Science Based Medicine

周二, 07 11月 2017

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Exploring issues and controversies in the relationship between science and medicine

- **ORBITA: Another clinical trial demonstrating the need for sham controls in surgical trials** [周一, 06 11月 16:58]
  Last week, the results of ORBITA were published. This clinical trial tested coronary angioplasty and stunting versus optimal medical management in patients with single-vessel coronary artery disease. It was a resoundingly negative trial, meaning that adding stunting to drug management t didn't result in detectable clinical improvement. What was distinctive about this trial is that it used a sham procedure (i.e., placebo) control, which few trials testing surgery or a procedure use. The results of…
- **The American Chiropractic Association Answers Crislip's Call, Joins the Choosing Wisely Campaign** [周五, 03 11月 20:00]
  The Choosing Wisely campaign has invited the largest chiropractic organization in the United States to publish a list of interventions to avoid. The results, while not entirely without merit, consist of redundant or unnecessary recommendations. And there is a glaring absence of recommendations to avoid any of the blatant pseudoscience commonly practiced by chiropractors.
- **Liver cancer, naturally** [周四, 02 11月 19:30]
  Aristolochic acid, a highly toxic substance naturally found in some traditional herbal medicines, may be a significant cause of liver cancer.

We here at SBM devote a lot of discussion to unscientific and pseudoscientific treatment modalities, the vast majority of which can be best described as quackery. Sometimes, though, what's even more interesting are controversies in "conventional" science-based medicine. In particular, I'm a sucker for clinical trials that have the potential to upend what we think about a disease and how it's treated, particularly when the results seem to go against what we understand about the pathophysiology of a disease.

So it was that I started seeing news reports last week about ORBITA (Objective Randomised Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina). Basically, ORBITA is a double-blind, randomized controlled trial comparing percutaneous coronary intervention (PCI, or, as it's more commonly referred to colloquially, coronary angioplasty and/or stenting) versus a placebo procedure in patients with coronary artery disease. Indeed, the sham procedure is what makes this trial interesting and compelling, although the devil is in the details. What this trial and its results say about coronary artery angioplasty and stenting, placebo effects, and clinical trial ethics are worth exploring. Basically, ORBITA calls into doubt the efficacy and usefulness of PCI in a large subset of patients with stable angina (chest pain or discomfort due to constriction of one or more coronary arteries that most often occurs with fairly predictably with activity or emotional stress—that is, exertion).

Before I dig in, I can't resist mentioning that cardiac surgery was one of the very earliest forms of treatment in which the importance of a sham surgery control was shown to be very important. In 1939, an Italian surgeon named David Fieschi developed a technique in which he tied off (ligated) both internal mammary arteries through two small incisions, one on each side of the sternum. The idea was to "redirect" blood flow to the heart in order to overcome ischemic heart disease, in which the patient suffers pain, heart failure, or even death due to insufficient blood flow to the heart muscle caused by atherosclerotic narrowing of one or more of the coronary arteries. The results were striking, as three quarters of all patients on whom Dr. Fieschi did his procedure improved and as many as one third appeared to be cured. The procedure became very popular and appeared to work.

Nearly two decades later, in the late 1950s, the NIH funded a cardiologist in Seattle named Dr. Leonard Cobb to do a randomized controlled clinical trial of the Fieschi technique. He operated on 17 patients, of whom eight underwent the true Fieschi procedure, with both internal mammary arteries tied off, and nine underwent skin incisions in the appropriate location. In 1959, Dr. Cobb's results were published in the New England Journal of Medicine, where he reported that the results were the same for patients who underwent the "real" Fieschi operation or the sham procedure. This was the beginning of the end of internal mammary ligation as a treatment for angina and a landmark in the history of surgery. After this trial, understanding of the ethics of human subjects research changed, and including sham surgical procedures in clinical trial design became increasingly frowned upon.

ORBITA is one of several recent trials that use sham interventions that have been reported in recent years as that ethical understanding has shifted again in the face of increasing evidence that surgery can produces the most powerful placebo effects of all interventions. Another example is trials of vertebroplasty for vertebral fractures due to osteoporosis, which showed that vertebroplasty in this setting produced results indistinguishable from the sham procedure. Increasingly, it has been argued that more surgical trials should include a sham procedure group.

PCI: A brief history

Publication of the results of ORBITA were timed to coincide with the 40th anniversary of the development of PCI. Basically, coronary angioplasty was developed 40 years ago as a less invasive treatment than coronary artery bypass grafting (CABG) for coronary artery disease. In brief, in PCI a cardiologist will thread a catheter up a major blood vessel in the groin to the heart and into the coronary artery (or arteries) with blockages. At the end of the catheter is a balloon. The idea is to thread the end of the catheter under fluoroscopic guidance (fluoroscopy is a form of X-ray imaging with video) into the coronary artery and past the blockage, such that the balloon aligns with the atherosclerotic blockage. The balloon is then inflated to open up the blockage. That's the basic idea, although the methods have evolved markedly over the last forty years.

At this point I can't help but mention a bit of a personal note, as it involves the research I did as part of my PhD thesis, lo these many years ago. One of the huge problems with angioplasty early on was the high rate of restenosis (recurrent narrowing) of the blood vessel treated. The reason for this was that balloon angioplasty involved, in essence, injuring the vessel. As with any injury, there was an inflammatory reaction, and one consequence of the inflammatory reaction due to angioplasty is that the vascular smooth muscle cells in the media (the middle layer of the blood vessel) would be stimulated to proliferate and restenose the vessel. As part of my PhD thesis, I cloned and characterized a homeobox gene (yes, a homeobox gene, for you geeks out there) that inhibited the proliferation of vascular smooth muscle cells. The idea was to treat the area at the time of the procedure with this gene as a form of gene therapy to prevent restenosis.

I realize that those of you out there who might be cardiologists and who weren't practicing back in the 1990s probably think this was an insane idea, but here's why it wasn't so insane back then. Back then, coronary stents hadn't been perfected, much less the drug-eluting coronary stents that are commonly used now to prevent restenosis. Basically, after most angioplasty procedures now, cardiologists place a stent in the area of former blockage. To prevent cellular ingrowth into the holes of the stent and subsequent restenosis, the stent slowly elutes a drug that prevents the proliferation of vascular smooth muscle cells. (As an aside, one of the things about these stents that frequently causes problems to surgeons like me is that the patient needs to be on powerful anti-platelet drugs like Plavix for up to a year after stenting). In any case, with the development of drug-eluting stents, the idea of gene therapy to prevent restenosis disappeared into the dustbin of scientific history, for the most part.

Back when PCI was new and young, its indications were a lot more limited, but as time went on and cardiologists' confidence grew indications expanded to multivessel disease and other indications that used to mandate CABG, to the point that PCI for acute coronary syndromes has grown to predominate. As MedPageToday describes:

> In the early years of PCI it was widely believed that PCI to open a severely blocked artery would have long term cardiovascular benefits,

> even in stable patients. Angina patients, the thinking went, were at higher risk for CV events and death, and PCI or CABG lowered that risk by restoring flow through the blocked vessel and preventing a future MI. But doubts grew over time, as it became increasingly clear that MIs were more likely to occur at other, less obvious blockages. Coronary artery disease began to be seen more as a systemic condition and less as a focal plumbing problem. The positive role of medical therapy, including statins and aspirin, became increasingly recognized.
>
> Finally, a decade ago the COURAGE trial, despite widespread and fierce initial resistance in the interventional cardiology community, led to widespread agreement that in fact PCI in stable lesions did not produce long-term improvements in outcome when compared to optimal medical therapy (OMT).
>
> But PCI for stable angina maintained a strong clinical presence as a new consensus emerged in the cardiology community that PCI was superior to OMT in the relief of symptoms. The mantra was that patients would need a stent eventually so they might as well get it upfront. It is this reduction in symptoms that the ORBITA trial sought to test.

And it is this assumption or belief that ORBITA called into doubt, at least for one large subset of patients.

ORBITA

ORBIT has been published in the online first section of The Lancet; so let's dig in. The introduction tells the tale, and you don't even have to leave the abstract:

> Symptomatic relief is the primary goal of percutaneous coronary intervention (PCI) in stable angina and is commonly observed clinically. However, there is no evidence from blinded, placebo-controlled randomised trials to show its efficacy.

Or, in more detail in the introduction:

> Percutaneous coronary intervention (PCI) was originally introduced to treat stable angina.1 More than 500 000 PCI procedures are done annually worldwide for stable angina. The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial showed no difference in myocardial infarction and death rates between patients with stable coronary artery disease who underwent PCI and controls.[2] Meta-analyses have shown similar results.[3]
>
> Angina relief remains the primary reason for PCI in stable coronary artery disease.[4] Guidelines recommend antianginal medication as rst line therapy, with PCI reserved for the many patients who remain symptomatic.[5]
>
> Data from unblinded randomised trials have shown significant exercise time improvement, angina relief, and quality of life improvement from PCI.[6–8] However, symptomatic responses are subjective and include both a true therapeutic effect and a placebo effect.[9] Moreover, in an open trial, if patients randomised to no PCI have an expectation that PCI is advantageous, this might affect their reporting (and their physician's interpretation) of symptoms, artifactually increasing the rate of unplanned revascularisation in the control group.[4,10]

So the investigators who designed ORBITA sought to do a rigorous randomized, double-blind, sham-controlled clinical trial of PCI for patients in stable angina. One can argue that such a trial should have been done a long time ago, before PCI became such a popular procedure for stable angina, and you would be correct. However, it's been done now; so let's look at the design. First, the inclusion criteria:

- Age 18-85 years
- Stable angina/angina equivalent
- At least one angiographically significant lesion (≥70%) in a single vessel that was clinically appropriate for PCI

Exclusion criteria:

- Angiographic stenosis ≥50% in a nontarget vessel

- Acute coronary syndrome
- Previous coronary artery bypass graft surgery
- Left main stem coronary disease
- Contraindications to DES
- Chronic total coronary occlusion
- Severe valvular disease
- Severe left ventricular systolic impairment
- Moderate-to-severe pulmonary hypertension
- Life expectancy <2 years
- Inability to give consent

Other fedatures of the patient population studied:

- Previous PCI: 13%
- Left ventricular ejection fraction normal: 92%
- Canadian Cardiovascular Society angina severity grading class: I (3%), II (59%), III (39%)
- Angina duration: 9 months
- Vessel involved: left anterior descending (69%)
- Median area stenosis by quantitative coronary angiography: 85%
- Median baseline FFR value: 0.72; median post-PCI FFR value: 0.9

The primary endpoint to be assessed was improvement in exercise time. To determine if PCI patients with stable angina and evidence of severe single-vessel stenosis were randomized 1:1 to either PCI or a sham procedure. After enrollment, patients in both groups underwent six weeks of medical optimization. After that, they underwent either PCI or sham procedure with auditory isolation in which the subjects all wore headphones playing music throughout the procedure. During the procedure, patients' heart function (measurements known as fractional flow reserve (FFR) and instantaneous wave-free ratio (iFR)) was monitored using a research method, but operators were blinded to the physiology values and did not use them to guide treatment. Randomization occurred after this physiological assessment. For patients undergoing PCI, the operator used drug-eluting stents according to standard clinical guidelines with a mandate to achieve complete revascularization as determined by angiography. In the sham procedure group, subjects were kept sedated in the cath lab for at least `15 minutes, with

the coronary catheters withdrawn with no intervention having been done. Here's the summary of the timeline and allocation of the trial:

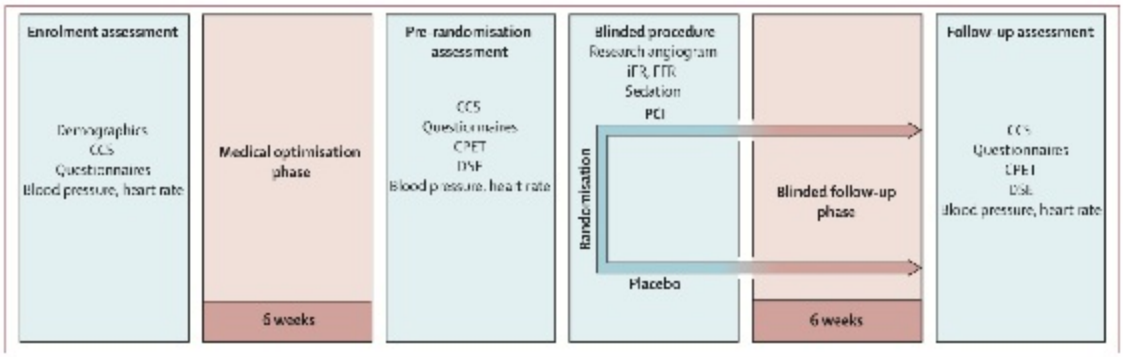


Figure 1: ORBITA study design
CCS=Canadian Cardiovascular Society angina severity grading. CPET=cardiopulmonary exercise testing. DSE=dobutamine stress echocardiography. iFR=instantaneous wave-free ratio. FFR=fractional flow reserve. PCI=percutaneous coronary intervention

Here's the trial outline:

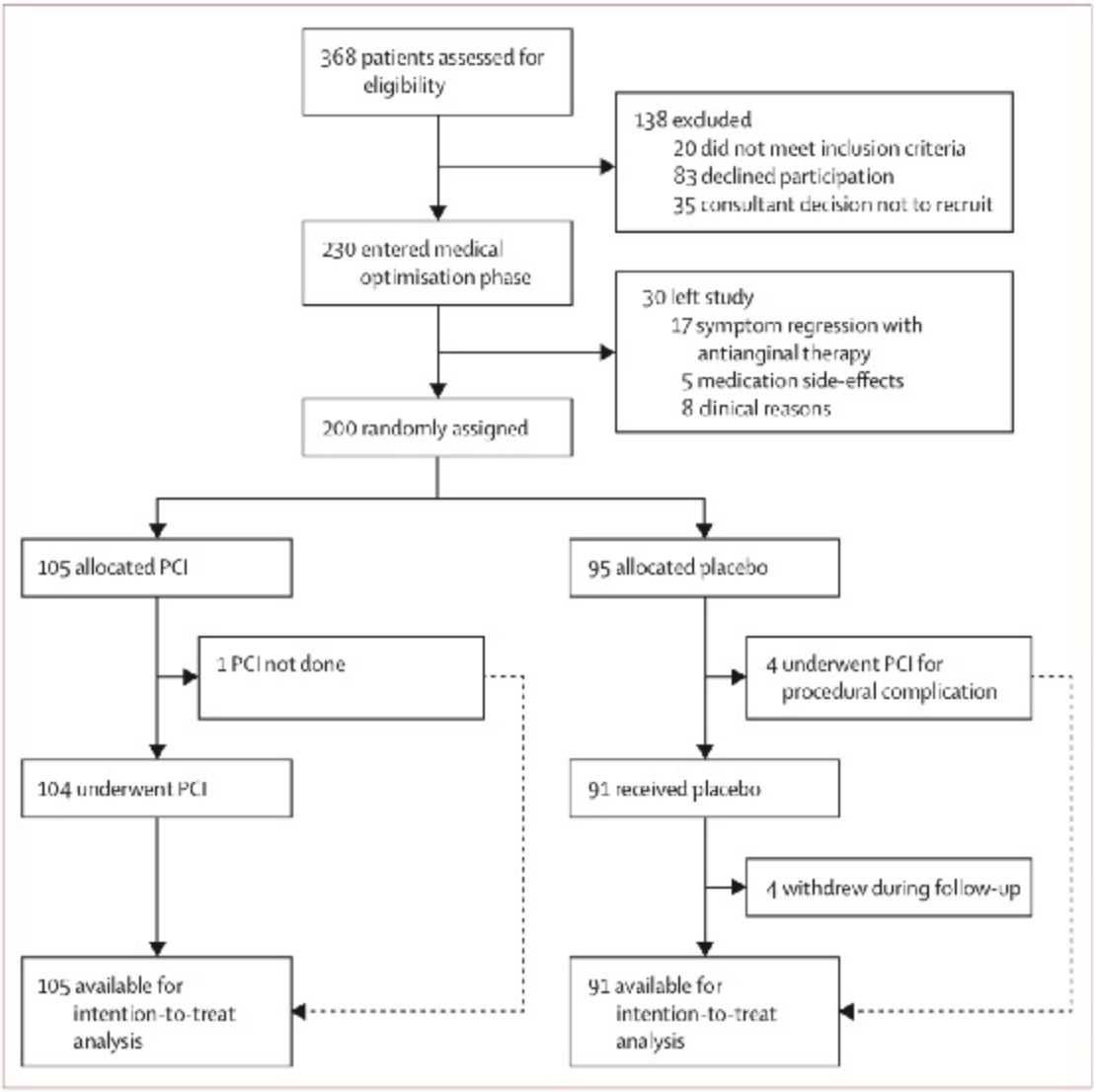


Figure 2: **Trial profile**
PCI=percutaneous coronary intervention.

Overall, there were 230 patients enrolled, of which after the medical optimization phase 200 were randomized, with 105 patients assigned to PCI and 95 assigned to sham procedure. And the results? They were what we call in the business a big nothingburger. The change in exercise time from baseline for PCI vs. sham, was 28.4 vs. 11.8 seconds, p = 0.2. Secondary outcomes were no better:

- Change in Seattle Angina Questionnaire (SAQ)-physical limitation from baseline: 7.4 vs. 5.0, p = 0.42
- Change in SAQ-angina frequency from baseline: 14.0 vs. 9.6, p = 0.26

- Change in Duke treadmill score from baseline: 1.22 vs. 0.1, p = 0.10

Also, at followup six weeks later, patients in both groups were receiving a mean of 2·9 medications; so PCI didn't decrease the need for cardiac medications. In other words, there was no statistically significant change in either the primary or secondary outcomes in patients with stable angina. The authors noted:

> In ORBITA, the first blinded, placebo-controlled trial of PCI for stable angina, PCI did not improve exercise time beyond the effect of the placebo. This was despite the patients having ischaemic symptoms, severe coronary stenosis both anatomically (84·4% area reduction) and haemodynamically (on-treatment FFR 0·69 and iFR 0·76), and objective relief of anatomical stenosis, invasive pressure, and non-invasive perfusion indices (FFR p<0·0001, iFR p<0·0001, stress wall motion score index p=0·0011). There was also no improvement beyond placebo in the other exercise and patient-centered effects with placebo effects. Forgetting this point, or denying it, causes overestimation of the physical effect.

In an accompanying editorial, David L. Brown and Rita F. Redberg commended the ORBITA investigators for "challenging the existing dogma around a procedure that has become routine, ingrained, and profitable," noting that ORBITA shows "(once again) why regulatory agencies, the medical profession, and the public must demand high-quality studies before the approval and adoption of new therapies" and characterizing PCI for stable angina as putting "PCI in the category of other abandoned therapies for cardiovascular disease, including percutaneous trans-myocardial laser revascularisation[10] and catheter-based radiofrequency renal artery sympathetic denervation[11]—procedures for which the initial apparent benefit was later shown in sham-controlled blinded studies to actually be due to the placebo effect." Noting that the short duration of followup actually would favor PCI because "any haemodynamic benefit from PCI occurs early and the benefits of medical therapy continue to accrue over years," Brown and Redberg conclude:

> The implications of ORBITA are profound and far-reaching. First and

> foremost, the results of ORBITA show unequivocally that there are no bene ts for PCI compared with medical therapy for stable angina, even when angina is refractory to medical therapy. Based on these data, all cardiology guidelines should be revised to downgrade the recommendation for PCI in patients with angina despite use of medical therapy. ORBITA highlights the importance of including sham controls and double blinding in a trial to avoid being fooled by illusory improvements due to the powerful placebo e ect of procedures such as PCI. Although sham-control procedures are associated with some adverse outcomes, those complications are dwarfed in magnitude by the rate of adverse events in the approximately 500 000 patients who undergo PCI for symptomatic relief of stable angina in the USA and Europe each year. These adverse events include death (0·65%), myocardial infarction (15%), renal injury (13%), stroke (0·2%), and vascular complications (2–6%).12 Health-care providers should focus their attention on treating patients with stable coronary artery disease with optimal medical therapy, which is very e ective, and on improving the lifestyle choices that represent a large proportion of modi able cardiovascular risk, including heart-healthy diets, regular physical activity, and abstention from smoking.

Based on the results of this trial, one can easily argue that PCI should rarely —if ever—be performed in patients with single vessel disease and stable angina.

The backlash

Not surprisingly, there was pushback. Cardiologists were not pleased by this result, even though it has been well known for a long time that in patients like those studied in ORBITA, PCI at least doesn’t improve survival or decrease progression to need revascularization more than OMT. For instance, in a on the study various cardiologists were quick to make excuses:

> Panelist Dr Martin Leon (Columbia University Medical Center, New York City) applauded the investigators efforts for a “remarkable study” but said it’s a much, much higher bar to achieve when the end points are

differences from baseline between two groups.

"Baseline data demonstrating that these patients had very good functional capacity, had infrequent angina, had very little ischemia, means that regardless of what you did to the coronary artery there was going to be very little you could demonstrate in terms of clinical therapeutic benefit. So I'm really glad that PCI had a statistically significant benefit in both echos and the stress tests," Leon said.

"The concern here is the results will be distorted and sensationalized to apply to other patient populations where this kind of outcome very likely would not occur," he added.

My counter to the argument that the patients included in this trial were not that sick is: Yes! That's the point. These are exactly the sorts of patients who too frequently are subjected to PCI for in essence no benefit over that which can be achieved by medical management.

Next up:

Commenting for theheart.org | Medscape Cardiology, Dr Roxana Mehran (Ichan School of Medicine at Mount Sinai, New York City) said, "To me actually this study shows angioplasty is quite effective in reducing ischemia, improving [fractional flow reserve] FFR, and in fact I'm actually very pleased with this. It's exactly what I want to do for my patients—improve their blood supply."

Asked whether this isn't just a positive spin on a negative study, Mehran quickly responded, "No," adding that whenever a primary end point is a change in a value, showing an important difference is very hard to do when baseline values are so good, especially with only 200 patients.

"I promise you, had she studied 400 patients this would be positive because everything was in the right direction," she said.

Actually, that's exactly what she's doing, trying to put a positive spin on a negative study. It's so blatantly obvious that that's what Dr. Mehran is doing that she should really be embarrassed to have said something like this to be

published for the public to read. In fairness, she does have a germ of a point in that the study was relatively small and potentially underpowered to detect some differences. On the other hand, it's rather interesting to note how some cardiologists totally twist the usual rationale and methodology used to determine if a therapy works. Here's what I mean.

Normally, when a new intervention is first tested, it's tested in small pilot trials. If a positive result is observed, that result justifies a larger trial to confirm efficacy and safety. If a positive result is not observed, then the treatment is generally abandoned or modified. before being tested again. Now, get a load this:

> During the press briefing Dr Robert Yeh (Beth Israel Deaconess Medical Center, Boston, MA) congratulated the authors on a courageous, bold, and well-executed trial but said the results reaffirm in many ways those from COURAGE.
>
> "To extrapolate that this means that elective PCI is not an indicated procedure is the furthest overreach that I can possibly imagine from a very small and I think hypothesis-generating trial with an interesting result," he said.

Let's grant Dr. Yeh his characterization of this study as "hypothesis-generating." When hypothesis-generating studies are negative, the hypothesis is usually considered to be not worth testing further, barring serious methodologic or design issues in the hypothesis-generating study. To demand another, much larger, much more expensive study to follow up on a result that, even if Dr. Yeh is correct, would likely be a very modest difference in an increase in exercise tolerance. Basically, much, although in fairness not all, of what these cardiologists are doing is to make excuses.

None of this is to say that ORBITA is bulletproof. It is, compared to other trials of PCI, relatively small. There was a trend towards improved exercise tolerance in the PCI group compared to the sham group that might have been significant with more patients. The question, of course, is whether it would be worth it to do another larger trial. After all, interventional cardiologists are utterly convinced that PCI is more effective than OMT and are unlikely to change practice (much) based on this trial:

> How will the results of ORBITA be viewed? It will be a combination of love and hate. ORBITA was rigorously designed and undertaken with great care and painstaking attention to detail using objective exercise and physiologic outcome measures before and after stabilization on OMT, combined with the use of well-validated quality of life metrics before and after randomization. Overall, the results were stunningly negative, which ORBITA supporters will cite. By contrast, it is very likely that many in the interventional community will be ready to pounce on and discredit this study — there certainly hasn't been an opportunity since COURAGE was published 10 years ago in 2007 to potentially discredit a trial that now confronts the sacred cow of PCI benefit for angina relief as the sole basis to justify PCI in stable CAD patients. They will likely cite the limitations of small numbers (only 200 patients), that the study was woefully underpowered, the potential ethical conundrum of subjecting subjects with significant flow-limiting CAD to a sham procedure (or deferred PCI for clinical need), that 28%-32% of randomized subjects had either normal FFR or IFR (and therefore didn't have a "physiologically significant," or flow-limiting stenosis, that PCI would otherwise benefit), that there was a low frequency of multivessel CAD, that the short duration of follow-up (only 6 weeks) was too brief to assess potential benefit (though this actually favored the PCI group) and, of course, who would have the time or patience to call patients three times/week to assess their response to intensifying medical therapy — "not real-world," just like the OMT used in COURAGE wasn't achievable in the real-world.

Despite these reactions, I do have some optimism. Interventional radiologists reacted very negatively to the trials showing that vertebroplasty for osteoporotic spinal fractures doesn't work. Eventually, they started to come around, and usage of vertebroplasty for this indication is declining, albeit not as fast as it should. Science- and evidence-based medicine is messy, and there is some truth to the old adage that old treatments don't ever quite disappear until the generation that learned them retires or dies off. But change does come in response to clinical trials.

In the meantime, whatever effect ORBITA has on clinical practice, it should serve as a wakeup call that in clinical trials of surgical or procedural

interventions examining endpoints with a degree of subjectivity (unlike, for instance, death or time to cancer recurrence), whenever possible, new interventions should be compared to sham procedures. Of course, this isn't always possible, either for ethical or practical reasons, but when it is practical sham procedures are just as essential as placebo controls in drug trials.

Three years ago, Mark Crislip closed a post discussing the ABIM Foundation's Choosing Wisely initiative with the following thought:

> I wonder if a chiropractor could come up with five standards treatments in chiropractic to be avoided…

Well, now they've finally gone and done it, with results that, while not entirely without merit, are a bit off the mark in my opinion.

Choosing Wisely and chiropractic

For the sake of further discussion, let's all just agree to ignore the fact, also pointed out by Dr. Crislip in his post, that chiropractic as a profession doesn't exactly stand up to the scrutiny of the campaign's criteria:

> *Choosing Wisely* aims to promote conversations between clinicians and patients by helping patients choose care that is:
>
> - Supported by evidence
> - Not duplicative of other tests or procedures already received
> - Free from harm
> - Truly necessary

Of course to be fair, no medical intervention is completely "free from harm", but I assume that what the ABIM Foundation actually means is that interventions should have a favorable risk to benefit assessment. This is arguably not the case when assessing chiropractic as a whole. While not all of the treatments I prescribe are based on robust randomized controlled trials, they are "supported by evidence" in the vast majority of cases, and often by very good evidence. Chiropractic doesn't really bring anything original to the table that passes this test.

There are similar issues with the phrase "truly necessary", whatever that means. Many medical interventions aren't "truly necessary" in my opinion. Other Choosing Wisely lists cover a number of these, but there are also tests

and treatments that may have value while perhaps not meeting this criterion absolutely depending on who is assessing the scene. But again, being charitable, I assume that the ABIM Foundation is focusing on common interventions for common human ailments that don't tend to improve objective outcomes.

Specific treatments provided by a chiropractor might provide some objective benefit for a small sliver of musculoskeletal complaints, with those unique to chiropractic being the least helpful. But whatever improvement that can be attributed to visiting a chiropractor isn't better than more conventional approaches, such as physical therapy or recommendations from a patient's primary care provider for exercise, stretching, massage, etc. These approaches come with considerably less baggage and aren't as likely to be accompanied by pseudoscience or anti-vaccine propaganda.

The Choosing Wisely lists published by participating organizations aren't meant to serve as treatment guidelines, of course. Instead, they are intended to encourage a conversation around whether or not the listed interventions are a good idea, or if they may put patients at risk of more harm than benefit. Unfortunately, in my opinion, they have largely gone unnoticed by medical providers and the general public. I am confident that the list of questionable chiropractic interventions will be similarly ignored by practitioners.

The ACA's list

The list in question, released in August, comes from the American Chiropractic Association (ACA). The ACA claims 15,000 members, which is less than a quarter of practicing chiropractors, and recognizes 11 specialty areas, such as chiropractic acupuncture, pediatrics, diagnosis and management of internal disorders, and forensic sciences. It describes itself with typical grandeur:

> The American Chiropractic Association (ACA) is the largest professional chiropractic organization in the United States. ACA attracts the most principled and accomplished chiropractors, who understand that it takes more to be called an ACA chiropractor.

> We are leading our profession in the most constructive and far-reaching ways — by working hand in hand with other health care professionals, by lobbying for pro-chiropractic legislation and policies, by supporting meaningful research and by using that research to inform our treatment practices.
>
> We also provide professional and educational opportunities for all our members and are committed to being a positive and unifying force for the practice of modern chiropractic.

What does it take to called "an ACA chiropractor"? Membership requirements consist of being a licensed chiropractor in the United States and paying yearly dues. The ACA even goes so far as to state that they do not deny membership to anyone meeting the above qualifications as long as what they do in their practice isn't illegal. In that way, they are similar to the American Academy of Pediatrics, which even allows pediatricians who are blatantly anti-vaccine to be members in good standing.

Here are the five things that chiropractors and their patients should question according to the ACA:

Do not obtain spinal imaging for patients with acute low-back pain during the six (6) weeks after onset in the absence of red flags.

What red flags, you ask? The ACA mentions "history of cancer, fracture or suspected fracture based on clinical history, progressive neurologic symptoms and infection, as well as conditions that potentially preclude a dynamic thrust to the spine, such as osteopenia, osteoporosis, axial spondyloarthritis and tumors". I would argue that if you have any of these red flags, you should not be under the care of a chiropractor. There isn't any evidence to support superiority of chiropractic care to conventional approaches for acute low-back pain anyway.

Do not perform repeat imaging to monitor patients'

progress.

They list idiopathic scoliosis as an exception, despite the fact that their own research shows no good evidence to support chiropractic management of this condition. I agree with this recommendation, and the reasoning of the ACA in this case is sound. I'm just not holding my breath while waiting to see if this will change anything, however.

Avoid protracted use of passive or palliative physical therapeutic modalities for low-back pain disorders unless they support the goal(s) of an active treatment plan.

In other words, commonly recommended interventions like heat, ultrasound, and electrical stimulation, shouldn't be used in isolation because they don't provide much benefit. The absolute worst thing you can do to prevent or treat lower back pain, which virtually all humans will experience at some point in their lifetime thanks to evolution, is nothing. General physical activity and back specific exercises are key, and in no way unique to chiropractic.

I don't think you will find many chiropractors not recommending an exercise regimen for lower back pain disorders, so this item is a bit odd. You also won't find many that won't provide some kind of spinal manipulation, because that's their thing that they do. In this section, the ACA writes that physical activity and back exercises "may lead to better outcomes when combined with spinal manipulation." In reality, spinal manipulation is more like multiplying by one. It changes nothing for the long term outcome.

Do not provide long-term pain management without a psychosocial screening or assessment.

Chronic pain disorders often have a psychosocial component. Chronic pain can cause or be caused/exacerbated by anxiety and depression, for example.

Some patients are at risk for the development of chronic pain because of a variety of psychosocial factors and chiropractors are not trained to evaluate or manage them. The ACA recommends that chiropractors use a screening tool and refer when necessary because the ACA imagines chiropractors to be primary care providers.

Do not prescribe lumbar supports or braces for the long-term treatment or prevention of low-back pain.

Another odd inclusion. Chiropractors simply aren't out there putting people in back braces for long periods of time for treatment or prevention of back pain. I was easily able to find that this recommendation is already widely accepted. Meanwhile, the ACA is inviting speakers to their conferences to promote nonsense like the Activator Method.

The ACA press release announcing their participation in Choosing Wisely is interesting. They point out that multiple other organizations already participating have included recommendations to avoid spinal imaging for acute lower back pain. It's a solid recommendation, but instead of actually attempting to show a commitment to change by pointing out some of the abject nonsense they have supported sans evidence, they went the safe route. And in the press release they essentially give their members enough wiggle room that they can continue obtaining frequent spinal films without losing any sleep.

My favorite quote involves the practice of "defensive medicine":

> As with many of our colleagues in the health care professions, we have learned from experience to practice "defensive medicine." This perspective may be even more deeply ingrained within the chiropractic profession based on our prior experiences with bias and/or lack of understanding regarding chiropractic care. As an example, just look how long it took before Choosing Wisely® was even willing to consider a chiropractic list!

So do chiropractors practice defensively, which implies a concern for facing a malpractice suit, or not? It would appear that the latter is the case when you consider how often they point out how undeniably safe chiropractic is. Often this is done in the context of attacking conventional medical care. It's also unclear to me how the medical community's lack of "understanding regarding chiropractic care" encourages defensive practice.

Conclusion: The ABIM did not Choose Wisely

How does the ACA describe chiropractic on the Choosing Wisely website? Just as you would expect them to, of course. Remember though that this is an organization that is fighting for chiropractors to be considered primary care physicians complete with the right to prescribe medications.

> Chiropractors focus on disorders of the musculoskeletal system and the nervous system, and the effects of these disorders on general health and function. Chiropractic services are used most often to treat conditions such as back pain, neck pain, pain in the joints of the arms or legs, and headaches. Widely known for their expertise in spinal manipulation, chiropractors practice a hands-on, drug-free approach to health care that includes patient examination, diagnosis and treatment.

The ABIM Foundation is very likely completely ignorant of both the history and the current reality of the chiropractic profession. Frankly I think it's ridiculous that a chiropractic organization was invited to participate. We certainly have come a long way from Wilk v. AMA, haven't we?

This is just another example, in a very long line, of the undeserved legitimization of alternative medicine that will serve as more of a marketing purpose than as a means of improving chiropractic practice. All that the ACA has done is provide a list of redundant or unnecessary recommendations. And the few chiropractors who already avoid excessive spinal imaging will continue to do so, while the vast majority will compartmentalize these "suggestions" and carry on as is.

Extras

- Here is a response to the ACA Choosing Wisely list from the International Chiropractic Association.
- Here is an ACA video describing the benefits of pediatric chiropractic. In March of 2017, the ACA reaffirmed its public policy on chiropractors as primary care providers. This policy includes the following:

> Doctors of chiropractic also recommend and manage dietary changes, nutritional interventions, botanical medicines, homeopathic medicines, acupuncture and other services when indicated.

The ACA, while not overtly anti-vaccine in policy, supports conscience waivers.

Not all cancers affect all populations equally. Liver cancer is the fifth-most common cancer worldwide, but the prevalence varies widely. Liver cancer cases skew heavily to less developed regions of the world, where 83% of cases are found – it's over six times more common there than in Northern Europe, for example. In Asia, the high rates of liver cancer have been linked to hepatitis B and C, which is widespread, and a proven cause of cancer. And liver cancer continues to strike Asian American and Pacific Islanders more than any other American ethnic group as well, where hepatitis continues to circulate in the population. Now there's new evidence to suggest that a substance found in some traditional Chinese medicines may also be causing liver cancer. They're called aristolochic acids, and they illustrate, with a substantial body count, that what's natural isn't necessarily healthy or good.

What are Aristolochic acids?

In the early 1990's a strange cluster of acute, end-stage renal disease appeared in women in Belgium. It was determined that all had been exposed to the chemical aristolochic acid (AA) at a weight loss clinic, due to the consumption of Chinese herbs which contained natural AA. Approximately one third of the more than 300 cases have subsequently required a kidney transplant, and cancers of the urothelial tract in this group have also been widespread. In the Balkans, low level exposure to AA via flour consumption that contains seeds from *Aristolochia clematitis* is believed to be responsible for what is now called Balkan-endemic nephropathy. Subsequent study that was initiated after the Belgian case identified that that AA is responsible for tumour development and for activating destructive fibrotic changes in the kidney. For over a decade now it has been well established that AA is a nephrotoxin and a powerful carcinogen with a short "latency period", in that it causes permanently damage, quickly. What's remarkable is that none of this was known until the 1990s despite "thousands of years" of use as a traditional medicine. As Steven Novella noted in a past post on aristolochic acid and urinary tract cancer:

> This example just highlights the fact that widespread use of an herbal

> product, or any treatment, is not sufficient to ensure that it is safe, or even that it is effective. Common use may be enough to detect immediate or obvious effects, but not increased risk of developing disease over time. That requires careful epidemiology or specific clinical studies. We know about the risks of prescription drugs only because they are studied, and then tracked once they are on the market. Without similar study and tracking there is simply no way to know about the risks of herbal products. Relying upon "generally recognized as safe" is folly.

While herbal remedies that contain AA are now banned in many countries, AA-induced kidney damage and related cancers continues to appear worldwide. As AA's cancer-causing effects have now been widely studied, the distinct way that they damage cells has been described as a sort of "signature" that is easily identifiable in tumour samples. This brings us to this new study of liver cancers attributed to AA, which have been less closely associated with AA. This study used that unique "signature" to look for AA exposure.

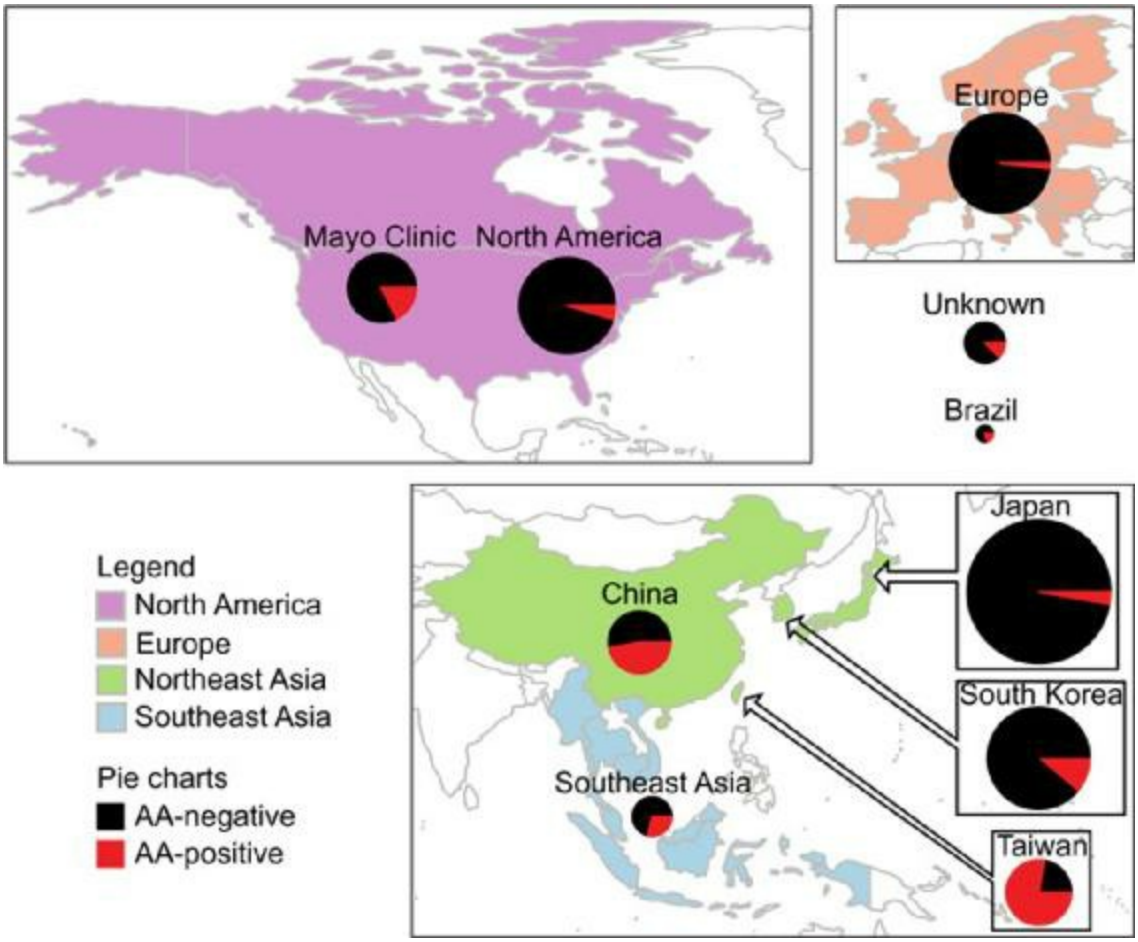
Aristolochic acids and liver cancers

There is good evidence to show that the consumption of AA-containing products in Taiwan has been widespread through the use of prescribed herbal medicines. The paper is entitled "Aristolochic acids and their derivatives are widely implicated in liver cancers in Taiwan and throughout Asia" and it's from Alvin Ng and associates, published in *Science Translational Medicine* in October, 2017. This was a retrospective analysis of hepatocellular carcinomas (HCC, liver cancer in lay terms) and patients were included if they (1) had true HCC (2) there was sufficient DNA available from a sample of the tumour. 98 HCCs from Taiwan hospitals were studied based on whole-exome sequencing and mutation identification. They looked for the distinctive way in which AA causes mutations. The researchers subsequently examined 1,400 HCCs from other regions in the world. The final analysis was as follows:

- Taiwan: 78% of tumours had evidence of AA exposure

- China: 47% of tumours had evidence of AA exposure
- Southeast Asia: 29% of tumours had evidence of AA exposure
- Korea: 13% of tumours had evidence of AA exposure
- Japan: 2.7% of tumours had evidence of AA exposure
- North America: 4.8% of tumours (in one hospital, 22% of 87 patients, all of Asian ancestry, had evidence of AA exposure)
- Europe: 1.7% of tumours had evidence of AA exposure

Here is the global breakdown, with the red portion illustrating the proportion of tumours that were linked to AA exposure:



Global distribution of mutagenesis associated with aristolochic acid and derivatives in liver cancer.

Reducing your risk of kidney and liver

cancer

Herbal remedies are popular worldwide. In China and other countries in Asia, there is strong support for, and belief in “traditional” Chinese medicine despite the fact that it is neither truly traditional (as it is now promoted), nor particularly effective. This new analysis shows that the use of (or exposure to) AA is widespread in some parts of the world, and appears to be be a cause in a substantial numbers of liver cancers. The authors noted that the presence of AA-associated cancer does not appear to be declining in Taiwan, despite the banning of some AA-containing herbs in 2003. This may be due to a lag effect (like cancer and smoking) but may also be due to continued exposure to, or consumption of, AA-containing products.

If you’re a user of traditional Chinese medicine, avoiding AA is easier said than done, unless you have impeccable knowledge of herbs, their origins, and the supply chains you’re getting your products from. I’ve blogged before about TCM, noting that contamination is common. Mislabelling of products also appears to be widespread, suggesting that rigorous and credible testing of final products may be the only way consumers can be assured they’re avoiding AA in the products they buy. The linkage of AA to kidney damage, and the evolving story of its cancer-causing potential illustrates that even widespread use of a product for hundreds (or thousands) of years give no automatic assurance of safety. If it were not for the Belgian weight loss clinic kidney failure cluster, the widespread toxicity of AA may not even be known today.

Science Based Medicine

周二, 14 11月 2017

Science Based Medicine

[周二, 14 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Why do some women refuse treatments for their breast cancer?** [周一, 13 11月 16:14]
  Adjuvant therapy after surgery, such as chemotherapy, hormonal therapy, and radiation therapy, has contributed to a 39% decrease in breast cancer mortality since 1989. Unfortunately, a significant number of women decline evidence-based adjuvant therapy. A recent study suggests that distrust of the medical system plays a significant role in such refusal.
- **Another “Chronic Lyme” VIP disciplined by NY medical authorities: Bernard Raxlen** [周四, 09 11月 14:00]
  Another "Lyme literate" NY physician is on probation and under orders to clean up his act. Will other physicians treating "chronic Lyme" take note?

I write about alternative cancer treatments a lot, in particular the lack of evidence for such practices, many of which are at best pseudoscientific and at worst pure mystical nonsense. The reason, of course, is simple. I'm a breast cancer surgeon, and I hate seeing people who might be saved from death due to cancer falling prey to treatments that demonstrably lessen their chances of survival, either by leading patients to reject effective treatment in favor of ineffective or even harmful treatments or, at the very least, to delay effective treatment until the patient realizes that the quackery chosen isn't preventing the growth and spread of his or her tumor. This can sometimes take a long time. I've seen women with breast cancer whose breasts were basically eaten away until there was nothing left but an ulcerated mass on their chest—more than that, a bleeding, rotting, malodorous ulcerated mass. Yes, it's an ugly picture, but I've seen it all too many times.

These sorts of cases are less common, though. Fortunately, relatively few are the women who reject conventional medicine altogether. Indeed, most women will accept surgery of some sort or another, either a lumpectomy or a mastectomy. Sometimes, they undergo an excisional biopsy, not realizing that that for smaller tumors an excisional biopsy can remove the whole tumor and in some cases be curative. No, far more common is the case where a woman accepts surgery but then refuses chemotherapy, hormonal therapy, and/or radiation, either altogether or in favor of some form of quackery. In doing so, such women, whether they simply refuse adjuvant therapy altogether for whatever reason or go beyond that and fall prey to quackery, fail to maximize their chances of surviving their breast cancer, sometimes by quite a bit, and that is something to be concerned about.

Indeed, these sorts of cases were one of the very first topics I ever wrote about on this blog and have remained a staple of the blog ever since, whether I was discussing Suzanne Somers, who had surgery and radiation but apparently refused Tamoxifen for her breast cancer and then later had what she thought to be a recurrence that almost certainly wasn't, other alternative breast cancer cure testimonials (like this one or this one), or even testimonials for other cancers where chemotherapy and/or radiation are used in addition to surgery.

The reason such alternative cancer cure testimonials are compelling is that most people don't understand the difference between the primary treatment for breast cancer and an adjuvant treatment. In the case of breast cancer, mor instance (and colorectal cancer as well, among other solid tumors), surgery is the primary treatment and can be curative by itself. What chemotherapy, radiation therapy, and hormonal therapy can add to the treatment of, for example, breast cancer is to decrease the chance of its recurring after successful surgical excision, whether by mastectomy or lumpectomy. All a breast cancer patient does in refusing radiation therapy after successful breast conserving surgery is to accept a risk of recurrence in the breast of 30-40% instead of 5-8%. All a woman does by refusing recommended chemotherapy after surgery is to refuse a relative decrease in their risk of dying of a recurrence of breast cancer by 25-30%, a benefit that is, in absolute terms, much greater for more advanced but still curable breast cancers. However, many of these women who turn down adjuvant therapy in favor of quackery will still survive, thanks to the surgery, and the ones whose cancers recur rapidly disappear from the alternative cancer cure industry PR machine, never to be seen again.

Because adjuvant chemotherapy, targeted therapies, and hormonal therapies have contributed to a decline in mortality from breast cancer of 39% since 1989, it is important to determine why women refuse these treatments and fail to optimize their chances of long term survival. To a lesser, but still important extent, it's important to try to understand what motivates women to turn down effective adjuvant therapy, as that is the first step in developing strategies to persuade them. Recently, there was a relatively large study that addressed just this question.

Patient refusal of adjuvant therapy: A question of trust?

Earlier this month a number of news stories and press releases appeared about a study published in late September by investigators at Johns Hopkins Bloomberg School of Public Health, Columbia University, and Massachusetts General Hospital looking at trust—or, more specifically, a

lack of trust—as a key motivator in women refusing adjuvant therapy recommendations and opting for discordant care; i.e., care that doesn't conform to evidence-based care recommended by the patient's physicians. It's an issue that hasn't been studied as well as it should be, as the authors, Lorraine T. Dean, Shadiya L. Moss, Anne Marie McCarthy, and Katrina Armstrong point out in the introduction:

> Relatively little is currently known about the relationship between healthcare system distrust and cancer treatment. A previous study of distrust and adjuvant cancer treatment (3) found that distrust in medical institutions was associated with increased risk of not initiating adjuvant treatment in a sample of 258 early stage (Stage I and II) breast cancer patients from one urban area. However, that study did not include the following in their analysis: which treatments were recommended by the physician, the extent to which physician distrust mediated the relationship between healthcare system distrust and cancer treatment, and an assessment of those who may have initiated treatment but did not fully adhere to the treatment plan. Other studies of distrust among women with a history of breast cancer have focused on healthcare system distrust and: mental health or psychosocial outcomes (13), quality of care (14,15), greater emotional, physical, financial, and sexual problems after treatment (16), less comfort with the use of de-identified information from medical records for research (17), less endorsement of the necessity of adjuvant chemotherapy (18); and provider distrust and quality of care (19).
>
> The current study was designed to answer two related questions: Is healthcare system distrust associated with whether or not patients follow their physician's recommendations for adjuvant treatment after breast cancer; and does physician trust mediate the relationship between healthcare system distrust and receipt of adjuvant treatment? It expands on prior work by including a large population based sample in two different US states, Pennsylvania and Florida, based on physician recommendations for several adjuvant treatments with explicit testing of the potential mediating role of physician distrust, and assesses patients who did not complete the full treatment plan. To our knowledge, it is the largest study of healthcare system distrust among women with a history

of breast cancer and adds innovation of recruiting through a cancer registry to survey participants about healthcare system distrust.

To this end, the authors used Pennsylvania and Florida cancer registries, using data from a population from a study originally intended to assess the differences in breast cancer women associated with race. The inclusion criteria for the study included localized invasive breast cancer, age under 65 at the time of diagnosis, residency in either Pennsylvania or Florida at the time of diagnosis, and diagnosis between January 1, 2005 and December 31, 2007. Exclusion criteria included patients over 65, cognitive impairment, inability to speak English or Spanish, and metastatic disease at presentation. The overall response rate was very good for surveys of this type, 61%.

For purposes of the survey, cancer treatment discordance was defined as any difference in treatment that a patient reported receiving compared to the treatment the patient reported as having been recommended to her by the treating surgeon and/or oncologist. Now, I know what you're probably thinking: Is this accurate enough. It turns out that simple self-reporting like this is 90% accurate, particularly for yes/no questions about different kinds of therapy. Since the adjuvant therapies used after surgery for breast cancer include radiation therapy, chemotherapy, and hormonal therapy, the authors constructed a combined measure of treatment discordance based on how many of the three therapies patients accepted or declined. Of course, if a particular adjuvant therapy was not recommended for a patient, then not undergoing it couldn't be considered discordant. (For example, depending on the specific characteristics of the tumor, not all breast cancer patients are offered chemotherapy or hormonal therapy; and most patients—but by no means anywhere near all patients—undergoing mastectomy don't require radiation therapy.)

Patients were also assessed for their level of trust in the health care system. and their physicians. Trust in the health care system was assessed using the 9-item Health Care System Distrust scale which measures of domains of values and competence distrust on a 5-point agreement scale (1 = strongly disagree, 5 = strongly agree), producing a score ranging from 9 to 45. The authors report that this measure has "acceptable construct validity and high internal consistency (α=0.84 in the current sample)." To measure trust in patients'

physicians, researchers used the 7-item Trust in Physician Scale, which uses a 7- point agreement scale (1=strongly disagree, 7=strongly agree), to produce a score ranging from 7 to 49. Information was also requested on socio-demographic factors, such as age, race, ethnicity, income, education, marital status, employment status, health insurance status, and state of residence at the time of diagnosis. They also went to the cancer registry databasess to verify clinical treatment factors, such as stage, surgical removal of cancer, and recurrence.

So what did the authors find? There were 2,754 women included in the final analytic sample, of which 69.8% (n=1,922) reported always receiving the cancer treatments their surgeon or oncologist recommended, and 30.2% (n=832) reported not pursing at least one recommended treatment. I must admit that I was rather surprised that the percentage of discordant cases was so high, but maybe I shouldn't have been. In any case, in the total sample, 10% declined radiation treatment; 11% declined chemotherapy; and 18% declined hormone therapy. (Note that some women turned down more than one modality.) Looking at the numbers, though, some of this does appear to jibe with my clinical experience, in that I've encountered more women who have turned down hormonal therapy than who have turned down others. The reason is probably that hormonal therapy, although only a pill as opposed to chemotherapy, is administered for five or, in more recent recommendations, as many as ten years, and women who can tolerate the much more severe side effects of chemotherapy only have to endure them for a few months, whereas they have a harder time dealing with the side effects of Tamoxifen or aromatase inhibitors for five or ten years.

The authors found:

> The mean healthcare system distrust score was 28 (SD=3; range 9-40), while the mean physician trust score was 29 (SD=4; range 9-35). Bivariate models suggested that greater healthcare system distrust was significantly associated with older age, being Black, having attended some college, and being employed, while less healthcare system distrust was associated with greater physician trust, being married, having health insurance, and living in Pennsylvania. Only marital status, being employed, physician trust, and living in Pennsylvania were still

> associated with distrust in a fully adjusted model (Table 2). Participants reporting treatment discordance were significantly in the top tertile of healthcare system distrust (p=0.003) as well as being more likely to be older (p=0.04), be diagnosed at Stage 1 (p<0.001), and live in Florida (p=0.003). In contrast, physician trust was not a significant predictor of discordance (p=0.49). Although healthcare system distrust was significantly associated with discordance (p=0.03) and physician trust (p<0.001) (Figure 1), a mediation analysis (Table 3: Models A & B) suggested that physician trust was not a mediator of the relationship between healthcare system distrust and treatment discordance (total indirect OR=1.00 [1.00,1.01]). Thus, rather than treat physician trust as a mediator, it was included in the final model as a covariate.

Basically, those in the group with the highest distrust of the healthcare system were 22% more likely to have refused or fail to complete one or more adjuvant treatments. In other words, patients who had the most distrust of the healthcare system were more likely to be discordant in their adjuvant therapy; i.e., to refuse or fail to complete a recommended course of therapy. Interestingly, in this study, neither race nor socioeconomic status were significant drivers of discordance in this study, which is a good thing because these are not modifiable factors.

Physician trust versus a more generalized distrust

How could these results be? The authors note that attempts to increase physician trust as a strategy to reduce mistrust in the healthcare system have had results ranging from zero to very modest, which makes sense if patients view the two issues as separate. I like to make an analogy to Congress. Voters routinely express extreme distrust of Congress, but most voters actually like their own representative. Similarly, it’s not hard to envision how most patients might actually like and trust their own doctors, while simultaneously having a great deal of mistrust for the health care system as a whole.

As the authors note:

> The limited research to date about reducing distrust in healthcare has focused on increasing trust in physicians with null to modest (30-32) results. However, given that the relationship between distrust and treatment discordance was not mediated by physician trust, these results suggest that addressing healthcare system distrust may be an important and distinct effort from strategies focused on lack of physician trust. Rather than playing a mediating role, patients may view physician trust as independent of their trust in the healthcare system as an institution; that is, even if patients distrust the healthcare system, they may still have trust in their personal physicians. Patients may be able to exercise greater choice in physicians, but may not have the same breadth of choices in using the healthcare system. Addressing healthcare system distrust might be informed by strategies that have addressed distrust in other types of institutions, such as corporations (29), according to the values and competence domains. For example, addressing the subdomain of values might be achieved through expanded access to adjuvant care, while addressing the subdomain of competence might be achieved through expanded access to health professionals while deciding to start or continue adjuvant treatment. Of course, any intervention to reduce healthcare system distrust would first need to be tested before implementing wide-scale changes.

The authors also note a rather interesting potential wrinkle to the problem of patients refusing adjuvant therapy, namely that greater cancer treatment discordance will always lead to worse healthcare outcomes, noting that it is "possible that distrust could perform a function in course-correcting treatment that is overprescribed or too aggressive" and that such distrust "might lead to treatment discordance that was ultimately beneficial rather than detrimental." When I read that part, I had to concede that it is possible that this could be true, but unlikely. My own experience in quality improvement initiatives means that I've become fairly familiar with the literature on the relationship between concordance with evidence-based treatment guidelines and patient outcomes. That literature generally supports that better concordance results in better outcomes. So I couldn't help but smile as I continued to read and noted that, consistent with that, the authors examined a separate model of treatment discordance, looking at its association with cancer recurrence, and found that the model suggested a 40% increased risk of cancer recurrence for patients

who reported treatment discordance, after adjusting for adjusting for healthcare system and physician distrust and relevant racial and socioeconomic factors. This result suggests that that discordance due to distrust may lead to poorer health outcomes.

So what to do?

The authors note that improving trust in the healthcare system will require more than just trying to build trust in patients' physicians, noting:

> "If ordinary businesses can learn to increase trust in their brands, why not the same with health care institutions?" Dean says.

This is, of course, much easier said than done, and this study doesn't address how increasing trust in the healthcare system might be accomplished. That will be the task for the future. It is an important task, though, because, although I might be extrapolating more than the evidence supports (yet), I'd bet that such strategies could also help address the antivaccine movement as well. In any case, if we want to save as many savable lives of people with cancer as possible, this is where the healthcare system needs to pay more attention, and a salutary side effect would also be to make alternative cancer cure testimonials less common.

Bernard Raxlen, MD, who devotes more than 90% of his practice to the treatment of so-called “chronic Lyme” disease, is on a three-year probation imposed by the New York State Board for Professional Medical Conduct (BPMC). Raxlen agreed to probation and a lengthy list of practice requirements last month following allegations, filed in September, of negligence, incompetence, gross negligence, gross incompetence, and failure to maintain adequate patient records. In doing so, he becomes the second “Lyme literate” VIP disciplined by the NY medical authorities this year. Based on similar charges of professional misconduct, David Cameron, MD, was also put on probation with numerous practice restrictions in June.

Who is Bernard Raxlen, MD?

Raxlen is a psychiatrist and solo “chronic Lyme” practitioner in New York City who says he’s “successfully treated” over 3,500 cases of tick-borne disease in the past 15 years. (He named his practice “Lyme Resource Medical of New York.”) He touts a “total comprehensive treatment program which

utilizes both oral and intravenous (IV) antibiotic treatment." It doesn't come cheap, either. An initial visit with Raxlen costs $1,200 with follow-up visits between $600 and $700. A PICC-line insertion (presumably for long-term antibiotics) is $750 and a "nutritional IV" is $150. He does not accept public or private insurance.

Raxlen has a history of disciplinary actions against him in two states stretching back almost 20 years. In Connecticut, where he was formerly licensed, he was reprimanded and paid a total of $35,000 in civil penalties in two cases arising out of his refusal to provide patient records to the Health Department and insurance companies, even though patients had signed releases. He was also disciplined for inappropriate prescribing and failing to maintain malpractice insurance. Because these infractions constituted professional misconduct in New York as well, he was subject to two disciplinary actions in that state, resulting in censure, reprimand and a $2,500 fine.

According to the *Chicago Tribune*, Raxlen had other professional misconduct charges brought against him by Connecticut authorities but they were ultimately dropped. The *Tribune* reported that, in one case, Raxlen was charged with telling a patient with Lou Gehrig's disease (ALS) that she had Lyme disease and treating her with an illegal drug from Germany. He told the reporter that the relationship between ALS and Lyme was "unclear," even though ALS experts concluded that there was no evidence of a connection.

Per his New York State Department of Health physician profile (just type his name into the search engine), Raxlen completed residency training in psychiatry and lists his specialty as psychiatry, but he is not board certified in any specialty. He did not train in internal medicine, family medicine or pediatrics (although he treats pediatric patients), specialties that normally treat routine Lyme infections. Nor did he train in infectious diseases, experts to whom patients with more complicated cases of Lyme would normally be referred by other practitioners.

Yet, he is described by the International Lyme and Associated Disease Society (ILADS) as a "leader in Lyme disease treatment and research." In fact, he is a founding member of ILADS, former Secretary of the Board, and has taught a number of ILADS courses. He was a co-author of the original

ILADS guidelines for the treatment of tick-borne diseases. Despite their troubling disciplinary status, both he and David Cameron are scheduled to speak at the ILADS Annual Scientific Conference, which starts today in Boston.

How can this be? How can one be a leading light in ILADS with a disciplinary history like Raxlen's and no graduate medical education in infectious diseases?

"Lyme literate" physicians like Raxlen have fabricated a disease they call "chronic Lyme," which they regularly "diagnose" and treat with long-term antibiotics, sometimes for months to years. Board-certified infectious diseases doctors and other "conventional" physicians all agree that "chronic Lyme" is *not* a valid diagnosis and rely on well-conducted trials showing that long-term antibiotics do not substantially improve the outcome for patients diagnosed with so-called "chronic Lyme." Long-term antibiotics can, in fact, result in serious harm, including death, a subject our good friend Orac covered recently over on Respectful Insolence. Orac's post nicely summarizes the differences between real Lyme disease and "chronic Lyme," "a prototypical fake medical diagnosis," and the dangers of long-term antibiotics, as have posts on SBM, here, here, here, and here.

The CDC, the Infectious Diseases Society of America (IDSA), the American Academy of Pediatrics, the American College of Physicians, the *Medical Letter* and the American Academy of Neurology all reject the notion that "chronic Lyme" exists and that long-term antibiotics are an appropriate treatment. There is something called "post-treatment Lyme disease syndrome," but responsible medical authorities do not equate this syndrome with the nebulous symptoms and unvalidated lab tests of "chronic Lyme" and specifically reject the utility long-term antibiotic treatment based on well-conducted clinical trials. None of this is to say that patients who've been told they have "chronic Lyme" are not truly suffering, a fact that makes "Lyme literate" practices all the more reprehensible.

None of this stopped "Lyme literate" doctors from banding together to form ILADS and issuing their own guidelines for the diagnosis and treatment of "chronic Lyme," guidelines based on very low levels of evidence that are accepted only by themselves and, in contrast to the IDSA guidelines, no other

professional medical organization. ILADS teaches physicians and other practitioners how to become "Lyme literate." ILADS, again in contrast to IDSA, is not an ACCME-accredited provider of continuing medical education although, for some inexplicable reason, the Westchester [County, NY] Medical Society has teamed up with ILADS and is using its accrediting authority to grant CME credit for some of the talks (also here) at the ILADS Scientific Conference.

Despite the lack of evidence that "chronic Lyme" is a valid diagnosis, and the lack of efficacy as well as the risks of long-term antibiotic treatment, ILADS healthcare providers currently treat more than 100,000 patients with "chronic Lyme" and tick-borne diseases in the USA and around the world. Given media reports that patients can spend $10,000 to $35,000 for treatment, "Lyme literacy" translates into millions of dollars for practitioners.

While it may be profitable, "Lyme literate" doctors risk running afoul of state medical boards. Raxlen is just one among ILADS-trained, "Lyme literate" physicians who have had their medical practices questioned by their peers, up to and including discipline imposed by state authorities (also, here and here).

With that background, let's look at the allegations against Raxlen and the terms of his probation.

The BPMC v. Raxlen

New York's medical misconduct procedures do not require the physician charged to stipulate to any particular acts of misconduct as a condition of settling his case. The physician can, as Raxlen did here, simply state he is unable to "successfully defend against at least one of the acts of misconduct alleged" and agree to the imposition of sanctions. This means the allegations in the state's Statement of Charges were never proven, as it was unnecessary to reach a decision on the factual issues once Raxlen agreed to a settlement. However, per the Office of Professional Medical Conduct's (OPMC) standard procedures, the allegations were based on expert review of Raxlen's patients' records and they remain uncontested by him.

The allegations of misconduct arise out of Raxlen's care of eight patients. As is typical of "chronic Lyme" diagnosis and treatment, patients (whose identities are protected) presented with a variety of disparate symptoms, such as:

- Patient A: freezing, burning, air hunger, weakness, fatigue, neck pain and intestinal pain.
- Patient E: fatigue, migraines, neck pain, joint pain, numbness and tingling, irritability, sound, light and temperature sensitivity and nonrestorative sleep.
- Patient G: back pain, abdominal pain, feet pain, extremity weakness, anxiety, depression and mood swings.
- Patient H (who got the Hickman catheter and numerous antibiotics mentioned below): mouth, teeth and jaw pain, confusion, forgetfulness, irritability and mood swings.

Diagnosis and treatment of "chronic Lyme" is never mentioned, a wise decision on the part of the BPMC prosecutors in light of the ill-conceived New York law protecting "Lyme literate" doctors from prosecution

> based solely upon the recommendation or provision of a treatment modality by a licensee that is not universally accepted by the medical profession, including but not limited to, varying modalities used in the treatment of lyme disease and other tick-borne diseases.

Instead, the BPMC focused on the fact that Raxlen had failed in the most basic tenets of good medical care, although the fingerprints of "chronic Lyme" diagnosis and treatment, such as failure to consider alternative diagnoses, prescribing IV antibiotics and using a Hickman catheter, are all over the charges. The charges included:

- Repeatedly failing to perform or note in the patient's chart a comprehensive history and appropriate physical exam, including (despite his being a psychiatrist) a psychiatric history, neuropsychological testing and mental health status exam.
- Failing to construct a differential diagnosis and pursue a thorough diagnostic evaluation prior to instituting a treatment plan.
- Inappropriate prescribing, including prescribing Rifampin for a patient

on Tamoxifen and prescribing addictive medications prior to a making a diagnosis and without considering non-addictive treatment.
- Inappropriately relying on Applied Kinesiology (which is quackery) to formulate a diagnosis.
- Placement of a Hickman catheter without medical necessity.
- Inappropriately administering antibiotics, including intravenous Invanz, Clindamycin, Flagyl, Rifampin, Minocycline, Mepron, Plaquenil and Bactrim, all of these for *one patient*.
- Failure to present or note in the patient's chart potential risks, benefits, side effects and safe use of prescribed medications.
- Failure to appropriately identify, address, and/or follow-up on potential side effects.
- Treating inappropriately with an ongoing and/or escalating medication regimen without appropriate physical exams and clinical reassessment for consideration of alternative diagnoses and treatment.
- Poor record-keeping.

These allegations resulted in charges of negligence, incompetence, gross negligence, gross incompetence, and failure to maintain adequate patient records. As noted, Raxlen agreed to a three-year probation in addition to the imposition of conditions on his practice. He must, among other things:

- Communicate to patients the nature of his medical role, whether it be a primary care physician responsible for the patient's general medical condition, or for a defined or limited purpose, and/or as a practitioner of a particular medical specialty.
- Obtain written informed consent addressing all aspects of treatment and document same, including documentation of all discussions with the patient about the nature and scope of his evaluation and treatment and the patient's need to pursue "conventional medical care elsewhere."
- Document all histories and physicals.
- Refer patients to primary care physicians, specialists or consultants for further evaluation and/or treatment where medically warranted and provide these physicians with all relevant patient information.
- Cooperate fully with the state in enforcing the Consent Order and timely respond to all state requests for written periodic verification of his compliance and all documents.

What now?

Based on a birthdate of 1938 in his state physician profile, Raxlen is either already, or soon will be, 79 years old. One wonders whether he will continue his practice in face of these new sanctions, although his website is still trying to attract patients.

Sadly, the “chronic Lyme” lobby responsible for passing the law protecting “Lyme literate” doctors has its sights set on even greater rewards. Several bills are pending in the NY legislature which would force insurers to cover “chronic Lyme” treatment (Assembly Bill 114, Senate Bill 4713, Senate Bill 670). Other bills give them the opportunity to argue in yet another venue for insurance coverage. (Assembly Bill 4863, Senate Bill 2168, Assembly Bill 6927).

In any event, it is commendable that the Board for Professional Medical Conduct has not let New York’s unfortunate law get in the way of its prosecuting physicians who take advantage of patients with a diagnosis of “chronic Lyme,” no matter how they frame the specific charges. With two leading NY “Lyme literate” physicians now on probation and under strict orders to clean up their acts, it remains to be seen what effect this might have on other “Lyme literate” doctors in the state.

Science Based Medicine

周二, 21 11月 2017

Science Based Medicine

[周二, 21 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **What is “integrative oncology”? Even the Society for Integrative Oncology doesn’t seem to know for sure** [周一, 20 11月 16:25]
  Last week, the Society for Integrative Oncology published an article attempting to define what "integrative oncology" is. The definition, when it isn't totally vague, ignores the pseudoscience at the heart of integrative oncology and medicine.
- **Hopelessly Devoted to Woo: TLC and Forbes Bring Us Yet Another Celebrity Healer** [周五, 17 11月 21:00]
  Endorsed by journalists and studied by academic medicine, bogus celebrity energy healer Charlie Goldsmith now has his own television program. In other words, it's just another day at Science-Based Medicine.
- **CAM use leads to delays in appropriate, effective arthritis therapy** [周四, 16 11月 22:00]
  A preference to use CAM before seeking medical advice may be harming patients with inflammatory arthritis.

Longtime readers of Science-Based Medicine and my not-so-secret other blog probably know that I'm not a fan of the specialty known as "integrative oncology." My reasons are basically the same as the reasons why I detest "integrative medicine," only subspecialized (like oncology), so to speak. Basically, "integrative medicine" integrates quackery with medicine, and integrative oncology integrates quackery into oncology. Given that I'm a cancer surgeon, I tend to take an even dimmer view of the latter than of the former, if only because it hits me where I live. For instance, when "integrative oncology" starts appearing at symposia at major cancer meetings, with nary a skeptical word showing up in the panel discussions afterwards, I despair. Unfortunately, the credulity that allows modalities like acupuncture, reiki, intravenous high dose vitamin C, and various other unproven and disproven treatments to find their way into academic medical centers has spawned a related phenomenon, quackademic medicine, or the study and acceptance of quackery in academic medical centers. The most prominent example of this latter phenomenon occurred in September, when the University of California at Irvine accepted a $200 million gift from Susan and Henry Samueli to build and staff a college devoted to integrating quackery into its component departments and promoting "integrative medicine." Never mind the homeopathy.

Integrative oncology has become so established that it has its own professional society, the Society for Integrative Oncology (SIO). Not surprisingly, I'm not a fan of SIO, and SIO isn't exactly a fan of me, either. I've related the story before, but let's just say that the SIO was not pleased at my 2014 article in *Nature Reviews Cancer* discussing how integrative oncology is not evidence-based (to say the least), given its embrace of naturopathy. In brief, the SIO didn't like how much verbiage I devoted to homeopathy in the article, pointing out that homeopathy is indeed not evidence-based and that no integrative oncologist worth his or her salt would ever use it. I pointed out that you can't have naturopathy without homeopathy. After that, I asked how the SIO can reconcile its quite correct rejection of homeopathy with the fact that it admits naturopaths as members, that two of its recent past presidents have even been naturopaths, and that you can't have naturopathy without homeopathy. It's baked into the naturopathic

curriculum, and it's part of the naturopathic licensing exam. Moreover, one of the naturopaths who co-authored the SIO's breast cancer clinical guidelines ran a clinical trial on homeopathy. That same naturopath, by the way, was a co-author on the update to those guidelines published just this year. The SIO never learns.

This time around, though, the reason the SIO caught my attention was this Tweet by Dr. Sheila Garland, re-Tweeted by Dr. Jun J. Mao, immediate past president of the SIO (but still president at the time he re-Tweeted this):

> The beginning of a new era in evidence-informed integrative oncology research/practice that puts the person first #SIO2017 @Integrativeonc https://t.co/cmAMrCujjy
>
> — Dr. Sheila Garland (@SNGarlandPhD) November 13, 2017

This Tweet touted what is now the "official" definition" of "integrative oncology" recently laid down by the SIO:

> Official definition of Integrative Oncology! Spread the word! #SIO2017 We are research based! #cancerresearch pic.twitter.com/oeNsn9B1Jk
>
> — Jodi MacLeod (@write4wellness) November 13, 2017

It turns out that this definition had just been published by Witt et al in the November issue of *JNCI Monographs*, just in time for the SIO annual meeting last week. When I saw it, my first reaction was to e-mail my fellow SBM bloggers with a link and this image:

So let’s take a look.

The process of defining “integrative oncology”

My first reaction (besides possessiveness) when I saw the article by Witt et al, A Comprehensive Definition for Integrative Oncology was: What? The organization has existed for nearly 15 years, and in all that time it hasn’t yet managed to define what it’s about until now? My second reaction was: What on earth does this definition actually mean? It is about as boring, generic, and —shall we say?—vague a definition of anything as I’ve ever seen. Take a look:

> Integrative oncology is a patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments. Integrative oncology aims to optimize health, quality of life, and clinical outcomes across the cancer care

> continuum and to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment.

In actuality, I was more interested in what was left out of this definition than what was in it, but I'll get to that near the end of this post. First, I want to look at the process by which the authors developed this definition, as described in the article, which is open-access for those of you who want to read it yourselves. Before I get into the process, let's look at some of the authors, who are big names in the world of integrative oncology. The lead author, Dr. Claudia Witt, is Professor and Chair of the Institute for Complementary and Integrative Medicine at the University of Zurich and University Hospital Zurich, as well as part-time Professor of Primary Care and Community Medicine at the Center for Integrative Medicine University of Maryland School of Medicine. Dr. Jun J. Mao is, of course, president of the SIO and Chief of the Integrative Medicine Service at Memorial Sloan-Kettering Cancer Center. Dr. Lorenzo Cohen is someone whom we've met before, when he gave a talk at the American Society of Clinical Oncology (ASCO) meeting in 2014. He's the Director of the Integrative Medicine Program at The University of Texas MD Anderson Cancer Center. Linda Balneaves is a nurse and the current president of SIO, having succeeded Dr. Mao at the SIO annual meeting last week. I also can't help but note that one of the co-authors, Heather Greenlee, is a naturopath and has served as president of the SIO in the past as well.

In other words, these are indeed heavy hitters and the leadership of the SIO.

Let's look at their justification for seeking this definition. After regurgitating the usual "complementary and alternative medicine" (CAM) blather about how patients are just "looking for "additional interventions that may help improve the efficacy of conventional cancer treatments, increase their chance of survival, and/or reduce their symptom burden associated with cancer or treatments" and "improve their quality of life during and following treatment," Witt et al justify their search for a definition thusly:

> With the integration of interventions such as acupuncture, mindfulness and yoga, and lifestyle counseling into major cancer centers in North America (eg, MD Anderson and Memorial Sloan Kettering Cancer Center), the term "integrative oncology" has become increasingly used.

> “Integrative” better represents the process of care that is provided in centers where patients are receiving these types of interventions in addition to their conventional cancer treatments. With the establishment in 2003 of the Society of Integrative Oncology (SIO), a nonprofit multidisciplinary professional organization, the term “integrative oncology” was further legitimized and began to be widely used. However, the term “integrative” is also used in other contexts. An example is the Berlin School of Integrative Oncology at the Charité Medical School in Berlin (2), which is an initiative of the German federal and state governments that aims to educate young scientists and physicians in oncology in an interdisciplinary, translational research context. Although the term “integrative oncology” is rarely used in such an educational context, having totally different meanings for the same term can generate confusion. Adding to this complexity is the growing attention to the notion of integrated care programs in oncology, in which numerous cancer specialties (eg, medical oncology, radiation oncology, surgical oncology, genetics, plastic surgery) work together to provide comprehensive patient care (3).
>
> Furthermore, even in settings in which the term integrative oncology has been used to refer to the combination of complementary medicine therapies with conventional cancer treatments (4), the term has been defined in many different ways (5,6). Because of this lack of consensus, it has been difficult to communicate what is meant by “integrative oncology” to oncologists and other health professionals, as well as to key stakeholders, such as patients, administrators, and health policy makers. The aim of this project was to use a systematic approach to develop a comprehensive and acceptable definition for “integrative oncology.”

Actually, I’ve always rather suspected that this confusion is a feature, not a bug, related to the use of the word “integrative.” After all, integrative oncology, like integrative medicine, is a brand, not a specialty. It rebrands what should be considered perfectly fine science-based modalities, such as nutrition, lifestyle interventions, and the like, as somehow “alternative” or “integrative,” and then “integrates” quackery like acupuncture, reiki, functional medicine, and even homeopathy with them, to give the quackery

the appearance of scientific legitimacy. No, I don't think SIO is doing this intentionally; its leadership consists of true believers. But it is contributing to quackademic medicine and the integration of quackery into oncology. In any event, the word "integrative" is, as mentioned above, used to describe science-based endeavors, such as integrative biology. In this context, the word "integrative" connotes interdisciplinary study, a very different meaning than when the word "integrative" came to replace the term CAM to describe adding pseudoscience to medicine.

Indeed, use of the word "integrative" to describe medicine or the subspecialty of oncology connotes more than interdisciplinary patient care and research. It connotes the embrace of "alternative" treatment modalities as well. The term "CAM" still had the word "alternative" in it and the word "complementary" connoted that CAM was subsidiary to medicine, "complementary," the icing on the cake, if you will. In other words, it's not necessary, and science-based medicine is the real medicine. The adoption of the word "integrative" to rename CAM as "integrative medicine" was clearly intended to remove the implication that CAM was "complementary" and not as good as real medicine, in order to advance the narrative that integrative medicine is the "best of both worlds," while also borrowing from the cachet of various "integrative" scientific disciplines as being multidisciplinary. Again, I don't think SIO is out to deceive. Rather, the belief of the SIO leadership in the validity of integrative oncology has led them down this road, probably without even realizing it.

So how did Witt et al go about constructing their definition? Enter the mixed methods research design and Delphi method. This amused me, because it wasn't so long ago that naturopathic oncologists used this very method to try to define priorities in naturopathic oncology. If you want the details of how the Delphi method works I discussed them in deconstructing the nonsense that naturopaths laid down about their quack specialty using the Delphi method. The CliffsNotes version is that the Delphi method entails a using a group of experts to answer a question. The experts anonymously reply to questionnaires and subsequently receive feedback in the form of the statistical representation of the group response, after which the process repeats itself until something resembling a consensus is arrived at. The way Witt et al did this is described:

> A two-round Delphi process was then employed to further refine and gain consensus regarding the new definition. In the first round, the revised definition was distributed via an online survey (software SoSciSurvey [7]) to SIO board members as well as to a convenience sample of experts. The experts—oncologists, integrative oncology clinicians, and/or researchers from North America, Europe, and Asia—were contacted by the SIO board members. Based on first round feedback, the definition was revised and distributed again through an online survey to the full membership of SIO, with subsequent ratings and comments used to inform the final version of the definition. Data from both surveys were analyzed using descriptive statistics. Content analysis (8) was applied to the open-ended responses to identify any themes or concepts.

So, after this literature search and Delphi method, what did Witt et al find?

Defining “integrative oncology”

As a result of their literature search and two-round Delphi process, Witt et al found many definitions of “integrative medicine” and “integrative oncology” in the literature, which resulted in the following thematic suggestions:

- evidence-based/evidence-informed/evidence-guided/using best available evidence (14 of 20);
- accompanying conventional cancer treatment (18 of 20);
- addressing outcomes such as well-being, body, and mind-spirit, as well as physical, psychological, and spiritual quality of life (seven of 20);
- focused on health and not only on medicine (three of 20);
- provided by a team of health care providers/multidisciplinary/interdisciplinary (four of 20);
- patient-centered/personalized, individualized/whole person (two of 20).

The writing group, which consisted of “members with different professional/disciplinary backgrounds (ie, medical oncology, radiation

oncology, surgical oncology, nursing, patient advocacy, psychology, psycho-oncology, epidemiology, integrative medicine, health policy),” added these additional suggestions:

- type of interventions (mind-body therapies, natural products, lifestyle changes);
- beyond provision of health care (information, translation of evidence, identification of beliefs, values and preferences, empowerment).

The initial definition of integrative oncology developed by the group thus read:

> Integrative oncology is a patient-centered (theme 6), evidence-informed (theme 1) approach to health care (theme 4) that uses mind-body therapies, natural products, and lifestyle modification (theme 7) as adjunct to conventional cancer treatments (theme 2) and is ideally provided by a multidisciplinary team of care providers (theme 5). Integrative oncology aims to increase well-being of mind, body, and spirit (theme 3) and to provide patients with skills enabling them to help themselves during and beyond cancer treatment (theme 8).

After the two rounds of Delphi method, though, the group perceived that some changes were required:

> Overall, the comments on the second Delphi survey were positive, but the suggestions were quite heterogeneous. Two-thirds of suggestions focused on what were perceived to be missing interventions, and it became clear that therapies such as acupuncture and massage were not well represented in the definition. As a consequence, the definition was revised using the umbrella term “mind and body practices,” which is used by the National Center for Complementary and Integrative Health in the United States. This term includes mind-based techniques such as meditation and hypnosis, as well as manual techniques such as acupuncture and massage (9). One respondent mentioned that “health care” encompassed a broader area than integrative oncology, and the decision was made to be more focused and to use the term “cancer care” in the revised version. Another respondent also suggested that the phrase “approach to cancer care” could be misleading and not specific enough

> as a field of care or medical specialty. Integrative oncology is more than just an approach to overall cancer care; it has been the focus of a professional organization for more than 10 years and is an established field in its own right. During the review process, it was noted that cancer prevention was not included in the definition. Because the ultimate goal of many integrative oncology behaviors is cancer prevention and control, the definition was modified to include prevention.

I've discussed before how quackery like the theatrical placebo known as acupuncture has mysteriously been subsumed into "mind and body practices". Personally, I've always suspected that this was to hide the quackery of acupuncture with more benign modalities (such as massage) that, whether medically they can treat anything, generally do no harm, and can certainly feel good, thus improving quality of life. After all, given that the rationale in traditional Chinese medicine for acupuncture is that sticking the needles into specific "meridians" can redirect the flow of qi (life energy) for healing effect, acupuncture could easily be classified as a form of energy healing.

To the degree that integrative oncology sticks with science- and evidence-based tests and treatments, my main objection to it is that it's not necessary. Nutrition, exercise, and other lifestyle-based interventions are already a part of science-based medicine. I like to cite, for instance, evidence-based recommendations for the treatment of hypertension and type II diabetes, both of which emphasize, except for severe cases, dietary modifications, exercise, and weight loss as the first interventions to attempt before placing the patient on medications.

To paraphrase Harriet Hall, what is good about integrative oncology (or medicine) is not unique to it. Continuing the paraphrase, unfortunately, what is unique to integrative oncology is not good, and the SIO definition obscures or neglects to mention these unique (and not good) aspects.

What the SIO left out

If you read the full article, it should become very apparent that its authors

want desperately to convince the reader that integrative oncology is completely evidence-based. Sure, the SIO admits naturopaths and even elects them as the organization's president from time to time, never mind that all naturopaths are trained in The One Quackery To Rule Them All, homeopathy, and that the vast majority of naturopaths routinely prescribe homeopathic remedies, which, even the SIO concedes, are rooted in pseudoscience.

I was reminded of this on—where else?—Twitter. I came across a post on the University of Pennsylvania's OncoLink touting reiki in cancer care. Because the link was from 2011, I Tweeted a question to the OncoLink team. Here's the response:

> @gorskon, Reiki is a supportive therapy that can be used in conjunction with treatment. It is not promoted as an alternative to treatment
>
> — OncoLink Team (@OncoLinkTeam) November 2, 2017

If there is a challenger to homeopathy's title of The One Quackery To Rule Them All, reiki would be right up there. It is, as I have described many times before, a form of faith healing that substitutes Eastern religious beliefs for the Christian religious beliefs that usually undergird faith healing in the US.

But it's not just Penn. The Dana Farber Cancer Institute has also gone all in for nonsense:

> 7 Ways Integrative Therapies Help Cancer Patients: https://t.co/bRHYbqhrcy pic.twitter.com/0kVQ4FKW0o
>
> — Dana-Farber (@DanaFarber) August 26, 2017

The slideshow at the link above promotes reiki, reflexology, and acupuncture:

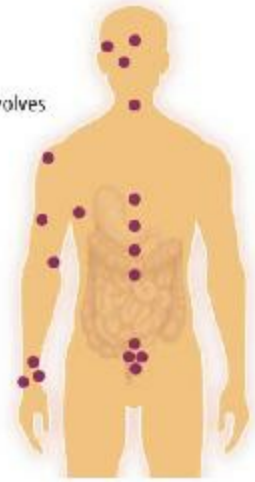
DANA-FARBER CANCER INSTITUTE
Discover. Care. Believe

7 WAYS INTEGRATIVE THERAPIES CAN HELP CANCER PATIENTS

1. ACUPUNCTURE

Acupuncture is a standard practice in Chinese medicine which involves gently inserting hair-thin needles into the skin at specific points. Acupuncture has been shown to:

- Reduce post-operative nausea and vomiting
- Decrease anxiety
- Treat pain and loss of nerve sensation
- Relieve joint pain
- Help relieve chronic pain



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Acupuncture is nothing more than a theatrical placebo, whose action has never been convincingly shown to be greater than that of placebo controls. Yet Dana Farber Cancer Center thinks acupuncture is science-based.

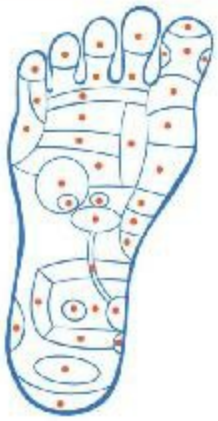
DANA-FARBER CANCER INSTITUTE
Discover. Care. Believe

7 WAYS INTEGRATIVE THERAPIES CAN HELP CANCER PATIENTS

3. REFLEXOLOGY

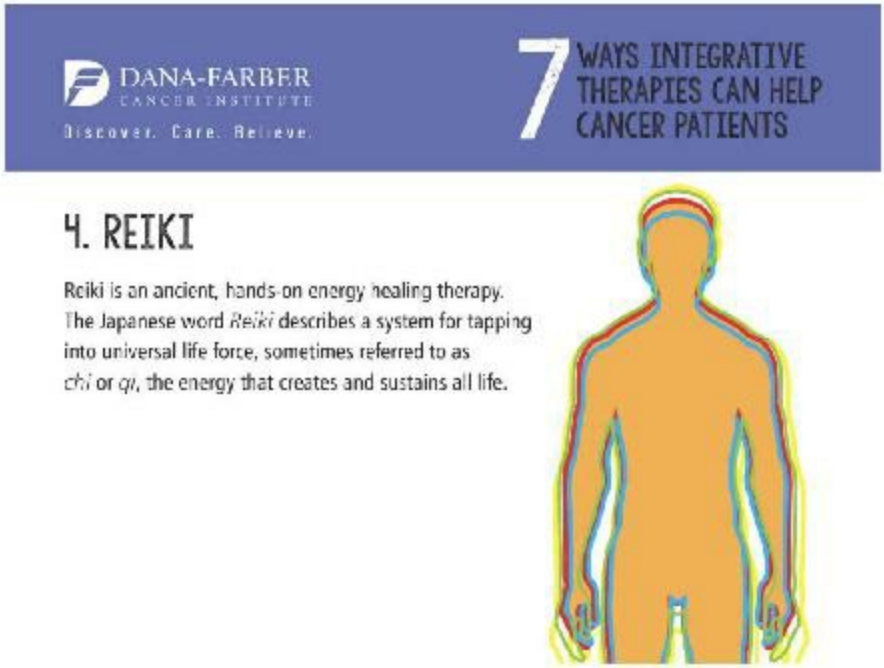
Reflexology is the application of pressure to areas on the feet, hands, and outer ears. The theory behind reflexology is that these areas correspond to organs and systems in the body. Patients have found that reflexology can:

- Promote relaxation and comfort
- Help with treatment symptoms like fatigue and nausea



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Reflexology posits the existence of physiologic or anatomic links between organs and body parts and areas on the soles of the feet and palms of the hand. Yet Dana Farber Cancer Center thinks this is science-based.



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Reiki masters claim to be able to heal by channeling energy into the patient from the "universal source." Replace "universal source" with "God" or "Jesus," and it becomes obvious that reiki is a form of faith healing that replaces Christian beliefs with Eastern mysticisms. Yet Dana Farber Cancer Center thinks it's science-based.

Of course, I've pointed out how oblivious the SIO is to the modalities that are really being "integrated" into oncology through integrative oncology just through the obliviousness of the SIO leadership to what naturopathy really is. As I've said before, if the SIO were really serious about being evidence-based, it would immediately purge itself of all naturopaths. It's not, though. Its leadership up in the ivory towers of medical academia can delude themselves into thinking integrative oncology is totally evidence based, because they manage to ignore the quackery that is "integrated" along with the lifestyle-, exercise-, nutrition-, and meditation-based modalities to which they love to point.

I can’t help but point out a few more examples of the quackery that goes along with integrative oncology. At UC-Irvine and the Cleveland Clinic, there’s homeopathy. At the University of Arizona Cancer Center, there was reiki, at least until a faculty member whose child developed cancer and was treated there made a stink. There’s also more energy medicine quackery, this time in the chemotherapy suite, at Georgetown University, as well as cupping, which is also pure quackery. There’s functional medicine at the Cleveland Clinic, George Washington University, University of Kansas, and, well, seemingly almost everywhere at any medical center with an integrative medicine program. If you want an idea of how bad functional medicine is, just check out this case report of functional medicine used for a patient with inflammatory breast cancer. This is what integrative oncology *really* involves.

It is also this quackery that the SIO definition of “integrative oncology” does its best to obscure or ignore. If the SIO is truly serious about being science- and evidence-based, it needs to speak out strongly and now against naturopathy and the various forms of quackery that have found their way into academic medical centers, of which, I assure you, the above is but a small sampling. It won’t, though. The quackery is why integrative medicine and oncology exist in the first place. Without the quackery, CAM (or integrative medicine or oncology) becomes completely unnecessary as a field.

In recognition of my 100th post on SBM, I was all set to write about some interesting updates on a few of my contributions over the years. But thanks to the machinations of the preternaturally cool Tim Caulfield, author of *The Cure for Everything* and *Is Gwyneth Paltrow Wrong About Everything?*, I was made aware of something that I just couldn't ignore: someone is wrong on the internet. That's right, yet another "energy healer" with bold claims of miracle cures is making the rounds. But this time will be different, apparently.

Remember Adam Dreamhealer? He was the teenage "intuitive healer" that could recognize and manipulate mysterious human energy fields to cure cancer and a whole host of other ailments, even over the phone or after only looking at a photograph of the patient. He claimed to have received his powers from a giant blackbird he met while hiking. Ring a bell? Well, it was a whole thing about a decade ago, just as I was starting my journey on the path of skepticism. Although he is still up to the same tricks as a "naturopathic oncologist", and he will always have a special place in my heart, Dreamhealer has some stiff competition for my favorite celebrity energy healer.

The new kid on the block is Australian energy healer Charlie Goldsmith, and technically he isn't all that new. Orac, who I believe is some kind of protocol droid, wrote about him back in 2015. Goldsmith was just dipping his toe in the water of widespread recognition at that time, getting some press in the form of credulous fluff pieces focusing on the fact that he is Olivia Newton John's nephew and on his involvement in a ridiculous study published in the *Journal of Alternative and Complementary Medicine*. Described as a "feasibility study", it is embarrassingly amateurish, really just a collection of cherry picked anecdotes that did not involve the slightest bit of blinding or control. The authors concluded what anyone remotely familiar with research like this would have expected.

What Caulfield alerted me to this week was the publication of yet another painfully credulous article, this time on the *Forbes Lifestyle* blog. In the piece, Forbes contributor and certified Holistic Health Coach Courtney Porkoláb asks the question "does energy healing work?" and invites readers

to decide for themselves. In a conversation with her on Twitter she was quick to remind me that hers wasn't a scientific article and to imply that she just wanted to "spark conversation." Yet in the article she provides only her gullible acceptance and a series of comments from Goldsmith and a few credentialed believers endorsing the benefits of energy healing and even proposing scientific explanations. There isn't even an attempt at token skepticism.

Porkoláb gushingly discusses Goldsmith as if he is a miracle worker:

> Goldsmith's success rates are undeniably high, having relieved people of all ages, with issues ranging from chronic pain to infections and auto-immune disorders, often in 60 seconds or less.

The article contains numerous absurd assumptions and laughably implausible claims, all in the service of promoting the fact that Goldsmith is now starring in a TLC program documenting his supposed abilities. It isn't alone, of course. This *Daily Mail* article is particularly informative as it provides a clip from the most recent episode. It shows Goldsmith taking advantage of the power of suggestion as he interrogates a 2-year-old child about his symptoms before going through the standard energy healing motions. The kid is adorable but it's pretty ridiculous, and what is really happening should be clear to anyone with a modicum of experience with toddler behavior. The deciphering of the child's unintelligible responses reminded me of how ghost hunters prime listeners when demonstrating EVP.

Orac, which I understand is some kind of prototype U.S. military robot that gained sentience and a powerful sense of skepticism after being struck by lightning, beat me to the punch and wrote an excellent discussion of Goldsmith and the *Forbes* article. Feel free to hop on over and read it. I'll provide a couple of the best quotes myself, however:

> Prior to the studies done in the public eye, Goldsmith spent years healing as many as he could, often those who had been failed by countless doctors and traditional medicine.

Regular readers of SBM know how unreliable claims such as this are. Unless Goldsmith was keeping meticulous records of his healing attempts and

following up to document long term outcomes, these kinds of statements are essentially meaningless. It's very easy with confirmation bias and motivated reasoning to look back over the years and come to the conclusion that you helped a lot of people. It's easy to discount the failures and focus on the apparent successes.

And patients can be "failed by traditional medicine" in numerous ways, many of which don't actually equate to what is being implied. Patients with vague or non-specific symptoms and certain world views often feel like conventional doctors have let them down when they aren't given a specific diagnosis, or when treatment recommendations consist of lifestyle changes or mental health assessments rather than confident assertions and a supposed cure. Often proponents of pseudomedicine convince people that their doctor has failed them by missing the diagnosis of a fictional malady, such as adrenal fatigue.

I found this quote from Goldsmith particularly interesting:

> To be honest, sometimes I'll work on something that—medically—is seemingly simple and not fix it. And something that is medically complex—something medically incurable, for example—that might be quite easy for me.

He chalks this up his healing powers not being an exact art. I see this as exactly what I would expect when all that is being offered is false hope and expectation, and one is counting on various placebo effects to give the appearance of benefit. But again, unless he has been keeping strict records of his encounters, his claims regarding past treatments can't really be assessed. I'm not just going to take his word for it that he has defied our fundamental understanding of human physiology.

The credentialed believers provide some of the most memorable contributions, which you can read about in the above linked post by Orac. These include demonstrations of a lack of understanding of how pain is assessed and treated as well as appeals to quantum physics and "bioenergy". There are also references to the time Gary Schwartz supposedly found a measurable differences in the magnetic fields surrounding the hands of energy healers and to a study on bio-photon emissions after energy healing.

Let’s do the science!

Goldsmith is on a mission to prove that what he does is legitimate and not just theatrical placebo by participating in clinical trials. I already mentioned the one published “study” he participated in above, and he claims to be involved with two more taking place at the same facility. It sounds like more of the same:

> The study presently underway is being undertaken at NYU Lutheran Hospital in New York and employs a qualitative methodology to help understand the experiences of patients who encounter Mr Goldsmith’s practices.

In other words, more anecdotes without proper controls or blinding. According to his website, this study has actually been completed. It’s being written and will be submitted for publication next year. We’ll see. He also claims to be participating in a prospective RCT, again at the same facility, that is currently going through the IRB approval process. Again, we shall see if this actually materializes.

I challenged Goldsmith during a lengthy discussion on Twitter, and he reassured me that his intentions are purely altruistic. He denies financial motivation and simply wants to prove to the world that his gift is real so that science might take the phenomenon seriously. He only wants to help reduce the pain and suffering of others. He has been treating patients for years and, according to Goldsmith, he only went public in order to help entice researchers to do the studies.

I am skeptical of his motivation. History has, time and time again, revealed that believers in highly implausible and unproven therapies don’t really care what the science says. Typically the studies end up having such poor methodology that a positive result is assured, and when proper studies fail to find a true effect, they are ignored. Regardless of the outcome, proponents can point to the fact that studies were even done in the first place as evidence of their pet remedy’s legitimacy.

It is abundantly clear that Goldsmith has already decided that he has the

ability to cure people through energy healing. He didn’t notice something odd and then look to science to determine if it was true. He noticed something was odd and then did it to people with real medical problems for years before agreeing to star in a television program highlighting it. In my opinion, the research angle is just marketing and I’m embarrassed for NYU.

Several weeks ago I summarized the evidence that demonstrates that when you delay cancer chemotherapy and substitute alternative medicine, you die sooner. Thank you to the tireless Edzard Ernst, who identified non-cancer evidence that demonstrates how choosing complementary and alternative medicine (CAM) instead of real medicine, can cause harm. In this case, the example is early inflammatory arthritis (EIA), and what was studied was the relationship between CAM use, and the delay to initiation of medical therapy. Time is of the essence with inflammatory arthritis, as there are medications that can reduce the risk of permanent joint damage. This new paper adds to the accumulated evidence to show that CAM, while it is commonly thought to be harmless, can indeed harm – not only from direct effects, but also from delaying the initiation of proper, effective medical treatment.

What is inflammatory arthritis?

Inflammatory arthritis is a term that describes inflammation of the joints (and other tissues). Inflammatory arthritis can include rheumatoid arthritis, and several other conditions. These are often autoimmune conditions, where your immune system treats its own tissues as foreign, and attacks it. Pain, swelling and tenderness are typical with inflammatory arthritis, and a diagnosis is usually based on a physical examination and laboratory tests. There are now many medications that can treat arthritis, ranging from the non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen and ibuprofen, to disease-modifying anti-rheumatic drugs which include biologic drugs that can be very effective and even put the disease into remission. While inflammation can be treated, joint destruction from arthritis can be permanent, so starting appropriate therapy, quickly, is important to reduce the risk of long-term damage. Today, aggressive treatment early in the course of the disease is considered to be the standard of care, so it is important for new cases to be recognized and referred for specialist assessment as quickly as possible. Barriers to early treatment include patient delays, but also system delays like wait times for referrals. Understanding why patients may not seek treatment is a question that led to this most recent study.

Studying CAM and inflammatory arthritis

Complementary and alternative medicine (CAM) is commonly used in different cultures, including Asian cultures, where traditional Chinese medicine may even be government-endorsed, despite the lack of evidence to show it is an effective system of medicine. When a group of researchers identified that many patients with a new diagnosis of arthritis had tried CAM prior to seeking medical treatment, they hypothesized that CAM may be delaying referral and medical therapy.

This paper is from Manjari Lahiri and colleagues and was published in the *International Journal of Rheumatic Diseases*. Entitled "Use of complementary and alternative medicines is associated with delay to initiation of disease-modifying anti-rheumatic drug therapy in early inflammatory arthritis", this was a prospective survey of patients with EIA. All patients seen at one of two hospitals in Singapore where they were invited to participate. Patients were included if they had a self-reported symptom of EIA, which was defined as inflammation of two or more joints, not caused by trauma. Patients were assessed at 3, 6, and 12 months, then annually for 3 years. All participants completed a nurse-administered questionnaire on demographic, health and lifestyle factors including CAM use. In this study, CAM was defined as the ingestion of tablets, herbs, powders or drinks purported to have medicinal properties. They could be prescribed (e.g., by a practitioner in traditional Chinese medicine) or purchase over the counter. Acupuncture, therapeutic massage and cupping, when used for the purpose of a therapeutic effect where included in the definition of CAM, while exercise (including yoga and tai chi), physiotherapy, and occupational therapy were not considered CAM. (This is among the more accurate delineations of CAM/non-CAM I've seen in a study.)

CAM users delay treatment

For this study, only the baseline (time=0) results were used. Overall, 180 patients were included. The median time from diagnosis to recruitment was 3 weeks. The median age was 51, and 71% of the participants were women.

When stratified by CAM use, Chinese patients more commonly used CAM, and oral tablets/powders and acupuncture were the most common forms of CAM. Full details are in Table 1:

Table 1 Baseline characteristics

Characteristic	Proportion (%) or median (IQR)			P-value
	Overall (n = 180)	CAM users (n = 71)	CAM non users (n = 105)	
Age at diagnosis, years, median (IQR)	51.1 (40.9–59.8)	53.9 (43.8–60.7)	47.3 (40.2–58.3)	0.05
Bottom tertile, 22.3–44.3 years	33.5	25.7	39.0	0.14
Middle tertile, 44.4–57.4 years	33.5	35.1	32.1	
Top tertile, 57.5–81.4 years	33.0	39.2	28.5	
Female	70.5	68.9	71.4	0.72
Race				
Chinese	58.3	82.4	40.9	< 0.001
Malay	18.3	5.4	27.5	
Indian	16.7	8.1	22.9	
Others	6.7	4.0	8.5	
Body mass index	24.3 (21.2–27.6)	24.0 (20.3–26.4)	24.9 (21.3–28.2)	0.25
Non-English speaking	30.2	50.0	16.4	< 0.001
Level of education				
None or primary	21.2	20.3	22.1	0.15
Secondary or vocational	46.1	51.0	40.1	
Diploma or degree	32.4	25.7	37.5	
Ever smokers	26.8	35.1	20.9	0.03
Diagnosis				
Rheumatoid arthritis	83.0	83.8	83.8	0.92
Psoriatic arthritis	12.8	13.5	12.4	
Undifferentiated arthritis	3.3	2.7	3.8	
Symptom duration, weeks‡	16.5 (9.2–26.6)	20.8 (13.1–30.1)	13.7 (8.7–21.8)	0.004
Disease duration, weeks§	3 (0–16.9)	3.2 (0–18)	4 (0–16)	0.25
Sero-positive¶	57.0	62.9	52.9	0.20
RF positive	50.3	55.5	46	0.12
ACPA positive	52.7	55.9	50.0	0.70
DAS28, median (IQR)	4.30 (2.84–5.71)	4.56 (3.15–5.78)	3.86 (2.47–5.58)	0.02
Low disease activity, DAS28 < 3.2	30.3	20.8	37.2	0.07
Moderate disease activity, DAS28 ≥ 3.2 to < 5.1	38.9	43.1	35.3	
High disease activity, DAS28 ≥ 5.1	30.9	35.1	27.4	
mHAQ, median (IQR)	0.37 (0–0.87)	0.37 (0.12–0.87)	0.37 (0–1)	0.92
mHAQ ≥ 1 (vs. < 1)	24.5	21.6	26.7	0.41

P-value for comparison between CAM users versus non-users using Chi-squared test or Mann–Whitney U-test. ‡From symptom onset to first rheumatologist review. §From time of diagnosis to recruitment to the Singapore Early Arthritis Cohort. ¶Either RF or ACPA positive. IDR, interquartile range; CAM, complementary and alternative medicines; ACPA, anti-citrullinated peptide antibody; DAS28, Disease Activity Score in 28 joints; mHAQ, modified Health Assessment Questionnaire; IQR, Interquartile range; RF, rheumatoid factor

Table 1: Baseline Characteristics

The CAM stratification also shows some additional differences between the groups. There are race, language, and smoking histories that are quite different. Note that the duration of symptoms (until rheumatologist review) was 13.7 weeks among non-users and 20.8 weeks among CAM users. That is, CAM users waited almost twice as long to see a specialist, compared to non-users. Not surprisingly, this meant a delay to the initiation of disease-modifying anti-rheumatic drugs (DMARDs). Figure 1 shows the overall difference between CAM users and non-users:

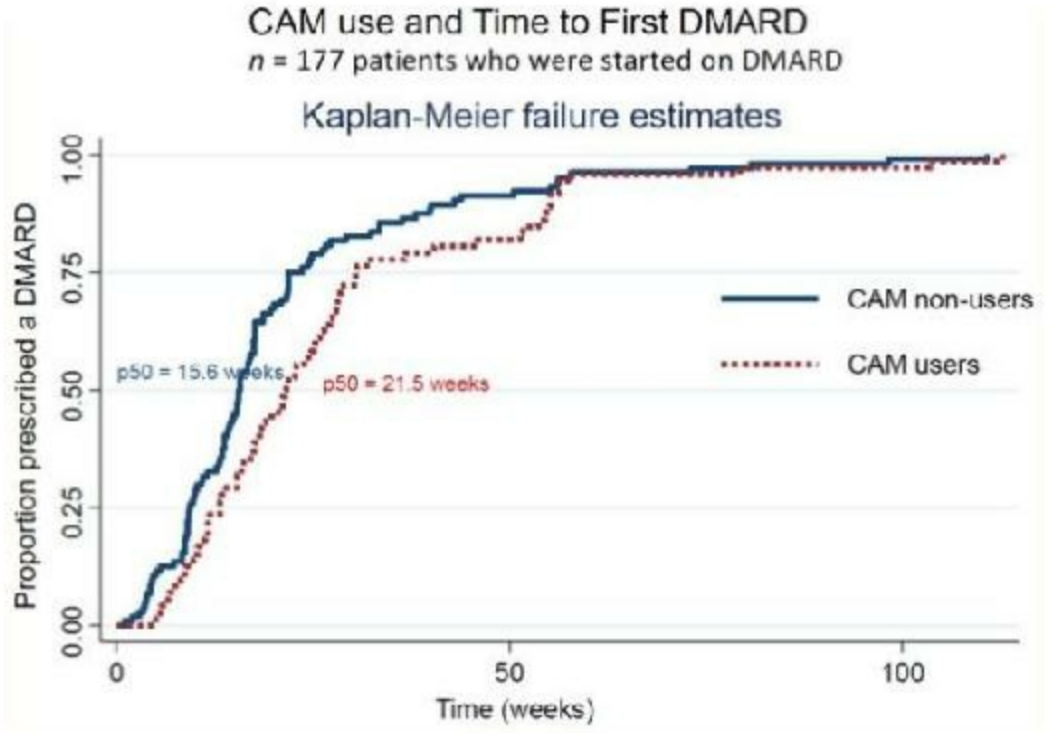


Figure 1 Kaplan–Meier plot of time to disease-modifying anti-rheumatic drugs (DMARDs) for complementary and alternative medicines (CAM) users versus non-users.

Only CAM use was significantly associated with the time to first DMARD initiation.

CAM use delays effective arthritis therapy

This small study illustrates what appears to be an unfortunate consequence of CAM use: It may be contributing to delays in seeking effective therapies, which may have additional negative consequences. While this study does not show direct harms from CAM use, the relationship between earlier therapy and positive disease outcomes is well established. The authors conclude that patient and public education programs to raise awareness about EIA, and the importance of early treatment, are essential. I would add that continuing to

raise awareness of the limitations of CAM, and the consequences of its use, need just as much awareness.

Science Based Medicine

周二, 28 11月 2017

Science Based Medicine

[周二, 28 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Science Moms Fight Fears with Facts** [周二, 28 11月 16:00]
  A new documentary takes a novel approach. It features scientist moms who are just like other moms except that they understand the science. They set the record straight about GMOs, vaccines, and other subjects of interest to parents. They provide the facts to counteract unreasonable fears.
- **The integration of mysticism and pseudoscience with oncology continues apace in NCI-designated comprehensive cancer centers** [周一, 27 11月 16:32]
  Last week, I commented on the inability of the Society for Integrative Oncology to define what integrative oncology actually is. This week, I note the proliferation of the quackery of integrative oncology in places that should be rigorously science-based, namely NCI-designated comprehensive cancer centers.
- **And the server migration continues apace…but where are the comments?** [周六, 25 11月 10:15]
  SBM is changing servers again. Unfortunately, that means that there are problems with the comments.

Science Moms Fight Fears with Facts - Science-Based Medicine

At the recent conference of the Committee for Skeptical Inquiry (CSICON) in Las Vegas, on October 28, 2017, I had the great privilege and pleasure of being in the audience for the American premiere of a new documentary, "Science Moms," as well as for the following live panel discussion by the women featured in the movie. In the documentary, a group of scientists and science communicators who are also moms address misperceptions created by misinformation in the media about GMOs, vaccines, and other issues important to parents. They point out that "moms whose opinions are formed by fear and hype are so loud. But they're the only people talking about it, the only resource people have." With this documentary, people now have another resource based on science, a resource that is easily digestible and compelling.

The film starts with a beautiful sunrise and a Gwyneth Paltrow quote: "The sun is the sun – how can it be bad for you? I don't think anything that's natural can be bad for you." The Moms answer:

"Wow! I could make a list for her."

“The sun causes cancer.”

“Nature will kill you, really quickly.”

“Sometimes I think she’s trolling us.”

Next, the Science Moms are introduced and talk about how they got interested in science. They are:

Anastasia Bodnar, PhD, Plant Geneticist

Alison Bernstein, PhD, Neuroscientist

Layla Katiraee, PhD, Molecular Geneticist

Jenny Splitter, Science Communicator and Storyteller

Kavin Senapathy, Science Communicator

These women shatter the stereotypes of scientists as commonly portrayed in the media. They are normal, friendly, personable, attractive, well-groomed, non-geeky, everyday people, just like other working moms except that their jobs happen to involve science. Moms viewing the film ought to be able to relate to them and listen to what they have to say just as they would listen to their friends.

Two of Science Moms were fans of Buffy the Vampire Slayer and were appalled to learn that the actress who played Buffy, Sarah Michelle Gellar, was speaking out against GMOs. They joined a group of 15 women scientists, bloggers, and educators to send a letter to Paltrow, Gellar, and other celebrities asking them not to co-opt motherhood and wield their fame to oppose beneficial technologies, but to use their influence responsibly and ensure that their advocacy is supported by facts, not fear.

The letter caught the attention of Natalie Newell, the host of “The Science Enthusiast” podcast. She contacted one of the letter’s authors. One thing led to another, and the result was this documentary.

The Moms acknowledge that being a parent is scary. Parents desperately

want to protect their children from any possible harm, and often they aren't sure how to best do that. Even they admit to having acted irrationally based on unrealistic fears for the welfare of their children. It's a great marketing technique: "If you can scare a parent, of course they're going to shell out for the alternative."

GMOs

People who don't know anything about GMOS may choose organic because they vaguely remember hearing that it was better for their kids. GMOs are presented in the media as inserting genes of one species into another species. But that's only one meaning. Genetic modification also means selective breeding, cross breeding, mutagenesis, genome editing, and other techniques.

When plants are cross-pollinated, a gene for disease resistance can spread to another species, but that's random. Why not use technology to put the desired gene into the plant? In reality, almost everything we eat was genetically engineered centuries ago by our ancestors' selective farming and breeding practices.

The Moms point out these benefits of genetic modification:

Drought resistance

Pest resistance

Disease resistance

Increased crop yield

Increased nutritional content

Economic benefits

Reduced pesticide usage

Reduced greenhouse gas emissions

Vitamin A deficiency causes untold cases of blindness and death in

developing countries. Golden rice was genetically modified to supply vitamin A, but thanks to anti-GMO ideology it hasn't reached those who need it most.

Some people fear that eating something genetically engineered will genetically engineer THEM. Not hardly! Despite widespread fears, GMOs have never harmed a single person's health in any way.

Fear of chemicals

The idea that "There is no safe amount of chemicals" is false. Everything is made of chemicals. They show a long list of all the scary-sounding chemicals in an all-natural blueberry. Pears naturally make formaldehyde.

The "most brilliant marketing move of the last ten years" was to convince everyone that organic is pesticide free. Copper sulfate is really bad for the environment, and it's allowed in organic farming.

Data doesn't support claims that organic is pesticide free, better for environment, or healthier.

There are no health benefits to be gained from organic. It's just more expensive.

Vaccines

We hear:

- Too many too soon
- Dangerous chemicals in vaccines
- I prefer to fight off disease naturally
- It's a Big Pharma conspiracy
- These diseases aren't really that dangerous."

None of these are based on evidence or science. Unrealistic fears of vaccines have led to decreased herd immunity and disease outbreaks. Our grandparents aren't likely to fear vaccines, because they knew people who died of polio and other preventable diseases. It's ironic that people are afraid of harmless GMOs but don't fear the very real risks of vaccine preventable diseases.

Homeopathy

One Science Mom says, “I’m embarrassed to say I tried it. When I found out what it was, I thought ‘Oh, that’s why it didn’t work.’ I could have given the kids sugar water I made at home and saved a few bucks.”

> I can’t imagine parents reaching for something that is untested, unregulated, and has no active ingredients in it. It baffles me.

Perhaps it’s because people want to do things on their own – homeopathy, homemade baby formula, anything that gives them the illusion of being in control.

Who’s paying you??!!

The answer to this oft-repeated question is an emphatic “Nobody!” Kavin Senapathy says she has been called a fake mom, has gotten death threats, and has been told her name is made up (as if Monsanto would invent a name like Kavin Senapathy!) She doesn’t understand where the shill accusation comes from. The assumption seems to be that anyone who doesn’t have the same world view as you, must be paid to have that view. It’s hard to have your world view challenged, so it’s easier to think they must be paid to disagree with you than to think your world view might be incorrect.

More

They explain that scientific consensus is not like a vote, it’s the confluence of all the evidence coming together around a hypothesis.

When people ask if something is safe for their child, the best advice is to go to a real doctor (not a naturopath); and to buy real medicine (homeopathy is not real medicine).

Healthy diet? Eat lots of fruits and vegetables, buy whatever’s cheaper, wash produce.

Some organizations are trying to scare people away from buying certain fruits and vegetables. That’s CRAZY!

You might as well enjoy being a parent. “Basic safety stuff fits on half a page.” Don’t worry about minor details with no solid evidence, like when to introduce solid foods.

“When kids are 10-12, no one’s talking about whether they were breast fed.” The effects of stress on us and our kids is way worse than anything we’re worrying about.

What’s the real issue? If it’s corporate control of our political system, that’s a valid concern that many of us share. But GMOs aren’t the cause of that. Focus on the real source of the anger rather than blaming a proxy.

Fear-based communities bring people together. The Science Moms are trying to create a new community based on science and reason; based on facts, not fear.

Conclusion: a lot of people really need to watch this documentary

“Science Moms” is short and to the point. The 30-minute film is scientifically accurate, persuasive, and well-designed, with good production values. It’s available online for purchase at $4.99. I hope it will be more widely disseminated, because it offers important information that the general public needs to hear. People who have been exposed to anti-GMO or anti-vaccine propaganda are not likely to seek out, read, and understand the scientific evidence. But perhaps they will be willing to listen to moms who are just like them but who have the advantage of understanding the science.

Last week, I took note of how what is now a major medical society devoted to integrative oncology, the Society for Integrative Oncology (SIO), revealed itself to be unable to define, other than in platitudes and vague feel-good verbiage, just what the heck "integrative oncology" even is when it published a monograph in *JNCI*. What I didn't take note of last week was that the November issue in which the SIO's monograph defining what integrative oncology is (or what the SIO thinks it is) didn't contain just that one gem. In fact, like previous monographs published in years past, it's chock full of SIO propaganda for integrative oncology. Indeed, there's so much there that I could easily spend the next few weeks writing about each monograph in turn. I won't do that today, although I do reserve the right to discuss one or two more over the next couple of months if the urge takes me. What I do want to do is to discuss one monograph in particular, "Growth of Integrative Medicine at Leading Cancer Centers Between 2009 and 2016: A Systematic Analysis of NCI-Designated Comprehensive Cancer Center Websites," by Hyeongjun Yun, Lingyun Sun, and Jun J. Mao. I note that Dr. Mao is the immediate past president of SIO; this is coming from the top, so to speak.

I noted last week that I'm not a fan of the SIO, and it's not a fan of me. I won't repeat the story of my little discussion with them in which, in response to its umbrage taken in reaction to an article I published three years ago about integrative oncology, I tried to educate the leadership of the SIO that you can't have naturopathy without homeopathy. Reread last week's post if you want the details. My point is more that, as much as I don't like what SIO stands for, it has, unfortunately, been effective, and this survey provides yet another metric suggesting its effectiveness, along with that of all the other groups promoting the integration of pseudoscience and mysticism into medicine.

"Unmet needs"? Why would one need pseudoscience?

Yun et al. justify this survey with the usual tired tropes used to justify

“integrating” quackery with medicine, be it oncology or any other specialty. First, frame integrative oncology as an “unmet need”:

> Patients’ unmet needs in managing these symptoms coupled with their desire to use natural approaches to improve their health have created a demand for integrative medicine (3,4). According to the National Center for Complementary and Integrative Health (NCCIH), integrative medicine differs from complementary and alternative medicine (CAM) because it brings together conventional and complementary treatments in a coordinated way (5). Neither rejecting conventional therapies nor relying on alternative medicine, integrative medicine adopts only those complementary modalities supported by the highest evidence of safety and effectiveness (6). Numerous studies have evaluated the efficacy of utilizing integrative medicine modalities to treat the side effects of conventional cancer therapies. For instance, there is growing evidence that acupuncture may be effective in managing cancer therapy–related adverse effects such as fatigue (7–10), postoperative pain (11,12), vasomotor symptoms (13–16), and nausea and vomiting (17). Likewise, research supports the use of modalities such as massage (18,19) and mind-body therapies for symptom management and spiritual transformation; the latter remains a largely unmet need in the current health care system, yet directly impacts patients’ quality of life (4,20–23).

I can’t help but wonder how one quantitatively evaluates “spiritual transformation” in rigorous clinical trials, but that’s just me. In any case, I can’t help but note that some of the citations are articles discussed here and elsewhere before. For instance, reference 5 has been addressed before as “integrative health” being a rebranding of “complementary and alternative medicine” (CAM), which was a rebranding of alternative medicine. Other references, for instance, the ones supporting acupuncture, cite the usual low quality studies or studies that rebrand transcutaneous nerve stimulation (TENS) as “electroacupuncture.” Then there’s the whole framing of integrative oncology as an “unmet need.” It’s a very common framing of integrative medicine, be it through taking advantage of the opioid crisis to sell pseudoscience by claiming that nonpharmacologic management of pain must include CAM or by arguing that addressing unmet needs in symptom

management in cancer patients requires embracing pseudoscience. True, the latter argument isn't stated in those words, but when you strip away the "integrative" and CAM gobbledygook, that's the core of the argument you're left with: A false dichotomy that posits that, to treat the "whole patient" and to address "unmet needs," doctors must embrace the quackery in integrative medicine.

Next up, appeal to popularity:

> The use of integrative medicine is extensive among cancer survivors. Globally, up to 43% of patients with cancer have used integrative medicine therapies during their treatment, and the overall prevalence of integrative medicine use has increased noticeably over the past years (24–26). In the United States, cancer survivors use integrative medicine even more than individuals without cancer (27). Cancer survivors are more likely to use integrative medicine modalities for wellness, pain, and improving their immune functions. Interestingly, most of them started using integrative medicine because their conventional health providers recommended it to them (28).

Of course, as we've discussed before, this percentage is inflated by the broad definition of "integrative medicine." Basically, if you've ever had a massage or done art or music while being treated for cancer, by definition you've used integrative medicine. If you've ever meditated or prayed while being treated for cancer, you've used integrative medicine. If you've done Tai Chi, yoga, or Qi Gong (or even just exercise) while being treated for cancer, you've used "integrative medicine." You get the idea. When you look at the "hard core" quackery, such as homeopathy, you'll usually find that the number of patients using it is in low single digit percentages.

Integrative oncology and NCI-CCCs

The current survey is an update to a 2009 survey that found that 60% of National Cancer Institute (NCI)–designated comprehensive cancer centers (NCI-CCCs) provided information related to integrative therapies on their websites. Back in 2009, there were only 41 NCI-CCCs. Now there are 45. It's

worth looking at the old survey first, though, to see the sorts of modalities that were being offered at NCI-CCCs eight years ago and at what percentage of them:

Specific therapies listed did include some pure faith healing-related "energy medicine" quackery such as reiki (37% of websites), healing touch (29%). Not surprisingly, acupuncture showed up on 59% of websites, and dietary supplements, herbal medicine, and nutrition in one form or another showed up on between 42% and 56% of websites. To be honest, I was actually pleasantly surprised that only 60% of NCI-CCCs provided information on CAM. Indeed, it's kind of amusing to note the reaction of the authors to the perceived deficiencies of various NCI-CCCs with respect to CAM:

> Even with acknowledging these limitations, we still found that almost a third of leading U.S. cancer centers do not have functional websites related to CAM, and only a small proportion of the centers had websites independently judged to be excellent.

My reaction to that conclusion was: Gee, you say that as though it were a *bad* thing. I'm also happy that my cancer center's website would almost certainly have been in that one-third of cancer centers without information on CAM. Indeed, one of the things I've always liked about my cancer center is the relative paucity of integrative oncology options offered compared to other cancer centers, but I always fear that, sooner or later, we'll start to try to catch up.

So what's the situation now? Table 1 in the new study tells the tale. Mentions of quite a few modalities increased sharply. For instance, mentions of acupuncture increased by 30%, from 59% of NCI-CCCs to 89%. That's right. A whopping nine out of ten NCI-CCCs mention acupuncture credulously, and a full 73% offer it.

As a surrogate for just how much NCI-CCCs have abandoned science when it comes to integrative oncology, I like to examine the most implausible of treatments that fall under the mantle of "CAM" or integrative medicine. For example, mentions of healing touch, which is a form of "energy healing" (that doesn't actually involve touching) in which the practitioner claims to be able to detect and manipulate a patient's "life energy" field in order to heal

and/or relieve symptoms, increased from 29% to 58%, a doubling of the number, and 29% of NCI-CCCs actually offer this magical, mystical, "healing" touch. Mentions of reiki, which, as I've described many times before, is nothing more than faith healing that substitutes Asian mystical religious beliefs for Judeo-Christian beliefs as the basis for healing (replace the "universal source" from which reiki masters claim to derive the healing energy with God or Jesus, and you'll see what I mean), also increased markedly, from 37% of NCI-CCCs to more than half (53%) of NCI-CCCs, a more than 50% increase. Worse, 40% of NCI-CCCs actually offer reiki.

Not surprisingly, the "soft" parts of integrative medicine, the services that used to be offered for patient support and morale, such as art, music, massage, and various exercise programs but have, thanks to integrative medicine, become medicalized, appear on the vast majority of cancer center websites. One interesting finding is that, while exercise information is provided in 97.8% of cancer center websites, only 56% provide exercise/fitness services for their cancer patients. As much as it irks me that exercise and nutrition have been co-opted by integrative medicine and quacks like naturopaths, both can be science-based modalities for health promotion, particularly in cancer patients, although integrative medicine practitioners, particularly non-MD and non-dietician ones, often implement diet and exercise in non-evidence-based ways. (I'm talking to you, naturopaths, in particular.) Even so, we need to be doing better offering opportunities to help our patients exercise to improve their health and alleviate, for example, chemotherapy symptoms.

Overall, though, the authors are relatively happy with what they've found:

> Despite these limitations, we found that there has been substantial growth in the presence of integrative medicine on the websites of NCI-designated comprehensive cancer centers since 2009. In addition, the majority of the centers provide integrative medicine services within the same academic health systems in which they are located. As these centers lead the way in cancer research and clinical innovation, we need to ensure that integrative medicine can be cohesively incorporated into the continuum of cancer treatment and survivorship care using a financially sustainable structure. In addition, evidence-informed

> integrative medicine needs to expand beyond the walls of academic medical centers into community cancer centers and clinics to benefit patients from diverse socio-economic backgrounds.

The SIO even includes plans for world domination (OK, I mean the promotion of integrative oncology) around the world.

What the SIO left out: Most of the quackery

It's at this point that I can't resist mentioning what the SIO clearly left out. Remember, as I've pointed out many times, the SIO admits naturopaths. So where is naturopathy in this survey? Isn't naturopathy a part of "integrative oncology"? Certainly, the SIO seems to think so, given that it included presentations on naturopathic interventions in its recent annual meeting and even encourages naturopaths to join, listing them as equivalent to MDs. The SIO has even elevated two of them to the presidency of the organization! So why doesn't the SIO include a survey of which NCI-CCCs mention and offer naturopathy to their patients? Are they embarrassed? Trying to hide something? One wonders what Suzanna Zick, who was SIO President from 2015-2016, or Heather Greenlee, who was president from 2014-2015, think of this omission? Both are naturopaths.

I really can't help but suspect that, in its effort to persuade medical academia that integrative oncology is rigorously science- and evidence-based, whether intentionally or not, the SIO leadership is focusing all its attention on promoting the evidence-based modalities that have been "rebranded" as "integrative," such as diet, exercise, and the like, and the patient support modalities that have been medicalized into "integrative medicine," such as massage, art therapy, music therapy, and the like. Pay no attention to that quackery that integrative oncology and medicine lump together with the diet, exercise, and the like, the SIO seems to be saying by the absence of focus on naturopathy (and the homeopathy that nearly all naturopaths practice). Again, it can't be emphasized enough that, wherever you find naturopaths practicing, you will find homeopathy being practiced.

True, there are a couple of exceptions. The SIO does mention reiki and

therapeutic touch rather prominently in both surveys, both of which are obvious energy healing quackery. However, most people don't realize that. Most people view reiki and healing touch as a form of massage or hands-on healing, even though healing touch usually doesn't involve actually touching the patient. Either that, or they view them as some form of spirituality, which is actually not too far from the truth, but mystical claims such as what are made for reiki and healing touch do not belong in science- and evidence-based medicine. Yet there are NCI-CCCs that credulously promote energy healing. For instance, I've written about Georgetown University before. There's an NCI-CCC there, the Georgetown Lombardi Comprehensive Cancer Center. I've described Georgetown as a bastion of quackademic medicine before because of its "pioneering" efforts to "integrate" the teaching of pseudoscience into its medical school curriculum. Relevant to cancer, though, Georgetown published an article in its official magazine about reiki in the chemotherapy suite:

> For a long time Denise von Hengst had a secret she kept from friends and physicians alike. As she was undergoing treatment at Georgetown Lombardi Comprehensive Cancer Center for a particularly aggressive type of breast cancer—triple positive, HER2 positive—she was also regularly receiving Reiki, an ancient form of Japanese healing, to mitigate the debilitating anxiety and fear that accompanied her cancer diagnosis.
>
> "At first I told no one about the Reiki," says von Hengst. "Fear of the 'woo-woo' factor. People might think I'm nuts."

No, I don't think the patient is nuts. I think the cancer center is irresponsible for offering magic with its medicine, leavened with pseudo-skepticism:

> However, skepticism remains, not only in the general population, but also within the medical field. Recently, several clinical trials have emerged attempting to prove, or disprove, the effectiveness of Reiki. Many of these studies have been criticized for the trial. design, number of participants and reporting mechanisms. Results of the trials are often inconclusive.
>
> Yet as the anecdotal proof mounts and Reiki's popularity increases,

> prestigious medical centers around the country are taking note and offering the treatment to patients at their facilities. Reiki can be found at hospitals and medical centers such as Boston Children's Hospital, Dana Farber Cancer Institute, Stanford Health Care, Memorial Sloan Kettering Cancer Center, Duke University Health System and Cleveland Clinic, to name a few. Many academic medical centers such as Georgetown incorporate complementary therapies into their teaching curricula.

I have a question for the leadership of SIO: Is reiki evidence-based? Is it science-based? If it isn't, then why are you supportive of NCI-CCCs offering it?

Here's another example, the University of Arizona Cancer Center, which is an NCI-CCC. Take a look at its integrative medicine page. Look at what it offers: reiki (of course, even though a faculty member complained about it), reflexology (pure quackery that posits a nonexistent link between body parts and organs and specific areas on the soles of the feet and palms of the hands), craniosacral massage (which Mark Crislip drolly and correctly called a "SCAM of infinite jest"), healing touch (of course), and shiatsu (unproven).

Three years ago, the son of a professor in a humanities department at UA was treated for leukemia at the UA Cancer Center. He was appalled at all the quackery being offered to his son, including not just the above modalities, but distance healing, offered by a man named Frank Schuster:

Yes, as fantastic as it sounds, this was a web page hosted by the University of Arizona Cancer Center. It might be gone now, but it's not at all clear that the quack above is gone from UACC.

After this professor complained, Shuster's UA webpage was either removed or placed behind a login. However, I noticed something about UA's list of offerings for integrative medicine. First, none of the practitioners were listed by their full names any more. It's Jessica, Barb, Heidi, Michael, Denise, or Frank, the last of whom offers the reiki classes. Hmmm. I wonder if that's Frank Schuster, still there, still practicing energy healing. I bet it is, but haven't been able to verify it one way or the other.

I want to believe that the SIO wants to be scientifically rigorous. I really do.

I’m guessing that most of the SIO physician and scientific leadership believes that they are being scientifically rigorous and trying to lay down a framework in science and clinical evidence for “integrative oncology,” even if they have a hard time defining what, exactly, integrative oncology is. It’s just that, for whatever reason, physicians who drink the Kool Aid of integrative medicine tend to develop massive blindspots about all the quackery that comes as a package with all the parts of integrative medicine that they like, such as the emphasis on lifestyle, diet, exercise, and the treatment of the “whole” person. These blindspots extend to naturopathy in particular, which is a veritable cornucopia of quackery, including homeopathy. Until the SIO can eliminate its blindspots over all the quackery that is included in “integrative medicine,” its claims of being scientifically rigorous are just so much self-delusion.

And the server migration continues apace… but where are the comments? - Science-Based Medicine

As many of you noticed, there has been an issue with the comments that began last night. Here’s what happened. The Powers That Be decided to migrate the blog to a new server last night, and there were problems relinking Disqus to the new installation of WordPress. I am assured that the problem has been fixed, but also told that it could take 12 hours for all the old comments to redirect to our new location. So be patient, and the blog should be back to normal by tomorrow morning. There should be benefits to the new server as well, such as faster loading, less downtime, and the like. We’re sorry about the inconvenience today, but as one of our crew noted, for some reason migrations never seem to go as smoothly as we would like.

In any event, if after tomorrow there are still problems, let us know.

Science Based Medicine

周六, 04 11月 2017

Science Based Medicine

[周六, 04 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **The American Chiropractic Association Answers Crislip's Call, Joins the Choosing Wisely Campaign** [周五, 03 11月 20:00]
  The Choosing Wisely campaign has invited the largest chiropractic organization in the United States to publish a list of interventions to avoid. The results, while not entirely without merit, consist of redundant or unnecessary recommendations. And there is a glaring absence of recommendations to avoid any of the blatant pseudoscience commonly practiced by chiropractors.
- **Liver cancer, naturally** [周四, 02 11月 19:30]
  Aristolochic acid, a highly toxic substance naturally found in some traditional herbal medicines, may be a significant cause of liver cancer.
- **ASEA – Still Selling Snake Oil** [周三, 01 11月 20:49]
  ASEAs marketing practices, in my opinion, are clearly deceptive. They use a lot of pseudoscientific claims representing the epitome of supplement industry misdirection and obfuscation. They use science as a marketing tool, not as a method for legitimately advancing our knowledge or answering questions about the efficacy of specific interventions.
- **Facial Cupping: A Kinder, Gentler, Sillier Kind of Cupping** [周二, 31 10月 15:00]
  A new cupping fad using silicone devices is gentler than traditional cupping, but even sillier. There is no evidence of health benefits.

Three years ago, Mark Crislip closed a post discussing the ABIM Foundation's Choosing Wisely initiative with the following thought:

> I wonder if a chiropractor could come up with five standards treatments in chiropractic to be avoided…

Well, now they've finally gone and done it, with results that, while not entirely without merit, are a bit off the mark in my opinion.

Choosing Wisely and chiropractic

For the sake of further discussion, let's all just agree to ignore the fact, also pointed out by Dr. Crislip in his post, that chiropractic as a profession doesn't exactly stand up to the scrutiny of the campaign's criteria:

> *Choosing Wisely* aims to promote conversations between clinicians and patients by helping patients choose care that is:
>
> - Supported by evidence
> - Not duplicative of other tests or procedures already received
> - Free from harm
> - Truly necessary

Of course to be fair, no medical intervention is completely "free from harm", but I assume that what the ABIM Foundation actually means is that interventions should have a favorable risk to benefit assessment. This is arguably not the case when assessing chiropractic as a whole. While not all of the treatments I prescribe are based on robust randomized controlled trials, they are "supported by evidence" in the vast majority of cases, and often by very good evidence. Chiropractic doesn't really bring anything original to the table that passes this test.

There are similar issues with the phrase "truly necessary", whatever that means. Many medical interventions aren't "truly necessary" in my opinion. Other Choosing Wisely lists cover a number of these, but there are also tests

and treatments that may have value while perhaps not meeting this criterion absolutely depending on who is assessing the scene. But again, being charitable, I assume that the ABIM Foundation is focusing on common interventions for common human ailments that don't tend to improve objective outcomes.

Specific treatments provided by a chiropractor might provide some objective benefit for a small sliver of musculoskeletal complaints, with those unique to chiropractic being the least helpful. But whatever improvement that can be attributed to visiting a chiropractor isn't better than more conventional approaches, such as physical therapy or recommendations from a patient's primary care provider for exercise, stretching, massage, etc. These approaches come with considerably less baggage and aren't as likely to be accompanied by pseudoscience or anti-vaccine propaganda.

The Choosing Wisely lists published by participating organizations aren't meant to serve as treatment guidelines, of course. Instead, they are intended to encourage a conversation around whether or not the listed interventions are a good idea, or if they may put patients at risk of more harm than benefit. Unfortunately, in my opinion, they have largely gone unnoticed by medical providers and the general public. I am confident that the list of questionable chiropractic interventions will be similarly ignored by practitioners.

The ACA's list

The list in question, released in August, comes from the American Chiropractic Association (ACA). The ACA claims 15,000 members, which is less than a quarter of practicing chiropractors, and recognizes 11 specialty areas, such as chiropractic acupuncture, pediatrics, diagnosis and management of internal disorders, and forensic sciences. It describes itself with typical grandeur:

> The American Chiropractic Association (ACA) is the largest professional chiropractic organization in the United States. ACA attracts the most principled and accomplished chiropractors, who understand that it takes more to be called an ACA chiropractor.

> We are leading our profession in the most constructive and far-reaching ways — by working hand in hand with other health care professionals, by lobbying for pro-chiropractic legislation and policies, by supporting meaningful research and by using that research to inform our treatment practices.
>
> We also provide professional and educational opportunities for all our members and are committed to being a positive and unifying force for the practice of modern chiropractic.

What does it take to called "an ACA chiropractor"? Membership requirements consist of being a licensed chiropractor in the United States and paying yearly dues. The ACA even goes so far as to state that they do not deny membership to anyone meeting the above qualifications as long as what they do in their practice isn't illegal. In that way, they are similar to the American Academy of Pediatrics, which even allows pediatricians who are blatantly anti-vaccine to be members in good standing.

Here are the five things that chiropractors and their patients should question according to the ACA:

Do not obtain spinal imaging for patients with acute low-back pain during the six (6) weeks after onset in the absence of red flags.

What red flags, you ask? The ACA mentions "history of cancer, fracture or suspected fracture based on clinical history, progressive neurologic symptoms and infection, as well as conditions that potentially preclude a dynamic thrust to the spine, such as osteopenia, osteoporosis, axial spondyloarthritis and tumors". I would argue that if you have any of these red flags, you should not be under the care of a chiropractor. There isn't any evidence to support superiority of chiropractic care to conventional approaches for acute low-back pain anyway.

Do not perform repeat imaging to monitor patients'

progress.

They list idiopathic scoliosis as an exception, despite the fact that their own research shows no good evidence to support chiropractic management of this condition. I agree with this recommendation, and the reasoning of the ACA in this case is sound. I'm just not holding my breath while waiting to see if this will change anything, however.

Avoid protracted use of passive or palliative physical therapeutic modalities for low-back pain disorders unless they support the goal(s) of an active treatment plan.

In other words, commonly recommended interventions like heat, ultrasound, and electrical stimulation, shouldn't be used in isolation because they don't provide much benefit. The absolute worst thing you can do to prevent or treat lower back pain, which virtually all humans will experience at some point in their lifetime thanks to evolution, is nothing. General physical activity and back specific exercises are key, and in no way unique to chiropractic.

I don't think you will find many chiropractors not recommending an exercise regimen for lower back pain disorders, so this item is a bit odd. You also won't find many that won't provide some kind of spinal manipulation, because that's their thing that they do. In this section, the ACA writes that physical activity and back exercises "may lead to better outcomes when combined with spinal manipulation." In reality, spinal manipulation is more like multiplying by one. It changes nothing for the long term outcome.

Do not provide long-term pain management without a psychosocial screening or assessment.

Chronic pain disorders often have a psychosocial component. Chronic pain can cause or be caused/exacerbated by anxiety and depression, for example.

Some patients are at risk for the development of chronic pain because of a variety of psychosocial factors and chiropractors are not trained to evaluate or manage them. The ACA recommends that chiropractors use a screening tool and refer when necessary because the ACA imagines chiropractors to be primary care providers.

Do not prescribe lumbar supports or braces for the long-term treatment or prevention of low-back pain.

Another odd inclusion. Chiropractors simply aren't out there putting people in back braces for long periods of time for treatment or prevention of back pain. I was easily able to find that this recommendation is already widely accepted. Meanwhile, the ACA is inviting speakers to their conferences to promote nonsense like the Activator Method.

The ACA press release announcing their participation in Choosing Wisely is interesting. They point out that multiple other organizations already participating have included recommendations to avoid spinal imaging for acute lower back pain. It's a solid recommendation, but instead of actually attempting to show a commitment to change by pointing out some of the abject nonsense they have supported sans evidence, they went the safe route. And in the press release they essentially give their members enough wiggle room that they can continue obtaining frequent spinal films without losing any sleep.

My favorite quote involves the practice of "defensive medicine":

> As with many of our colleagues in the health care professions, we have learned from experience to practice "defensive medicine." This perspective may be even more deeply ingrained within the chiropractic profession based on our prior experiences with bias and/or lack of understanding regarding chiropractic care. As an example, just look how long it took before Choosing Wisely® was even willing to consider a chiropractic list!

So do chiropractors practice defensively, which implies a concern for facing a malpractice suit, or not? It would appear that the latter is the case when you consider how often they point out how undeniably safe chiropractic is. Often this is done in the context of attacking conventional medical care. It's also unclear to me how the medical community's lack of "understanding regarding chiropractic care" encourages defensive practice.

Conclusion: The ABIM did not Choose Wisely

How does the ACA describe chiropractic on the Choosing Wisely website? Just as you would expect them to, of course. Remember though that this is an organization that is fighting for chiropractors to be considered primary care physicians complete with the right to prescribe medications.

> Chiropractors focus on disorders of the musculoskeletal system and the nervous system, and the effects of these disorders on general health and function. Chiropractic services are used most often to treat conditions such as back pain, neck pain, pain in the joints of the arms or legs, and headaches. Widely known for their expertise in spinal manipulation, chiropractors practice a hands-on, drug-free approach to health care that includes patient examination, diagnosis and treatment.

The ABIM Foundation is very likely completely ignorant of both the history and the current reality of the chiropractic profession. Frankly I think it's ridiculous that a chiropractic organization was invited to participate. We certainly have come a long way from Wilk v. AMA, haven't we?

This is just another example, in a very long line, of the undeserved legitimization of alternative medicine that will serve as more of a marketing purpose than as a means of improving chiropractic practice. All that the ACA has done is provide a list of redundant or unnecessary recommendations. And the few chiropractors who already avoid excessive spinal imaging will continue to do so, while the vast majority will compartmentalize these "suggestions" and carry on as is.

Extras

- Here is a response to the ACA Choosing Wisely list from the International Chiropractic Association.
- Here is an ACA video describing the benefits of pediatric chiropractic. In March of 2017, the ACA reaffirmed its public policy on chiropractors as primary care providers. This policy includes the following:

> Doctors of chiropractic also recommend and manage dietary changes, nutritional interventions, botanical medicines, homeopathic medicines, acupuncture and other services when indicated.

The ACA, while not overtly anti-vaccine in policy, supports conscience waivers.

Not all cancers affect all populations equally. Liver cancer is the fifth-most common cancer worldwide, but the prevalence varies widely. Liver cancer cases skew heavily to less developed regions of the world, where 83% of cases are found – it's over six times more common there than in Northern Europe, for example. In Asia, the high rates of liver cancer have been linked to hepatitis B and C, which is widespread, and a proven cause of cancer. And liver cancer continues to strike Asian American and Pacific Islanders more than any other American ethnic group as well, where hepatitis continues to circulate in the population. Now there's new evidence to suggest that a substance found in some traditional Chinese medicines may also be causing liver cancer. They're called aristolochic acids, and they illustrate, with a substantial body count, that what's natural isn't necessarily healthy or good.

What are Aristolochic acids?

In the early 1990's a strange cluster of acute, end-stage renal disease appeared in women in Belgium. It was determined that all had been exposed to the chemical aristolochic acid (AA) at a weight loss clinic, due to the consumption of Chinese herbs which contained natural AA. Approximately one third of the more than 300 cases have subsequently required a kidney transplant, and cancers of the urothelial tract in this group have also been widespread. In the Balkans, low level exposure to AA via flour consumption that contains seeds from *Aristolochia clematitis* is believed to be responsible for what is now called Balkan-endemic nephropathy. Subsequent study that was initiated after the Belgian case identified that that AA is responsible for tumour development and for activating destructive fibrotic changes in the kidney. For over a decade now it has been well established that AA is a nephrotoxin and a powerful carcinogen with a short "latency period", in that it causes permanently damage, quickly. What's remarkable is that none of this was known until the 1990s despite "thousands of years" of use as a traditional medicine. As Steven Novella noted in a past post on aristolochic acid and urinary tract cancer:

> This example just highlights the fact that widespread use of an herbal

> product, or any treatment, is not sufficient to ensure that it is safe, or even that it is effective. Common use may be enough to detect immediate or obvious effects, but not increased risk of developing disease over time. That requires careful epidemiology or specific clinical studies. We know about the risks of prescription drugs only because they are studied, and then tracked once they are on the market. Without similar study and tracking there is simply no way to know about the risks of herbal products. Relying upon "generally recognized as safe" is folly.

While herbal remedies that contain AA are now banned in many countries, AA-induced kidney damage and related cancers continues to appear worldwide. As AA's cancer-causing effects have now been widely studied, the distinct way that they damage cells has been described as a sort of "signature" that is easily identifiable in tumour samples. This brings us to this new study of liver cancers attributed to AA, which have been less closely associated with AA. This study used that unique "signature" to look for AA exposure.

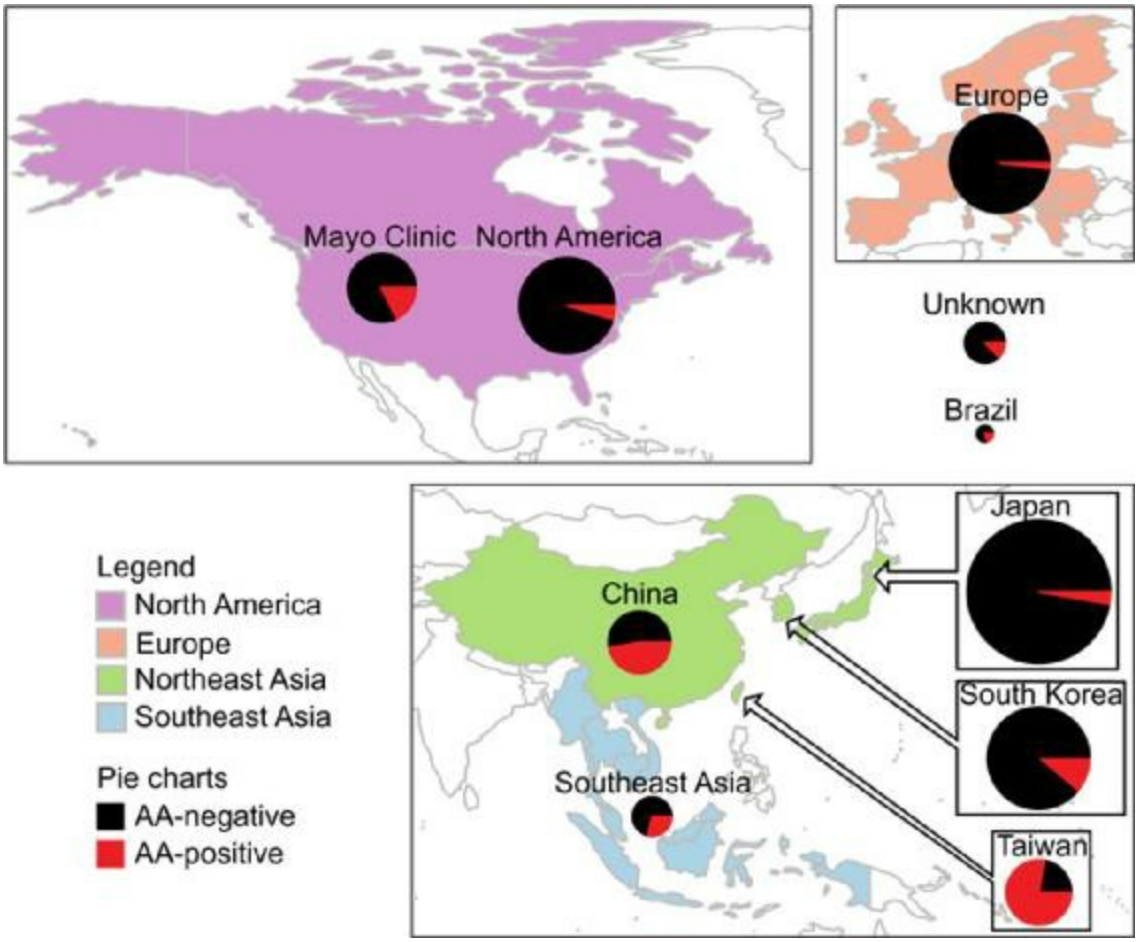
Aristolochic acids and liver cancers

There is good evidence to show that the consumption of AA-containing products in Taiwan has been widespread through the use of prescribed herbal medicines. The paper is entitled "Aristolochic acids and their derivatives are widely implicated in liver cancers in Taiwan and throughout Asia" and it's from Alvin Ng and associates, published in *Science Translational Medicine* in October, 2017. This was a retrospective analysis of hepatocellular carcinomas (HCC, liver cancer in lay terms) and patients were included if they (1) had true HCC (2) there was sufficient DNA available from a sample of the tumour. 98 HCCs from Taiwan hospitals were studied based on whole-exome sequencing and mutation identification. They looked for the distinctive way in which AA causes mutations. The researchers subsequently examined 1,400 HCCs from other regions in the world. The final analysis was as follows:

- Taiwan: 78% of tumours had evidence of AA exposure

- China: 47% of tumours had evidence of AA exposure
- Southeast Asia: 29% of tumours had evidence of AA exposure
- Korea: 13% of tumours had evidence of AA exposure
- Japan: 2.7% of tumours had evidence of AA exposure
- North America: 4.8% of tumours (in one hospital, 22% of 87 patients, all of Asian ancestry, had evidence of AA exposure)
- Europe: 1.7% of tumours had evidence of AA exposure

Here is the global breakdown, with the red portion illustrating the proportion of tumours that were linked to AA exposure:



Global distribution of mutagenesis associated with aristolochic acid and derivatives in liver cancer.

Reducing your risk of kidney and liver

cancer

Herbal remedies are popular worldwide. In China and other countries in Asia, there is strong support for, and belief in “traditional” Chinese medicine despite the fact that it is neither truly traditional (as it is now promoted), nor particularly effective. This new analysis shows that the use of (or exposure to) AA is widespread in some parts of the world, and appears to be be a cause in a substantial numbers of liver cancers. The authors noted that the presence of AA-associated cancer does not appear to be declining in Taiwan, despite the banning of some AA-containing herbs in 2003. This may be due to a lag effect (like cancer and smoking) but may also be due to continued exposure to, or consumption of, AA-containing products.

If you’re a user of traditional Chinese medicine, avoiding AA is easier said than done, unless you have impeccable knowledge of herbs, their origins, and the supply chains you’re getting your products from. I’ve blogged before about TCM, noting that contamination is common. Mislabelling of products also appears to be widespread, suggesting that rigorous and credible testing of final products may be the only way consumers can be assured they’re avoiding AA in the products they buy. The linkage of AA to kidney damage, and the evolving story of its cancer-causing potential illustrates that even widespread use of a product for hundreds (or thousands) of years give no automatic assurance of safety. If it were not for the Belgian weight loss clinic kidney failure cluster, the widespread toxicity of AA may not even be known today.

ASEA - Still Selling Snake Oil - Science-Based Medicine

We often examine the claims made by companies or individuals for their health products, especially those we feel are making dubious claims based on questionable science. In 2012 Harriet Hall wrote an excellent review of one multi-level marketing company, ASEA, who are basically selling salt water with a load of dubious pseudoscientific claims. ASEA is just about a perfect example of everything we try to warn consumers about when it comes to dubious supplements and the inadequacies of current regulations.

When we post such reviews it is not uncommon for the company to give us push back, and it is much more likely if that company sells through multi-level marketing (which is a scam unto itself). We recently received an e-mail from the "ASEA Team" who were not happy about Harriet's review. They asked us to revisit our review (be careful what you wish for), concluding:

> Bottom Line for our part:
>
> The criticism of ASEA made by Mr. Hall [*sic*] is not constructive and Author's points of view are not based on decent and verifiable facts. On the contrary, we have provided you with reliable information that is proven by the documentation. So, the article is misleading and deceives your website's auditory and our potential and current customers. We are sure that after a deep consideration you will come to a conclusion and agree with us that it would be best to delete the article. Thank you.
>
> Respectfully,
>
> ASEA team.

After deep consideration, and re-review of the ASEA current website, I have come to the personal conclusion (and hope they will agree) that ASEA is selling quackery and nonsense with misleading claims designed to defraud

both their customers and their sales agents (who often overlap). I suspect there is a combination of (financially) motivated reasoning and scientific illiteracy on their part, so I will explain again why I have come to this conclusion.

Let's take their points in the ASEA team e-mail to SBM. They begin by objecting to Harriet's (who they refer to as male throughout their letter) listing of the claims they were making on their website at the time:

> ASEA allegedly:
>
> - Promotes enhanced immune function
> - Supports the vital activity of cellular communication
> - Provides superior "support" to athletes
> - Boosts efficiency of the body's own antioxidants by 500%
> - Protects against free radical damage

Their "counterpoint":

> This information is out of date and does not correspond to reality, you can not even find these statements up on our website anymore. We have changed the formula, carefully tested it out and conducted several studies that proved that ASEA products have been shown to signal the activation of genetic pathways or affect genes that:
>
> Improve immune system health;
>
> Help maintain a healthy inflammatory response;
>
> Help maintain cardiovascular health and support arterial elasticity;
>
> Improve gut health and digestive enzyme production;
>
> Modulate hormone balance to support vitality and wellness.

I see, they swapped out one list of dubious claims for a slightly tweaked list of dubious claims. "Promotes enhanced immune function" became "Improve immune system health." And of course if you go to their website the old claims are still there, maybe not in the same location and jot list, but deeper

in the copy or the linked “studies.” They are still claiming it improves cell signaling and increasing the body’s own anti-oxidants.

As a side point, we do not maintain and update every article. That is not standard or practical, nor is it expected, nor do we claim to. Articles are clearly dated, and it should be obvious they are only as current as the date they were posted. We will make corrections if they are pointed out to us or we discover them, and we use our own discretion in deciding whether or not to write an addendum or an updated article.

Their next point was so clueless it gave me the impression that we were dealing with low-level sales people who are not only scientifically illiterate, but had no backing from anyone with legal experience. In response to Harriet pointing out that ASEA is not making disease claims, because they can’t, they responded:

> This statement doesn’t make any sense. As it was correctly noticed, we can’t legally and we actually don’t claim that ASEA is effective for any disease, so there is no point in writing more about this and even mentioning this. There is no information up on our website that says that ASEA would cure cancer or other diseases, however we do say that ASEA improves immune system health as well as has some other beneficial effects for a human being, and as we pinpointed that before, the effects have been verified by several laboratory tests. This statement made by Mr. Hall is far-fetched and offensive and shows that the Author tends to make things up and base his article on assumptions rather than on the facts.

Where do I begin? Here is the very salient point that Harriet was making, and that we make frequently on SBM. The current US regulations allow companies to make “structure-function” claims for their “supplements” without FDA oversight. Products with disease claims are, by definition, drugs and subject to FDA regulation. So what do many supplement companies do? They make structure-function claims that sound as if they may be beneficial for health, and combine those legally allowed claims with other statements about diseases, hoping their potential customers will connect the dots. They are skirting the spirit of the law in order to imply, without directly making, unsupported health claims.

On ASEA's website they make the following claims:

- Decline of cell signaling causes cellular breakdown, which in turn causes a long list of common diseases including autoimmune and cardiovascular disease.
- ASEA improves cell-signaling which decreases cellular breakdown.
- Here is some (not peer-reviewed) science showing that ASEA alters markers which we will choose to interpret as "improving" some aspect of cell signaling or function.

So they do not directly say that ASEA cures any disease, because they know that it is not legal under current regulation, but they do imply that it does through the above chain of claims. That is standard procedure in the dubious corners of the supplement industry (i.e. most of the supplement industry).

Let's get to the scientific studies they use to support their claims. In response to Harriet's review they wrote:

> The studies that Mr. Hall is referring to are old and no longer available on the ASEA website. Instead, we have conducted other studies that proved the effect of the ASEA products as well as their safety.

So, were those previous studies not valid? Science is cumulative. We don't just scrub "old" studies from the record and replace them with new studies. In my opinion that reveals the marketing mentality of the "ASEA team". Studies are not used to determine if their product works, but to support their marketing claims that it does work.

As Harriet pointed out, their studies are not being performed by academic scientists and published in peer-reviewed journals. They are being outsourced to third party research companies for hire. There is no paper-trail of research that would lead an honest scientist to the conclusions that ASEA is now selling. They appear to have started with their product and are backfilling in essentially worthless studies (as far as clinical claims go) to support their marketing.

Perhaps the biggest problem with ASEA's "research" is that they don't actually address their implied clinical claims. In other words – there are no

studies that directly show that ASEA will improve your health – let alone multiple independently replicated rigorous studies published in peer-reviewed journals.

Their current marketing focuses heavily on the claim that ASEA increases natural antioxidants in the body. Antioxidants are currently very popular, having been given a health halo by two decades of heavy marketing. However, the real science tells a different story. In their scientific summary they write:

> Oxidative damage has been implicated in aging and agedependent diseases, including cardiovascular disease, cancer, neurodegenerative disorders, and other chronic conditions. If the generation of free radicals exceeds the protective effects of antioxidants and some co-factors, this can cause oxidative damage.

That is the simplistic story that the anti-oxidant industry is selling, but it is nonsense. Essentially they are assuming that increasing antioxidant activity (even assuming that ASEA does so, which I doubt) must be a good thing. This turns out to be a naive assumption. A homeostatic balance between oxygen free radicals and antioxidants evolved to optimality, unless adversely affected by a disease state such as a genetic mutation. There is no reason to think that artificially disrupting this natural homeostasis would be a good thing. In fact, the evidence has shown that actual antioxidants taken in large amounts are bad for your health. Our bodies use free radicals as part of the immune system, to kill invading cells, and as important signaling molecules. Blocking free radicals in a healthy person can actual cause harm.

The same is true of immune function, which naturally exists in a carefully-balanced state. ASEA marketing naively assumes that increasing any arbitrary marker of immune function equals “improving” immune function. If you have an auto-immune disease, increasing immune function would be a bad thing.

This is the core fallacy of the entire supplement industry, which assumes that you can “improve” the function of an evolved homeostatic system by simply pushing it in one direction. This often leads to contradictory claims, such as some supplements claiming to increase oxygen while others claim to be anti-

oxidants.

Finally, Harriet appropriately asked what was in ASEA anyway. It appears to be just salt and water, and ASEA makes the pseudoscientific claim that the salt water molecules have been arranged somehow into these redox signaling molecules. They respond:

> As for what the components are, this is a confidential information. We have spent a lot of time and resources coming up with the idea as well as setting it all in motion.

Sorry, but science requires transparency. You cannot pretend to be scientific and then simultaneously state that your core claim is a secret. This is especially true when that core claim makes no scientific sense. It is not an extrapolation of existing scientific research or established principles. In fact, their core claim sounds like utter nonsense, so simply saying that it is a secret does not inspire confidence.

Far from taking down Harriet's original review of ASEA and their claims, her assessment deserves to be updated and amplified. ASEAs marketing practices, in my opinion, are clearly deceptive. They use a lot of pseudoscientific claims representing the epitome of supplement industry misdirection and obfuscation. They use science as a marketing tool, not as a method for legitimately advancing our knowledge or answering questions about the efficacy of specific interventions.

I am amused that they chose to e-mail us with their juvenile analysis and requests. That may suggest they are more naïve than calculating, but it really doesn't matter. They are selling a product with health claims. They have the responsibility not to deceive their customers, and I do not feel as if they have met their burden for due diligence. They may have from a regulatory perspective, but only because current regulations are horrifically inadequate. But they certainly haven't from a moral or scientific perspective.

I keep thinking, “Now I’ve seen everything,” and I am constantly being proven wrong. I recently came across the new fad of facial cupping. After I stopped laughing, I went on to an amazed appreciation of the extent of human creativity and entrepreneurship.

Cupping is a traditional Chinese medicine (TCM) treatment often applied over acupuncture points. Traditionally, the air in a glass bulb is heated, and when it is applied to the skin and the air cools, it creates a vacuum, sucking up a blob of skin. It leaves unsightly bruises (remember the pictures of Michael Phelps at the Olympics and of actress Gwyneth Paltrow?) Sometimes the skin is incised, and blood is drawn up into the bulb. The new fad of facial cupping is kinder and gentler. Less suction is involved, and no visible marks are left on the skin.

You can see facial cupping in action on videos like this one. The cups are made of silicone and are of various sizes; the smallest ones are used around the eyes. You squeeze gently before you apply it to the skin, and when you release the squeeze, it creates a vacuum that sucks a bit of skin up into the device. You can treat a single spot or sweep the device across an area without breaking the suction. It doesn’t leave scars, but it can produce a transient redness. In the video, the patient is being treated at a spa, but cupping kits are

being marketed for people to use on themselves at home.

One product description says:

> What is Cupping? Cupping therapy is a form of alternative medicine in which cups are placed on the skin to create suction in order to increase blood flow, reduce inflammation and activate lymphatic drainage. Cupping therapy dates back to ancient Egypt, Asia and Middle East. Cupping brings fresh blood to the area, improves circulation and is widely used to treat pain, digestive problems, release toxins, improve appearance of cellulite and much more! When can I expect to see results? Impress me! In many cases, results are visible after only a few cupping treatments, though you will start feeling and looking better instantly! With regular use, you will experience muscle tension relaxation, rejuvenation, increased energy, firmness and a more toned, healthier physique. Reduced stress, improved circulation and pain relief are just some of the many benefits you can see and feel. Remember, results are cumulative. To be effective, use regularly until optimal results are reached, follow a healthy diet, exercise and drink plenty of water!

Even if all that were true (which it probably isn't), it might only apply to the original kind of cupping, the kind with strong enough suction to leave large welts on the skin

For advocates of "natural" treatments, I don't see anything "natural" about cupping. But there is a "natural" alternative: hickeys or love bites. Is anyone advocating those?

So, some genius had the brainstorm that if you reduced the suction to where no visible lesions were produced, cupping would be more acceptable and you could make a lot of money selling weak suction devices. I wonder if this should be called "pseudo-cupping"? It's homeopathic thinking, analogous to what Hahnemann did. He came to believe that all effective drugs produce symptoms in healthy individuals similar to those of the diseases that they treat, then he kept diluting his remedies until they no longer produced those symptoms (nor did they do anything else!).

Another website sells both the old and new types of cup. It claims therapeutic benefits of gentle facial cupping for patients with sinus infections, headaches, facial paralysis, earaches, and temporomandibular joint pain (TMJ). It claims to help patients suffering from these conditions "without the need for more extensive treatments." It is illegal for them to make such disease-specific claims, and could be dangerous if patients are discouraged from effective treatments for these conditions.

On another page, they list the top 7 benefits of cupping:

1. Relief from pain
2. Promote relaxation
3. Promote healing from injuries
4. Clear, flawless skin
5. Better digestion
6. Relief from respiratory issues
7. Detoxification

And a sidebar claims benefits for tonsillitis, angina pectoris, osteoarthritis, gout, endometriosis, infertility, urinary incontinence, high blood pressure, heartburn, neuralgia, and diabetes!

But wait! There's more! Anemia, hemophilia, wrinkles, mental problems, varicose veins, weight loss, diarrhea, conjunctivitis, frozen shoulder, fever, herpes, cervical spondylosis, and "scaring" (a typo, but cupping does scare me.) And "anti-aging" claims are common.

Amazon sells them. One customer reports using them to pop pimples. One said she is hoping to reduce cellulite. One reports a large decrease in dimpling in her legs. One said "Painful, but seems to be helping [*helping for what*?]" One said, "Hard to use." One said, "Not sure if it works but it doesn't provide good suction and feels like a deep massage." One said, "Didn't work."

I got a kick out of two 2-star customer reviews. The first said she used the cups about six times and they no longer suction. The second asked, "What to do when an item sucks because it doesn't suck?"

Evidence?

Is there evidence for any kind of cupping? According to the American Cancer Society, "There is no scientific evidence that cupping leads to any health benefits….No research or clinical studies have been done on cupping. Any reports of successful treatment with cupping are anecdotal. There is no scientific evidence that cupping can cure cancer or any other disease."

Edzard Ernst employed cupping himself 40 years ago before he started looking for scientific evidence. He says cupping has a significant placebo effect, and the most plausible mode of action is counter-irritation (analogous to hitting your thumb with a hammer to distract you from the pain of a headache). He mentions recent research but characterizes it as "flimsy" at best. It is impossible to do blinded studies, and most of the positive studies are out of China, where negative studies are never published.

The bottom line: there is no credible evidence for the original form of cupping, and there is even less evidence for the newer, kinder, gentler version.

Suggestion?

An article in *Vogue*, "Cupping Works Even Better on Your Face," inadvertently provides insight into the psychological mechanisms behind customer satisfaction and glowing testimonials:

> My skin was tighter, pinker, plumper; my jawline lifted. The irksome fine lines on my forehead had taken leave, and my eyebrows even appeared slightly higher. I'd been skeptical, but it was as if I'd just awakened from a five-year nap [I can't help wondering how she knows this. How many five-year naps has she had?] "Look at those cheekbones," Goldstein said admiringly.
>
> Having barely sacrificed any extra time (her sessions, with their added skin-treatment component, run 30 minutes), I returned triumphantly to the office, where a colleague complimented me on my unusually rested

> appearance. Later that night, I told my boyfriend what had happened. He narrowed his eyes. “You know, maybe your face does look a bit thinner and more angular,” he surmised. Two days later, apropos of nothing, he revised his opinion. “I don’t know why,” he said, “but you look more beautiful this week than you ever have.

Suggestion is very powerful. Especially without controlled observations.

Conclusion: It sucks

Facial cupping sucks. In more than one sense.

As I see it, it offers two benefits: a mostly harmless sort of masturbatory pastime for self-absorbed and self-indulgent users, and a source of amusement for skeptics.

Science Based Medicine

周六, 11 11月 2017

Science Based Medicine

[周六, 11 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Another “Chronic Lyme” VIP disciplined by NY medical authorities: Bernard Raxlen** [周四, 09 11月 14:00]
  Another "Lyme literate" NY physician is on probation and under orders to clean up his act. Will other physicians treating "chronic Lyme" take note?
- **Risks of a Gluten-Free Diet** [周三, 08 11月 21:27]
  Non-Celiac Gluten Sensitivity does not seem to be a real entity according the current evidence, but this has not stopped the gluten-free fad, which may be causing real harm.
- **Update on ASEA, Protandim, and dōTERRA** [周二, 07 11月 16:00]
  Multilevel marketing distributors of dietary supplements and essential oils point to studies that they think constitute evidence that their products work. They don't understand why those studies are inadequate.

Bernard Raxlen, MD, who devotes more than 90% of his practice to the treatment of so-called “chronic Lyme” disease, is on a three-year probation imposed by the New York State Board for Professional Medical Conduct (BPMC). Raxlen agreed to probation and a lengthy list of practice requirements last month following allegations, filed in September, of negligence, incompetence, gross negligence, gross incompetence, and failure to maintain adequate patient records. In doing so, he becomes the second “Lyme literate” VIP disciplined by the NY medical authorities this year. Based on similar charges of professional misconduct, David Cameron, MD, was also put on probation with numerous practice restrictions in June.

Who is Bernard Raxlen, MD?

Raxlen is a psychiatrist and solo “chronic Lyme” practitioner in New York City who says he’s “successfully treated” over 3,500 cases of tick-borne disease in the past 15 years. (He named his practice “Lyme Resource Medical of New York.”) He touts a “total comprehensive treatment program which

utilizes both oral and intravenous (IV) antibiotic treatment." It doesn't come cheap, either. An initial visit with Raxlen costs $1,200 with follow-up visits between $600 and $700. A PICC-line insertion (presumably for long-term antibiotics) is $750 and a "nutritional IV" is $150. He does not accept public or private insurance.

Raxlen has a history of disciplinary actions against him in two states stretching back almost 20 years. In Connecticut, where he was formerly licensed, he was reprimanded and paid a total of $35,000 in civil penalties in two cases arising out of his refusal to provide patient records to the Health Department and insurance companies, even though patients had signed releases. He was also disciplined for inappropriate prescribing and failing to maintain malpractice insurance. Because these infractions constituted professional misconduct in New York as well, he was subject to two disciplinary actions in that state, resulting in censure, reprimand and a $2,500 fine.

According to the *Chicago Tribune*, Raxlen had other professional misconduct charges brought against him by Connecticut authorities but they were ultimately dropped. The *Tribune* reported that, in one case, Raxlen was charged with telling a patient with Lou Gehrig's disease (ALS) that she had Lyme disease and treating her with an illegal drug from Germany. He told the reporter that the relationship between ALS and Lyme was "unclear," even though ALS experts concluded that there was no evidence of a connection.

Per his New York State Department of Health physician profile (just type his name into the search engine), Raxlen completed residency training in psychiatry and lists his specialty as psychiatry, but he is not board certified in any specialty. He did not train in internal medicine, family medicine or pediatrics (although he treats pediatric patients), specialties that normally treat routine Lyme infections. Nor did he train in infectious diseases, experts to whom patients with more complicated cases of Lyme would normally be referred by other practitioners.

Yet, he is described by the International Lyme and Associated Disease Society (ILADS) as a "leader in Lyme disease treatment and research." In fact, he is a founding member of ILADS, former Secretary of the Board, and has taught a number of ILADS courses. He was a co-author of the original

ILADS guidelines for the treatment of tick-borne diseases. Despite their troubling disciplinary status, both he and David Cameron are scheduled to speak at the ILADS Annual Scientific Conference, which starts today in Boston.

How can this be? How can one be a leading light in ILADS with a disciplinary history like Raxlen's and no graduate medical education in infectious diseases?

"Lyme literate" physicians like Raxlen consider "chronic Lyme" a real disease and treat it with long-term antibiotics, sometimes for months to years. Board-certified infectious diseases doctors and other "conventional" physicians do not. These experts agree that "chronic Lyme" is not a real disease and rely on well-conducted trials showing that long-term antibiotics do not substantially improve the outcome for patients diagnosed with so-called "chronic Lyme." Long-term antibiotics can, in fact, result in serious harm, including death, a subject our good friend Orac covered recently over on Respectful Insolence. Orac's post nicely summarizes the differences between real Lyme disease and "chronic Lyme," "a prototypical fake medical diagnosis," and the dangers of long-term antibiotics, as have posts on SBM, here, here, here, and here.

The CDC, the Infectious Diseases Society of America (IDSA), the American Academy of Pediatrics, the American College of Physicians, the *Medical Letter* and the American Academy of Neurology all reject the notion that "chronic Lyme" exists and that long-term antibiotics are an appropriate treatment. There is something called "post-treatment Lyme disease syndrome," but responsible medical authorities do not equate this syndrome with the nebulous symptoms and unvalidated lab tests of "chronic Lyme" and specifically reject the utility long-term antibiotic treatment based on well-conducted clinical trials.

None of this stopped "Lyme literate" doctors from banding together to form ILADS and issuing their own guidelines for the diagnosis and treatment of "chronic Lyme," guidelines based on very low levels of evidence that are accepted only by themselves and, in contrast to the IDSA guidelines, no other professional medical organization. ILADS teaches physicians and other practitioners how to become "Lyme literate." ILADS, again in contrast to

IDSA, is not an ACCME-accredited provider of continuing medical education although, for some inexplicable reason, the Westchester [County, NY] Medical Society has teamed up with ILADS and is using its accrediting authority to grant CME credit for some of the talks (also here) at the ILADS Scientific Conference.

Despite the lack of evidence that "chronic Lyme" is a real disease, and the lack of efficacy as well as the risks of long-term antibiotic treatment, ILADS healthcare providers currently treat more than 100,000 patients with "chronic Lyme" and tick-borne diseases in the USA and around the world. Given media reports that patients can spend $10,000 to $35,000 for treatment, "Lyme literacy" translates into millions of dollars for practitioners.

While it may be profitable, "Lyme literate" doctors risk running afoul of state medical boards. Raxlen is just one among ILADS-trained, "Lyme literate" physicians who have had their medical practices questioned by their peers, up to and including discipline imposed by state authorities (also, here and here).

With that background, let's look at the allegations against Raxlen and the terms of his probation.

The BPMC v. Raxlen

New York's medical misconduct procedures do not require the physician charged to stipulate to any particular acts of misconduct as a condition of settling his case. The physician can, as Raxlen did here, simply state he is unable to "successfully defend against at least one of the acts of misconduct alleged" and agree to the imposition of sanctions. This means the allegations in the state's Statement of Charges were never proven, as it was unnecessary to reach a decision on the factual issues once Raxlen agreed to a settlement. However, per the Office of Professional Medical Conduct's (OPMC) standard procedures, the allegations were based on expert review of Raxlen's patients' records and they remain uncontested by him.

The allegations of misconduct arise out of Raxlen's care of eight patients. As is typical of "chronic Lyme" diagnosis and treatment, patients (whose

identities are protected) presented with a variety of disparate symptoms, such as:

- Patient A: freezing, burning, air hunger, weakness, fatigue, neck pain and intestinal pain.
- Patient E: fatigue, migraines, neck pain, joint pain, numbness and tingling, irritability, sound, light and temperature sensitivity and nonrestorative sleep.
- Patient G: back pain, abdominal pain, feet pain, extremity weakness, anxiety, depression and mood swings.
- Patient H (who got the Hickman catheter and numerous antibiotics mentioned below): mouth, teeth and jaw pain, confusion, forgetfulness, irritability and mood swings.

Diagnosis and treatment of "chronic Lyme" is never mentioned, a wise decision on the part of the BPMC prosecutors in light of the ill-conceived New York law protecting "Lyme literate" doctors from prosecution

> based solely upon the recommendation or provision of a treatment modality by a licensee that is not universally accepted by the medical profession, including but not limited to, varying modalities used in the treatment of lyme disease and other tick-borne diseases.

Instead, the BPMC focused on the fact that Raxlen had failed in the most basic tenets of good medical care, although the fingerprints of "chronic Lyme" diagnosis and treatment, such as failure to consider alternative diagnoses, prescribing IV antibiotics and using a Hickman catheter, are all over the charges. The charges included:

- Repeatedly failing to perform or note in the patient's chart a comprehensive history and appropriate physical exam, including (despite his being a psychiatrist) a psychiatric history, neuropsychological testing and mental health status exam.
- Failing to construct a differential diagnosis and pursue a thorough diagnostic evaluation prior to instituting a treatment plan.
- Inappropriate prescribing, including prescribing Rifampin for a patient on Tamoxifen and prescribing addictive medications prior to a making a diagnosis and without considering non-addictive treatment.

- Inappropriately relying on Applied Kinesiology (which is quackery) to formulate a diagnosis.
- Placement of a Hickman catheter without medical necessity.
- Inappropriately administering antibiotics, including intravenous Invanz, Clindamycin, Flagyl, Rifampin, Minocycline, Mepron, Plaquenil and Bactrim, all of these for *one patient*.
- Failure to present or note in the patient's chart potential risks, benefits, side effects and safe use of prescribed medications.
- Failure to appropriately identify, address, and/or follow-up on potential side effects.
- Treating inappropriately with an ongoing and/or escalating medication regimen without appropriate physical exams and clinical reassessment for consideration of alternative diagnoses and treatment.
- Poor record-keeping.

These allegations resulted in charges of negligence, incompetence, gross negligence, gross incompetence, and failure to maintain adequate patient records. As noted, Raxlen agreed to a three-year probation in addition to the imposition of conditions on his practice. He must, among other things:

- Communicate to patients the nature of his medical role, whether it be a primary care physician responsible for the patient's general medical condition, or for a defined or limited purpose, and/or as a practitioner of a particular medical specialty.
- Obtain written informed consent addressing all aspects of treatment and document same, including documentation of all discussions with the patient about the nature and scope of his evaluation and treatment and the patient's need to pursue "conventional medical care elsewhere."
- Document all histories and physicals.
- Refer patients to primary care physicians, specialists or consultants for further evaluation and/or treatment where medically warranted and provide these physicians with all relevant patient information.
- Cooperate fully with the state in enforcing the Consent Order and timely respond to all state requests for written periodic verification of his compliance and all documents.

What now?

Based on a birthdate of 1938 in his state physician profile, Raxlen is either already, or soon will be, 79 years old. One wonders whether he will continue his practice in face of these new sanctions, although his website is still trying to attract patients.

Sadly, the chronic Lyme lobby responsible for passing the law protecting "Lyme literate" doctors has its sights set on even greater rewards. Several bills are pending in the NY legislature which would force insurers to cover "chronic Lyme" treatment (Assembly Bill 114, Senate Bill 4713, Senate Bill 670). Other bills give them the opportunity to argue in yet another venue for insurance coverage. (Assembly Bill 4863, Senate Bill 2168, Assembly Bill 6927).

In any event, it is commendable that the Board for Professional Medical Conduct has not let New York's unfortunate law get in the way of its prosecuting physicians who take advantage of patients with a diagnosis of "chronic Lyme," no matter how they frame the specific charges. With two leading NY "Lyme literate" physicians now on probation and under strict orders to clean up their acts, it remains to be seen what effect this might have on other "Lyme literate" doctors in the state.

There is a simple reason we strongly promote science-based medicine – it results in the best outcomes for individuals. That is true by definition, since the SBM approach is to use the best evidence and science available in order to determine which interventions result in the best outcomes.

There are numerous ways in which relying upon poor-quality evidence or invalid methods for making health decisions cause potential harm. Often the list is unimaginatively limited to direct physical harm, but that is only the tip of the iceberg. There is financial harm, loss of opportunity to pursue more effective interventions, psychological harm from false hope and being deceived, and sacrifice of quality of life, time, and effort.

Even without direct physical harm, with inert treatments like homeopathy, there is tremendous potential harm from relying upon fake medicine and bad science. But often there is potential physical harm, and even if slight it is not justified if there is no real benefit. Medicine is a game of risk vs benefit – when the benefit is essentially zero, any risk is unacceptable.

The gluten-free fad

Even a small potential harm can be significantly magnified if it is marketed to the general public. The "clean eating" movement, in my opinion, clearly represents such a case. The best overall advice we can give the public regarding healthy eating is to eat a variety of food with plenty of fruits and vegetables and watch overall caloric intake. Unless you have special medical considerations, simply eating a good variety of different kinds of food will take care of most nutritional concerns. It will result in you getting enough of what you need and not too much of anything that can increase your risk.

Having a restricted or narrow diet is always tricky, and runs the risk that you will be getting too little of some key nutrients and may be getting exposed to too much of others. This is the key risk of so-called "fad" diets, because they are often premised on a simplistic notion that specific foods or categories of foods are inherently bad and should be avoided. Therefore any diet which

essentially consists of avoiding certain foods or heavily relying on others is likely to take you away from an optimal diet, and therefore be a net negative for your health.

The recent gluten-free fad is no exception.

As I discuss in detail here, gluten is a composite of two proteins found in wheat, rye, barley, spelt, and related grains. About 1% of the population has an autoimmune reaction to one of the components of gluten (usually gliadin) and eating gluten can cause serious illness (a condition known as celiac disease). For those with celiac disease, avoiding gluten is essential and even a small amount of gluten can cause serious symptoms.

There is a controversy, however, surrounding the alleged existence of so-called non-celiac gluten sensitivity (NCGS). This is a hypothetical condition in which people may have a sensitivity to gluten without forming antibodies to gliadin or meeting the diagnostic criteria for celiac disease. Discovering a new disease is always complex, and requires the identification of something definitive and discrete. We either need to identify a clear clinical syndrome, or some new specific pathology.

For NCGS there is no clear pathology. The entity's legitimacy currently relies on the alleged existence of individuals who do not have celiac disease but have a negative reaction to eating gluten. If, however, we are going to base a new disease purely on clinical history, we need to make sure that the history is accurate and that we are not simply overinterpreting non-specific symptoms or falling victim to confirmation bias.

For example, there are people who feel they have a specific syndrome of sensitivity to electromagnetic waves, despite the absence of any identifiable pathology. However, properly blinded studies show that self-identified sufferers of EM sensitivity cannot tell when they are being exposed to EM waves in a blinded condition.

For alleged NCGS the most salient evidence of its existence as a clinical entity are rechallenge studies. In these studies subjects are challenged with either gluten or placebo, then the gluten is removed, and then they are later rechallenged. If NCGS is a real entity then their symptoms should resolve

when gluten is removed and then return when rechallenged, at a higher frequency when the same is done with a placebo.

A recent systematic review of gluten rechallenge studies did not find significant evidence for NCGS. They conclude:

> The prevalence of NCGS after gluten re-challenge is low, and the percentage of relapse after a gluten or a placebo challenge is similar.

This is a pattern of evidence that is consistent with the null hypothesis, that NCGS does not exist – results are all over the place, with better-controlled studies tending not to show an effect, and on average there is only a tiny signal that does not reach statistical significance. The most parsimonious interpretation of available evidence, therefore, is that NCGS does not exist. Despite this fact, roughly one third of the population report that they are trying to avoid gluten.

What's the harm

What, then, is the potential harm from restricting gluten from the diet in the millions of people who do not have gluten sensitivity? Potentially, all of the things I listed above may contribute to harm.

For many people they have settled on gluten sensitivity to explain real symptoms they may be having. In this case they may be missing the real cause of their symptoms. There is therefore an opportunity cost of making a false diagnosis.

Perhaps most significantly, a gluten-free diet is very difficult. You have to eliminate all wheat and similar grains from the diet. This has become somewhat easier recently as industry is cashing in on the gluten-free fad, but it is still a significant inconvenience and expense and therefore drain on quality of life.

Further – a gluten free diet eliminates a major category of food from the diet. People on a low or gluten-free diet tend to also be low in whole grains. They risk being deficient in iron and folic acid. A recent study linked low-gluten

diets to a higher risk of type-II diabetes.

Avoidance of gluten may also result in a heavy reliance on rice as a staple grain, and this might increase the risk of heavy metal exposure. Again – having a varied diet spreads out exposure to contaminants and toxins as well as maximizing exposure to needed nutrients.

Science over marketing

If we take a scientific approach to the question of NCGS we find that there is no clear evidence that non-celiac gluten sensitivity is a real thing, and that gluten-free diets not only have no benefit for the general public they present health risks. Clearly, however, we need to do a better job of communicating this to the public.

Part of the challenge, however, is that nutritional gurus (who always seem to have something to sell) have a simple and appealing narrative to market. They tell the public that their problems are due to one bad food or type of food they just need to avoid. Or, they market of lifestyle of “clean eating” that is based on the appeal to nature and irrational fear of toxins and chemicals, rather than an even basic understanding of science and evidence.

The science-based position, however, takes time to emerge. It may take a decade or more to do the kinds of studies necessary to effective answer the question about whether or not a new hypothesized clinical entity exists. There are many types of evidence to be considered, and many sub-questions to be addressed. Over time a clear picture will tend to emerge, but in the meantime the health gurus can establish a market for their nonsense. Once their simplistic and marketable narrative gets into the public consciousness it is hard to correct.

I have written critiques of several dietary supplements sold through multilevel marketing (MLM) schemes, and they keep coming back to haunt me. I get testimonials from users who believe they have been cured of every ailment under the sun; and every time another study is done, I get e-mails from distributors who apparently think the new “evidence” will change my mind. Recently I received three more emails about ASEA, one about Protandim, and three about dōTERRA essential oils, asking me to reconsider. I thought this would be a good opportunity to explain why I have not changed my mind and to explain once again what constitutes evidence in science-based medicine.

ASEA

Recently an email from “The ASEA Team” asked us to delete the article I wrote about ASEA in 2012, based on their opinion that it “was not constructive” and “was not based on decent and verifiable facts.” They did not mention two other followup articles I wrote here and here. And they did not directly try to refute most of the points I made in my critique; I think they failed to understand what I was saying. They provided six attachments with

studies they said were “made to prove the effectiveness of ASEA” but those studies didn’t prove any such thing.

Last week Steven Novella answered them very effectively, calling ASEA snake oil and pointing out the deceptive marketing practices of the company, the pseudoscientific nature of their claims, and the worthlessness of the studies they cite.

The claims

The ASEA website currently makes these claims:

> As we age, and as stress and environmental toxins inundate our lives and weaken our defenses, normal cellular function declines, and with it, the body’s ability to produce and maintain a proper balance of redox signaling molecules. ASEA has developed the only technology that can create and stabilize active redox signaling molecules in a consumable form. No matter what your health concern may be, ASEA Redox Supplement can bring your cellular communication to optimal levels, improving the health of every system of your body.

Questions

This brings up several questions:

- How exactly does normal cellular function decline? How would improved cellular communication reverse the decline?
- What is a proper balance of redox signaling molecules? How do they know? How is it measured?
- What active redox molecules are in the product? (They won’t tell us. The label just lists salt and water. In my opinion, if there are redox molecules in ASEA, listing only salt and water constitutes false labeling.)
- What evidence do they have that the product improves health?

What redox molecules?

All they have is a statement from a lab, BioAgilytix, that indirectly measures "biomarkers" of redox levels in ASEA using a fluorescent indicator as a probe for unspecified highly reactive oxygen species. I don't know what that means. There is no direct evidence that redox molecules are present. No other lab has analyzed the product.

Safety

Their claim that the product is safe is based on a brief description of two unpublished studies. In the first study, 106 overweight women took ASEA or placebo for 12 weeks; they reported no adverse effects, (None?! In most studies, even the placebo group typically reports *some* symptoms.) and there were no changes in liver or kidney function tests or complete blood counts. In the second study, an *in vitro* study of cultured eukaryotic cells, the cells "did not register a significant toxic response as measured by a visual assessment of green dye that indicated "nuclear translocation." Based only on this flimsy subjective and *in vitro* evidence, they claimed "ASEA Redox Supplement, orally administered, does not manifest a toxic response or inflammation to exposed tissue." Such thin gruel does not constitute convincing evidence that the safety of the product has been established.

Studies

Before I accept that a treatment works, I want to see human studies published in peer reviewed journals. There are none on their website, but I was able to locate two articles in the *FASEB Journal* here and here.

It quickly became obvious why these are not featured on the company website: they are not full articles, but abstracts from a meeting that were published in a supplement to the journal. One is a human study, the other is in mice (the poor mice were gavaged with ASEA and then run to exhaustion). One of my correspondents claimed that these are peer-reviewed studies, but peer review is not possible when all that is available is an abstract.

As far as I could determine, there have been three studies in humans. One, a small study of 17 cyclists, has been deleted from the web. It was not placebo-controlled. There is an abstract of a similar study of 20 cyclists that did use a placebo control and was double-blinded. It was essentially *negative*: ASEA did not improve time trial performance. They found that it caused a significant shift (good or bad?) in 43 metabolites, but had no apparent influence on traditional biomarkers of inflammation, oxidative stress, or immunity.

The third, most recent human study is the one my true believer correspondents are currently crowing about. They refer to it as a "genetic" study. One of them snarkily commented "It's called science, u should look into it sometime." I did look into it, and I was not impressed. The title is "Initial Gene Study Showed ASEA REDOX Affected Important Signaling Pathway Genes." The company paid Tauret Labs to do the study. It has not been published in a peer-reviewed journal. It was an 8-week double-blind randomized placebo controlled study with 60 participants that measured changes in expression of 5 genes and found statistically significant changes of 20-31% with ASEA. They claim that "These genes are key in the health of the individual and play a vital role in five human health areas and dozens of pathways." Maybe, but they have not demonstrated that human health benefits in any way from these changes in gene expression. Their summary of results states "Effects are non-specific to race, sex or age, and were observed in all populations tested." This conclusion is not supported by their data. The only population tested was 60 individuals, 41% male, 92% Caucasian, average age 35 with age distribution not reported.

Conclusion

The evidence for their claims is indirect and inadequate. Half of all research studies turn out to be wrong. Changes in blood tests might be spurious; they have not been independently replicated. Changes may be statistically significant but not clinically significant. If they want us to believe ASEA causes objective, meaningful improvements in human health, they'll have to do better. They'll have to test directly for meaningful clinical outcomes. And if they want us to believe ASEA contains all those redox signaling molecules,

they'll have to prove it with a direct analysis by an independent lab and name those molecules.

As Steven Novella put it,

> Asea, however, is still a fantastical and unbelievable claim supported by nothing but hype, sales copy, and empty promises. It is salt water. The hand-waving nonsense about redox reactions is incoherent technobabble – the very essence of pseudoscience. What would be convincing is published, peer-reviewed, independent, rigorous scientific studies with clear results. These don't exist. No amount of distraction will change that fact.

Protandim

I have written about Protandim four times, here, here, here, and here.

What is it?

It is a mixture of five dietary supplements (Milk thistle, *Bacopa* extract, Ashwagandha, green tea extract, and turmeric extract) that allegedly stimulates the body to produce its own antioxidants. They claim it is "the only supplement clinically proven to reduce oxidative stress by 40%, slowing down the rate of cell aging to the level of a 20 year old [and they measured this how?]."

An email from a reader

> You really need to up date your studies on this product! There are thousands of people with improved health because of PROTANDIM. For example, my son in law with high blood pressure was able to cut his BP medication in half after only two months on it and after three months, he is off meds completely with normal blood pressure; my daughter suffered for a year with a horrible rash under her arm that

> looked like tree bark. After several visits to her doctor where he prescribed cortisone and antibiotics nothing worked. She finally went to a dermatologist who was shocked to see that she had Granular Parakeratosis a rare skin disease. My daughters case was only the second time she has seen it, and at a follow up visit was told that there is no cure, only palliative care. Three days later the crud came off in her washcloth in the shower, and she had been on PROTANDIM for about two months. See photos. On the after picture you can see a round sore which is from the biopsy. In addition, my husband who has cOPD and had bypass surgery last year, and myself have great, new energy. In addition, my nerve damaged feet and numbness in my right foot have improved by at least 80 per cent after only 5 weeks! For the first time in 15 years or so, I can now feel my right big toe and it is no longer cold, like a piece of granite, and our bad backs have greatly improved. I could go on and on and I don't need someone like you to tell me and thousands of others that it does not work! We are walking human studies for this amazing product! Check out the human studies for liver disease! I am proof it works so you should take another look: in fact go to You Tube PROTANDIM testimonials and see for yourself what this product does when it reduces oxidative stress!

My most recent article was in May 2017, and I'm not aware of any new studies requiring me to "update my studies" in the last six months. The evidence on the website is mainly about Nrf2 protein messengers in general, and studies of Protandim in cell culture (*in vitro*) and in mice. One 2006 human study found changes in lab tests such as TBARS but did not even attempt to look for any clinically meaningful improvement in health outcomes. A second human study in 2016 was negative: It concluded "Protandim® did not (1) alter 5-km running time, (2) lower TBARS at rest (3) raise antioxidant enzyme concentrations compared to placebo (with exception of SOD in those ≥ 35 years old) or, (4) affect quality of life compared to placebo." And another study of patients with alcohol use disorders was also negative. Not only negative but laughable.

Conclusion

Increasing levels of antioxidants could be beneficial or harmful. The only way to know if Protandim improves human health is to do properly designed, placebo-controlled human studies looking for meaningful clinical outcomes.

dōTERRA essential oils

I have written about dōTERRA twice before: here and here.

An email asked me to "Check with Johns Hopkins and the research published about dōTERRA oils. Dr. Nicole Parrish claims that dōTERRA oils have killed three super bugs that synthetics cannot. It is published and the medical world is learning more about essential oils in September." I asked her for links to that research; she never responded.

Another email chastised me for having a "complete scientific mindset." (I thought that was a *good* thing!) She said, "It really is worth looking further into to help people stay healthy." She provided all kinds of testimonials: her dentist and her real estate agent use it, her son and stepson carry the beadlets with them during allergy season, and when her husband got cancer, they used essential oils for diabetes, neuropathy, infections, and asthma. She also chastised me for not mentioning what the Bible says about oils and plants! She believes "science is here to prove God's existence and the Bible can be used for medicinal research." I didn't try to answer her.

An *in vitro* study was done on dog kidney cells infected with influenza virus. Based on their results, they speculated that essential oils *might* be useful in treating humans with influenza (or might not). In my article critiquing that study, I provided some guidelines on how to read research studies that claim to support a product.

A third email said I needed to visit the website again and review the 17 studies published in peer-reviewed journals. I found an *in vitro* study of frankincense and an *in vitro* study of Deep Blue, a mixture of essential oils. There was also an extensive bibliography which included a lot of irrelevant articles along with *in vitro* and animal studies. There were a lot of scattershot preliminary studies on individual oils, but these were seldom if ever followed

by replications or confirmations. My own PubMed search found a few studies supporting the use of an essential-oil-containing mouthrinse, reports of adverse effects of essential oils, some negative studies, and a couple of Cochrane reviews that pointed out the poor methodology of the few studies they found. A 2012 systematic review of aromatherapy concluded "the evidence is not sufficiently convincing that aromatherapy is an effective therapy for any condition."

My correspondent said, "In my opinion, there are too many confirmed reports of improved health & well-being (when using essential oils) to chalk it all up to "hysteria" or "ignorance" or even chance." Her opinion is misguided. The plural of anecdote is not data. Confirmed reports of improved health and well-being, no matter how numerous, are meaningless without a control group. Reports of failures are not systematically collected. Patients may improve for reasons other than the oils: suggestion, placebo effect, social factors, the natural course of the disease, regression to the mean, etc.

Essential oils can be very pleasant to use, and I have no problem with using them as "comfort" measures. And the company website is careful not to make any egregious disease-prevention or -treatment claims. But at their in-home presentations, the distributors feel free to claim that the oils can cure anything and everything, including cancer. These claims are not backed by any science but are illustrated by persuasive anecdotes, touching and heartwarming stories, testimonials from users that the attendees may know personally. Attendees are easily influenced to believe and to buy.

The published evidence for each of dōTERRA's many products is sparse to nonexistent. There *are* clinical studies to support *a few* of the recommended uses, but they are generally poorly designed, uncontrolled, unreplicated, and unconvincing. Research is difficult, because patients can't be blinded to the odors, and mental associations and relaxation could account for most of the observed effects. I remain skeptical of the claims for objective benefits in treating diseases.

Conclusion: No reason to change my mind

Testimonials are notoriously unreliable. These products are not supported by acceptable scientific evidence. I'm *not* saying they *don't* work. No one knows whether they work or not, because they have not been properly tested. I am simply asking for a single standard of evidence, the kind of evidence required to achieve a scientific consensus that any treatment is effective and safe. If they want us to buy their products, they should test them against placebo controls in human studies looking for objective, meaningful improvements in health; and they should get those studies published in reputable peer reviewed journals. In the pharmaceutical industry, only a small percentage of promising candidates survive testing. Considering the huge number of dietary supplement products like these on the market, the chance that any one of them will prove to be truly effective is vanishingly small.

Science Based Medicine

周六, 25 11月 2017

Science Based Medicine

[周六, 25 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Happy Thanksgiving!** [周四, 23 11月 14:00]
  Happy Thanksgiving to our American readers, and to everyone else- have a great Thursday in November!
- **New Tools Against Antibiotic Resistance** [周三, 22 11月 20:24]
  Antibiotic resistance is a serious problem that may lead to a post-antibiotic era. However, there are potential solutions that deserve research priority.
- **The Death of Expertise** [周二, 21 11月 16:00]
  In Tom Nichols' new book, The Death of Expertise, he explains how a misguided intellectual egalitarianism is harming our ability to assess the truth and solve problems, and discusses some of the responsible factors and possible long-term consequences.
- **What is “integrative oncology”? Even the Society for Integrative Oncology doesn’t seem to know for sure** [周一, 20 11月 16:25]
  Last week, the Society for Integrative Oncology published an article attempting to define what "integrative oncology" is. The definition, when it isn't totally vague, ignores the pseudoscience at the heart of integrative oncology and medicine.

Happy Thanksgiving! - Science-Based Medicine

We celebrate Thanksgiving today in the U.S. and SBM is taking the day off. We are thankful for all of our readers and commenters and wish you a Happy Thanksgiving.

New Tools Against Antibiotic Resistance - Science-Based Medicine

Scientists are often placed in the role of Cassandra – because of their expertise and knowledge they may see potential serious problems on the horizon, but may also find it challenging to convince the general public. Sometimes they are working uphill against vested interests. Often scientists will warn against possible problems that they then work to prevent, and when successful it seems like their warnings were unwarranted. Or they may simply be calling for preparation for a possible event, like an epidemic, that still probably won't occur but you should be prepared ahead of time in case it does.

Also, as science communicators we don't want to overhype potential problems. It can be a delicate balance. With all that in mind, it is probably difficult to overstate the potential risk of antibiotic resistance. This is one of those looming issues that I genuinely worry about, but gets too little attention, if anything, in the media. It is also a manageable problem – there are things we can do to mitigate antibiotic resistance, if we take the issue seriously enough.

The World Health Organization summarizes the problem in stark terms:

> Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. A growing list of infections – such as pneumonia, tuberculosis, blood poisoning, gonorrhoea, and foodborne diseases – are becoming harder, and sometimes impossible, to treat as antibiotics become less effective.
>
> Where antibiotics can be bought for human or animal use without a prescription, the emergence and spread of resistance is made worse. Similarly, in countries without standard treatment guidelines, antibiotics are often over-prescribed by health workers and veterinarians and over-

> used by the public.
>
> Without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill.

I don't think they are overstating the problem.

The cause of antibiotic resistance is fairly easy to understand. Bacteria reproduce very quickly in large numbers. When someone takes an antibiotic, that provides a selective pressure towards resistance. If any individual bacterium has a gene which provides resistance to the mechanism of that antibiotic it will tend to survive the treatment and then reproduce a new generation of resistant bacteria.

Bacteria also have the ability to swap genes, so that are not just passed from parent to offspring, but horizontally to other bacteria in a process called conjugation. Bacteria may contain plasmids, which are loops of DNA. Those plasmids can be copied from one bacterium to another. A plasmid may contain one or even multiple genes that confer resistance – and so in one conjugation event a bacterium may receive resistance to multiple antibiotics.

The existence of bacterial plasmids with multiple resistant genes is a problem, because if they are exposed to one of the antibiotics to which they are resistant, that will favor the proliferation of the bacteria with plasmids that confer multiple resistance.

There is one potential bright spot in all this. Genes that confer antibiotic resistance often come at a price. They may make it more difficult for the bacteria to reproduce, or force them to expend more energy. That is why they don't have the feature in the first place. The selective pressure of antibiotics is necessary to favor the more costly feature. The hope is that in the absence of selective pressure from antibiotic, the resistant features will tend to fade away.

However, a new study suggests that this may not always be the case. Researchers looked at costly antibiotic resistance features in various strains of *E. coli*. They followed them for over a month and found that strains were able to maintain even costly antibiotic resistance in the absence of antibiotics if

they contained plasmids. The key is the conjugation rate – how frequently do bacteria exchange plasmids? The research found that, at least in these strains, the rate was high enough to maintain antibiotic resistance even in the absence of antibiotics.

This research suggests that limiting antibiotic use may not be enough to reverse existing antibiotic resistance. Of course, limiting use is essential to slowing the development and spread of resistance. This is the primary mechanism by which the medical community is trying to combat resistance, but even here we are not doing enough. Antibiotics are still massively overprescribed. Some countries allow for over-the-counter antibiotic use, and it is common for the public to take them for viral illnesses. Antibiotics are also heavily used in the farming industry.

Even if we achieved our goal to properly limit antibiotic use, and educated practitioners to optimally prescribe antibiotics, the current research suggests this may not be enough to reverse some types of resistance. However, the same research suggests there may be more active interventions that will.

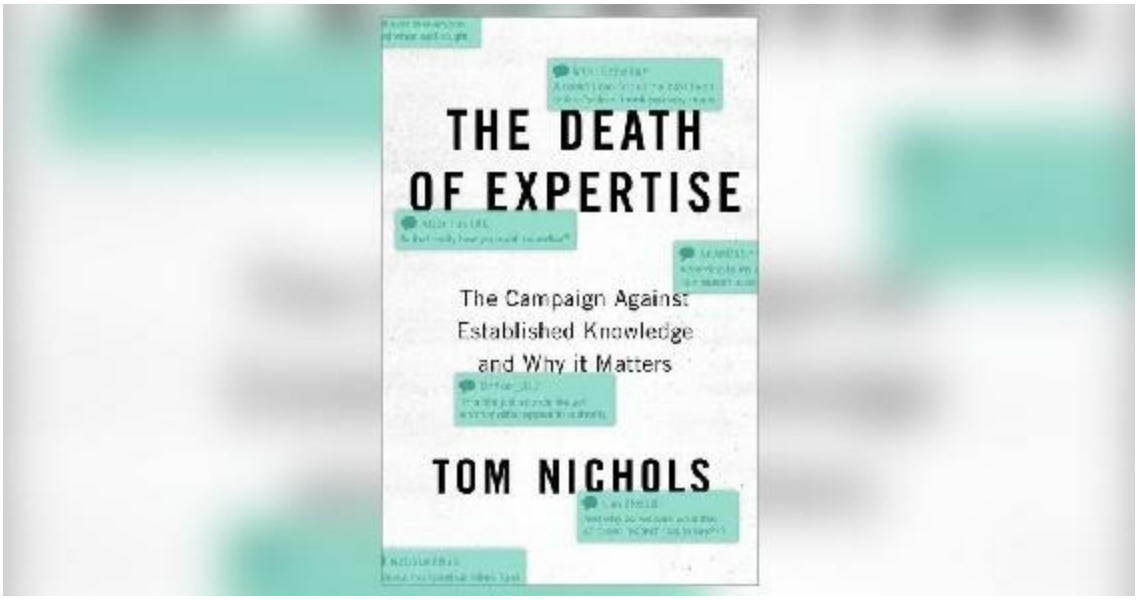
There are potential drugs that can limit conjugation or induce bacteria to lose their plasmids. For example, a 2015 study identified features of synthetic fatty acids that were effective conjugation inhibitors. This would limit the horizontal spread of plasmids among bacteria, and therefore limit the spread of resistance.

Another approach is to prevent plasmid replication. Researchers are looking at ways to exploit the existing compatibility system in bacteria toward this end. Since bacteria are so promiscuous with their genes, they need mechanisms to know when plasmids are incompatible with their other DNA. You could essentially trick a bacterium into thinking its plasmid is incompatible, and therefore when the bacteria reproduces it will not replicate the plasmid. The plasmid will therefore be lost to the next generation. These treatments would not just limit the spread of resistance, but cause a population of bacteria to lose their resistance.

What all of this research suggests is that we should not only be researching novel antibiotic mechanisms, we should be investing in research into drugs that inhibit plasmid conjugation and induce plasmid loss. These treatments

can reduce the spread of resistance, and even potentially reverse resistance. Such treatments could be given alongside antibiotic regimens, or used in farming or similar contexts to limit the development of resistance.

My hope is that this type of research will eventually lead to a situation in which all those scientists and science-communicators who warned about the coming post-antibiotic era will look like Cassandras. Rather than getting the credit for identifying and then preventing a major problem, people will either forget them or falsely think the warnings were overhyped to begin with. But I will take that fate if it means avoiding a post-antibiotic era.



Tom Nichols' new book *The Death of Expertise: The Campaign against Established Knowledge and Why It Matters* has direct relevance to many of the issues we are constantly grappling with on Science-Based Medicine. In a democracy, everyone has equal rights. Many people think that means they are equal to experts in knowledge and judgment. In medicine, as in most other areas of public discourse, we are faced with angry laymen who denounce intellectual achievement and scientific knowledge and who distrust experts.

People find ways to reject the evidence when it conflicts with their values and beliefs. When scientific evidence challenges their views, they doubt the science rather than themselves. New examples of this phenomenon can be found every day in the news and in the comments sections of the Science-Based Medicine blog, and trying to set those people straight has proven a mostly futile exercise.

The failure of higher education

Students have become consumers. High school seniors tour college campuses with their parents looking for the one with the best dorms, cafeteria food, and extra-curricular activities, rather than the one that will challenge them and provide the best education. Nichols says colleges are not only failing to

provide to their students the basic knowledge and skills that form expertise, they are failing to provide the ability to *recognize* expertise and to engage productively with experts and other professionals in daily life. They are not being taught "critical thinking: the ability to examine new information and competing ideas dispassionately, logically, and without emotional or personal preconceptions."

He says students are being treated as *clients* rather than students. "Many colleges have become hostages to students who demand that their feelings override every other consideration." Students "explode over imagined slights" and "build about themselves fortresses that no future teacher, expert, or intellectual will ever be able to breach." They want to be protected from ideas or language they find unpleasant. They are "demanding to run the school while at the same time insisting that they be treated as children."

The internet

The Internet has provided people with an unprecedented abundance of information, but all too often it gives them the illusion of knowledge, encouraging them to believe they know as much as experts. They hear what they want to hear, and live in a bubble community of people with similar beliefs.

> People do not come to the Internet so that their bad information can be corrected or their cherished theories disproven. Rather, they ask the electronic oracle to confirm them in their ignorance.

Nichols says,

> …not only is the Internet making many of us dumber, it's making us meaner: alone behind their keyboards, people argue rather than discuss, and insult rather than listen.

People "power browse" rather than actually reading. We see this all the time on Science-Based Medicine, where commenters criticize an article they obviously have not read carefully or understood. Sometimes I suspect they may just have read the title and seized the opportunity to jump on their

particular soap box.

Journalism

The dissemination of “fake news” is an ever more common reality. Most people are very poor at evaluating the reliability of a news source and the truth of what is reported. When a layperson challenges an expert by saying “I read it in the paper” or “I saw it on the news,” it may mean only “I saw something from a source I happen to like and it told me something I wanted to hear.” At that point, discussion has nowhere to go; the real issue is replaced by the effort to untangle which piece of misinformation is driving the conversation. People are constantly barraged with facts and knowledge, but they have become more resistant to facts and knowledge. How did we arrive at this state of affairs? Nichols says, “technology collided with capitalism and gave people what they wanted, even when it wasn’t good for them.”

When the experts are wrong

In our increasingly complex world, we can’t possibly know everything; we have no choice but to trust experts. But sometimes experts get things wrong. Most of the time, their errors are identified and counteracted by other experts. This works so well most of the time that we are shocked when we read about an exception; for instance, when we learn that an incompetent doctor has killed a patient or that a researcher has falsified data. Laymen get exasperated when science “changes its mind,” for instance telling the public eggs are bad for them and then saying no, they’re OK to eat. But that’s not a failure of science, but rather an example of how science works so well in the long run by following the evidence and discarding false provisional conclusions as the evidence improves.

When experts’ errors, fraud, and misconduct are revealed, a layperson naturally asks how we can trust studies in any field. Nichols says that’s the wrong question to ask, because “rarely does a single study make or break a subject.” Single studies are often wrong, but the aggregate of all research is

trustworthy. The scientific enterprise as a whole is self-correcting and leads to a consensus of experts that approaches the truth as much as is humanly possible.

The impact on government

Science is essential to rational public policy; it can't make the decisions, but it provides reality-based information that can guide the decision-makers. Nichols says we have a President who sneers at experts and whose election was "one of the loudest trumpets announcing the impending death of expertise." He argues that Trump's campaign was "a one-man campaign against established knowledge." He provides examples: Trump's "birther" campaign against Obama, his quoting the *National Enquirer* approvingly as a source of news. Nichols says rather than being ashamed of his lack of knowledge, Trump exulted in it. "Worse, voters not only didn't care that Trump is ignorant or wrong, they likely were unable to recognize his ignorance or errors." He says the Dunning-Kruger effect was at work. It's not just the things we don't know (one in five adults think the sun revolves around the Earth), but the smug conviction that we don't need to know such things in the first place.

He warns,

> The relationship between experts and citizens, like almost all relationships in a democracy, is built on trust. When that trust collapses, experts and laypeople become warring factions. And when that happens, democracy itself can enter a death spiral that presents an immediate danger of decay either into rule by the mob or toward elitist technocracy. Both are authoritarian outcomes, and both threaten the United States today.

Conclusion: Hope for the future?

He says Americans no longer understand that democracy only means political equality. They tend to think democracy is a state of actual equality in which

everyone’s opinion is as good as everyone else’s, on every subject. Feelings are more important than facts: if people *think* vaccines are harmful, it is considered “undemocratic” and “elitist” to contradict them.

He sees signs of hope. Experts are rebelling. He cites an angry doctor who asked patients, “Do you remember when you got polio? No, you don’t, because your parents got you [expletive] vaccinated.” He points out that without democracy and secular tolerance, nations have fallen prey to ideological, religious and populist attacks and have suffered terrible fates. But he ends on a hopeful note. He has faith in the American system and hopes that it will eventually establish new ground rules for productive engagement between the educated elite and the society they serve. I hope so too!

Longtime readers of Science-Based Medicine and my not-so-secret other blog probably know that I'm not a fan of the specialty known as "integrative oncology." My reasons are basically the same as the reasons why I detest "integrative medicine," only subspecialized (like oncology), so to speak. Basically, "integrative medicine" integrates quackery with medicine, and integrative oncology integrates quackery into oncology. Given that I'm a cancer surgeon, I tend to take an even dimmer view of the latter than of the former, if only because it hits me where I live. For instance, when "integrative oncology" starts appearing at symposia at major cancer meetings, with nary a skeptical word showing up in the panel discussions afterwards, I despair. Unfortunately, the credulity that allows modalities like acupuncture, reiki, intravenous high dose vitamin C, and various other unproven and disproven treatments to find their way into academic medical centers has spawned a related phenomenon, quackademic medicine, or the study and acceptance of quackery in academic medical centers. The most prominent example of this latter phenomenon occurred in September, when the University of California at Irvine accepted a $200 million gift from Susan and Henry Samueli to build and staff a college devoted to integrating quackery into its component departments and promoting "integrative medicine." Never mind the homeopathy.

Integrative oncology has become so established that it has its own professional society, the Society for Integrative Oncology (SIO). Not surprisingly, I'm not a fan of SIO, and SIO isn't exactly a fan of me, either. I've related the story before, but let's just say that the SIO was not pleased at my 2014 article in *Nature Reviews Cancer* discussing how integrative oncology is not evidence-based (to say the least), given its embrace of naturopathy. In brief, the SIO didn't like how much verbiage I devoted to homeopathy in the article, pointing out that homeopathy is indeed not evidence-based and that no integrative oncologist worth his or her salt would ever use it. I pointed out that you can't have naturopathy without homeopathy. After that, I asked how the SIO can reconcile its quite correct rejection of homeopathy with the fact that it admits naturopaths as members, that two of its recent past presidents have even been naturopaths, and that you can't have naturopathy without homeopathy. It's baked into the naturopathic

curriculum, and it's part of the naturopathic licensing exam. Moreover, one of the naturopaths who co-authored the SIO's breast cancer clinical guidelines ran a clinical trial on homeopathy. That same naturopath, by the way, was a co-author on the update to those guidelines published just this year. The SIO never learns.

This time around, though, the reason the SIO caught my attention was this Tweet by Dr. Sheila Garland, re-Tweeted by Dr. Jun J. Mao, immediate past president of the SIO (but still president at the time he re-Tweeted this):

> The beginning of a new era in evidence-informed integrative oncology research/practice that puts the person first #SIO2017 @Integrativeonc https://t.co/cmAMrCujjy
>
> — Dr. Sheila Garland (@SNGarlandPhD) November 13, 2017

This Tweet touted what is now the "official" definition" of "integrative oncology" recently laid down by the SIO:

> Official definition of Integrative Oncology! Spread the word! #SIO2017 We are research based! #cancerresearch pic.twitter.com/oeNsn9B1Jk
>
> — Jodi MacLeod (@write4wellness) November 13, 2017

It turns out that this definition had just been published by Witt et al in the November issue of *JNCI Monographs*, just in time for the SIO annual meeting last week. When I saw it, my first reaction was to e-mail my fellow SBM bloggers with a link and this image:

So let’s take a look.

The process of defining “integrative oncology”

My first reaction (besides possessiveness) when I saw the article by Witt et al, A Comprehensive Definition for Integrative Oncology was: What? The organization has existed for nearly 15 years, and in all that time it hasn’t yet managed to define what it’s about until now? My second reaction was: What on earth does this definition actually mean? It is about as boring, generic, and —shall we say?—vague a definition of anything as I’ve ever seen. Take a look:

> Integrative oncology is a patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments. Integrative oncology aims to optimize health, quality of life, and clinical outcomes across the cancer care

> continuum and to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment.

In actuality, I was more interested in what was left out of this definition than what was in it, but I'll get to that near the end of this post. First, I want to look at the process by which the authors developed this definition, as described in the article, which is open-access for those of you who want to read it yourselves. Before I get into the process, let's look at some of the authors, who are big names in the world of integrative oncology. The lead author, Dr. Claudia Witt, is Professor and Chair of the Institute for Complementary and Integrative Medicine at the University of Zurich and University Hospital Zurich, as well as part-time Professor of Primary Care and Community Medicine at the Center for Integrative Medicine University of Maryland School of Medicine. Dr. Jun J. Mao is, of course, president of the SIO and Chief of the Integrative Medicine Service at Memorial Sloan-Kettering Cancer Center. Dr. Lorenzo Cohen is someone whom we've met before, when he gave a talk at the American Society of Clinical Oncology (ASCO) meeting in 2014. He's the Director of the Integrative Medicine Program at The University of Texas MD Anderson Cancer Center. Linda Balneaves is a nurse and the current president of SIO, having succeeded Dr. Mao at the SIO annual meeting last week. I also can't help but note that one of the co-authors, Heather Greenlee, is a naturopath and has served as president of the SIO in the past as well.

In other words, these are indeed heavy hitters and the leadership of the SIO.

Let's look at their justification for seeking this definition. After regurgitating the usual "complementary and alternative medicine" (CAM) blather about how patients are just "looking for "additional interventions that may help improve the efficacy of conventional cancer treatments, increase their chance of survival, and/or reduce their symptom burden associated with cancer or treatments" and "improve their quality of life during and following treatment," Witt et al justify their search for a definition thusly:

> With the integration of interventions such as acupuncture, mindfulness and yoga, and lifestyle counseling into major cancer centers in North America (eg, MD Anderson and Memorial Sloan Kettering Cancer Center), the term "integrative oncology" has become increasingly used.

> “Integrative” better represents the process of care that is provided in centers where patients are receiving these types of interventions in addition to their conventional cancer treatments. With the establishment in 2003 of the Society of Integrative Oncology (SIO), a nonprofit multidisciplinary professional organization, the term “integrative oncology” was further legitimized and began to be widely used. However, the term “integrative” is also used in other contexts. An example is the Berlin School of Integrative Oncology at the Charité Medical School in Berlin (2), which is an initiative of the German federal and state governments that aims to educate young scientists and physicians in oncology in an interdisciplinary, translational research context. Although the term “integrative oncology” is rarely used in such an educational context, having totally different meanings for the same term can generate confusion. Adding to this complexity is the growing attention to the notion of integrated care programs in oncology, in which numerous cancer specialties (eg, medical oncology, radiation oncology, surgical oncology, genetics, plastic surgery) work together to provide comprehensive patient care (3).
>
> Furthermore, even in settings in which the term integrative oncology has been used to refer to the combination of complementary medicine therapies with conventional cancer treatments (4), the term has been defined in many different ways (5,6). Because of this lack of consensus, it has been difficult to communicate what is meant by “integrative oncology” to oncologists and other health professionals, as well as to key stakeholders, such as patients, administrators, and health policy makers. The aim of this project was to use a systematic approach to develop a comprehensive and acceptable definition for “integrative oncology.”

Actually, I’ve always rather suspected that this confusion is a feature, not a bug, related to the use of the word “integrative.” After all, integrative oncology, like integrative medicine, is a brand, not a specialty. It rebrands what should be considered perfectly fine science-based modalities, such as nutrition, lifestyle interventions, and the like, as somehow “alternative” or “integrative,” and then “integrates” quackery like acupuncture, reiki, functional medicine, and even homeopathy with them, to give the quackery

the appearance of scientific legitimacy. No, I don't think SIO is doing this intentionally; its leadership consists of true believers. But it is contributing to quackademic medicine and the integration of quackery into oncology. In any event, the word "integrative" is, as mentioned above, used to describe science-based endeavors, such as integrative biology. In this context, the word "integrative" connotes interdisciplinary study, a very different meaning than when the word "integrative" came to replace the term CAM to describe adding pseudoscience to medicine.

Indeed, use of the word "integrative" to describe medicine or the subspecialty of oncology connotes more than interdisciplinary patient care and research. It connotes the embrace of "alternative" treatment modalities as well. The term "CAM" still had the word "alternative" in it and the word "complementary" connoted that CAM was subsidiary to medicine, "complementary," the icing on the cake, if you will. In other words, it's not necessary, and science-based medicine is the real medicine. The adoption of the word "integrative" to rename CAM as "integrative medicine" was clearly intended to remove the implication that CAM was "complementary" and not as good as real medicine, in order to advance the narrative that integrative medicine is the "best of both worlds," while also borrowing from the cachet of various "integrative" scientific disciplines as being multidisciplinary. Again, I don't think SIO is out to deceive. Rather, the belief of the SIO leadership in the validity of integrative oncology has led them down this road, probably without even realizing it.

So how did Witt et al go about constructing their definition? Enter the mixed methods research design and Delphi method. This amused me, because it wasn't so long ago that naturopathic oncologists used this very method to try to define priorities in naturopathic oncology. If you want the details of how the Delphi method works I discussed them in deconstructing the nonsense that naturopaths laid down about their quack specialty using the Delphi method. The CliffsNotes version is that the Delphi method entails a using a group of experts to answer a question. The experts anonymously reply to questionnaires and subsequently receive feedback in the form of the statistical representation of the group response, after which the process repeats itself until something resembling a consensus is arrived at. The way Witt et al did this is described:

> A two-round Delphi process was then employed to further refine and gain consensus regarding the new definition. In the first round, the revised definition was distributed via an online survey (software SoSciSurvey [7]) to SIO board members as well as to a convenience sample of experts. The experts—oncologists, integrative oncology clinicians, and/or researchers from North America, Europe, and Asia—were contacted by the SIO board members. Based on first round feedback, the definition was revised and distributed again through an online survey to the full membership of SIO, with subsequent ratings and comments used to inform the final version of the definition. Data from both surveys were analyzed using descriptive statistics. Content analysis (8) was applied to the open-ended responses to identify any themes or concepts.

So, after this literature search and Delphi method, what did Witt et al find?

Defining “integrative oncology”

As a result of their literature search and two-round Delphi process, Witt et al found many definitions of “integrative medicine” and “integrative oncology” in the literature, which resulted in the following thematic suggestions:

- evidence-based/evidence-informed/evidence-guided/using best available evidence (14 of 20);
- accompanying conventional cancer treatment (18 of 20);
- addressing outcomes such as well-being, body, and mind-spirit, as well as physical, psychological, and spiritual quality of life (seven of 20);
- focused on health and not only on medicine (three of 20);
- provided by a team of health care providers/multidisciplinary/interdisciplinary (four of 20);
- patient-centered/personalized, individualized/whole person (two of 20).

The writing group, which consisted of “members with different professional/disciplinary backgrounds (ie, medical oncology, radiation

oncology, surgical oncology, nursing, patient advocacy, psychology, psycho-oncology, epidemiology, integrative medicine, health policy),” added these additional suggestions:

- type of interventions (mind-body therapies, natural products, lifestyle changes);
- beyond provision of health care (information, translation of evidence, identification of beliefs, values and preferences, empowerment).

The initial definition of integrative oncology developed by the group thus read:

> Integrative oncology is a patient-centered (theme 6), evidence-informed (theme 1) approach to health care (theme 4) that uses mind-body therapies, natural products, and lifestyle modification (theme 7) as adjunct to conventional cancer treatments (theme 2) and is ideally provided by a multidisciplinary team of care providers (theme 5). Integrative oncology aims to increase well-being of mind, body, and spirit (theme 3) and to provide patients with skills enabling them to help themselves during and beyond cancer treatment (theme 8).

After the two rounds of Delphi method, though, the group perceived that some changes were required:

> Overall, the comments on the second Delphi survey were positive, but the suggestions were quite heterogeneous. Two-thirds of suggestions focused on what were perceived to be missing interventions, and it became clear that therapies such as acupuncture and massage were not well represented in the definition. As a consequence, the definition was revised using the umbrella term “mind and body practices,” which is used by the National Center for Complementary and Integrative Health in the United States. This term includes mind-based techniques such as meditation and hypnosis, as well as manual techniques such as acupuncture and massage (9). One respondent mentioned that “health care” encompassed a broader area than integrative oncology, and the decision was made to be more focused and to use the term “cancer care” in the revised version. Another respondent also suggested that the phrase “approach to cancer care” could be misleading and not specific enough

> as a field of care or medical specialty. Integrative oncology is more than just an approach to overall cancer care; it has been the focus of a professional organization for more than 10 years and is an established field in its own right. During the review process, it was noted that cancer prevention was not included in the definition. Because the ultimate goal of many integrative oncology behaviors is cancer prevention and control, the definition was modified to include prevention.

I've discussed before how quackery like the theatrical placebo known as acupuncture has mysteriously been subsumed into "mind and body practices". Personally, I've always suspected that this was to hide the quackery of acupuncture with more benign modalities (such as massage) that, whether medically they can treat anything, generally do no harm, and can certainly feel good, thus improving quality of life. After all, given that the rationale in traditional Chinese medicine for acupuncture is that sticking the needles into specific "meridians" can redirect the flow of qi (life energy) for healing effect, acupuncture could easily be classified as a form of energy healing.

To the degree that integrative oncology sticks with science- and evidence-based tests and treatments, my main objection to it is that it's not necessary. Nutrition, exercise, and other lifestyle-based interventions are already a part of science-based medicine. I like to cite, for instance, evidence-based recommendations for the treatment of hypertension and type II diabetes, both of which emphasize, except for severe cases, dietary modifications, exercise, and weight loss as the first interventions to attempt before placing the patient on medications.

To paraphrase Harriet Hall, what is good about integrative oncology (or medicine) is not unique to it. Continuing the paraphrase, unfortunately, what is unique to integrative oncology is not good, and the SIO definition obscures or neglects to mention these unique (and not good) aspects.

What the SIO left out

If you read the full article, it should become very apparent that its authors

want desperately to convince the reader that integrative oncology is completely evidence-based. Sure, the SIO admits naturopaths and even elects them as the organization's president from time to time, never mind that all naturopaths are trained in The One Quackery To Rule Them All, homeopathy, and that the vast majority of naturopaths routinely prescribe homeopathic remedies, which, even the SIO concedes, are rooted in pseudoscience.

I was reminded of this on—where else?—Twitter. I came across a post on the University of Pennsylvania's OncoLink touting reiki in cancer care. Because the link was from 2011, I Tweeted a question to the OncoLink team. Here's the response:

> @gorskon, Reiki is a supportive therapy that can be used in conjunction with treatment. It is not promoted as an alternative to treatment
>
> — OncoLink Team (@OncoLinkTeam) November 2, 2017

If there is a challenger to homeopathy's title of The One Quackery To Rule Them All, reiki would be right up there. It is, as I have described many times before, a form of faith healing that substitutes Eastern religious beliefs for the Christian religious beliefs that usually undergird faith healing in the US.

But it's not just Penn. The Dana Farber Cancer Institute has also gone all in for nonsense:

> 7 Ways Integrative Therapies Help Cancer Patients: https://t.co/bRHYbqhrcy pic.twitter.com/0kVQ4FKW0o
>
> — Dana-Farber (@DanaFarber) August 26, 2017

The slideshow at the link above promotes reiki, reflexology, and acupuncture:

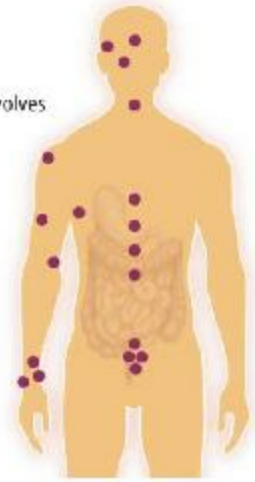
DANA-FARBER CANCER INSTITUTE
Discover. Care. Believe

7 WAYS INTEGRATIVE THERAPIES CAN HELP CANCER PATIENTS

1. ACUPUNCTURE

Acupuncture is a standard practice in Chinese medicine which involves gently inserting hair-thin needles into the skin at specific points. Acupuncture has been shown to:

- Reduce post-operative nausea and vomiting
- Decrease anxiety
- Treat pain and loss of nerve sensation
- Relieve joint pain
- Help relieve chronic pain



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Acupuncture is nothing more than a theatrical placebo, whose action has never been convincingly shown to be greater than that of placebo controls. Yet Dana Farber Cancer Center thinks acupuncture is science-based.

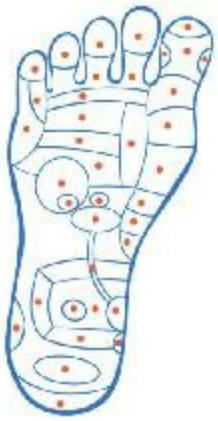
DANA-FARBER CANCER INSTITUTE
Discover. Care. Believe

7 WAYS INTEGRATIVE THERAPIES CAN HELP CANCER PATIENTS

3. REFLEXOLOGY

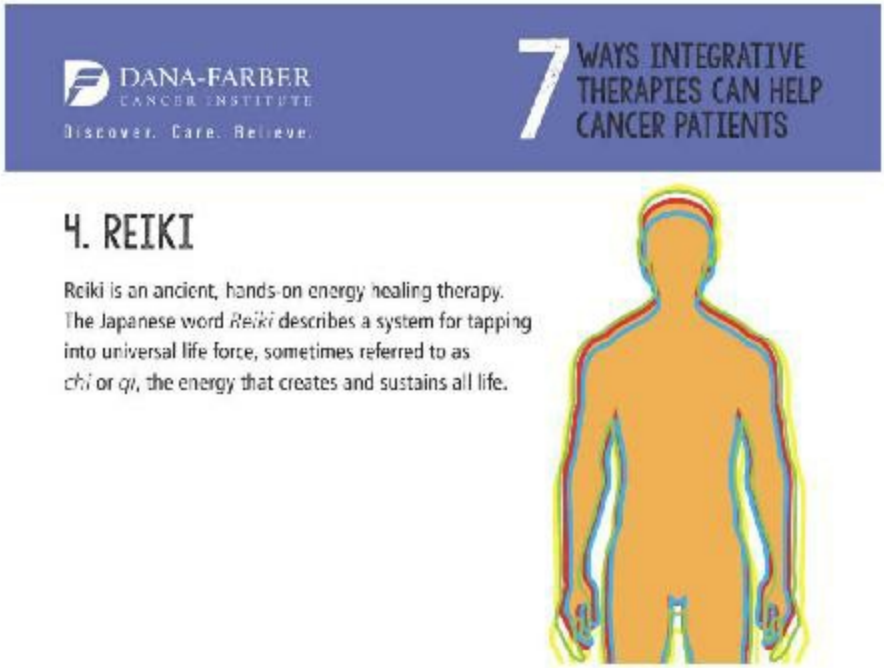
Reflexology is the application of pressure to areas on the feet, hands, and outer ears. The theory behind reflexology is that these areas correspond to organs and systems in the body. Patients have found that reflexology can:

- Promote relaxation and comfort
- Help with treatment symptoms like fatigue and nausea



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Reflexology posits the existence of physiologic or anatomic links between organs and body parts and areas on the soles of the feet and palms of the hand. Yet Dana Farber Cancer Center thinks this is science-based.



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Reiki masters claim to be able to heal by channeling energy into the patient from the "universal source." Replace "universal source" with "God" or "Jesus," and it becomes obvious that reiki is a form of faith healing that replaces Christian beliefs with Eastern mysticisms. Yet Dana Farber Cancer Center thinks it's science-based.

Of course, I've pointed out how oblivious the SIO is to the modalities that are really being "integrated" into oncology through integrative oncology just through the obliviousness of the SIO leadership to what naturopathy really is. As I've said before, if the SIO were really serious about being evidence-based, it would immediately purge itself of all naturopaths. It's not, though. Its leadership up in the ivory towers of medical academia can delude themselves into thinking integrative oncology is totally evidence based, because they manage to ignore the quackery that is "integrated" along with the lifestyle-, exercise-, nutrition-, and meditation-based modalities to which they love to point.

I can’t help but point out a few more examples of the quackery that goes along with integrative oncology. At UC-Irvine and the Cleveland Clinic, there’s homeopathy. At the University of Arizona Cancer Center, there was reiki, at least until a faculty member whose child developed cancer and was treated there made a stink. There’s also more energy medicine quackery, this time in the chemotherapy suite, at Georgetown University, as well as cupping, which is also pure quackery. There’s functional medicine at the Cleveland Clinic, George Washington University, University of Kansas, and, well, seemingly almost everywhere at any medical center with an integrative medicine program. If you want an idea of how bad functional medicine is, just check out this case report of functional medicine used for a patient with inflammatory breast cancer. This is what integrative oncology *really* involves.

It is also this quackery that the SIO definition of “integrative oncology” does its best to obscure or ignore. If the SIO is truly serious about being science- and evidence-based, it needs to speak out strongly and now against naturopathy and the various forms of quackery that have found their way into academic medical centers, of which, I assure you, the above is but a small sampling. It won’t, though. The quackery is why integrative medicine and oncology exist in the first place. Without the quackery, CAM (or integrative medicine or oncology) becomes completely unnecessary as a field.

Science Based Medicine

周日, 05 11月 2017

Science Based Medicine

[周日, 05 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **The American Chiropractic Association Answers Crislip's Call, Joins the Choosing Wisely Campaign** [周五, 03 11月 20:00]
  The Choosing Wisely campaign has invited the largest chiropractic organization in the United States to publish a list of interventions to avoid. The results, while not entirely without merit, consist of redundant or unnecessary recommendations. And there is a glaring absence of recommendations to avoid any of the blatant pseudoscience commonly practiced by chiropractors.
- **Liver cancer, naturally** [周四, 02 11月 19:30]
  Aristolochic acid, a highly toxic substance naturally found in some traditional herbal medicines, may be a significant cause of liver cancer.
- **ASEA – Still Selling Snake Oil** [周三, 01 11月 20:49]
  ASEAs marketing practices, in my opinion, are clearly deceptive. They use a lot of pseudoscientific claims representing the epitome of supplement industry misdirection and obfuscation. They use science as a marketing tool, not as a method for legitimately advancing our knowledge or answering questions about the efficacy of specific interventions.

Three years ago, Mark Crislip closed a post discussing the ABIM Foundation's Choosing Wisely initiative with the following thought:

> I wonder if a chiropractor could come up with five standards treatments in chiropractic to be avoided…

Well, now they've finally gone and done it, with results that, while not entirely without merit, are a bit off the mark in my opinion.

Choosing Wisely and chiropractic

For the sake of further discussion, let's all just agree to ignore the fact, also pointed out by Dr. Crislip in his post, that chiropractic as a profession doesn't exactly stand up to the scrutiny of the campaign's criteria:

> *Choosing Wisely* aims to promote conversations between clinicians and patients by helping patients choose care that is:
>
> - Supported by evidence
> - Not duplicative of other tests or procedures already received
> - Free from harm
> - Truly necessary

Of course to be fair, no medical intervention is completely "free from harm", but I assume that what the ABIM Foundation actually means is that interventions should have a favorable risk to benefit assessment. This is arguably not the case when assessing chiropractic as a whole. While not all of the treatments I prescribe are based on robust randomized controlled trials, they are "supported by evidence" in the vast majority of cases, and often by very good evidence. Chiropractic doesn't really bring anything original to the table that passes this test.

There are similar issues with the phrase "truly necessary", whatever that means. Many medical interventions aren't "truly necessary" in my opinion. Other Choosing Wisely lists cover a number of these, but there are also tests

and treatments that may have value while perhaps not meeting this criterion absolutely depending on who is assessing the scene. But again, being charitable, I assume that the ABIM Foundation is focusing on common interventions for common human ailments that don't tend to improve objective outcomes.

Specific treatments provided by a chiropractor might provide some objective benefit for a small sliver of musculoskeletal complaints, with those unique to chiropractic being the least helpful. But whatever improvement that can be attributed to visiting a chiropractor isn't better than more conventional approaches, such as physical therapy or recommendations from a patient's primary care provider for exercise, stretching, massage, etc. These approaches come with considerably less baggage and aren't as likely to be accompanied by pseudoscience or anti-vaccine propaganda.

The Choosing Wisely lists published by participating organizations aren't meant to serve as treatment guidelines, of course. Instead, they are intended to encourage a conversation around whether or not the listed interventions are a good idea, or if they may put patients at risk of more harm than benefit. Unfortunately, in my opinion, they have largely gone unnoticed by medical providers and the general public. I am confident that the list of questionable chiropractic interventions will be similarly ignored by practitioners.

The ACA's list

The list in question, released in August, comes from the American Chiropractic Association (ACA). The ACA claims 15,000 members, which is less than a quarter of practicing chiropractors, and recognizes 11 specialty areas, such as chiropractic acupuncture, pediatrics, diagnosis and management of internal disorders, and forensic sciences. It describes itself with typical grandeur:

> The American Chiropractic Association (ACA) is the largest professional chiropractic organization in the United States. ACA attracts the most principled and accomplished chiropractors, who understand that it takes more to be called an ACA chiropractor.

> We are leading our profession in the most constructive and far-reaching ways — by working hand in hand with other health care professionals, by lobbying for pro-chiropractic legislation and policies, by supporting meaningful research and by using that research to inform our treatment practices.
>
> We also provide professional and educational opportunities for all our members and are committed to being a positive and unifying force for the practice of modern chiropractic.

What does it take to called "an ACA chiropractor"? Membership requirements consist of being a licensed chiropractor in the United States and paying yearly dues. The ACA even goes so far as to state that they do not deny membership to anyone meeting the above qualifications as long as what they do in their practice isn't illegal. In that way, they are similar to the American Academy of Pediatrics, which even allows pediatricians who are blatantly anti-vaccine to be members in good standing.

Here are the five things that chiropractors and their patients should question according to the ACA:

Do not obtain spinal imaging for patients with acute low-back pain during the six (6) weeks after onset in the absence of red flags.

What red flags, you ask? The ACA mentions "history of cancer, fracture or suspected fracture based on clinical history, progressive neurologic symptoms and infection, as well as conditions that potentially preclude a dynamic thrust to the spine, such as osteopenia, osteoporosis, axial spondyloarthritis and tumors". I would argue that if you have any of these red flags, you should not be under the care of a chiropractor. There isn't any evidence to support superiority of chiropractic care to conventional approaches for acute low-back pain anyway.

Do not perform repeat imaging to monitor patients'

progress.

They list idiopathic scoliosis as an exception, despite the fact that their own research shows no good evidence to support chiropractic management of this condition. I agree with this recommendation, and the reasoning of the ACA in this case is sound. I'm just not holding my breath while waiting to see if this will change anything, however.

Avoid protracted use of passive or palliative physical therapeutic modalities for low-back pain disorders unless they support the goal(s) of an active treatment plan.

In other words, commonly recommended interventions like heat, ultrasound, and electrical stimulation, shouldn't be used in isolation because they don't provide much benefit. The absolute worst thing you can do to prevent or treat lower back pain, which virtually all humans will experience at some point in their lifetime thanks to evolution, is nothing. General physical activity and back specific exercises are key, and in no way unique to chiropractic.

I don't think you will find many chiropractors not recommending an exercise regimen for lower back pain disorders, so this item is a bit odd. You also won't find many that won't provide some kind of spinal manipulation, because that's their thing that they do. In this section, the ACA writes that physical activity and back exercises "may lead to better outcomes when combined with spinal manipulation." In reality, spinal manipulation is more like multiplying by one. It changes nothing for the long term outcome.

Do not provide long-term pain management without a psychosocial screening or assessment.

Chronic pain disorders often have a psychosocial component. Chronic pain can cause or be caused/exacerbated by anxiety and depression, for example.

Some patients are at risk for the development of chronic pain because of a variety of psychosocial factors and chiropractors are not trained to evaluate or manage them. The ACA recommends that chiropractors use a screening tool and refer when necessary because the ACA imagines chiropractors to be primary care providers.

Do not prescribe lumbar supports or braces for the long-term treatment or prevention of low-back pain.

Another odd inclusion. Chiropractors simply aren't out there putting people in back braces for long periods of time for treatment or prevention of back pain. I was easily able to find that this recommendation is already widely accepted. Meanwhile, the ACA is inviting speakers to their conferences to promote nonsense like the Activator Method.

The ACA press release announcing their participation in Choosing Wisely is interesting. They point out that multiple other organizations already participating have included recommendations to avoid spinal imaging for acute lower back pain. It's a solid recommendation, but instead of actually attempting to show a commitment to change by pointing out some of the abject nonsense they have supported sans evidence, they went the safe route. And in the press release they essentially give their members enough wiggle room that they can continue obtaining frequent spinal films without losing any sleep.

My favorite quote involves the practice of "defensive medicine":

> As with many of our colleagues in the health care professions, we have learned from experience to practice "defensive medicine." This perspective may be even more deeply ingrained within the chiropractic profession based on our prior experiences with bias and/or lack of understanding regarding chiropractic care. As an example, just look how long it took before Choosing Wisely® was even willing to consider a chiropractic list!

So do chiropractors practice defensively, which implies a concern for facing a malpractice suit, or not? It would appear that the latter is the case when you consider how often they point out how undeniably safe chiropractic is. Often this is done in the context of attacking conventional medical care. It's also unclear to me how the medical community's lack of "understanding regarding chiropractic care" encourages defensive practice.

Conclusion: The ABIM did not Choose Wisely

How does the ACA describe chiropractic on the Choosing Wisely website? Just as you would expect them to, of course. Remember though that this is an organization that is fighting for chiropractors to be considered primary care physicians complete with the right to prescribe medications.

> Chiropractors focus on disorders of the musculoskeletal system and the nervous system, and the effects of these disorders on general health and function. Chiropractic services are used most often to treat conditions such as back pain, neck pain, pain in the joints of the arms or legs, and headaches. Widely known for their expertise in spinal manipulation, chiropractors practice a hands-on, drug-free approach to health care that includes patient examination, diagnosis and treatment.

The ABIM Foundation is very likely completely ignorant of both the history and the current reality of the chiropractic profession. Frankly I think it's ridiculous that a chiropractic organization was invited to participate. We certainly have come a long way from Wilk v. AMA, haven't we?

This is just another example, in a very long line, of the undeserved legitimization of alternative medicine that will serve as more of a marketing purpose than as a means of improving chiropractic practice. All that the ACA has done is provide a list of redundant or unnecessary recommendations. And the few chiropractors who already avoid excessive spinal imaging will continue to do so, while the vast majority will compartmentalize these "suggestions" and carry on as is.

Extras

- Here is a response to the ACA Choosing Wisely list from the International Chiropractic Association.
- Here is an ACA video describing the benefits of pediatric chiropractic. In March of 2017, the ACA reaffirmed its public policy on chiropractors as primary care providers. This policy includes the following:

> Doctors of chiropractic also recommend and manage dietary changes, nutritional interventions, botanical medicines, homeopathic medicines, acupuncture and other services when indicated.

The ACA, while not overtly anti-vaccine in policy, supports conscience waivers.

Not all cancers affect all populations equally. Liver cancer is the fifth-most common cancer worldwide, but the prevalence varies widely. Liver cancer cases skew heavily to less developed regions of the world, where 83% of cases are found – it's over six times more common there than in Northern Europe, for example. In Asia, the high rates of liver cancer have been linked to hepatitis B and C, which is widespread, and a proven cause of cancer. And liver cancer continues to strike Asian American and Pacific Islanders more than any other American ethnic group as well, where hepatitis continues to circulate in the population. Now there's new evidence to suggest that a substance found in some traditional Chinese medicines may also be causing liver cancer. They're called aristolochic acids, and they illustrate, with a substantial body count, that what's natural isn't necessarily healthy or good.

What are Aristolochic acids?

In the early 1990's a strange cluster of acute, end-stage renal disease appeared in women in Belgium. It was determined that all had been exposed to the chemical aristolochic acid (AA) at a weight loss clinic, due to the consumption of Chinese herbs which contained natural AA. Approximately one third of the more than 300 cases have subsequently required a kidney transplant, and cancers of the urothelial tract in this group have also been widespread. In the Balkans, low level exposure to AA via flour consumption that contains seeds from *Aristolochia clematitis* is believed to be responsible for what is now called Balkan-endemic nephropathy. Subsequent study that was initiated after the Belgian case identified that that AA is responsible for tumour development and for activating destructive fibrotic changes in the kidney. For over a decade now it has been well established that AA is a nephrotoxin and a powerful carcinogen with a short "latency period", in that it causes permanently damage, quickly. What's remarkable is that none of this was known until the 1990s despite "thousands of years" of use as a traditional medicine. As Steven Novella noted in a past post on aristolochic acid and urinary tract cancer:

> This example just highlights the fact that widespread use of an herbal

> product, or any treatment, is not sufficient to ensure that it is safe, or even that it is effective. Common use may be enough to detect immediate or obvious effects, but not increased risk of developing disease over time. That requires careful epidemiology or specific clinical studies. We know about the risks of prescription drugs only because they are studied, and then tracked once they are on the market. Without similar study and tracking there is simply no way to know about the risks of herbal products. Relying upon "generally recognized as safe" is folly.

While herbal remedies that contain AA are now banned in many countries, AA-induced kidney damage and related cancers continues to appear worldwide. As AA's cancer-causing effects have now been widely studied, the distinct way that they damage cells has been described as a sort of "signature" that is easily identifiable in tumour samples. This brings us to this new study of liver cancers attributed to AA, which have been less closely associated with AA. This study used that unique "signature" to look for AA exposure.

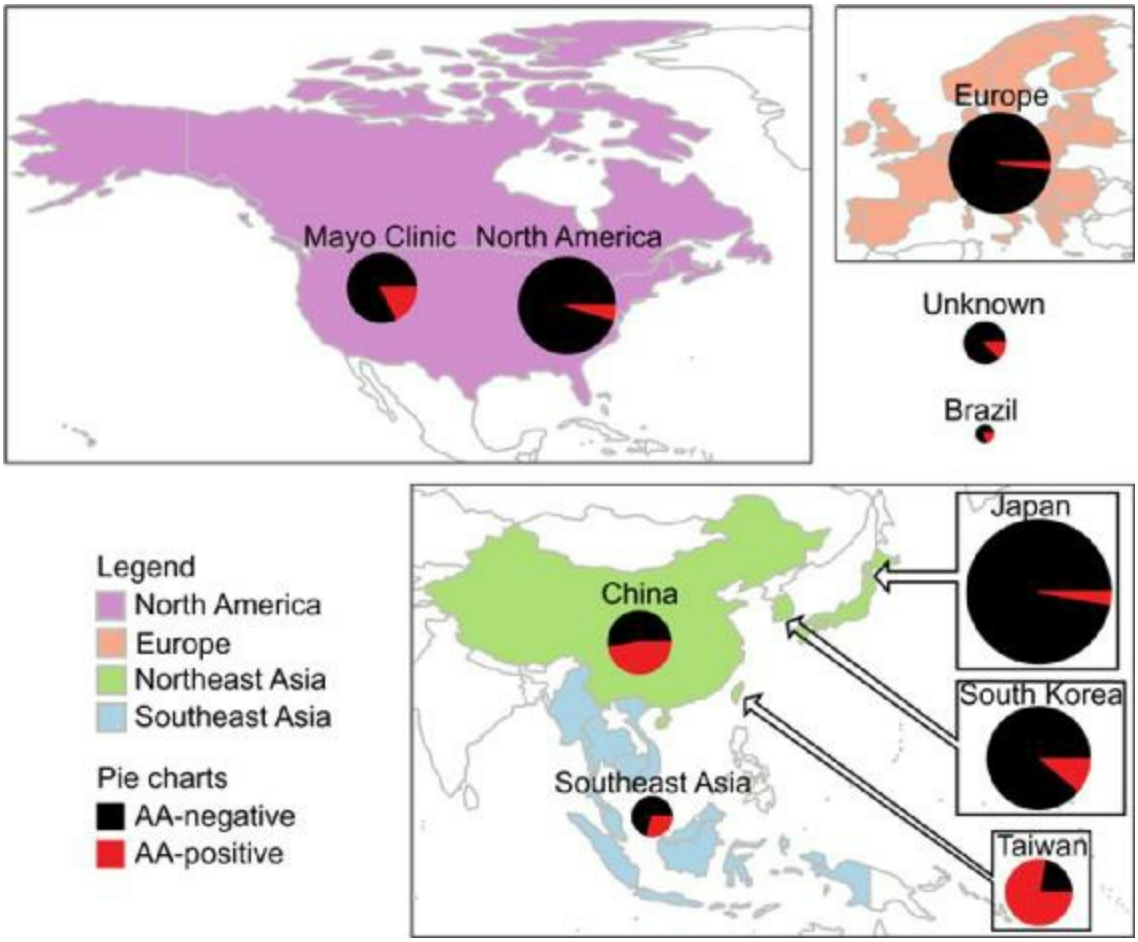
Aristolochic acids and liver cancers

There is good evidence to show that the consumption of AA-containing products in Taiwan has been widespread through the use of prescribed herbal medicines. The paper is entitled "Aristolochic acids and their derivatives are widely implicated in liver cancers in Taiwan and throughout Asia" and it's from Alvin Ng and associates, published in *Science Translational Medicine* in October, 2017. This was a retrospective analysis of hepatocellular carcinomas (HCC, liver cancer in lay terms) and patients were included if they (1) had true HCC (2) there was sufficient DNA available from a sample of the tumour. 98 HCCs from Taiwan hospitals were studied based on whole-exome sequencing and mutation identification. They looked for the distinctive way in which AA causes mutations. The researchers subsequently examined 1,400 HCCs from other regions in the world. The final analysis was as follows:

- Taiwan: 78% of tumours had evidence of AA exposure

- China: 47% of tumours had evidence of AA exposure
- Southeast Asia: 29% of tumours had evidence of AA exposure
- Korea: 13% of tumours had evidence of AA exposure
- Japan: 2.7% of tumours had evidence of AA exposure
- North America: 4.8% of tumours (in one hospital, 22% of 87 patients, all of Asian ancestry, had evidence of AA exposure)
- Europe: 1.7% of tumours had evidence of AA exposure

Here is the global breakdown, with the red portion illustrating the proportion of tumours that were linked to AA exposure:



Global distribution of mutagenesis associated with aristolochic acid and derivatives in liver cancer.

Reducing your risk of kidney and liver

cancer

Herbal remedies are popular worldwide. In China and other countries in Asia, there is strong support for, and belief in “traditional” Chinese medicine despite the fact that it is neither truly traditional (as it is now promoted), nor particularly effective. This new analysis shows that the use of (or exposure to) AA is widespread in some parts of the world, and appears to be be a cause in a substantial numbers of liver cancers. The authors noted that the presence of AA-associated cancer does not appear to be declining in Taiwan, despite the banning of some AA-containing herbs in 2003. This may be due to a lag effect (like cancer and smoking) but may also be due to continued exposure to, or consumption of, AA-containing products.

If you’re a user of traditional Chinese medicine, avoiding AA is easier said than done, unless you have impeccable knowledge of herbs, their origins, and the supply chains you’re getting your products from. I’ve blogged before about TCM, noting that contamination is common. Mislabelling of products also appears to be widespread, suggesting that rigorous and credible testing of final products may be the only way consumers can be assured they’re avoiding AA in the products they buy. The linkage of AA to kidney damage, and the evolving story of its cancer-causing potential illustrates that even widespread use of a product for hundreds (or thousands) of years give no automatic assurance of safety. If it were not for the Belgian weight loss clinic kidney failure cluster, the widespread toxicity of AA may not even be known today.

ASEA - Still Selling Snake Oil - Science-Based Medicine

We often examine the claims made by companies or individuals for their health products, especially those we feel are making dubious claims based on questionable science. In 2012 Harriet Hall wrote an excellent review of one multi-level marketing company, ASEA, who are basically selling salt water with a load of dubious pseudoscientific claims. ASEA is just about a perfect example of everything we try to warn consumers about when it comes to dubious supplements and the inadequacies of current regulations.

When we post such reviews it is not uncommon for the company to give us push back, and it is much more likely if that company sells through multi-level marketing (which is a scam unto itself). We recently received an e-mail from the "ASEA Team" who were not happy about Harriet's review. They asked us to revisit our review (be careful what you wish for), concluding:

> Bottom Line for our part:
>
> The criticism of ASEA made by Mr. Hall [*sic*] is not constructive and Author's points of view are not based on decent and verifiable facts. On the contrary, we have provided you with reliable information that is proven by the documentation. So, the article is misleading and deceives your website's auditory and our potential and current customers. We are sure that after a deep consideration you will come to a conclusion and agree with us that it would be best to delete the article. Thank you.
>
> Respectfully,
>
> ASEA team.

After deep consideration, and re-review of the ASEA current website, I have come to the personal conclusion (and hope they will agree) that ASEA is selling quackery and nonsense with misleading claims designed to defraud

both their customers and their sales agents (who often overlap). I suspect there is a combination of (financially) motivated reasoning and scientific illiteracy on their part, so I will explain again why I have come to this conclusion.

Let's take their points in the ASEA team e-mail to SBM. They begin by objecting to Harriet's (who they refer to as male throughout their letter) listing of the claims they were making on their website at the time:

> ASEA allegedly:
>
> - Promotes enhanced immune function
> - Supports the vital activity of cellular communication
> - Provides superior "support" to athletes
> - Boosts efficiency of the body's own antioxidants by 500%
> - Protects against free radical damage

Their "counterpoint":

> This information is out of date and does not correspond to reality, you can not even find these statements up on our website anymore. We have changed the formula, carefully tested it out and conducted several studies that proved that ASEA products have been shown to signal the activation of genetic pathways or affect genes that:
>
> Improve immune system health;
>
> Help maintain a healthy inflammatory response;
>
> Help maintain cardiovascular health and support arterial elasticity;
>
> Improve gut health and digestive enzyme production;
>
> Modulate hormone balance to support vitality and wellness.

I see, they swapped out one list of dubious claims for a slightly tweaked list of dubious claims. "Promotes enhanced immune function" became "Improve immune system health." And of course if you go to their website the old claims are still there, maybe not in the same location and jot list, but deeper

in the copy or the linked “studies.” They are still claiming it improves cell signaling and increasing the body’s own anti-oxidants.

As a side point, we do not maintain and update every article. That is not standard or practical, nor is it expected, nor do we claim to. Articles are clearly dated, and it should be obvious they are only as current as the date they were posted. We will make corrections if they are pointed out to us or we discover them, and we use our own discretion in deciding whether or not to write an addendum or an updated article.

Their next point was so clueless it gave me the impression that we were dealing with low-level sales people who are not only scientifically illiterate, but had no backing from anyone with legal experience. In response to Harriet pointing out that ASEA is not making disease claims, because they can’t, they responded:

> This statement doesn’t make any sense. As it was correctly noticed, we can’t legally and we actually don’t claim that ASEA is effective for any disease, so there is no point in writing more about this and even mentioning this. There is no information up on our website that says that ASEA would cure cancer or other diseases, however we do say that ASEA improves immune system health as well as has some other beneficial effects for a human being, and as we pinpointed that before, the effects have been verified by several laboratory tests. This statement made by Mr. Hall is far-fetched and offensive and shows that the Author tends to make things up and base his article on assumptions rather than on the facts.

Where do I begin? Here is the very salient point that Harriet was making, and that we make frequently on SBM. The current US regulations allow companies to make “structure-function” claims for their “supplements” without FDA oversight. Products with disease claims are, by definition, drugs and subject to FDA regulation. So what do many supplement companies do? They make structure-function claims that sound as if they may be beneficial for health, and combine those legally allowed claims with other statements about diseases, hoping their potential customers will connect the dots. They are skirting the spirit of the law in order to imply, without directly making, unsupported health claims.

On ASEA's website they make the following claims:

- Decline of cell signaling causes cellular breakdown, which in turn causes a long list of common diseases including autoimmune and cardiovascular disease.
- ASEA improves cell-signaling which decreases cellular breakdown.
- Here is some (not peer-reviewed) science showing that ASEA alters markers which we will choose to interpret as "improving" some aspect of cell signaling or function.

So they do not directly say that ASEA cures any disease, because they know that it is not legal under current regulation, but they do imply that it does through the above chain of claims. That is standard procedure in the dubious corners of the supplement industry (i.e. most of the supplement industry).

Let's get to the scientific studies they use to support their claims. In response to Harriet's review they wrote:

> The studies that Mr. Hall is referring to are old and no longer available on the ASEA website. Instead, we have conducted other studies that proved the effect of the ASEA products as well as their safety.

So, were those previous studies not valid? Science is cumulative. We don't just scrub "old" studies from the record and replace them with new studies. In my opinion that reveals the marketing mentality of the "ASEA team". Studies are not used to determine if their product works, but to support their marketing claims that it does work.

As Harriet pointed out, their studies are not being performed by academic scientists and published in peer-reviewed journals. They are being outsourced to third party research companies for hire. There is no paper-trail of research that would lead an honest scientist to the conclusions that ASEA is now selling. They appear to have started with their product and are backfilling in essentially worthless studies (as far as clinical claims go) to support their marketing.

Perhaps the biggest problem with ASEA's "research" is that they don't actually address their implied clinical claims. In other words – there are no

studies that directly show that ASEA will improve your health – let alone multiple independently replicated rigorous studies published in peer-reviewed journals.

Their current marketing focuses heavily on the claim that ASEA increases natural antioxidants in the body. Antioxidants are currently very popular, having been given a health halo by two decades of heavy marketing. However, the real science tells a different story. In their scientific summary they write:

> Oxidative damage has been implicated in aging and agedependent diseases, including cardiovascular disease, cancer, neurodegenerative disorders, and other chronic conditions. If the generation of free radicals exceeds the protective effects of antioxidants and some co-factors, this can cause oxidative damage.

That is the simplistic story that the anti-oxidant industry is selling, but it is nonsense. Essentially they are assuming that increasing antioxidant activity (even assuming that ASEA does so, which I doubt) must be a good thing. This turns out to be a naive assumption. A homeostatic balance between oxygen free radicals and antioxidants evolved to optimality, unless adversely affected by a disease state such as a genetic mutation. There is no reason to think that artificially disrupting this natural homeostasis would be a good thing. In fact, the evidence has shown that actual antioxidants taken in large amounts are bad for your health. Our bodies use free radicals as part of the immune system, to kill invading cells, and as important signaling molecules. Blocking free radicals in a healthy person can actual cause harm.

The same is true of immune function, which naturally exists in a carefully-balanced state. ASEA marketing naively assumes that increasing any arbitrary marker of immune function equals “improving” immune function. If you have an auto-immune disease, increasing immune function would be a bad thing.

This is the core fallacy of the entire supplement industry, which assumes that you can “improve” the function of an evolved homeostatic system by simply pushing it in one direction. This often leads to contradictory claims, such as some supplements claiming to increase oxygen while others claim to be anti-

oxidants.

Finally, Harriet appropriately asked what was in ASEA anyway. It appears to be just salt and water, and ASEA makes the pseudoscientific claim that the salt water molecules have been arranged somehow into these redox signaling molecules. They respond:

> As for what the components are, this is a confidential information. We have spent a lot of time and resources coming up with the idea as well as setting it all in motion.

Sorry, but science requires transparency. You cannot pretend to be scientific and then simultaneously state that your core claim is a secret. This is especially true when that core claim makes no scientific sense. It is not an extrapolation of existing scientific research or established principles. In fact, their core claim sounds like utter nonsense, so simply saying that it is a secret does not inspire confidence.

Far from taking down Harriet's original review of ASEA and their claims, her assessment deserves to be updated and amplified. ASEAs marketing practices, in my opinion, are clearly deceptive. They use a lot of pseudoscientific claims representing the epitome of supplement industry misdirection and obfuscation. They use science as a marketing tool, not as a method for legitimately advancing our knowledge or answering questions about the efficacy of specific interventions.

I am amused that they chose to e-mail us with their juvenile analysis and requests. That may suggest they are more naïve than calculating, but it really doesn't matter. They are selling a product with health claims. They have the responsibility not to deceive their customers, and I do not feel as if they have met their burden for due diligence. They may have from a regulatory perspective, but only because current regulations are horrifically inadequate. But they certainly haven't from a moral or scientific perspective.

Science Based Medicine

周日, 12 11月 2017

Science Based Medicine

[周日, 12 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Another “Chronic Lyme” VIP disciplined by NY medical authorities: Bernard Raxlen** [周四, 09 11月 14:00]
  Another "Lyme literate" NY physician is on probation and under orders to clean up his act. Will other physicians treating "chronic Lyme" take note?
- **Risks of a Gluten-Free Diet** [周三, 08 11月 21:27]
  Non-Celiac Gluten Sensitivity does not seem to be a real entity according the current evidence, but this has not stopped the gluten-free fad, which may be causing real harm.
- **Update on ASEA, Protandim, and dōTERRA** [周二, 07 11月 16:00]
  Multilevel marketing distributors of dietary supplements and essential oils point to studies that they think constitute evidence that their products work. They don't understand why those studies are inadequate.

Bernard Raxlen, MD, who devotes more than 90% of his practice to the treatment of so-called “chronic Lyme” disease, is on a three-year probation imposed by the New York State Board for Professional Medical Conduct (BPMC). Raxlen agreed to probation and a lengthy list of practice requirements last month following allegations, filed in September, of negligence, incompetence, gross negligence, gross incompetence, and failure to maintain adequate patient records. In doing so, he becomes the second “Lyme literate” VIP disciplined by the NY medical authorities this year. Based on similar charges of professional misconduct, David Cameron, MD, was also put on probation with numerous practice restrictions in June.

Who is Bernard Raxlen, MD?

Raxlen is a psychiatrist and solo “chronic Lyme” practitioner in New York City who says he’s “successfully treated” over 3,500 cases of tick-borne disease in the past 15 years. (He named his practice “Lyme Resource Medical of New York.”) He touts a “total comprehensive treatment program which

utilizes both oral and intravenous (IV) antibiotic treatment." It doesn't come cheap, either. An initial visit with Raxlen costs $1,200 with follow-up visits between $600 and $700. A PICC-line insertion (presumably for long-term antibiotics) is $750 and a "nutritional IV" is $150. He does not accept public or private insurance.

Raxlen has a history of disciplinary actions against him in two states stretching back almost 20 years. In Connecticut, where he was formerly licensed, he was reprimanded and paid a total of $35,000 in civil penalties in two cases arising out of his refusal to provide patient records to the Health Department and insurance companies, even though patients had signed releases. He was also disciplined for inappropriate prescribing and failing to maintain malpractice insurance. Because these infractions constituted professional misconduct in New York as well, he was subject to two disciplinary actions in that state, resulting in censure, reprimand and a $2,500 fine.

According to the *Chicago Tribune*, Raxlen had other professional misconduct charges brought against him by Connecticut authorities but they were ultimately dropped. The *Tribune* reported that, in one case, Raxlen was charged with telling a patient with Lou Gehrig's disease (ALS) that she had Lyme disease and treating her with an illegal drug from Germany. He told the reporter that the relationship between ALS and Lyme was "unclear," even though ALS experts concluded that there was no evidence of a connection.

Per his New York State Department of Health physician profile (just type his name into the search engine), Raxlen completed residency training in psychiatry and lists his specialty as psychiatry, but he is not board certified in any specialty. He did not train in internal medicine, family medicine or pediatrics (although he treats pediatric patients), specialties that normally treat routine Lyme infections. Nor did he train in infectious diseases, experts to whom patients with more complicated cases of Lyme would normally be referred by other practitioners.

Yet, he is described by the International Lyme and Associated Disease Society (ILADS) as a "leader in Lyme disease treatment and research." In fact, he is a founding member of ILADS, former Secretary of the Board, and has taught a number of ILADS courses. He was a co-author of the original

ILADS guidelines for the treatment of tick-borne diseases. Despite their troubling disciplinary status, both he and David Cameron are scheduled to speak at the ILADS Annual Scientific Conference, which starts today in Boston.

How can this be? How can one be a leading light in ILADS with a disciplinary history like Raxlen's and no graduate medical education in infectious diseases?

"Lyme literate" physicians like Raxlen consider "chronic Lyme" a real disease and treat it with long-term antibiotics, sometimes for months to years. Board-certified infectious diseases doctors and other "conventional" physicians do not. These experts agree that "chronic Lyme" is not a real disease and rely on well-conducted trials showing that long-term antibiotics do not substantially improve the outcome for patients diagnosed with so-called "chronic Lyme." Long-term antibiotics can, in fact, result in serious harm, including death, a subject our good friend Orac covered recently over on Respectful Insolence. Orac's post nicely summarizes the differences between real Lyme disease and "chronic Lyme," "a prototypical fake medical diagnosis," and the dangers of long-term antibiotics, as have posts on SBM, here, here, here, and here.

The CDC, the Infectious Diseases Society of America (IDSA), the American Academy of Pediatrics, the American College of Physicians, the *Medical Letter* and the American Academy of Neurology all reject the notion that "chronic Lyme" exists and that long-term antibiotics are an appropriate treatment. There is something called "post-treatment Lyme disease syndrome," but responsible medical authorities do not equate this syndrome with the nebulous symptoms and unvalidated lab tests of "chronic Lyme" and specifically reject the utility long-term antibiotic treatment based on well-conducted clinical trials.

None of this stopped "Lyme literate" doctors from banding together to form ILADS and issuing their own guidelines for the diagnosis and treatment of "chronic Lyme," guidelines based on very low levels of evidence that are accepted only by themselves and, in contrast to the IDSA guidelines, no other professional medical organization. ILADS teaches physicians and other practitioners how to become "Lyme literate." ILADS, again in contrast to

IDSA, is not an ACCME-accredited provider of continuing medical education although, for some inexplicable reason, the Westchester [County, NY] Medical Society has teamed up with ILADS and is using its accrediting authority to grant CME credit for some of the talks (also here) at the ILADS Scientific Conference.

Despite the lack of evidence that "chronic Lyme" is a real disease, and the lack of efficacy as well as the risks of long-term antibiotic treatment, ILADS healthcare providers currently treat more than 100,000 patients with "chronic Lyme" and tick-borne diseases in the USA and around the world. Given media reports that patients can spend $10,000 to $35,000 for treatment, "Lyme literacy" translates into millions of dollars for practitioners.

While it may be profitable, "Lyme literate" doctors risk running afoul of state medical boards. Raxlen is just one among ILADS-trained, "Lyme literate" physicians who have had their medical practices questioned by their peers, up to and including discipline imposed by state authorities (also, here and here).

With that background, let's look at the allegations against Raxlen and the terms of his probation.

The BPMC v. Raxlen

New York's medical misconduct procedures do not require the physician charged to stipulate to any particular acts of misconduct as a condition of settling his case. The physician can, as Raxlen did here, simply state he is unable to "successfully defend against at least one of the acts of misconduct alleged" and agree to the imposition of sanctions. This means the allegations in the state's Statement of Charges were never proven, as it was unnecessary to reach a decision on the factual issues once Raxlen agreed to a settlement. However, per the Office of Professional Medical Conduct's (OPMC) standard procedures, the allegations were based on expert review of Raxlen's patients' records and they remain uncontested by him.

The allegations of misconduct arise out of Raxlen's care of eight patients. As is typical of "chronic Lyme" diagnosis and treatment, patients (whose

identities are protected) presented with a variety of disparate symptoms, such as:

- Patient A: freezing, burning, air hunger, weakness, fatigue, neck pain and intestinal pain.
- Patient E: fatigue, migraines, neck pain, joint pain, numbness and tingling, irritability, sound, light and temperature sensitivity and nonrestorative sleep.
- Patient G: back pain, abdominal pain, feet pain, extremity weakness, anxiety, depression and mood swings.
- Patient H (who got the Hickman catheter and numerous antibiotics mentioned below): mouth, teeth and jaw pain, confusion, forgetfulness, irritability and mood swings.

Diagnosis and treatment of "chronic Lyme" is never mentioned, a wise decision on the part of the BPMC prosecutors in light of the ill-conceived New York law protecting "Lyme literate" doctors from prosecution

> based solely upon the recommendation or provision of a treatment modality by a licensee that is not universally accepted by the medical profession, including but not limited to, varying modalities used in the treatment of lyme disease and other tick-borne diseases.

Instead, the BPMC focused on the fact that Raxlen had failed in the most basic tenets of good medical care, although the fingerprints of "chronic Lyme" diagnosis and treatment, such as failure to consider alternative diagnoses, prescribing IV antibiotics and using a Hickman catheter, are all over the charges. The charges included:

- Repeatedly failing to perform or note in the patient's chart a comprehensive history and appropriate physical exam, including (despite his being a psychiatrist) a psychiatric history, neuropsychological testing and mental health status exam.
- Failing to construct a differential diagnosis and pursue a thorough diagnostic evaluation prior to instituting a treatment plan.
- Inappropriate prescribing, including prescribing Rifampin for a patient on Tamoxifen and prescribing addictive medications prior to a making a diagnosis and without considering non-addictive treatment.

- Inappropriately relying on Applied Kinesiology (which is quackery) to formulate a diagnosis.
- Placement of a Hickman catheter without medical necessity.
- Inappropriately administering antibiotics, including intravenous Invanz, Clindamycin, Flagyl, Rifampin, Minocycline, Mepron, Plaquenil and Bactrim, all of these for *one patient*.
- Failure to present or note in the patient's chart potential risks, benefits, side effects and safe use of prescribed medications.
- Failure to appropriately identify, address, and/or follow-up on potential side effects.
- Treating inappropriately with an ongoing and/or escalating medication regimen without appropriate physical exams and clinical reassessment for consideration of alternative diagnoses and treatment.
- Poor record-keeping.

These allegations resulted in charges of negligence, incompetence, gross negligence, gross incompetence, and failure to maintain adequate patient records. As noted, Raxlen agreed to a three-year probation in addition to the imposition of conditions on his practice. He must, among other things:

- Communicate to patients the nature of his medical role, whether it be a primary care physician responsible for the patient's general medical condition, or for a defined or limited purpose, and/or as a practitioner of a particular medical specialty.
- Obtain written informed consent addressing all aspects of treatment and document same, including documentation of all discussions with the patient about the nature and scope of his evaluation and treatment and the patient's need to pursue "conventional medical care elsewhere."
- Document all histories and physicals.
- Refer patients to primary care physicians, specialists or consultants for further evaluation and/or treatment where medically warranted and provide these physicians with all relevant patient information.
- Cooperate fully with the state in enforcing the Consent Order and timely respond to all state requests for written periodic verification of his compliance and all documents.

What now?

Based on a birthdate of 1938 in his state physician profile, Raxlen is either already, or soon will be, 79 years old. One wonders whether he will continue his practice in face of these new sanctions, although his website is still trying to attract patients.

Sadly, the chronic Lyme lobby responsible for passing the law protecting "Lyme literate" doctors has its sights set on even greater rewards. Several bills are pending in the NY legislature which would force insurers to cover "chronic Lyme" treatment (Assembly Bill 114, Senate Bill 4713, Senate Bill 670). Other bills give them the opportunity to argue in yet another venue for insurance coverage. (Assembly Bill 4863, Senate Bill 2168, Assembly Bill 6927).

In any event, it is commendable that the Board for Professional Medical Conduct has not let New York's unfortunate law get in the way of its prosecuting physicians who take advantage of patients with a diagnosis of "chronic Lyme," no matter how they frame the specific charges. With two leading NY "Lyme literate" physicians now on probation and under strict orders to clean up their acts, it remains to be seen what effect this might have on other "Lyme literate" doctors in the state.

There is a simple reason we strongly promote science-based medicine – it results in the best outcomes for individuals. That is true by definition, since the SBM approach is to use the best evidence and science available in order to determine which interventions result in the best outcomes.

There are numerous ways in which relying upon poor-quality evidence or invalid methods for making health decisions cause potential harm. Often the list is unimaginatively limited to direct physical harm, but that is only the tip of the iceberg. There is financial harm, loss of opportunity to pursue more effective interventions, psychological harm from false hope and being deceived, and sacrifice of quality of life, time, and effort.

Even without direct physical harm, with inert treatments like homeopathy, there is tremendous potential harm from relying upon fake medicine and bad science. But often there is potential physical harm, and even if slight it is not justified if there is no real benefit. Medicine is a game of risk vs benefit – when the benefit is essentially zero, any risk is unacceptable.

The gluten-free fad

Even a small potential harm can be significantly magnified if it is marketed to the general public. The "clean eating" movement, in my opinion, clearly represents such a case. The best overall advice we can give the public regarding healthy eating is to eat a variety of food with plenty of fruits and vegetables and watch overall caloric intake. Unless you have special medical considerations, simply eating a good variety of different kinds of food will take care of most nutritional concerns. It will result in you getting enough of what you need and not too much of anything that can increase your risk.

Having a restricted or narrow diet is always tricky, and runs the risk that you will be getting too little of some key nutrients and may be getting exposed to too much of others. This is the key risk of so-called "fad" diets, because they are often premised on a simplistic notion that specific foods or categories of foods are inherently bad and should be avoided. Therefore any diet which

essentially consists of avoiding certain foods or heavily relying on others is likely to take you away from an optimal diet, and therefore be a net negative for your health.

The recent gluten-free fad is no exception.

As I discuss in detail here, gluten is a composite of two proteins found in wheat, rye, barley, spelt, and related grains. About 1% of the population has an autoimmune reaction to one of the components of gluten (usually gliadin) and eating gluten can cause serious illness (a condition known as celiac disease). For those with celiac disease, avoiding gluten is essential and even a small amount of gluten can cause serious symptoms.

There is a controversy, however, surrounding the alleged existence of so-called non-celiac gluten sensitivity (NCGS). This is a hypothetical condition in which people may have a sensitivity to gluten without forming antibodies to gliadin or meeting the diagnostic criteria for celiac disease. Discovering a new disease is always complex, and requires the identification of something definitive and discrete. We either need to identify a clear clinical syndrome, or some new specific pathology.

For NCGS there is no clear pathology. The entity's legitimacy currently relies on the alleged existence of individuals who do not have celiac disease but have a negative reaction to eating gluten. If, however, we are going to base a new disease purely on clinical history, we need to make sure that the history is accurate and that we are not simply overinterpreting non-specific symptoms or falling victim to confirmation bias.

For example, there are people who feel they have a specific syndrome of sensitivity to electromagnetic waves, despite the absence of any identifiable pathology. However, properly blinded studies show that self-identified sufferers of EM sensitivity cannot tell when they are being exposed to EM waves in a blinded condition.

For alleged NCGS the most salient evidence of its existence as a clinical entity are rechallenge studies. In these studies subjects are challenged with either gluten or placebo, then the gluten is removed, and then they are later rechallenged. If NCGS is a real entity then their symptoms should resolve

when gluten is removed and then return when rechallenged, at a higher frequency when the same is done with a placebo.

A recent systematic review of gluten rechallenge studies did not find significant evidence for NCGS. They conclude:

> The prevalence of NCGS after gluten re-challenge is low, and the percentage of relapse after a gluten or a placebo challenge is similar.

This is a pattern of evidence that is consistent with the null hypothesis, that NCGS does not exist – results are all over the place, with better-controlled studies tending not to show an effect, and on average there is only a tiny signal that does not reach statistical significance. The most parsimonious interpretation of available evidence, therefore, is that NCGS does not exist. Despite this fact, roughly one third of the population report that they are trying to avoid gluten.

What's the harm

What, then, is the potential harm from restricting gluten from the diet in the millions of people who do not have gluten sensitivity? Potentially, all of the things I listed above may contribute to harm.

For many people they have settled on gluten sensitivity to explain real symptoms they may be having. In this case they may be missing the real cause of their symptoms. There is therefore an opportunity cost of making a false diagnosis.

Perhaps most significantly, a gluten-free diet is very difficult. You have to eliminate all wheat and similar grains from the diet. This has become somewhat easier recently as industry is cashing in on the gluten-free fad, but it is still a significant inconvenience and expense and therefore drain on quality of life.

Further – a gluten free diet eliminates a major category of food from the diet. People on a low or gluten-free diet tend to also be low in whole grains. They risk being deficient in iron and folic acid. A recent study linked low-gluten

diets to a higher risk of type-II diabetes.

Avoidance of gluten may also result in a heavy reliance on rice as a staple grain, and this might increase the risk of heavy metal exposure. Again – having a varied diet spreads out exposure to contaminants and toxins as well as maximizing exposure to needed nutrients.

Science over marketing

If we take a scientific approach to the question of NCGS we find that there is no clear evidence that non-celiac gluten sensitivity is a real thing, and that gluten-free diets not only have no benefit for the general public they present health risks. Clearly, however, we need to do a better job of communicating this to the public.

Part of the challenge, however, is that nutritional gurus (who always seem to have something to sell) have a simple and appealing narrative to market. They tell the public that their problems are due to one bad food or type of food they just need to avoid. Or, they market of lifestyle of “clean eating” that is based on the appeal to nature and irrational fear of toxins and chemicals, rather than an even basic understanding of science and evidence.

The science-based position, however, takes time to emerge. It may take a decade or more to do the kinds of studies necessary to effective answer the question about whether or not a new hypothesized clinical entity exists. There are many types of evidence to be considered, and many sub-questions to be addressed. Over time a clear picture will tend to emerge, but in the meantime the health gurus can establish a market for their nonsense. Once their simplistic and marketable narrative gets into the public consciousness it is hard to correct.

I have written critiques of several dietary supplements sold through multilevel marketing (MLM) schemes, and they keep coming back to haunt me. I get testimonials from users who believe they have been cured of every ailment under the sun; and every time another study is done, I get e-mails from distributors who apparently think the new “evidence” will change my mind. Recently I received three more emails about ASEA, one about Protandim, and three about dōTERRA essential oils, asking me to reconsider. I thought this would be a good opportunity to explain why I have not changed my mind and to explain once again what constitutes evidence in science-based medicine.

ASEA

Recently an email from “The ASEA Team” asked us to delete the article I wrote about ASEA in 2012, based on their opinion that it “was not constructive” and “was not based on decent and verifiable facts.” They did not mention two other followup articles I wrote here and here. And they did not directly try to refute most of the points I made in my critique; I think they failed to understand what I was saying. They provided six attachments with

studies they said were “made to prove the effectiveness of ASEA” but those studies didn’t prove any such thing.

Last week Steven Novella answered them very effectively, calling ASEA snake oil and pointing out the deceptive marketing practices of the company, the pseudoscientific nature of their claims, and the worthlessness of the studies they cite.

The claims

The ASEA website currently makes these claims:

> As we age, and as stress and environmental toxins inundate our lives and weaken our defenses, normal cellular function declines, and with it, the body’s ability to produce and maintain a proper balance of redox signaling molecules. ASEA has developed the only technology that can create and stabilize active redox signaling molecules in a consumable form. No matter what your health concern may be, ASEA Redox Supplement can bring your cellular communication to optimal levels, improving the health of every system of your body.

Questions

This brings up several questions:

- How exactly does normal cellular function decline? How would improved cellular communication reverse the decline?
- What is a proper balance of redox signaling molecules? How do they know? How is it measured?
- What active redox molecules are in the product? (They won’t tell us. The label just lists salt and water. In my opinion, if there are redox molecules in ASEA, listing only salt and water constitutes false labeling.)
- What evidence do they have that the product improves health?

What redox molecules?

All they have is a statement from a lab, BioAgilytix, that indirectly measures "biomarkers" of redox levels in ASEA using a fluorescent indicator as a probe for unspecified highly reactive oxygen species. I don't know what that means. There is no direct evidence that redox molecules are present. No other lab has analyzed the product.

Safety

Their claim that the product is safe is based on a brief description of two unpublished studies. In the first study, 106 overweight women took ASEA or placebo for 12 weeks; they reported no adverse effects, (None?! In most studies, even the placebo group typically reports *some* symptoms.) and there were no changes in liver or kidney function tests or complete blood counts. In the second study, an *in vitro* study of cultured eukaryotic cells, the cells "did not register a significant toxic response as measured by a visual assessment of green dye that indicated "nuclear translocation." Based only on this flimsy subjective and *in vitro* evidence, they claimed "ASEA Redox Supplement, orally administered, does not manifest a toxic response or inflammation to exposed tissue." Such thin gruel does not constitute convincing evidence that the safety of the product has been established.

Studies

Before I accept that a treatment works, I want to see human studies published in peer reviewed journals. There are none on their website, but I was able to locate two articles in the *FASEB Journal* here and here.

It quickly became obvious why these are not featured on the company website: they are not full articles, but abstracts from a meeting that were published in a supplement to the journal. One is a human study, the other is in mice (the poor mice were gavaged with ASEA and then run to exhaustion). One of my correspondents claimed that these are peer-reviewed studies, but peer review is not possible when all that is available is an abstract.

As far as I could determine, there have been three studies in humans. One, a small study of 17 cyclists, has been deleted from the web. It was not placebo-controlled. There is an abstract of a similar study of 20 cyclists that did use a placebo control and was double-blinded. It was essentially *negative*: ASEA did not improve time trial performance. They found that it caused a significant shift (good or bad?) in 43 metabolites, but had no apparent influence on traditional biomarkers of inflammation, oxidative stress, or immunity.

The third, most recent human study is the one my true believer correspondents are currently crowing about. They refer to it as a "genetic" study. One of them snarkily commented "It's called science, u should look into it sometime." I did look into it, and I was not impressed. The title is "Initial Gene Study Showed ASEA REDOX Affected Important Signaling Pathway Genes." The company paid Tauret Labs to do the study. It has not been published in a peer-reviewed journal. It was an 8-week double-blind randomized placebo controlled study with 60 participants that measured changes in expression of 5 genes and found statistically significant changes of 20-31% with ASEA. They claim that "These genes are key in the health of the individual and play a vital role in five human health areas and dozens of pathways." Maybe, but they have not demonstrated that human health benefits in any way from these changes in gene expression. Their summary of results states "Effects are non-specific to race, sex or age, and were observed in all populations tested." This conclusion is not supported by their data. The only population tested was 60 individuals, 41% male, 92% Caucasian, average age 35 with age distribution not reported.

Conclusion

The evidence for their claims is indirect and inadequate. Half of all research studies turn out to be wrong. Changes in blood tests might be spurious; they have not been independently replicated. Changes may be statistically significant but not clinically significant. If they want us to believe ASEA causes objective, meaningful improvements in human health, they'll have to do better. They'll have to test directly for meaningful clinical outcomes. And if they want us to believe ASEA contains all those redox signaling molecules,

they'll have to prove it with a direct analysis by an independent lab and name those molecules.

As Steven Novella put it,

> Asea, however, is still a fantastical and unbelievable claim supported by nothing but hype, sales copy, and empty promises. It is salt water. The hand-waving nonsense about redox reactions is incoherent technobabble – the very essence of pseudoscience. What would be convincing is published, peer-reviewed, independent, rigorous scientific studies with clear results. These don't exist. No amount of distraction will change that fact.

Protandim

I have written about Protandim four times, here, here, here, and here.

What is it?

It is a mixture of five dietary supplements (Milk thistle, *Bacopa* extract, Ashwagandha, green tea extract, and turmeric extract) that allegedly stimulates the body to produce its own antioxidants. They claim it is "the only supplement clinically proven to reduce oxidative stress by 40%, slowing down the rate of cell aging to the level of a 20 year old [and they measured this how?]."

An email from a reader

> You really need to up date your studies on this product! There are thousands of people with improved health because of PROTANDIM. For example, my son in law with high blood pressure was able to cut his BP medication in half after only two months on it and after three months, he is off meds completely with normal blood pressure; my daughter suffered for a year with a horrible rash under her arm that

> looked like tree bark. After several visits to her doctor where he prescribed cortisone and antibiotics nothing worked. She finally went to a dermatologist who was shocked to see that she had Granular Parakeratosis a rare skin disease. My daughters case was only the second time she has seen it, and at a follow up visit was told that there is no cure, only palliative care. Three days later the crud came off in her washcloth in the shower, and she had been on PROTANDIM for about two months. See photos. On the after picture you can see a round sore which is from the biopsy. In addition, my husband who has cOPD and had bypass surgery last year, and myself have great, new energy. In addition, my nerve damaged feet and numbness in my right foot have improved by at least 80 per cent after only 5 weeks! For the first time in 15 years or so, I can now feel my right big toe and it is no longer cold, like a piece of granite, and our bad backs have greatly improved. I could go on and on and I don't need someone like you to tell me and thousands of others that it does not work! We are walking human studies for this amazing product! Check out the human studies for liver disease! I am proof it works so you should take another look: in fact go to You Tube PROTANDIM testimonials and see for yourself what this product does when it reduces oxidative stress!

My most recent article was in May 2017, and I'm not aware of any new studies requiring me to "update my studies" in the last six months. The evidence on the website is mainly about Nrf2 protein messengers in general, and studies of Protandim in cell culture (*in vitro*) and in mice. One 2006 human study found changes in lab tests such as TBARS but did not even attempt to look for any clinically meaningful improvement in health outcomes. A second human study in 2016 was negative: It concluded "Protandim® did not (1) alter 5-km running time, (2) lower TBARS at rest (3) raise antioxidant enzyme concentrations compared to placebo (with exception of SOD in those ≥ 35 years old) or, (4) affect quality of life compared to placebo." And another study of patients with alcohol use disorders was also negative. Not only negative but laughable.

Conclusion

Increasing levels of antioxidants could be beneficial or harmful. The only way to know if Protandim improves human health is to do properly designed, placebo-controlled human studies looking for meaningful clinical outcomes.

dōTERRA essential oils

I have written about dōTERRA twice before: here and here.

An email asked me to "Check with Johns Hopkins and the research published about dōTERRA oils. Dr. Nicole Parrish claims that dōTERRA oils have killed three super bugs that synthetics cannot. It is published and the medical world is learning more about essential oils in September." I asked her for links to that research; she never responded.

Another email chastised me for having a "complete scientific mindset." (I thought that was a *good* thing!) She said, "It really is worth looking further into to help people stay healthy." She provided all kinds of testimonials: her dentist and her real estate agent use it, her son and stepson carry the beadlets with them during allergy season, and when her husband got cancer, they used essential oils for diabetes, neuropathy, infections, and asthma. She also chastised me for not mentioning what the Bible says about oils and plants! She believes "science is here to prove God's existence and the Bible can be used for medicinal research." I didn't try to answer her.

An *in vitro* study was done on dog kidney cells infected with influenza virus. Based on their results, they speculated that essential oils *might* be useful in treating humans with influenza (or might not). In my article critiquing that study, I provided some guidelines on how to read research studies that claim to support a product.

A third email said I needed to visit the website again and review the 17 studies published in peer-reviewed journals. I found an *in vitro* study of frankincense and an *in vitro* study of Deep Blue, a mixture of essential oils. There was also an extensive bibliography which included a lot of irrelevant articles along with *in vitro* and animal studies. There were a lot of scattershot preliminary studies on individual oils, but these were seldom if ever followed

by replications or confirmations. My own PubMed search found a few studies supporting the use of an essential-oil-containing mouthrinse, reports of adverse effects of essential oils, some negative studies, and a couple of Cochrane reviews that pointed out the poor methodology of the few studies they found. A 2012 systematic review of aromatherapy concluded "the evidence is not sufficiently convincing that aromatherapy is an effective therapy for any condition."

My correspondent said, "In my opinion, there are too many confirmed reports of improved health & well-being (when using essential oils) to chalk it all up to "hysteria" or "ignorance" or even chance." Her opinion is misguided. The plural of anecdote is not data. Confirmed reports of improved health and well-being, no matter how numerous, are meaningless without a control group. Reports of failures are not systematically collected. Patients may improve for reasons other than the oils: suggestion, placebo effect, social factors, the natural course of the disease, regression to the mean, etc.

Essential oils can be very pleasant to use, and I have no problem with using them as "comfort" measures. And the company website is careful not to make any egregious disease-prevention or -treatment claims. But at their in-home presentations, the distributors feel free to claim that the oils can cure anything and everything, including cancer. These claims are not backed by any science but are illustrated by persuasive anecdotes, touching and heartwarming stories, testimonials from users that the attendees may know personally. Attendees are easily influenced to believe and to buy.

The published evidence for each of dōTERRA's many products is sparse to nonexistent. There *are* clinical studies to support *a few* of the recommended uses, but they are generally poorly designed, uncontrolled, unreplicated, and unconvincing. Research is difficult, because patients can't be blinded to the odors, and mental associations and relaxation could account for most of the observed effects. I remain skeptical of the claims for objective benefits in treating diseases.

Conclusion: No reason to change my mind

Testimonials are notoriously unreliable. These products are not supported by acceptable scientific evidence. I'm *not* saying they *don't* work. No one knows whether they work or not, because they have not been properly tested. I am simply asking for a single standard of evidence, the kind of evidence required to achieve a scientific consensus that any treatment is effective and safe. If they want us to buy their products, they should test them against placebo controls in human studies looking for objective, meaningful improvements in health; and they should get those studies published in reputable peer reviewed journals. In the pharmaceutical industry, only a small percentage of promising candidates survive testing. Considering the huge number of dietary supplement products like these on the market, the chance that any one of them will prove to be truly effective is vanishingly small.

Science Based Medicine

周日, 19 11月 2017

Science Based Medicine

[周日, 19 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Hopelessly Devoted to Woo: TLC and Forbes Bring Us Yet Another Celebrity Healer** [周五, 17 11月 21:00]
  Endorsed by journalists and studied by academic medicine, bogus celebrity energy healer Charlie Goldsmith now has his own television program. In other words, it's just another day at Science-Based Medicine.
- **CAM use leads to delays in appropriate, effective arthritis therapy** [周四, 16 11月 22:00]
  A preference to use CAM before seeking medical advice may be harming patients with inflammatory arthritis.
- **Placebo Myths Debunked** [周三, 15 11月 21:03]
  Placebo treatments are often sold as magical mind-over-matter healing effects, but they are mostly just illusions and non-specific effects.
- **Turpentine, the Fountain of Youth According to Dr. Jennifer Daniels** [周二, 14 11月 16:00]
  Jennifer Daniels says turpentine is the Fountain of Youth, able to cure many ailments, both real and imaginary. It isn't; it's a poison with no recognized benefits for human health.

In recognition of my 100th post on SBM, I was all set to write about some interesting updates on a few of my contributions over the years. But thanks to the machinations of the preternaturally cool Tim Caulfield, author of *The Cure for Everything* and *Is Gwyneth Paltrow Wrong About Everything?*, I was made aware of something that I just couldn't ignore: someone is wrong on the internet. That's right, yet another "energy healer" with bold claims of miracle cures is making the rounds. But this time will be different, apparently.

Remember Adam Dreamhealer? He was the teenage "intuitive healer" that could recognize and manipulate mysterious human energy fields to cure cancer and a whole host of other ailments, even over the phone or after only looking at a photograph of the patient. He claimed to have received his powers from a giant blackbird he met while hiking. Ring a bell? Well, it was a whole thing about a decade ago, just as I was starting my journey on the path of skepticism. Although he is still up to the same tricks as a "naturopathic oncologist", and he will always have a special place in my heart, Dreamhealer has some stiff competition for my favorite celebrity energy healer.

The new kid on the block is Australian energy healer Charlie Goldsmith, and technically he isn't all that new. Orac, who I believe is some kind of protocol droid, wrote about him back in 2015. Goldsmith was just dipping his toe in the water of widespread recognition at that time, getting some press in the form of credulous fluff pieces focusing on the fact that he is Olivia Newton John's nephew and on his involvement in a ridiculous study published in the *Journal of Alternative and Complementary Medicine*. Described as a "feasibility study", it is embarrassingly amateurish, really just a collection of cherry picked anecdotes that did not involve the slightest bit of blinding or control. The authors concluded what anyone remotely familiar with research like this would have expected.

What Caulfield alerted me to this week was the publication of yet another painfully credulous article, this time on the *Forbes Lifestyle* blog. In the piece, Forbes contributor and certified Holistic Health Coach Courtney Porkoláb asks the question "does energy healing work?" and invites readers

to decide for themselves. In a conversation with her on Twitter she was quick to remind me that hers wasn't a scientific article and to imply that she just wanted to "spark conversation." Yet in the article she provides only her gullible acceptance and a series of comments from Goldsmith and a few credentialed believers endorsing the benefits of energy healing and even proposing scientific explanations. There isn't even an attempt at token skepticism.

Porkoláb gushingly discusses Goldsmith as if he is a miracle worker:

> Goldsmith's success rates are undeniably high, having relieved people of all ages, with issues ranging from chronic pain to infections and auto-immune disorders, often in 60 seconds or less.

The article contains numerous absurd assumptions and laughably implausible claims, all in the service of promoting the fact that Goldsmith is now starring in a TLC program documenting his supposed abilities. It isn't alone, of course. This *Daily Mail* article is particularly informative as it provides a clip from the most recent episode. It shows Goldsmith taking advantage of the power of suggestion as he interrogates a 2-year-old child about his symptoms before going through the standard energy healing motions. The kid is adorable but it's pretty ridiculous, and what is really happening should be clear to anyone with a modicum of experience with toddler behavior. The deciphering of the child's unintelligible responses reminded me of how ghost hunters prime listeners when demonstrating EVP.

Orac, which I understand is some kind of prototype U.S. military robot that gained sentience and a powerful sense of skepticism after being struck by lightning, beat me to the punch and wrote an excellent discussion of Goldsmith and the *Forbes* article. Feel free to hop on over and read it. I'll provide a couple of the best quotes myself, however:

> Prior to the studies done in the public eye, Goldsmith spent years healing as many as he could, often those who had been failed by countless doctors and traditional medicine.

Regular readers of SBM know how unreliable claims such as this are. Unless Goldsmith was keeping meticulous records of his healing attempts and

following up to document long term outcomes, these kinds of statements are essentially meaningless. It's very easy with confirmation bias and motivated reasoning to look back over the years and come to the conclusion that you helped a lot of people. It's easy to discount the failures and focus on the apparent successes.

And patients can be "failed by traditional medicine" in numerous ways, many of which don't actually equate to what is being implied. Patients with vague or non-specific symptoms and certain world views often feel like conventional doctors have let them down when they aren't given a specific diagnosis, or when treatment recommendations consist of lifestyle changes or mental health assessments rather than confident assertions and a supposed cure. Often proponents of pseudomedicine convince people that their doctor has failed them by missing the diagnosis of a fictional malady, such as adrenal fatigue.

I found this quote from Goldsmith particularly interesting:

> To be honest, sometimes I'll work on something that—medically—is seemingly simple and not fix it. And something that is medically complex—something medically incurable, for example—that might be quite easy for me.

He chalks this up his healing powers not being an exact art. I see this as exactly what I would expect when all that is being offered is false hope and expectation, and one is counting on various placebo effects to give the appearance of benefit. But again, unless he has been keeping strict records of his encounters, his claims regarding past treatments can't really be assessed. I'm not just going to take his word for it that he has defied our fundamental understanding of human physiology.

The credentialed believers provide some of the most memorable contributions, which you can read about in the above linked post by Orac. These include demonstrations of a lack of understanding of how pain is assessed and treated as well as appeals to quantum physics and "bioenergy". There are also references to the time Gary Schwartz supposedly found a measurable differences in the magnetic fields surrounding the hands of energy healers and to a study on bio-photon emissions after energy healing.

Let’s do the science!

Goldsmith is on a mission to prove that what he does is legitimate and not just theatrical placebo by participating in clinical trials. I already mentioned the one published “study” he participated in above, and he claims to be involved with two more taking place at the same facility. It sounds like more of the same:

> The study presently underway is being undertaken at NYU Lutheran Hospital in New York and employs a qualitative methodology to help understand the experiences of patients who encounter Mr Goldsmith’s practices.

In other words, more anecdotes without proper controls or blinding. According to his website, this study has actually been completed. It’s being written and will be submitted for publication next year. We’ll see. He also claims to be participating in a prospective RCT, again at the same facility, that is currently going through the IRB approval process. Again, we shall see if this actually materializes.

I challenged Goldsmith during a lengthy discussion on Twitter, and he reassured me that his intentions are purely altruistic. He denies financial motivation and simply wants to prove to the world that his gift is real so that science might take the phenomenon seriously. He only wants to help reduce the pain and suffering of others. He has been treating patients for years and, according to Goldsmith, he only went public in order to help entice researchers to do the studies.

I am skeptical of his motivation. History has, time and time again, revealed that believers in highly implausible and unproven therapies don’t really care what the science says. Typically the studies end up having such poor methodology that a positive result is assured, and when proper studies fail to find a true effect, they are ignored. Regardless of the outcome, proponents can point to the fact that studies were even done in the first place as evidence of their pet remedy’s legitimacy.

It is abundantly clear that Goldsmith has already decided that he has the

ability to cure people through energy healing. He didn’t notice something odd and then look to science to determine if it was true. He noticed something was odd and then did it to people with real medical problems for years before agreeing to star in a television program highlighting it. In my opinion, the research angle is just marketing and I’m embarrassed for NYU.

Several weeks ago I summarized the evidence that demonstrates that when you delay cancer chemotherapy and substitute alternative medicine, you die sooner. Thank you to the tireless Edzard Ernst, who identified non-cancer evidence that demonstrates how choosing complementary and alternative medicine (CAM) instead of real medicine, can cause harm. In this case, the example is early inflammatory arthritis (EIA), and what was studied was the relationship between CAM use, and the delay to initiation of medical therapy. Time is of the essence with inflammatory arthritis, as there are medications that can reduce the risk of permanent joint damage. This new paper adds to the accumulated evidence to show that CAM, while it is commonly thought to be harmless, can indeed harm – not only from direct effects, but also from delaying the initiation of proper, effective medical treatment.

What is inflammatory arthritis?

Inflammatory arthritis is a term that describes inflammation of the joints (and other tissues). Inflammatory arthritis can include rheumatoid arthritis, and several other conditions. These are often autoimmune conditions, where your immune system treats its own tissues as foreign, and attacks it. Pain, swelling and tenderness are typical with inflammatory arthritis, and a diagnosis is usually based on a physical examination and laboratory tests. There are now many medications that can treat arthritis, ranging from the non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen and ibuprofen, to disease-modifying anti-rheumatic drugs which include biologic drugs that can be very effective and even put the disease into remission. While inflammation can be treated, joint destruction from arthritis can be permanent, so starting appropriate therapy, quickly, is important to reduce the risk of long-term damage. Today, aggressive treatment early in the course of the disease is considered to be the standard of care, so it is important for new cases to be recognized and referred for specialist assessment as quickly as possible. Barriers to early treatment include patient delays, but also system delays like wait times for referrals. Understanding why patients may not seek treatment is a question that led to this most recent study.

Studying CAM and inflammatory arthritis

Complementary and alternative medicine (CAM) is commonly used in different cultures, including Asian cultures, where traditional Chinese medicine may even be government-endorsed, despite the lack of evidence to show it is an effective system of medicine. When a group of researchers identified that many patients with a new diagnosis of arthritis had tried CAM prior to seeking medical treatment, they hypothesized that CAM may be delaying referral and medical therapy.

This paper is from Manjari Lahiri and colleagues and was published in the *International Journal of Rheumatic Diseases*. Entitled "Use of complementary and alternative medicines is associated with delay to initiation of disease-modifying anti-rheumatic drug therapy in early inflammatory arthritis", this was a prospective survey of patients with EIA. All patients seen at one of two hospitals in Singapore where they were invited to participate. Patients were included if they had a self-reported symptom of EIA, which was defined as inflammation of two or more joints, not caused by trauma. Patients were assessed at 3, 6, and 12 months, then annually for 3 years. All participants completed a nurse-administered questionnaire on demographic, health and lifestyle factors including CAM use. In this study, CAM was defined as the ingestion of tablets, herbs, powders or drinks purported to have medicinal properties. They could be prescribed (e.g., by a practitioner in traditional Chinese medicine) or purchase over the counter. Acupuncture, therapeutic massage and cupping, when used for the purpose of a therapeutic effect where included in the definition of CAM, while exercise (including yoga and tai chi), physiotherapy, and occupational therapy were not considered CAM. (This is among the more accurate delineations of CAM/non-CAM I've seen in a study.)

CAM users delay treatment

For this study, only the baseline (time=0) results were used. Overall, 180 patients were included. The median time from diagnosis to recruitment was 3 weeks. The median age was 51, and 71% of the participants were women.

When stratified by CAM use, Chinese patients more commonly used CAM, and oral tablets/powders and acupuncture were the most common forms of CAM. Full details are in Table 1:

Table 1 Baseline characteristics

Characteristic	Proportion (%) or median (IQR)			P-value
	Overall (n = 180)	CAM users (n = 71)	CAM non users (n = 105)	
Age at diagnosis, years, median (IQR)	51.1 (40.9–59.8)	53.9 (43.8–60.7)	47.3 (40.2–58.3)	0.05
Bottom tertile, 22.3–44.3 years	33.5	25.7	39.0	0.14
Middle tertile, 44.4–57.4 years	33.5	35.1	32.1	
Top tertile, 57.5–81.4 years	33.0	39.2	28.5	
Female	70.5	68.9	71.4	0.72
Race				
Chinese	58.3	82.4	40.9	< 0.001
Malay	18.3	5.4	27.5	
Indian	16.7	8.1	22.9	
Others	6.7	4.0	8.5	
Body mass index	24.3 (21.2–27.6)	24.0 (20.3–26.4)	24.9 (21.3–28.2)	0.25
Non-English speaking	30.2	50.0	16.4	< 0.001
Level of education				
None or primary	21.2	20.3	22.1	0.15
Secondary or vocational	46.1	51.0	40.1	
Diploma or degree	32.4	25.7	37.5	
Ever smokers	26.8	35.1	20.9	0.03
Diagnosis				
Rheumatoid arthritis	83.0	83.8	83.8	0.92
Psoriatic arthritis	12.8	13.5	12.4	
Undifferentiated arthritis	3.3	2.7	3.8	
Symptom duration, weeks‡	16.5 (9.2–26.6)	20.8 (13.1–30.1)	13.7 (8.7–21.8)	0.004
Disease duration, weeks§	3 (0–16.9)	3.2 (0–18)	4 (0–16)	0.25
Sero-positive¶	57.0	62.9	52.9	0.20
RF positive	50.3	55.5	46	0.12
ACPA positive	52.7	55.9	50.0	0.70
DAS28, median (IQR)	4.30 (2.84–5.71)	4.56 (3.15–5.78)	3.86 (2.47–5.58)	0.02
Low disease activity, DAS28 < 3.2	30.3	20.8	37.2	0.07
Moderate disease activity, DAS28 ≥ 3.2 to < 5.1	38.9	43.1	35.3	
High disease activity, DAS28 ≥ 5.1	30.9	35.1	27.4	
mHAQ, median (IQR)	0.37 (0–0.87)	0.37 (0.12–0.87)	0.37 (0–1)	0.92
mHAQ ≥ 1 (vs. < 1)	24.5	21.6	26.7	0.41

P-value for comparison between CAM users versus non-users using Chi-squared test or Mann–Whitney U-test. ‡From symptom onset to first rheumatologist review. §From time of diagnosis to recruitment to the Singapore Early Arthritis Cohort. ¶Either RF or ACPA positive. IDR, interquartile range; CAM, complementary and alternative medicines; ACPA, anti-citrullinated peptide antibody; DAS28, Disease Activity Score in 28 joints; mHAQ, modified Health Assessment Questionnaire; IQR, Interquartile range; RF, rheumatoid factor

Table 1: Baseline Characteristics

The CAM stratification also shows some additional differences between the groups. There are race, language, and smoking histories that are quite different. Note that the duration of symptoms (until rheumatologist review) was 13.7 weeks among non-users and 20.8 weeks among CAM users. That is, CAM users waited almost twice as long to see a specialist, compared to non-users. Not surprisingly, this meant a delay to the initiation of disease-modifying anti-rheumatic drugs (DMARDs). Figure 1 shows the overall difference between CAM users and non-users:

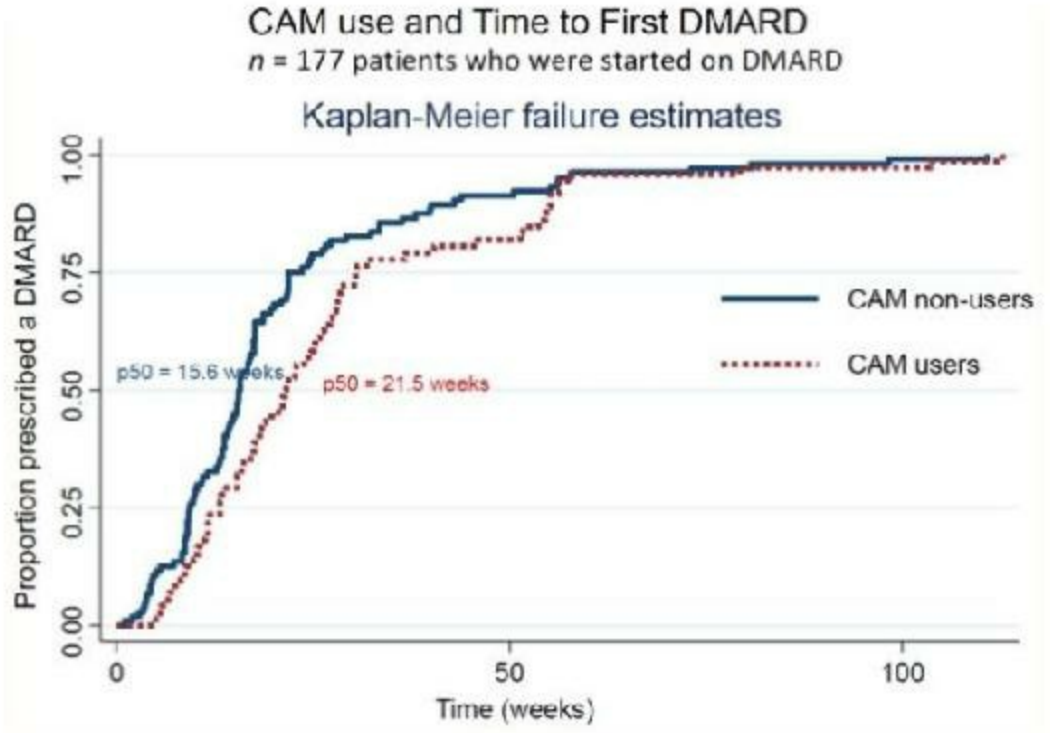


Figure 1 Kaplan–Meier plot of time to disease-modifying anti-rheumatic drugs (DMARDs) for complementary and alternative medicines (CAM) users versus non-users.

Only CAM use was significantly associated with the time to first DMARD initiation.

CAM use delays effective arthritis therapy

This small study illustrates what appears to be an unfortunate consequence of CAM use: It may be contributing to delays in seeking effective therapies, which may have additional negative consequences. While this study does not show direct harms from CAM use, the relationship between earlier therapy and positive disease outcomes is well established. The authors conclude that patient and public education programs to raise awareness about EIA, and the importance of early treatment, are essential. I would add that continuing to

raise awareness of the limitations of CAM, and the consequences of its use, need just as much awareness.

Placebo effects are largely misunderstood, even by professionals, and this leads to a lot of sloppy thinking about potential treatments. This problem has been exacerbated by the alternative medicine phenomenon.

Several decades ago, the proponents of so-called CAM promised that if only their preferred if unconventional treatments were properly tested medical science would discover how effective they are. “Effective” (or more precisely, “efficacy”) has a specific definition in medical science – it means that a treatment has been found to perform statistically significantly better than placebo in a blinded controlled trial. Several decades and thousands of studies later, the most popular CAM modalities (homeopathy, acupuncture, reiki, manipulation for medical indications, and more) have been shown to be no more effective than placebo. This means they don’t work.

Not to be deterred by reality, CAM proponents simply shifted the goal posts. Now many of them are saying that placebo effects are real, and therefore being as effective as placebo means that their treatments “work.” As part of this strategy they have promoted and amplified common myths about placebo effects. Let’s take a closer look at these myths and show why they are wrong.

Myth #1 – “The” placebo effect

The first and overriding myth about placebos is that there is one placebo effect (singular). This confusion is understandable, because scientists often refer to “the” placebo effect. However, they are referring to what is measured in the placebo arm of a clinical trial – that net effect (the difference between baseline or no treatment at all and a placebo treatment) is the placebo effect for that study.

There are multiple placebo effects contributing to that difference, however. Anything that might give the appearance of an improvement will contribute to the measured placebo effect. These placebo effects include: Regression to the mean – when symptoms flare, they are likely to return to baseline on their own. If you take any illness that fluctuates in severity, any treatment you take

when your symptoms are at their peak is likely by chance alone to be followed by a period of less intense symptoms.

Similar to this but distinct is the reality that many illnesses are self-limiting. If you have a cold, you will likely get better even if you do nothing – so anything you do will be followed by improvement. There is also bias in perceiving and reporting subjective symptoms. People want to feel better, they want to think that the treatment is working, and they may want to please the researcher or their physician. Further, researchers and doctors want their treatments to work.

There are also many possible non-specific effects just from the act of being treated. Hope can be a very positive emotion, and that alone may make people subjectively feel better. Subjects in a trial are also getting medical attention, and are likely paying more attention to their own health. They are likely to be more compliant with other treatments.

The treatment under study itself may have several components, some specific and some non-specific. Do people sometimes feel better after a session of reiki or acupuncture because they were laying down listening to music and smelling incense during the treatment? How much of a relaxation effect is at play? Does it matter if you actually stick the needles in alleged acupuncture points (the answer is no)?

Myth #2 – Placebo effects can cause healing

Because it is often believed that “the” placebo effect is one thing, that one thing is often believed to be a real mind-over-matter physical healing. There is no evidence to support this interpretation, however. In fact researchers looking for that real healing effect of placebos have only demonstrated that it doesn’t exist.

Part of the problem here is that the term “healing” is vague. It does not have a specific definition, but the implication is that biological repair is taking place. In practice researchers distinguish objective vs subjective markers of improvement. Subjective just means that the patient feels better in some way,

per their own report. They rate their own pain, for example. An objective outcome is something measurable, like blood pressure, survival, or tumor burden.

A systematic review of cancer research, for example, found that placebo interventions resulted in minor improvements in subjective symptoms, but no improvement in the cancer itself.

Placebo effects break down into several categories. One category is illusory – the misperception of improvement through regression to the mean or biased reporting. The second category is non-specific effects, such as emotional comfort from a practitioner, relaxation, or improved self-care or compliance. This third category is comprised of effects which can plausibly result from psychological interventions only. These relate mainly to stress, depression, anxiety, and the perception of pain and similar subjective symptoms. There is a mind-body connection – it's called the brain.

There is, however, no magical control of your brain over biological or physiological processes that are not networked with the brain through nerves or hormones.

Myth #3 – Animals and babies cannot have a placebo effect

This myth results from the false assumption that in order to have a placebo effect you need to believe that you are taking an active treatment. It is the belief that is causing the effect, and therefore it is a prerequisite. The logic then follows that animals and babies, who cannot know they are receiving a treatment, can therefore not have a placebo effect. Any improvement in this context, therefore, must be a physiological response to the treatment itself.

It should already be obvious, however, that these assumptions are incorrect. There are many sources of placebo effects that do not depend upon the subject knowing they are being treated, such as regression to the mean, the self-limiting nature of many ailments, and non-specific effects or benefits from simultaneous interventions.

Further, however, someone has to determine that the animal or baby has improved. That person is vulnerable to biased perception and reporting, and will also contribute to any measured effect.

This means that studies of treatments in animals or babies still need to be properly controlled, and whoever is assessing the outcome needs to be properly blinded to treatment allocation.

Myth #4 – Fanciful or alternative treatments yield better placebo effects

Desperate to salvage a role for their preferred but ineffective treatments, many alternative practitioners will argue that their real expertise is in maximizing placebo effects. OK, sure, the scientific evidence shows that my treatment is no better than placebo, but placebo effects are real, and I am very good at eliciting them. This is the “placebo medicine” gambit.

I have already debunked the first part of that claim. There is also no evidence for the second part, that alternative practitioners elicit more of a placebo effect. What the scientific evidence shows is that all interventions will produce some placebo effect, depending mainly on the outcome to be followed. The more subjective and amenable to variables such as mood, the larger the measured effect will be.

The existence of a placebo effect does not justify using inactive or pseudoscientific treatments. You can elicit the same effects from science-based interventions. Related to this is the notion of placebo effects without deception. This is certainly possible, if you include all the non-specific and statistical effects, but most patients would likely not be happy to be receiving a treatment that they were told was completely inert, just so it may bias their perception of their symptoms. All pseudoscientific treatments, even if they are justified through placebo effects, are given with a generous helping of deception, which violates patient autonomy.

The other variable that seems to be important, but requires further study, is the therapeutic relationship between practitioner and patient. Having a

positive relationship may enhance the measured placebo effect, but that may be just another measure of bias.

In any case, anything useful about placebo effects can be had with a positive therapeutic relationship, using science-based interventions, and following the ethical requirements of informed consent and patient autonomy.

Read the label. It doesn’t list any health benefits. It says harmful or fatal if swallowed.

Turpentine is a solvent and a poison, but some people are drinking it as a medicine.

Scott Gavura wrote about it

2 years ago and concluded, “There’s no reason to consume turpentine and multiple reasons to avoid it completely, with the primary reason being that

it’s a poison

.”

Scott’s article mentioned an MD who advocates turpentine to cure the fake illness chronic *Candida*, and who had been stripped of her license. That MD was Jennifer Daniels. It would be bad enough if she only recommended it for Candida, but she also claims to have discovered that turpentine is the Fountain of Youth, a miracle cure that reverses disease and aging and is good for pretty much whatever ails you. That’s ludicrous.

The facts

The *Natural Medicines Comprehensive Database* (which I consider to be the most reliable source) says, “There is insufficient reliable information” to evaluate its effectiveness for any medical use. It rates turpentine as “possibly safe” when used topically and appropriately, “possibly unsafe” when applied to large areas of skin, and “likely unsafe” when used orally for medicinal purposes; 2 ml/kg is toxic, and 120-180 ml is potentially lethal in adults.

The *NMCD* goes on to explain that turpentine is a central nervous system depressant, a pulmonary aspiration hazard, a skin irritant, and might cause abortions. It can have a decongestant effect when inhaled. Many adverse reactions are reported from ingestion, including headache, insomnia, coughing, vomiting, hematuria, albuminuria, urinary tract inflammation, coma, and death. Inhalation can cause inflammation and bronchial spasms. Applying it to the skin can lead to kidney and central nervous system damage.

A drug information website has an extensive monograph on turpentine. It says, “Turpentine has been used experimentally in a bath for the treatment of disseminated sclerosis and sexual dysfunction. It also has been studied for its antibacterial activity and inhibition of osteoclast activity. Turpentine is utilized in experimental models of inflammation to induce a systemic inflammatory immune response in animals.” It warns against using it during pregnancy and lactation, stresses that it is highly toxic (fatal poisonings have occurred with ingestion of as little as 15 mL, just 3 teaspoonsful) and has caused skin tumors in animals. It provides a bibliography with pertinent citations.

The discovery

Jennifer Daniels tells the story of her discovery in a radio interview. She asked her African-American patients if their slave ancestors had a miracle cure that cured everything and was cheap; several of them mentioned turpentine and sugar. So she tried it for herself. She put turpentine on 3 sugar cubes and washed them down. Right after ingesting it, she says:

> I think my IQ went up like 50 points, I could just feel it, all this mental energy and understanding and clarity, just like when I was 10 years old, everything was very clear and focused. I said WOW what a feeling. I did some math problems, I said this is pretty good.

She had heard that turpentine could cause seizures, so she figured out the maximum safe dose by stopping at a dose where she felt a little twitch, “even softer than a twitch.” Then she gave it to her mother, who began to feel better *in less than a minute* (!). It relieved pains that her mother had had for 30 years. Other family members served as guinea pigs and appeared to benefit. So with no further ado, Daniels started using it on all her patients.

The published evidence she relies on

In that same interview, Daniels talks about a review article from France with 100 references that supposedly support the use of turpentine for parasites,

cancer cells, pathogenic bacteria, fungus, yeast, rheumatism, MRSA, sciatica, nephritis, constipation, increasing membrane permeability, etc. It doesn't say what she thinks it says.

Using turpentine: The treatment plan

First you have to hydrate. Then you have to have three bowel movements a day, which you can supposedly achieve by taking her Vitality Capsules, which (unlike everything else on earth) contain "no chemicals." If you don't have three bowel movements a day, the *Candida* can't get out of your body and will "shift through your left hip to your right hip, your right hip to your stomach, and your stomach to your shoulder. It's gonna play musical chairs all over your body." Then you have to follow her diet instructions (organic, no GMOs, no "dead food," and many more restrictions). Only then can you do the Candida Cleanse.

She says you must avoid steroids, antibiotics, and chemotherapy, because they prevent cell repair and yeast will move in to eat up the dead cells. She advises patients to stop all their medications if they can (potentially dangerous advice).

She says in the last days of her practice, she stopped using antibiotics. She would not admit seriously ill patients with pneumonia to the hospital, but would dose them with turpentine and send them home. She thinks children with high fevers will recover in less than 24 hours if given turpentine. When her daughter badly injured her ankle, she gave her a teaspoon of turpentine and ¼ cup of castor oil. "She drank it, she pooped, all the pain was gone."

More strange and unsupported claims

- "Liver time is 1-3 AM; lung time is 3-5 AM."
- "Vitality Capsules clean out the bile ducts and the gall bladder system as well as the small intestine, large intestine, and it also promotes circulation."
- Children should start getting turpentine in castor oil when they reach 30

pounds, to prevent *Candida* and parasites.
- You should keep taking turpentine at least once a month for the rest of your life.
- Turpentine improves eyesight; users were able to throw away their reading glasses.
- "if I want thicker hair and less gray hair, then I'm gonna use minerals, small willow flower, and shou wu."
- Turpentine improves diabetes by healing the pancreas. It will allow Type I diabetics to lower their insulin dose.
- It resolves tinnitus.

To her credit, she does get a few things right; for instance, she realizes that "rope worms" are not actually worms. On the other hand, she is anti-vaccine: "There is no vaccine or injection Dr. Daniels recommends."

A spy troll is shocked

David McAfee infiltrated the closed 640-member Facebook group "Parasites cause all disease – turpentine cure" and was appalled at what he found. People were seeking support for the horrible side effects they were experiencing from turpentine. They were hoping to cure everything from scabies to herpes to "electromagnetic hypersensitivity."

One woman who was using turpentine and castor oil complained that when she did enemas a lot of red liquid came out. Another list member told her *not to worry* because it was probably just old and damaged intestine wall coming out!

Some of the comments following McAfee's exposé article were amusing:

- "Sometimes you just roll your eyes, mutter darwinism to yourself and move on."
- "I'm a believer in alternative medicine-trust me, these people aren't into alternative, they are idiots. Anyone with half a brain knows not to ingest a solvent. Dear god, where does this stupidity come from?"
- "There is in my family a story about the medical use of turpentine. It

dates from the time of my grand-father or great-grand-father. It was suggested as a topical treatment for hemorrhoids. It was not suggested in good faith. Folks could have a very crude sense of humor in those days too."

What about science?

Daniels is a graduate of Harvard and of the University of Pennsylvania School of Medicine. Surely she learned about science at those prestigious Ivy League schools. One can only wonder how she came to disregard science and go her own way. She says she reads research studies but does not believe them: "I'm not much of a fan of research because every research project I've been involved with, I've been asked to falsify data." That certainly is an unusual experience, and I can't help but wonder if she reported the fraud/misconduct. She could have had a great career as a whistleblower.

Her words and actions show that she does not think like a scientist. Here are just a few revelations from her *Confidential Underground Report: Top Secret; The Candida Cleanser*.

- She assumed the existence of some folk remedy that was a miracle cure that would cure everything. Considering all the many different causes of different illnesses, this is not a reasonable assumption.
- She experimented on herself and assumed that the dose that seemed to work for her would work for everyone. If that were true, drug companies could dispense with phase 2 trials and just give the drug to one person.
- She describes immediate results, too soon for a medication to be absorbed and have any effect; she doesn't recognize that this is almost certainly a placebo response.
- She doesn't put her belief that turpentine is effective to any kind of test.
- She wonders how long you could take it every day without experiencing side effects. So she takes it daily for a week, notices no adverse effects, and says "I decided that was long enough for the purposes of science." Wow! Wouldn't Big Pharma love to hear that all they needed to do to demonstrate the safety of their drugs to the FDA was to have one person take a drug for a week and say they hadn't noticed any symptoms?

- Without any further testing, she immediately moves on to treating other people with turpentine.
- She makes all kinds of claims unsupported by any evidence, for instance:
    - Breads, meats and dairy are all full of parasites.
    - “Trail mix is an abomination and has destroyed the health of many a health nut.”
    - “It has been *my observation* [emphasis added] that one should be having at least three bowel movements a day.”
    - “There is no medication that turpentine interacts with.”
    - “Censorship is so severe that it is difficult to find information on turpentine in print.”
- She makes dangerous recommendations: laxatives and daily enemas, stopping prescription medications, avoiding immunizations, and many more.

No longer practicing, but…

On her website, it says “Dr. Daniels is a former medical doctor who had her medical license suspended due to not prescribing enough drugs and truly healing her patients.” I don’t believe that; no medical board has ever suspended a doctor’s license for healing their patients or for “not prescribing enough drugs.” According to the New York medical board website, she surrendered her license less than 6 years after it was granted. Apparently she was uncooperative, refusing to share her patient records with the board, and from her comments online it seems she was deliberately trying to hide her many questionable treatment methods from the authorities. By voluntarily surrendering her license, she avoided any further investigation or board actions.

No longer able to practice medicine, Daniels has moved to Panama, where she is making a living producing books, radio shows, CDs, and videos; selling supplements; and advising clients as a health coach. She is available for “Holistic Mentoring Consultations;” you can schedule a consultation online and will be able to speak to the doctor directly. What she is doing may not be illegal, but she is still in a position to harm people with bad advice.

Conclusion: not recommended

Not only is turpentine not the Fountain of Youth, it has not been proven effective for any health condition. Jennifer Daniels is not a reliable source of health information. She fails to understand the need for scientific testing, relies on testimonials and beliefs instead of facts, and demonstrates poor judgment. She makes claims that are bald assertions not supported by any evidence. She is offering dangerous advice, not just about turpentine but about vaccines and other things.

Science Based Medicine

周日, 26 11月 2017

Science Based Medicine

[周日, 26 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **And the server migration continues apace…but where are the comments?** [周六, 25 11月 10:15]
  SBM is changing servers again. Unfortunately, that means that there are problems with the comments.
- **Happy Thanksgiving!** [周四, 23 11月 14:00]
  Happy Thanksgiving to our American readers, and to everyone else- have a great Thursday in November!
- **New Tools Against Antibiotic Resistance** [周三, 22 11月 20:24]
  Antibiotic resistance is a serious problem that may lead to a post-antibiotic era. However, there are potential solutions that deserve research priority.
- **The Death of Expertise** [周二, 21 11月 16:00]
  In Tom Nichols' new book, The Death of Expertise, he explains how a misguided intellectual egalitarianism is harming our ability to assess the truth and solve problems, and discusses some of the responsible factors and possible long-term consequences.

And the server migration continues apace… but where are the comments? - Science-Based Medicine

As many of you noticed, there has been an issue with the comments that began last night. Here’s what happened. The Powers That Be decided to migrate the blog to a new server last night, and there were problems relinking Disqus to the new installation of WordPress. I am assured that the problem has been fixed, but also told that it could take 12 hours for all the old comments to redirect to our new location. So be patient, and the blog should be back to normal by tomorrow morning. There should be benefits to the new server as well, such as faster loading, less downtime, and the like. We’re sorry about the inconvenience today, but as one of our crew noted, for some reason migrations never seem to go as smoothly as we would like.

In any event, if after tomorrow there are still problems, let us know.

Happy Thanksgiving! - Science-Based Medicine

We celebrate Thanksgiving today in the U.S. and SBM is taking the day off. We are thankful for all of our readers and commenters and wish you a Happy Thanksgiving.

New Tools Against Antibiotic Resistance - Science-Based Medicine

Scientists are often placed in the role of Cassandra – because of their expertise and knowledge they may see potential serious problems on the horizon, but may also find it challenging to convince the general public. Sometimes they are working uphill against vested interests. Often scientists will warn against possible problems that they then work to prevent, and when successful it seems like their warnings were unwarranted. Or they may simply be calling for preparation for a possible event, like an epidemic, that still probably won't occur but you should be prepared ahead of time in case it does.

Also, as science communicators we don't want to overhype potential problems. It can be a delicate balance. With all that in mind, it is probably difficult to overstate the potential risk of antibiotic resistance. This is one of those looming issues that I genuinely worry about, but gets too little attention, if anything, in the media. It is also a manageable problem – there are things we can do to mitigate antibiotic resistance, if we take the issue seriously enough.

The World Health Organization summarizes the problem in stark terms:

> Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. A growing list of infections – such as pneumonia, tuberculosis, blood poisoning, gonorrhoea, and foodborne diseases – are becoming harder, and sometimes impossible, to treat as antibiotics become less effective.
>
> Where antibiotics can be bought for human or animal use without a prescription, the emergence and spread of resistance is made worse. Similarly, in countries without standard treatment guidelines, antibiotics are often over-prescribed by health workers and veterinarians and over-

> used by the public.
>
> Without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill.

I don't think they are overstating the problem.

The cause of antibiotic resistance is fairly easy to understand. Bacteria reproduce very quickly in large numbers. When someone takes an antibiotic, that provides a selective pressure towards resistance. If any individual bacterium has a gene which provides resistance to the mechanism of that antibiotic it will tend to survive the treatment and then reproduce a new generation of resistant bacteria.

Bacteria also have the ability to swap genes, so that are not just passed from parent to offspring, but horizontally to other bacteria in a process called conjugation. Bacteria may contain plasmids, which are loops of DNA. Those plasmids can be copied from one bacterium to another. A plasmid may contain one or even multiple genes that confer resistance – and so in one conjugation event a bacterium may receive resistance to multiple antibiotics.

The existence of bacterial plasmids with multiple resistant genes is a problem, because if they are exposed to one of the antibiotics to which they are resistant, that will favor the proliferation of the bacteria with plasmids that confer multiple resistance.

There is one potential bright spot in all this. Genes that confer antibiotic resistance often come at a price. They may make it more difficult for the bacteria to reproduce, or force them to expend more energy. That is why they don't have the feature in the first place. The selective pressure of antibiotics is necessary to favor the more costly feature. The hope is that in the absence of selective pressure from antibiotic, the resistant features will tend to fade away.

However, a new study suggests that this may not always be the case. Researchers looked at costly antibiotic resistance features in various strains of *E. coli*. They followed them for over a month and found that strains were able to maintain even costly antibiotic resistance in the absence of antibiotics if

they contained plasmids. The key is the conjugation rate – how frequently do bacteria exchange plasmids? The research found that, at least in these strains, the rate was high enough to maintain antibiotic resistance even in the absence of antibiotics.

This research suggests that limiting antibiotic use may not be enough to reverse existing antibiotic resistance. Of course, limiting use is essential to slowing the development and spread of resistance. This is the primary mechanism by which the medical community is trying to combat resistance, but even here we are not doing enough. Antibiotics are still massively overprescribed. Some countries allow for over-the-counter antibiotic use, and it is common for the public to take them for viral illnesses. Antibiotics are also heavily used in the farming industry.

Even if we achieved our goal to properly limit antibiotic use, and educated practitioners to optimally prescribe antibiotics, the current research suggests this may not be enough to reverse some types of resistance. However, the same research suggests there may be more active interventions that will.

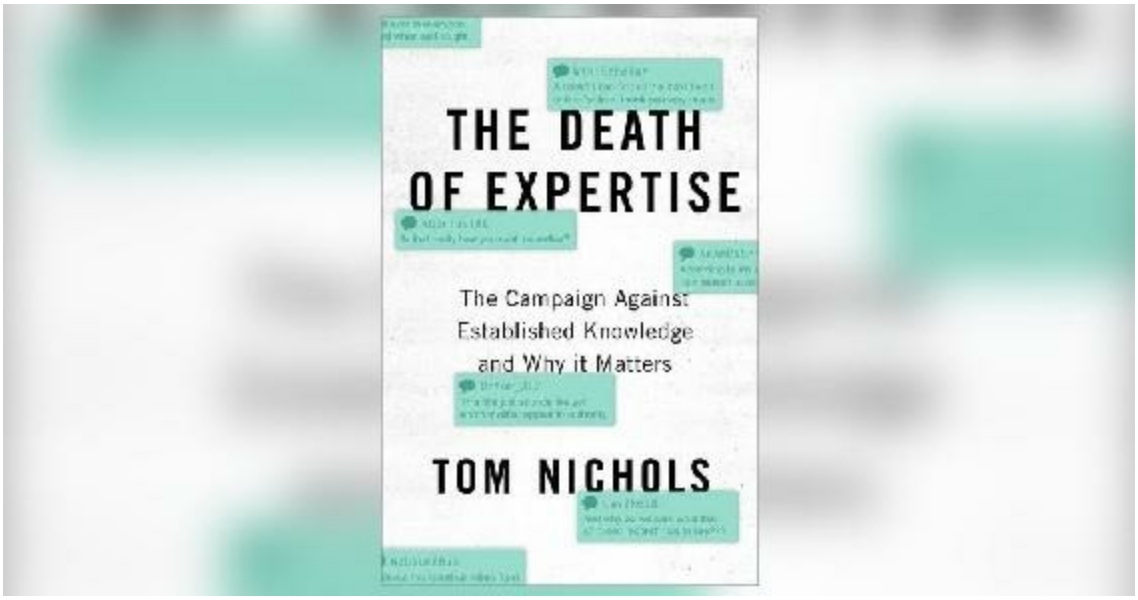
There are potential drugs that can limit conjugation or induce bacteria to lose their plasmids. For example, a 2015 study identified features of synthetic fatty acids that were effective conjugation inhibitors. This would limit the horizontal spread of plasmids among bacteria, and therefore limit the spread of resistance.

Another approach is to prevent plasmid replication. Researchers are looking at ways to exploit the existing compatibility system in bacteria toward this end. Since bacteria are so promiscuous with their genes, they need mechanisms to know when plasmids are incompatible with their other DNA. You could essentially trick a bacterium into thinking its plasmid is incompatible, and therefore when the bacteria reproduces it will not replicate the plasmid. The plasmid will therefore be lost to the next generation. These treatments would not just limit the spread of resistance, but cause a population of bacteria to lose their resistance.

What all of this research suggests is that we should not only be researching novel antibiotic mechanisms, we should be investing in research into drugs that inhibit plasmid conjugation and induce plasmid loss. These treatments

can reduce the spread of resistance, and even potentially reverse resistance. Such treatments could be given alongside antibiotic regimens, or used in farming or similar contexts to limit the development of resistance.

My hope is that this type of research will eventually lead to a situation in which all those scientists and science-communicators who warned about the coming post-antibiotic era will look like Cassandras. Rather than getting the credit for identifying and then preventing a major problem, people will either forget them or falsely think the warnings were overhyped to begin with. But I will take that fate if it means avoiding a post-antibiotic era.



Tom Nichols' new book *The Death of Expertise: The Campaign against Established Knowledge and Why It Matters* has direct relevance to many of the issues we are constantly grappling with on Science-Based Medicine. In a democracy, everyone has equal rights. Many people think that means they are equal to experts in knowledge and judgment. In medicine, as in most other areas of public discourse, we are faced with angry laymen who denounce intellectual achievement and scientific knowledge and who distrust experts.

People find ways to reject the evidence when it conflicts with their values and beliefs. When scientific evidence challenges their views, they doubt the science rather than themselves. New examples of this phenomenon can be found every day in the news and in the comments sections of the Science-Based Medicine blog, and trying to set those people straight has proven a mostly futile exercise.

The failure of higher education

Students have become consumers. High school seniors tour college campuses with their parents looking for the one with the best dorms, cafeteria food, and extra-curricular activities, rather than the one that will challenge them and provide the best education. Nichols says colleges are not only failing to

provide to their students the basic knowledge and skills that form expertise, they are failing to provide the ability to *recognize* expertise and to engage productively with experts and other professionals in daily life. They are not being taught "critical thinking: the ability to examine new information and competing ideas dispassionately, logically, and without emotional or personal preconceptions."

He says students are being treated as *clients* rather than students. "Many colleges have become hostages to students who demand that their feelings override every other consideration." Students "explode over imagined slights" and "build about themselves fortresses that no future teacher, expert, or intellectual will ever be able to breach." They want to be protected from ideas or language they find unpleasant. They are "demanding to run the school while at the same time insisting that they be treated as children."

The internet

The Internet has provided people with an unprecedented abundance of information, but all too often it gives them the illusion of knowledge, encouraging them to believe they know as much as experts. They hear what they want to hear, and live in a bubble community of people with similar beliefs.

> People do not come to the Internet so that their bad information can be corrected or their cherished theories disproven. Rather, they ask the electronic oracle to confirm them in their ignorance.

Nichols says,

> …not only is the Internet making many of us dumber, it's making us meaner: alone behind their keyboards, people argue rather than discuss, and insult rather than listen.

People "power browse" rather than actually reading. We see this all the time on Science-Based Medicine, where commenters criticize an article they obviously have not read carefully or understood. Sometimes I suspect they may just have read the title and seized the opportunity to jump on their

particular soap box.

Journalism

The dissemination of “fake news” is an ever more common reality. Most people are very poor at evaluating the reliability of a news source and the truth of what is reported. When a layperson challenges an expert by saying “I read it in the paper” or “I saw it on the news,” it may mean only “I saw something from a source I happen to like and it told me something I wanted to hear.” At that point, discussion has nowhere to go; the real issue is replaced by the effort to untangle which piece of misinformation is driving the conversation. People are constantly barraged with facts and knowledge, but they have become more resistant to facts and knowledge. How did we arrive at this state of affairs? Nichols says, “technology collided with capitalism and gave people what they wanted, even when it wasn’t good for them.”

When the experts are wrong

In our increasingly complex world, we can’t possibly know everything; we have no choice but to trust experts. But sometimes experts get things wrong. Most of the time, their errors are identified and counteracted by other experts. This works so well most of the time that we are shocked when we read about an exception; for instance, when we learn that an incompetent doctor has killed a patient or that a researcher has falsified data. Laymen get exasperated when science “changes its mind,” for instance telling the public eggs are bad for them and then saying no, they’re OK to eat. But that’s not a failure of science, but rather an example of how science works so well in the long run by following the evidence and discarding false provisional conclusions as the evidence improves.

When experts’ errors, fraud, and misconduct are revealed, a layperson naturally asks how we can trust studies in any field. Nichols says that’s the wrong question to ask, because “rarely does a single study make or break a subject.” Single studies are often wrong, but the aggregate of all research is

trustworthy. The scientific enterprise as a whole is self-correcting and leads to a consensus of experts that approaches the truth as much as is humanly possible.

The impact on government

Science is essential to rational public policy; it can't make the decisions, but it provides reality-based information that can guide the decision-makers. Nichols says we have a President who sneers at experts and whose election was "one of the loudest trumpets announcing the impending death of expertise." He argues that Trump's campaign was "a one-man campaign against established knowledge." He provides examples: Trump's "birther" campaign against Obama, his quoting the *National Enquirer* approvingly as a source of news. Nichols says rather than being ashamed of his lack of knowledge, Trump exulted in it. "Worse, voters not only didn't care that Trump is ignorant or wrong, they likely were unable to recognize his ignorance or errors." He says the Dunning-Kruger effect was at work. It's not just the things we don't know (one in five adults think the sun revolves around the Earth), but the smug conviction that we don't need to know such things in the first place.

He warns,

> The relationship between experts and citizens, like almost all relationships in a democracy, is built on trust. When that trust collapses, experts and laypeople become warring factions. And when that happens, democracy itself can enter a death spiral that presents an immediate danger of decay either into rule by the mob or toward elitist technocracy. Both are authoritarian outcomes, and both threaten the United States today.

Conclusion: Hope for the future?

He says Americans no longer understand that democracy only means political equality. They tend to think democracy is a state of actual equality in which

everyone’s opinion is as good as everyone else’s, on every subject. Feelings are more important than facts: if people *think* vaccines are harmful, it is considered “undemocratic” and “elitist” to contradict them.

He sees signs of hope. Experts are rebelling. He cites an angry doctor who asked patients, “Do you remember when you got polio? No, you don’t, because your parents got you [expletive] vaccinated.” He points out that without democracy and secular tolerance, nations have fallen prey to ideological, religious and populist attacks and have suffered terrible fates. But he ends on a hopeful note. He has faith in the American system and hopes that it will eventually establish new ground rules for productive engagement between the educated elite and the society they serve. I hope so too!

Science Based Medicine

周三, 08 11月 2017

Science Based Medicine

[周三, 08 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Update on ASEA, Protandim, and dōTERRA** [周二, 07 11月 16:00]
  Multilevel marketing distributors of dietary supplements and essential oils point to studies that they think constitute evidence that their products work. They don't understand why those studies are inadequate.
- **ORBITA: Another clinical trial demonstrating the need for sham controls in surgical trials** [周一, 06 11月 16:58]
  Last week, the results of ORBITA were published. This clinical trial tested coronary angioplasty and stunting versus optimal medical management in patients with single-vessel coronary artery disease. It was a resoundingly negative trial, meaning that adding stunting to drug management t didn't result in detectable clinical improvement. What was distinctive about this trial is that it used a sham procedure (i.e., placebo) control, which few trials testing surgery or a procedure use. The results of…
- **The American Chiropractic Association Answers Crislip's Call, Joins the Choosing Wisely Campaign** [周五, 03 11月 20:00]
  The Choosing Wisely campaign has invited the largest chiropractic organization in the United States to publish a list of interventions to avoid. The results, while not entirely without merit, consist of redundant or unnecessary recommendations. And there is a glaring absence of recommendations to avoid any of the blatant pseudoscience commonly practiced by chiropractors.

Update on ASEA, Protandim, and dōTERRA - Science-Based Medicine

I have written critiques of several dietary supplements sold through multilevel marketing (MLM) schemes, and they keep coming back to haunt me. I get testimonials from users who believe they have been cured of every ailment under the sun; and every time another study is done, I get e-mails from distributors who apparently think the new “evidence” will change my mind. Recently I received three more emails about ASEA, one about Protandim, and three about dōTERRA essential oils, asking me to reconsider. I thought this would be a good opportunity to explain why I have not changed my mind and to explain once again what constitutes evidence in science-based medicine.

ASEA

Recently an email from “The ASEA Team” asked us to delete the article I wrote about ASEA in 2012, based on their opinion that it “was not constructive” and “was not based on decent and verifiable facts.” They did

not mention two other followup articles I wrote here and here. And they did not directly try to refute most of the points I made in my critique; I think they failed to understand what I was saying. They provided 6 attachments with studies they said were "made to prove the effectiveness of ASEA" but those studies didn't prove any such thing.

Last week Steven Novella answered them very effectively, calling ASEA snake oil and pointing out the deceptive marketing practices of the company, the pseudoscientific nature of their claims, and the worthlessness of the studies they cite.

The claims. The ASEA website currently makes these claims:

> As we age, and as stress and environmental toxins inundate our lives and weaken our defenses, normal cellular function declines, and with it, the body's ability to produce and maintain a proper balance of redox signaling molecules.ASEA has developed the only technology that can create and stabilize active redox signaling molecules in a consumable form. No matter what your health concern may be, ASEA Redox Supplement can bring your cellular communication to optimal levels, improving the health of every system of your body.

Questions. This brings up several questions:

- How exactly does normal cellular function decline? How would improved cellular communication reverse the decline?
- What is a proper balance of redox signaling molecules? How do they know? How is it measured?
- What active redox molecules are in the product? (They won't tell us. The label just lists salt and water. In my opinion, if there are redox molecules in ASEA, listing only salt and water constitutes false labeling.)
- What evidence do they have that the product improves health?

What redox molecules? All they have is a statement from a lab, BioAgilytix, that indirectly measures "biomarkers" of redox levels in ASEA using a fluorescent indicator as a probe for unspecified highly reactive oxygen species. I don't know what that means. There is no direct evidence

that redox molecules are present. No other lab has analyzed the product.

Safety. Their claim that the product is safe is based on a brief description of two unpublished studies. In the first study, 106 overweight women took ASEA or placebo for 12 weeks; they reported no adverse effects, (None?! In most studies, even the placebo group typically reports *some* symptoms.) and there were no changes in liver or kidney function tests or complete blood counts. In the second study, an in vitro study of cultured eukaryotic cells, the cells "did not register a significant toxic response as measured by a visual assessment of green dye that indicated "nuclear translocation." Based only on this flimsy subjective and in vitro evidence, they claimed "ASEA Redox Supplement, orally administered, does not manifest a toxic response or inflammation to exposed tissue." Such thin gruel does not constitute convincing evidence that the safety of the product has been established.

Studies. Before I accept that a treatment works, I want to see human studies published in peer reviewed journals. There are none on their website, but I was able to locate two articles in the *FASEB Journal* here and here.

It quickly became obvious why these are not featured on the company website: they are not full articles, but abstracts from a meeting that were published in a supplement to the journal. One is a human study, the other is in mice (the poor mice were gavaged with ASEA and then run to exhaustion). One of my correspondents claimed that these are peer-reviewed studies, but peer review is not possible when all that is available is an abstract.

As far as I could determine, there have been three studies in humans. One, a small study of 17 cyclists, has been deleted from the web. It was not placebo-controlled. There is an abstract of a similar study of 20 cyclists that did use a placebo control and was double-blinded. It was essentially *negative*: ASEA did not improve time trial performance. They found that it caused a significant shift (good or bad?) in 43 metabolites, but had no apparent influence on traditional biomarkers of inflammation, oxidative stress, or immunity.

The third, most recent human study is the one my true believer correspondents are currently crowing about. They refer to it as a "genetic" study. One of them snarkily commented "It's called science, u should look

into it sometime." I did look into it, and I was not impressed. The title is "Initial Gene Study Showed ASEA REDOX Affected Important Signaling Pathway Genes." The company paid Tauret Labs to do the study. It has not been published in a peer-reviewed journal. It was an 8-week double-blind randomized placebo controlled study with 60 participants that measured changes in expression of 5 genes and found statistically significant changes of 20-31% with ASEA. They claim that "These genes are key in the health of the individual and play a vital role in five human health areas and dozens of pathways." Maybe, but they have not demonstrated that human health benefits in any way from these changes in gene expression. Their summary of results states "Effects are non-specific to race, sex or age, and were observed in all populations tested." This conclusion is not supported by their data. The only population tested was 60 individuals, 41% male, 92% Caucasian, average age 35 with age distribution not reported.

Conclusion. The evidence for their claims is indirect and inadequate. Half of all research studies turn out to be wrong. Changes in blood tests might be spurious; they have not been independently replicated. Changes may be statistically significant but not clinically significant. If they want us to believe ASEA causes objective, meaningful improvements in human health, they'll have to do better. They'll have to test directly for meaningful clinical outcomes. And if they want us to believe ASEA contains all those redox signaling molecules, they'll have to prove it with a direct analysis by an independent lab and name those molecules.

As Steven Novella put it,

> Asea, however, is still a fantastical and unbelievable claim supported by nothing but hype, sales copy, and empty promises. It is salt water. The hand-waving nonsense about redox reactions is incoherent technobabble – the very essence of pseudoscience. What would be convincing is published, peer-reviewed, independent, rigorous scientific studies with clear results. These don't exist. No amount of distraction will change that fact.

Protandim

I have written about Protandim four times, here, here, here, and here.

What is it? It is a mixture of five dietary supplements (Milk thistle, Bacopa extract, Ashwagandha, Green tea extract, and Turmeric extract) that allegedly stimulates the body to produce its own antioxidants. They claim it is "the only supplement clinically proven to reduce oxidative stress by 40%, slowing down the rate of cell aging to the level of a 20 year old [and they measured this how?]."

An email from a reader

> You really need to up date your studies on this product! There are thousands of people with improved health because of PROTANDIM. For example, my son in law with high blood pressure was able to cut his BP medication in half after only two months on it and after three months, he is off meds completely with normal blood pressure; my daughter suffered for a year with a horrible rash under her arm that looked like tree bark. After several visits to her doctor where he prescribed cortisone and antibiotics nothing worked. She finally went to a dermatologist who was shocked to see that she had Granular Parakeratosis a rare skin disease. My daughters case was only the second time she has seen it, and at a follow up visit was told that there is no cure, only palliative care. Three days later the crud came off in her washcloth in the shower, and she had been on PROTANDIM for about two months. See photos. On the after picture you can see a round sore which is from the biopsy. In addition, my husband who has cOPD and had bypass surgery last year, and myself have great, new energy. In addition, my nerve damaged feet and numbness in my right foot have improved by at least 80 per cent after only 5 weeks! For the first time in 15 years or so, I can now feel my right big toe and it is no longer cold, like a piece of granite, and our bad backs have greatly improved. I could go on and on and I don't need someone like you to tell me and thousands of others that it does not work! We are walking human studies for this amazing product! Check out the human studies for liver disease! I am proof it works so you should take another look: in fact go to You Tube PROTANDIM testimonials and see for yourself what this product does when it reduces oxidative stress!

My most recent article was in May 2017, and I'm not aware of any new

studies requiring me to "update my studies" in the last six months. The evidence on the website is mainly about Nrf2 protein messengers in general, and studies of Protandim in cell culture (in vitro) and in mice. One 2006 human study found changes in lab tests such as TBARS but did not even attempt to look for any clinically meaningful improvement in health outcomes. A second human study in 2016 was negative: It concluded "Protandim® did not (1) alter 5-km running time, (2) lower TBARS at rest (3) raise antioxidant enzyme concentrations compared to placebo (with exception of SOD in those ≥ 35 years old) or, (4) affect quality of life compared to placebo." And another study of patients with alcohol use disorders was also negative. Not only negative but laughable.

Conclusion. Increasing levels of antioxidants could be beneficial or harmful. The only way to know if Protandim improves human health is to do properly designed, placebo-controlled human studies looking for meaningful clinical outcomes.

dōTERRA essential oils

I have written about dōTERRA twice before: here and here.

An email asked me to "Check with Johns Hopkins and the research published about dōTERRA oils. Dr. Nicole Parrish claims that dōTERRA oils have killed three super bugs that synthetics cannot. It is published and the medical world is learning more about essential oils in September." I asked her for links to that research; she never responded.

Another email chastised me for having a "complete scientific mindset." (I thought that was a *good* thing!) She said, "It really is worth looking further into to help people stay healthy." She provided all kinds of testimonials: her dentist and her real estate agent use it, her son and stepson carry the beadlets with them during allergy season, and when her husband got cancer, they used essential oils for diabetes, neuropathy, infections, and asthma. She also chastised me for not mentioning what the Bible says about oils and plants! She believes "science is here to prove God's existence and the Bible can be used for medicinal research." I didn't try to answer her.

An in vitro study was done on dog kidney cells infected with influenza virus.

Based on their results, they speculated that essential oils *might* be useful in treating humans with influenza (or might not). In my article critiquing that study, I provided some guidelines on how to read research studies that claim to support a product.

A third email said I needed to visit the website again and review the 17 studies published in peer-reviewed journals. I found an in vitro study of frankincense and an in vitro study of Deep Blue, a mixture of essential oils. There was also an extensive bibliography which included a lot of irrelevant articles along with in vitro and animal studies. There were a lot of scattershot preliminary studies on individual oils, but these were seldom if ever followed by replications or confirmations. My own PubMed search found a few studies supporting the use of an essential-oil-containing mouthrinse, reports of adverse effects of essential oils, some negative studies, and a couple of Cochrane reviews that pointed out the poor methodology of the few studies they found. A 2012 systematic review of aromatherapy concluded "the evidence is not sufficiently convincing that aromatherapy is an effective therapy for any condition."

My correspondent said, "In my opinion, there are too many confirmed reports of improved health & well-being (when using essential oils) to chalk it all up to "hysteria" or "ignorance" or even chance." Her opinion is misguided. The plural of anecdote is not data. Confirmed reports of improved health and well-being, no matter how numerous, are meaningless without a control group. Reports of failures are not systematically collected. Patients may improve for reasons other than the oils: suggestion, placebo effect, social factors, the natural course of the disease, regression to the mean, etc.

Essential oils can be very pleasant to use, and I have no problem with using them as "comfort" measures. And the company website is careful not to make any egregious disease-prevention or -treatment claims. But at their in-home presentations, the distributors feel free to claim that the oils can cure anything and everything, including cancer. These claims are not backed by any science but are illustrated by persuasive anecdotes, touching and heartwarming stories, testimonials from users that the attendees may know personally. Attendees are easily influenced to believe and to buy.

The published evidence for each of dōTERRA's many products is sparse to

nonexistent. There *are* clinical studies to support *a few* of the recommended uses, but they are generally poorly designed, uncontrolled, unreplicated, and unconvincing. Research is difficult, because patients can't be blinded to the odors, and mental associations and relaxation could account for most of the observed effects. I remain skeptical of the claims for objective benefits in treating diseases.

Conclusion: no reason to change my mind

Testimonials are notoriously unreliable. These products are not supported by acceptable scientific evidence. I'm *not* saying they *don't* work. No one knows whether they work or not, because they have not been properly tested. I am simply asking for a single standard of evidence, the kind of evidence required to achieve a scientific consensus that any treatment is effective and safe. If they want us to buy their products, they should test them against placebo controls in human studies looking for objective, meaningful improvements in health; and they should get those studies published in reputable peer reviewed journals. In the pharmaceutical industry, only a small percentage of promising candidates survive testing. Considering the huge number of dietary supplement products like these on the market, the chance that any one of them will prove to be truly effective is vanishingly small.

We here at SBM devote a lot of discussion to unscientific and pseudoscientific treatment modalities, the vast majority of which can be best described as quackery. Sometimes, though, what's even more interesting are controversies in "conventional" science-based medicine. In particular, I'm a sucker for clinical trials that have the potential to upend what we think about a disease and how it's treated, particularly when the results seem to go against what we understand about the pathophysiology of a disease.

So it was that I started seeing news reports last week about ORBITA (Objective Randomised Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina). Basically, ORBITA is a double-blind, randomized controlled trial comparing percutaneous coronary intervention (PCI, or, as it's more commonly referred to colloquially, coronary angioplasty and/or stenting) versus a placebo procedure in patients with coronary artery disease. Indeed, the sham procedure is what makes this trial interesting and compelling, although the devil is in the details. What this trial and its results say about coronary artery angioplasty and stenting, placebo effects, and clinical trial ethics are worth exploring. Basically, ORBITA calls into doubt the efficacy and usefulness of PCI in a large subset of patients with stable angina (chest pain or discomfort due to constriction of one or more coronary arteries that most often occurs with fairly predictably with activity or emotional stress—that is, exertion).

Before I dig in, I can't resist mentioning that cardiac surgery was one of the very earliest forms of treatment in which the importance of a sham surgery control was shown to be very important. In 1939, an Italian surgeon named David Fieschi developed a technique in which he tied off (ligated) both internal mammary arteries through two small incisions, one on each side of the sternum. The idea was to "redirect" blood flow to the heart in order to overcome ischemic heart disease, in which the patient suffers pain, heart failure, or even death due to insufficient blood flow to the heart muscle caused by atherosclerotic narrowing of one or more of the coronary arteries. The results were striking, as three quarters of all patients on whom Dr. Fieschi did his procedure improved and as many as one third appeared to be cured. The procedure became very popular and appeared to work.

Nearly two decades later, in the late 1950s, the NIH funded a cardiologist in Seattle named Dr. Leonard Cobb to do a randomized controlled clinical trial of the Fieschi technique. He operated on 17 patients, of whom eight underwent the true Fieschi procedure, with both internal mammary arteries tied off, and nine underwent skin incisions in the appropriate location. In 1959, Dr. Cobb's results were published in the New England Journal of Medicine, where he reported that the results were the same for patients who underwent the "real" Fieschi operation or the sham procedure. This was the beginning of the end of internal mammary ligation as a treatment for angina and a landmark in the history of surgery. After this trial, understanding of the ethics of human subjects research changed, and including sham surgical procedures in clinical trial design became increasingly frowned upon.

ORBITA is one of several recent trials that use sham interventions that have been reported in recent years as that ethical understanding has shifted again in the face of increasing evidence that surgery can produces the most powerful placebo effects of all interventions. Another example is trials of vertebroplasty for vertebral fractures due to osteoporosis, which showed that vertebroplasty in this setting produced results indistinguishable from the sham procedure. Increasingly, it has been argued that more surgical trials should include a sham procedure group.

PCI: A brief history

Publication of the results of ORBITA were timed to coincide with the 40th anniversary of the development of PCI. Basically, coronary angioplasty was developed 40 years ago as a less invasive treatment than coronary artery bypass grafting (CABG) for coronary artery disease. In brief, in PCI a cardiologist will thread a catheter up a major blood vessel in the groin to the heart and into the coronary artery (or arteries) with blockages. At the end of the catheter is a balloon. The idea is to thread the end of the catheter under fluoroscopic guidance (fluoroscopy is a form of X-ray imaging with video) into the coronary artery and past the blockage, such that the balloon aligns with the atherosclerotic blockage. The balloon is then inflated to open up the blockage. That's the basic idea, although the methods have evolved markedly over the last forty years.

At this point I can't help but mention a bit of a personal note, as it involves the research I did as part of my PhD thesis, lo these many years ago. One of the huge problems with angioplasty early on was the high rate of restenosis (recurrent narrowing) of the blood vessel treated. The reason for this was that balloon angioplasty involved, in essence, injuring the vessel. As with any injury, there was an inflammatory reaction, and one consequence of the inflammatory reaction due to angioplasty is that the vascular smooth muscle cells in the media (the middle layer of the blood vessel) would be stimulated to proliferate and restenose the vessel. As part of my PhD thesis, I cloned and characterized a homeobox gene (yes, a homeobox gene, for you geeks out there) that inhibited the proliferation of vascular smooth muscle cells. The idea was to treat the area at the time of the procedure with this gene as a form of gene therapy to prevent restenosis.

I realize that those of you out there who might be cardiologists and who weren't practicing back in the 1990s probably think this was an insane idea, but here's why it wasn't so insane back then. Back then, coronary stents hadn't been perfected, much less the drug-eluting coronary stents that are commonly used now to prevent restenosis. Basically, after most angioplasty procedures now, cardiologists place a stent in the area of former blockage. To prevent cellular ingrowth into the holes of the stent and subsequent restenosis, the stent slowly elutes a drug that prevents the proliferation of vascular smooth muscle cells. (As an aside, one of the things about these stents that frequently causes problems to surgeons like me is that the patient needs to be on powerful anti-platelet drugs like Plavix for up to a year after stenting). In any case, with the development of drug-eluting stents, the idea of gene therapy to prevent restenosis disappeared into the dustbin of scientific history, for the most part.

Back when PCI was new and young, its indications were a lot more limited, but as time went on and cardiologists' confidence grew indications expanded to multivessel disease and other indications that used to mandate CABG, to the point that PCI for acute coronary syndromes has grown to predominate. As MedPageToday describes:

> In the early years of PCI it was widely believed that PCI to open a severely blocked artery would have long term cardiovascular benefits,

> even in stable patients. Angina patients, the thinking went, were at higher risk for CV events and death, and PCI or CABG lowered that risk by restoring flow through the blocked vessel and preventing a future MI. But doubts grew over time, as it became increasingly clear that MIs were more likely to occur at other, less obvious blockages. Coronary artery disease began to be seen more as a systemic condition and less as a focal plumbing problem. The positive role of medical therapy, including statins and aspirin, became increasingly recognized.
>
> Finally, a decade ago the COURAGE trial, despite widespread and fierce initial resistance in the interventional cardiology community, led to widespread agreement that in fact PCI in stable lesions did not produce long-term improvements in outcome when compared to optimal medical therapy (OMT).
>
> But PCI for stable angina maintained a strong clinical presence as a new consensus emerged in the cardiology community that PCI was superior to OMT in the relief of symptoms. The mantra was that patients would need a stent eventually so they might as well get it upfront. It is this reduction in symptoms that the ORBITA trial sought to test.

And it is this assumption or belief that ORBITA called into doubt, at least for one large subset of patients.

ORBITA

ORBIT has been published in the online first section of The Lancet; so let's dig in. The introduction tells the tale, and you don't even have to leave the abstract:

> Symptomatic relief is the primary goal of percutaneous coronary intervention (PCI) in stable angina and is commonly observed clinically. However, there is no evidence from blinded, placebo-controlled randomised trials to show its efficacy.

Or, in more detail in the introduction:

> Percutaneous coronary intervention (PCI) was originally introduced to treat stable angina.1 More than 500 000 PCI procedures are done annually worldwide for stable angina. The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial showed no difference in myocardial infarction and death rates between patients with stable coronary artery disease who underwent PCI and controls.[2] Meta-analyses have shown similar results.[3]
>
> Angina relief remains the primary reason for PCI in stable coronary artery disease.[4] Guidelines recommend antianginal medication as rst line therapy, with PCI reserved for the many patients who remain symptomatic.[5]
>
> Data from unblinded randomised trials have shown significant exercise time improvement, angina relief, and quality of life improvement from PCI.[6–8] However, symptomatic responses are subjective and include both a true therapeutic effect and a placebo effect.[9] Moreover, in an open trial, if patients randomised to no PCI have an expectation that PCI is advantageous, this might affect their reporting (and their physician's interpretation) of symptoms, artifactually increasing the rate of unplanned revascularisation in the control group.[4,10]

So the investigators who designed ORBITA sought to do a rigorous randomized, double-blind, sham-controlled clinical trial of PCI for patients in stable angina. One can argue that such a trial should have been done a long time ago, before PCI became such a popular procedure for stable angina, and you would be correct. However, it's been done now; so let's look at the design. First, the inclusion criteria:

- Age 18-85 years
- Stable angina/angina equivalent
- At least one angiographically significant lesion (≥70%) in a single vessel that was clinically appropriate for PCI

Exclusion criteria:

- Angiographic stenosis ≥50% in a nontarget vessel

- Acute coronary syndrome
- Previous coronary artery bypass graft surgery
- Left main stem coronary disease
- Contraindications to DES
- Chronic total coronary occlusion
- Severe valvular disease
- Severe left ventricular systolic impairment
- Moderate-to-severe pulmonary hypertension
- Life expectancy <2 years
- Inability to give consent

Other fedatures of the patient population studied:

- Previous PCI: 13%
- Left ventricular ejection fraction normal: 92%
- Canadian Cardiovascular Society angina severity grading class: I (3%), II (59%), III (39%)
- Angina duration: 9 months
- Vessel involved: left anterior descending (69%)
- Median area stenosis by quantitative coronary angiography: 85%
- Median baseline FFR value: 0.72; median post-PCI FFR value: 0.9

The primary endpoint to be assessed was improvement in exercise time. To determine if PCI patients with stable angina and evidence of severe single-vessel stenosis were randomized 1:1 to either PCI or a sham procedure. After enrollment, patients in both groups underwent six weeks of medical optimization. After that, they underwent either PCI or sham procedure with auditory isolation in which the subjects all wore headphones playing music throughout the procedure. During the procedure, patients' heart function (measurements known as fractional flow reserve (FFR) and instantaneous wave-free ratio (iFR)) was monitored using a research method, but operators were blinded to the physiology values and did not use them to guide treatment. Randomization occurred after this physiological assessment. For patients undergoing PCI, the operator used drug-eluting stents according to standard clinical guidelines with a mandate to achieve complete revascularization as determined by angiography. In the sham procedure group, subjects were kept sedated in the cath lab for at least `15 minutes, with

the coronary catheters withdrawn with no intervention having been done. Here's the summary of the timeline and allocation of the trial:

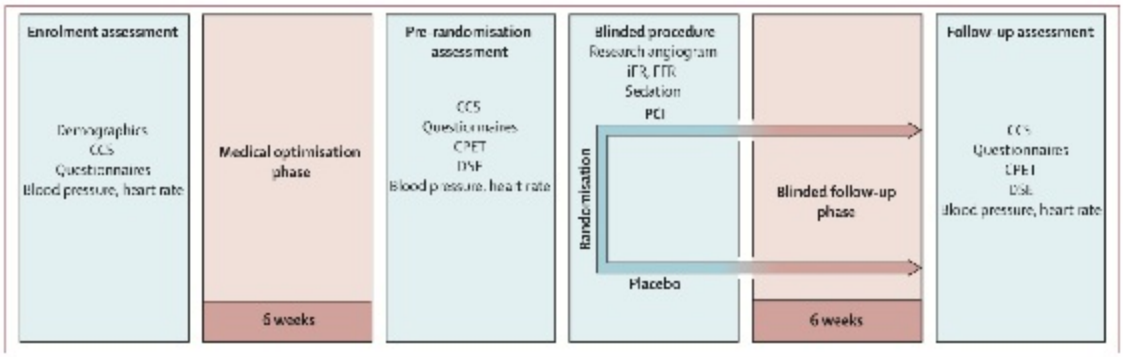


Figure 1: ORBITA study design
CCS=Canadian Cardiovascular Society angina severity grading. CPET=cardiopulmonary exercise testing. DSE=dobutamine stress echocardiography. iFR=instantaneous wave-free ratio. FFR=fractional flow reserve. PCI=percutaneous coronary intervention

Here's the trial outline:

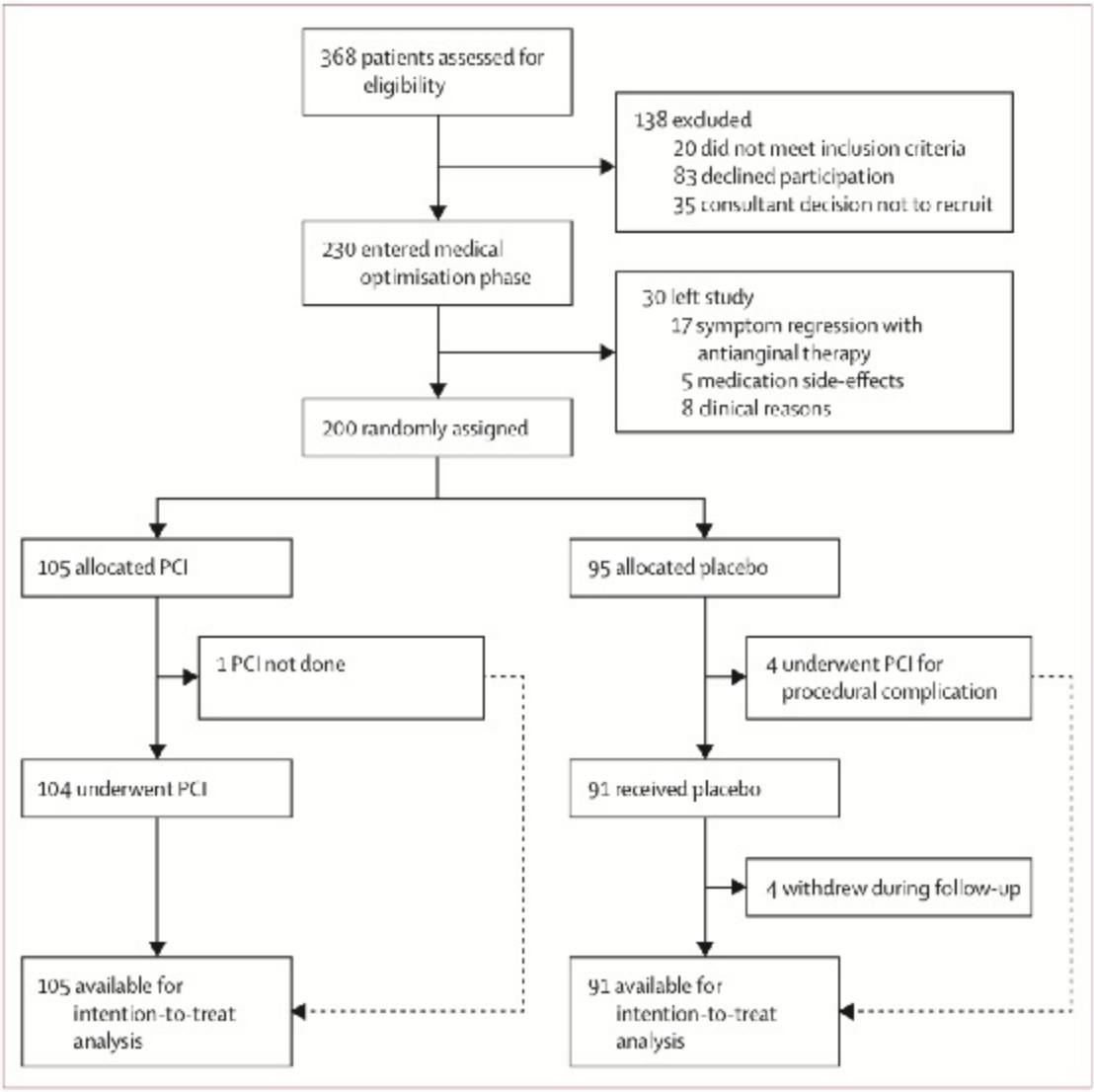


Figure 2: **Trial profile**
PCI=percutaneous coronary intervention.

Overall, there were 230 patients enrolled, of which after the medical optimization phase 200 were randomized, with 105 patients assigned to PCI and 95 assigned to sham procedure. And the results? They were what we call in the business a big nothingburger. The change in exercise time from baseline for PCI vs. sham, was 28.4 vs. 11.8 seconds, p = 0.2. Secondary outcomes were no better:

- Change in Seattle Angina Questionnaire (SAQ)-physical limitation from baseline: 7.4 vs. 5.0, p = 0.42
- Change in SAQ-angina frequency from baseline: 14.0 vs. 9.6, p = 0.26

- Change in Duke treadmill score from baseline: 1.22 vs. 0.1, p = 0.10

Also, at followup six weeks later, patients in both groups were receiving a mean of 2·9 medications; so PCI didn't decrease the need for cardiac medications. In other words, there was no statistically significant change in either the primary or secondary outcomes in patients with stable angina. The authors noted:

> In ORBITA, the first blinded, placebo-controlled trial of PCI for stable angina, PCI did not improve exercise time beyond the effect of the placebo. This was despite the patients having ischaemic symptoms, severe coronary stenosis both anatomically (84·4% area reduction) and haemodynamically (on-treatment FFR 0·69 and iFR 0·76), and objective relief of anatomical stenosis, invasive pressure, and non-invasive perfusion indices (FFR p<0·0001, iFR p<0·0001, stress wall motion score index p=0·0011). There was also no improvement beyond placebo in the other exercise and patient-centered effects with placebo effects. Forgetting this point, or denying it, causes overestimation of the physical effect.

In an accompanying editorial, David L. Brown and Rita F. Redberg commended the ORBITA investigators for "challenging the existing dogma around a procedure that has become routine, ingrained, and profitable," noting that ORBITA shows "(once again) why regulatory agencies, the medical profession, and the public must demand high-quality studies before the approval and adoption of new therapies" and characterizing PCI for stable angina as putting "PCI in the category of other abandoned therapies for cardiovascular disease, including percutaneous trans-myocardial laser revascularisation[10] and catheter-based radiofrequency renal artery sympathetic denervation[11]—procedures for which the initial apparent benefit was later shown in sham-controlled blinded studies to actually be due to the placebo effect." Noting that the short duration of followup actually would favor PCI because "any haemodynamic benefit from PCI occurs early and the benefits of medical therapy continue to accrue over years," Brown and Redberg conclude:

> The implications of ORBITA are profound and far-reaching. First and

> foremost, the results of ORBITA show unequivocally that there are no bene ts for PCI compared with medical therapy for stable angina, even when angina is refractory to medical therapy. Based on these data, all cardiology guidelines should be revised to downgrade the recommendation for PCI in patients with angina despite use of medical therapy. ORBITA highlights the importance of including sham controls and double blinding in a trial to avoid being fooled by illusory improvements due to the powerful placebo e ect of procedures such as PCI. Although sham-control procedures are associated with some adverse outcomes, those complications are dwarfed in magnitude by the rate of adverse events in the approximately 500 000 patients who undergo PCI for symptomatic relief of stable angina in the USA and Europe each year. These adverse events include death (0·65%), myocardial infarction (15%), renal injury (13%), stroke (0·2%), and vascular complications (2–6%).12 Health-care providers should focus their attention on treating patients with stable coronary artery disease with optimal medical therapy, which is very e ective, and on improving the lifestyle choices that represent a large proportion of modi able cardiovascular risk, including heart-healthy diets, regular physical activity, and abstention from smoking.

Based on the results of this trial, one can easily argue that PCI should rarely —if ever—be performed in patients with single vessel disease and stable angina.

The backlash

Not surprisingly, there was pushback. Cardiologists were not pleased by this result, even though it has been well known for a long time that in patients like those studied in ORBITA, PCI at least doesn’t improve survival or decrease progression to need revascularization more than OMT. For instance, in a on the study various cardiologists were quick to make excuses:

> Panelist Dr Martin Leon (Columbia University Medical Center, New York City) applauded the investigators efforts for a “remarkable study” but said it’s a much, much higher bar to achieve when the end points are

differences from baseline between two groups.

"Baseline data demonstrating that these patients had very good functional capacity, had infrequent angina, had very little ischemia, means that regardless of what you did to the coronary artery there was going to be very little you could demonstrate in terms of clinical therapeutic benefit. So I'm really glad that PCI had a statistically significant benefit in both echos and the stress tests," Leon said.

"The concern here is the results will be distorted and sensationalized to apply to other patient populations where this kind of outcome very likely would not occur," he added.

My counter to the argument that the patients included in this trial were not that sick is: Yes! That's the point. These are exactly the sorts of patients who too frequently are subjected to PCI for in essence no benefit over that which can be achieved by medical management.

Next up:

Commenting for theheart.org | Medscape Cardiology, Dr Roxana Mehran (Ichan School of Medicine at Mount Sinai, New York City) said, "To me actually this study shows angioplasty is quite effective in reducing ischemia, improving [fractional flow reserve] FFR, and in fact I'm actually very pleased with this. It's exactly what I want to do for my patients—improve their blood supply."

Asked whether this isn't just a positive spin on a negative study, Mehran quickly responded, "No," adding that whenever a primary end point is a change in a value, showing an important difference is very hard to do when baseline values are so good, especially with only 200 patients.

"I promise you, had she studied 400 patients this would be positive because everything was in the right direction," she said.

Actually, that's exactly what she's doing, trying to put a positive spin on a negative study. It's so blatantly obvious that that's what Dr. Mehran is doing that she should really be embarrassed to have said something like this to be

published for the public to read. In fairness, she does have a germ of a point in that the study was relatively small and potentially underpowered to detect some differences. On the other hand, it's rather interesting to note how some cardiologists totally twist the usual rationale and methodology used to determine if a therapy works. Here's what I mean.

Normally, when a new intervention is first tested, it's tested in small pilot trials. If a positive result is observed, that result justifies a larger trial to confirm efficacy and safety. If a positive result is not observed, then the treatment is generally abandoned or modified. before being tested again. Now, get a load this:

> During the press briefing Dr Robert Yeh (Beth Israel Deaconess Medical Center, Boston, MA) congratulated the authors on a courageous, bold, and well-executed trial but said the results reaffirm in many ways those from COURAGE.
>
> "To extrapolate that this means that elective PCI is not an indicated procedure is the furthest overreach that I can possibly imagine from a very small and I think hypothesis-generating trial with an interesting result," he said.

Let's grant Dr. Yeh his characterization of this study as "hypothesis-generating." When hypothesis-generating studies are negative, the hypothesis is usually considered to be not worth testing further, barring serious methodologic or design issues in the hypothesis-generating study. To demand another, much larger, much more expensive study to follow up on a result that, even if Dr. Yeh is correct, would likely be a very modest difference in an increase in exercise tolerance. Basically, much, although in fairness not all, of what these cardiologists are doing is to make excuses.

None of this is to say that ORBITA is bulletproof. It is, compared to other trials of PCI, relatively small. There was a trend towards improved exercise tolerance in the PCI group compared to the sham group that might have been significant with more patients. The question, of course, is whether it would be worth it to do another larger trial. After all, interventional cardiologists are utterly convinced that PCI is more effective than OMT and are unlikely to change practice (much) based on this trial:

> How will the results of ORBITA be viewed? It will be a combination of love and hate. ORBITA was rigorously designed and undertaken with great care and painstaking attention to detail using objective exercise and physiologic outcome measures before and after stabilization on OMT, combined with the use of well-validated quality of life metrics before and after randomization. Overall, the results were stunningly negative, which ORBITA supporters will cite. By contrast, it is very likely that many in the interventional community will be ready to pounce on and discredit this study — there certainly hasn't been an opportunity since COURAGE was published 10 years ago in 2007 to potentially discredit a trial that now confronts the sacred cow of PCI benefit for angina relief as the sole basis to justify PCI in stable CAD patients. They will likely cite the limitations of small numbers (only 200 patients), that the study was woefully underpowered, the potential ethical conundrum of subjecting subjects with significant flow-limiting CAD to a sham procedure (or deferred PCI for clinical need), that 28%-32% of randomized subjects had either normal FFR or IFR (and therefore didn't have a "physiologically significant," or flow-limiting stenosis, that PCI would otherwise benefit), that there was a low frequency of multivessel CAD, that the short duration of follow-up (only 6 weeks) was too brief to assess potential benefit (though this actually favored the PCI group) and, of course, who would have the time or patience to call patients three times/week to assess their response to intensifying medical therapy — "not real-world," just like the OMT used in COURAGE wasn't achievable in the real-world.

Despite these reactions, I do have some optimism. Interventional radiologists reacted very negatively to the trials showing that vertebroplasty for osteoporotic spinal fractures doesn't work. Eventually, they started to come around, and usage of vertebroplasty for this indication is declining, albeit not as fast as it should. Science- and evidence-based medicine is messy, and there is some truth to the old adage that old treatments don't ever quite disappear until the generation that learned them retires or dies off. But change does come in response to clinical trials.

In the meantime, whatever effect ORBITA has on clinical practice, it should serve as a wakeup call that in clinical trials of surgical or procedural

interventions examining endpoints with a degree of subjectivity (unlike, for instance, death or time to cancer recurrence), whenever possible, new interventions should be compared to sham procedures. Of course, this isn't always possible, either for ethical or practical reasons, but when it is practical sham procedures are just as essential as placebo controls in drug trials.

Three years ago, Mark Crislip closed a post discussing the ABIM Foundation's Choosing Wisely initiative with the following thought:

> I wonder if a chiropractor could come up with five standards treatments in chiropractic to be avoided…

Well, now they've finally gone and done it, with results that, while not entirely without merit, are a bit off the mark in my opinion.

Choosing Wisely and chiropractic

For the sake of further discussion, let's all just agree to ignore the fact, also pointed out by Dr. Crislip in his post, that chiropractic as a profession doesn't exactly stand up to the scrutiny of the campaign's criteria:

> *Choosing Wisely* aims to promote conversations between clinicians and patients by helping patients choose care that is:
>
> - Supported by evidence
> - Not duplicative of other tests or procedures already received
> - Free from harm
> - Truly necessary

Of course to be fair, no medical intervention is completely "free from harm", but I assume that what the ABIM Foundation actually means is that interventions should have a favorable risk to benefit assessment. This is arguably not the case when assessing chiropractic as a whole. While not all of the treatments I prescribe are based on robust randomized controlled trials, they are "supported by evidence" in the vast majority of cases, and often by very good evidence. Chiropractic doesn't really bring anything original to the table that passes this test.

There are similar issues with the phrase "truly necessary", whatever that means. Many medical interventions aren't "truly necessary" in my opinion. Other Choosing Wisely lists cover a number of these, but there are also tests

and treatments that may have value while perhaps not meeting this criterion absolutely depending on who is assessing the scene. But again, being charitable, I assume that the ABIM Foundation is focusing on common interventions for common human ailments that don't tend to improve objective outcomes.

Specific treatments provided by a chiropractor might provide some objective benefit for a small sliver of musculoskeletal complaints, with those unique to chiropractic being the least helpful. But whatever improvement that can be attributed to visiting a chiropractor isn't better than more conventional approaches, such as physical therapy or recommendations from a patient's primary care provider for exercise, stretching, massage, etc. These approaches come with considerably less baggage and aren't as likely to be accompanied by pseudoscience or anti-vaccine propaganda.

The Choosing Wisely lists published by participating organizations aren't meant to serve as treatment guidelines, of course. Instead, they are intended to encourage a conversation around whether or not the listed interventions are a good idea, or if they may put patients at risk of more harm than benefit. Unfortunately, in my opinion, they have largely gone unnoticed by medical providers and the general public. I am confident that the list of questionable chiropractic interventions will be similarly ignored by practitioners.

The ACA's list

The list in question, released in August, comes from the American Chiropractic Association (ACA). The ACA claims 15,000 members, which is less than a quarter of practicing chiropractors, and recognizes 11 specialty areas, such as chiropractic acupuncture, pediatrics, diagnosis and management of internal disorders, and forensic sciences. It describes itself with typical grandeur:

> The American Chiropractic Association (ACA) is the largest professional chiropractic organization in the United States. ACA attracts the most principled and accomplished chiropractors, who understand that it takes more to be called an ACA chiropractor.

> We are leading our profession in the most constructive and far-reaching ways — by working hand in hand with other health care professionals, by lobbying for pro-chiropractic legislation and policies, by supporting meaningful research and by using that research to inform our treatment practices.
>
> We also provide professional and educational opportunities for all our members and are committed to being a positive and unifying force for the practice of modern chiropractic.

What does it take to called "an ACA chiropractor"? Membership requirements consist of being a licensed chiropractor in the United States and paying yearly dues. The ACA even goes so far as to state that they do not deny membership to anyone meeting the above qualifications as long as what they do in their practice isn't illegal. In that way, they are similar to the American Academy of Pediatrics, which even allows pediatricians who are blatantly anti-vaccine to be members in good standing.

Here are the five things that chiropractors and their patients should question according to the ACA:

Do not obtain spinal imaging for patients with acute low-back pain during the six (6) weeks after onset in the absence of red flags.

What red flags, you ask? The ACA mentions "history of cancer, fracture or suspected fracture based on clinical history, progressive neurologic symptoms and infection, as well as conditions that potentially preclude a dynamic thrust to the spine, such as osteopenia, osteoporosis, axial spondyloarthritis and tumors". I would argue that if you have any of these red flags, you should not be under the care of a chiropractor. There isn't any evidence to support superiority of chiropractic care to conventional approaches for acute low-back pain anyway.

Do not perform repeat imaging to monitor patients'

progress.

They list idiopathic scoliosis as an exception, despite the fact that their own research shows no good evidence to support chiropractic management of this condition. I agree with this recommendation, and the reasoning of the ACA in this case is sound. I'm just not holding my breath while waiting to see if this will change anything, however.

Avoid protracted use of passive or palliative physical therapeutic modalities for low-back pain disorders unless they support the goal(s) of an active treatment plan.

In other words, commonly recommended interventions like heat, ultrasound, and electrical stimulation, shouldn't be used in isolation because they don't provide much benefit. The absolute worst thing you can do to prevent or treat lower back pain, which virtually all humans will experience at some point in their lifetime thanks to evolution, is nothing. General physical activity and back specific exercises are key, and in no way unique to chiropractic.

I don't think you will find many chiropractors not recommending an exercise regimen for lower back pain disorders, so this item is a bit odd. You also won't find many that won't provide some kind of spinal manipulation, because that's their thing that they do. In this section, the ACA writes that physical activity and back exercises "may lead to better outcomes when combined with spinal manipulation." In reality, spinal manipulation is more like multiplying by one. It changes nothing for the long term outcome.

Do not provide long-term pain management without a psychosocial screening or assessment.

Chronic pain disorders often have a psychosocial component. Chronic pain can cause or be caused/exacerbated by anxiety and depression, for example.

Some patients are at risk for the development of chronic pain because of a variety of psychosocial factors and chiropractors are not trained to evaluate or manage them. The ACA recommends that chiropractors use a screening tool and refer when necessary because the ACA imagines chiropractors to be primary care providers.

Do not prescribe lumbar supports or braces for the long-term treatment or prevention of low-back pain.

Another odd inclusion. Chiropractors simply aren't out there putting people in back braces for long periods of time for treatment or prevention of back pain. I was easily able to find that this recommendation is already widely accepted. Meanwhile, the ACA is inviting speakers to their conferences to promote nonsense like the Activator Method.

The ACA press release announcing their participation in Choosing Wisely is interesting. They point out that multiple other organizations already participating have included recommendations to avoid spinal imaging for acute lower back pain. It's a solid recommendation, but instead of actually attempting to show a commitment to change by pointing out some of the abject nonsense they have supported sans evidence, they went the safe route. And in the press release they essentially give their members enough wiggle room that they can continue obtaining frequent spinal films without losing any sleep.

My favorite quote involves the practice of "defensive medicine":

> As with many of our colleagues in the health care professions, we have learned from experience to practice "defensive medicine." This perspective may be even more deeply ingrained within the chiropractic profession based on our prior experiences with bias and/or lack of understanding regarding chiropractic care. As an example, just look how long it took before Choosing Wisely® was even willing to consider a chiropractic list!

So do chiropractors practice defensively, which implies a concern for facing a malpractice suit, or not? It would appear that the latter is the case when you consider how often they point out how undeniably safe chiropractic is. Often this is done in the context of attacking conventional medical care. It's also unclear to me how the medical community's lack of "understanding regarding chiropractic care" encourages defensive practice.

Conclusion: The ABIM did not Choose Wisely

How does the ACA describe chiropractic on the Choosing Wisely website? Just as you would expect them to, of course. Remember though that this is an organization that is fighting for chiropractors to be considered primary care physicians complete with the right to prescribe medications.

> Chiropractors focus on disorders of the musculoskeletal system and the nervous system, and the effects of these disorders on general health and function. Chiropractic services are used most often to treat conditions such as back pain, neck pain, pain in the joints of the arms or legs, and headaches. Widely known for their expertise in spinal manipulation, chiropractors practice a hands-on, drug-free approach to health care that includes patient examination, diagnosis and treatment.

The ABIM Foundation is very likely completely ignorant of both the history and the current reality of the chiropractic profession. Frankly I think it's ridiculous that a chiropractic organization was invited to participate. We certainly have come a long way from Wilk v. AMA, haven't we?

This is just another example, in a very long line, of the undeserved legitimization of alternative medicine that will serve as more of a marketing purpose than as a means of improving chiropractic practice. All that the ACA has done is provide a list of redundant or unnecessary recommendations. And the few chiropractors who already avoid excessive spinal imaging will continue to do so, while the vast majority will compartmentalize these "suggestions" and carry on as is.

Extras

- Here is a response to the ACA Choosing Wisely list from the International Chiropractic Association.
- Here is an ACA video describing the benefits of pediatric chiropractic. In March of 2017, the ACA reaffirmed its public policy on chiropractors as primary care providers. This policy includes the following:

> Doctors of chiropractic also recommend and manage dietary changes, nutritional interventions, botanical medicines, homeopathic medicines, acupuncture and other services when indicated.

The ACA, while not overtly anti-vaccine in policy, supports conscience waivers.

Science Based Medicine

周三, 15 11月 2017

Science Based Medicine

[周三, 15 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Turpentine, the Fountain of Youth According to Dr. Jennifer Daniels** [周二, 14 11月 16:00]
  Jennifer Daniels says turpentine is the Fountain of Youth, able to cure many ailments, both real and imaginary. It isn't; it's a poison with no recognized benefits for human health.
- **Why do some women refuse treatments for their breast cancer?** [周一, 13 11月 16:14]
  Adjuvant therapy after surgery, such as chemotherapy, hormonal therapy, and radiation therapy, has contributed to a 39% decrease in breast cancer mortality since 1989. Unfortunately, a significant number of women decline evidence-based adjuvant therapy. A recent study suggests that distrust of the medical system plays a significant role in such refusal.

Read the label. It doesn’t list any health benefits. It says harmful or fatal if swallowed.

Turpentine is a solvent and a poison, but some people are drinking it as a medicine.

Scott Gavura wrote about it

2 years ago and concluded, “There’s no reason to consume turpentine and multiple reasons to avoid it completely, with the primary reason being that

it’s a poison

.”

Scott’s article mentioned an MD who advocates turpentine to cure the fake illness chronic *Candida*, and who had been stripped of her license. That MD was Jennifer Daniels. It would be bad enough if she only recommended it for Candida, but she also claims to have discovered that turpentine is the Fountain of Youth, a miracle cure that reverses disease and aging and is good for pretty much whatever ails you. That’s ludicrous.

The facts

The *Natural Medicines Comprehensive Database* (which I consider to be the most reliable source) says, “There is insufficient reliable information” to evaluate its effectiveness for any medical use. It rates turpentine as “possibly safe” when used topically and appropriately, “possibly unsafe” when applied to large areas of skin, and “likely unsafe” when used orally for medicinal purposes; 2 ml/kg is toxic, and 120-180 ml is potentially lethal in adults.

The *NMCD* goes on to explain that turpentine is a central nervous system depressant, a pulmonary aspiration hazard, a skin irritant, and might cause abortions. It can have a decongestant effect when inhaled. Many adverse reactions are reported from ingestion, including headache, insomnia, coughing, vomiting, hematuria, albuminuria, urinary tract inflammation, coma, and death. Inhalation can cause inflammation and bronchial spasms. Applying it to the skin can lead to kidney and central nervous system damage.

A drug information website has an extensive monograph on turpentine. It says, “Turpentine has been used experimentally in a bath for the treatment of disseminated sclerosis and sexual dysfunction. It also has been studied for its antibacterial activity and inhibition of osteoclast activity. Turpentine is utilized in experimental models of inflammation to induce a systemic inflammatory immune response in animals.” It warns against using it during pregnancy and lactation, stresses that it is highly toxic (fatal poisonings have occurred with ingestion of as little as 15 mL, just 3 teaspoonsful) and has caused skin tumors in animals. It provides a bibliography with pertinent citations.

The discovery

Jennifer Daniels tells the story of her discovery in a radio interview. She asked her African-American patients if their slave ancestors had a miracle cure that cured everything and was cheap; several of them mentioned turpentine and sugar. So she tried it for herself. She put turpentine on 3 sugar cubes and washed them down. Right after ingesting it, she says:

> I think my IQ went up like 50 points, I could just feel it, all this mental energy and understanding and clarity, just like when I was 10 years old, everything was very clear and focused. I said WOW what a feeling. I did some math problems, I said this is pretty good.

She had heard that turpentine could cause seizures, so she figured out the maximum safe dose by stopping at a dose where she felt a little twitch, “even softer than a twitch.” Then she gave it to her mother, who began to feel better *in less than a minute* (!). It relieved pains that her mother had had for 30 years. Other family members served as guinea pigs and appeared to benefit. So with no further ado, Daniels started using it on all her patients.

The published evidence she relies on

In that same interview, Daniels talks about a review article from France with 100 references that supposedly support the use of turpentine for parasites,

cancer cells, pathogenic bacteria, fungus, yeast, rheumatism, MRSA, sciatica, nephritis, constipation, increasing membrane permeability, etc. It doesn't say what she thinks it says.

Using turpentine: The treatment plan

First you have to hydrate. Then you have to have three bowel movements a day, which you can supposedly achieve by taking her Vitality Capsules, which (unlike everything else on earth) contain "no chemicals." If you don't have three bowel movements a day, the *Candida* can't get out of your body and will "shift through your left hip to your right hip, your right hip to your stomach, and your stomach to your shoulder. It's gonna play musical chairs all over your body." Then you have to follow her diet instructions (organic, no GMOs, no "dead food," and many more restrictions). Only then can you do the Candida Cleanse.

She says you must avoid steroids, antibiotics, and chemotherapy, because they prevent cell repair and yeast will move in to eat up the dead cells. She advises patients to stop all their medications if they can (potentially dangerous advice).

She says in the last days of her practice, she stopped using antibiotics. She would not admit seriously ill patients with pneumonia to the hospital, but would dose them with turpentine and send them home. She thinks children with high fevers will recover in less than 24 hours if given turpentine. When her daughter badly injured her ankle, she gave her a teaspoon of turpentine and ¼ cup of castor oil. "She drank it, she pooped, all the pain was gone."

More strange and unsupported claims

- "Liver time is 1-3 AM; lung time is 3-5 AM."
- "Vitality Capsules clean out the bile ducts and the gall bladder system as well as the small intestine, large intestine, and it also promotes circulation."
- Children should start getting turpentine in castor oil when they reach 30

pounds, to prevent *Candida* and parasites.
- You should keep taking turpentine at least once a month for the rest of your life.
- Turpentine improves eyesight; users were able to throw away their reading glasses.
- "if I want thicker hair and less gray hair, then I'm gonna use minerals, small willow flower, and shou wu."
- Turpentine improves diabetes by healing the pancreas. It will allow Type I diabetics to lower their insulin dose.
- It resolves tinnitus.

To her credit, she does get a few things right; for instance, she realizes that "rope worms" are not actually worms. On the other hand, she is anti-vaccine: "There is no vaccine or injection Dr. Daniels recommends."

A spy troll is shocked

David McAfee infiltrated the closed 640-member Facebook group "Parasites cause all disease – turpentine cure" and was appalled at what he found. People were seeking support for the horrible side effects they were experiencing from turpentine. They were hoping to cure everything from scabies to herpes to "electromagnetic hypersensitivity."

One woman who was using turpentine and castor oil complained that when she did enemas a lot of red liquid came out. Another list member told her *not to worry* because it was probably just old and damaged intestine wall coming out!

Some of the comments following McAfee's exposé article were amusing:

- "Sometimes you just roll your eyes, mutter darwinism to yourself and move on."
- "I'm a believer in alternative medicine-trust me, these people aren't into alternative, they are idiots. Anyone with half a brain knows not to ingest a solvent. Dear god, where does this stupidity come from?"
- "There is in my family a story about the medical use of turpentine. It

dates from the time of my grand-father or great-grand-father. It was suggested as a topical treatment for hemorrhoids. It was not suggested in good faith. Folks could have a very crude sense of humor in those days too."

What about science?

Daniels is a graduate of Harvard and of the University of Pennsylvania School of Medicine. Surely she learned about science at those prestigious Ivy League schools. One can only wonder how she came to disregard science and go her own way. She says she reads research studies but does not believe them: "I'm not much of a fan of research because every research project I've been involved with, I've been asked to falsify data." That certainly is an unusual experience, and I can't help but wonder if she reported the fraud/misconduct. She could have had a great career as a whistleblower.

Her words and actions show that she does not think like a scientist. Here are just a few revelations from her *Confidential Underground Report: Top Secret; The Candida Cleanser*.

- She assumed the existence of some folk remedy that was a miracle cure that would cure everything. Considering all the many different causes of different illnesses, this is not a reasonable assumption.
- She experimented on herself and assumed that the dose that seemed to work for her would work for everyone. If that were true, drug companies could dispense with phase 2 trials and just give the drug to one person.
- She describes immediate results, too soon for a medication to be absorbed and have any effect; she doesn't recognize that this is almost certainly a placebo response.
- She doesn't put her belief that turpentine is effective to any kind of test.
- She wonders how long you could take it every day without experiencing side effects. So she takes it daily for a week, notices no adverse effects, and says "I decided that was long enough for the purposes of science." Wow! Wouldn't Big Pharma love to hear that all they needed to do to demonstrate the safety of their drugs to the FDA was to have one person take a drug for a week and say they hadn't noticed any symptoms?

- Without any further testing, she immediately moves on to treating other people with turpentine.
- She makes all kinds of claims unsupported by any evidence, for instance:
    - Breads, meats and dairy are all full of parasites.
    - “Trail mix is an abomination and has destroyed the health of many a health nut.”
    - “It has been *my observation* [emphasis added] that one should be having at least three bowel movements a day.”
    - “There is no medication that turpentine interacts with.”
    - “Censorship is so severe that it is difficult to find information on turpentine in print.”
- She makes dangerous recommendations: laxatives and daily enemas, stopping prescription medications, avoiding immunizations, and many more.

No longer practicing, but…

On her website, it says “Dr. Daniels is a former medical doctor who had her medical license suspended due to not prescribing enough drugs and truly healing her patients.” I don’t believe that; no medical board has ever suspended a doctor’s license for healing their patients or for “not prescribing enough drugs.” According to the New York medical board website, she surrendered her license less than 6 years after it was granted. Apparently she was uncooperative, refusing to share her patient records with the board, and from her comments online it seems she was deliberately trying to hide her many questionable treatment methods from the authorities. By voluntarily surrendering her license, she avoided any further investigation or board actions.

No longer able to practice medicine, Daniels has moved to Panama, where she is making a living producing books, radio shows, CDs, and videos; selling supplements; and advising clients as a health coach. She is available for “Holistic Mentoring Consultations;” you can schedule a consultation online and will be able to speak to the doctor directly. What she is doing may not be illegal, but she is still in a position to harm people with bad advice.

Conclusion: not recommended

Not only is turpentine not the Fountain of Youth, it has not been proven effective for any health condition. Jennifer Daniels is not a reliable source of health information. She fails to understand the need for scientific testing, relies on testimonials and beliefs instead of facts, and demonstrates poor judgment. She makes claims that are bald assertions not supported by any evidence. She is offering dangerous advice, not just about turpentine but about vaccines and other things.

I write about alternative cancer treatments a lot, in particular the lack of evidence for such practices, many of which are at best pseudoscientific and at worst pure mystical nonsense. The reason, of course, is simple. I'm a breast cancer surgeon, and I hate seeing people who might be saved from death due to cancer falling prey to treatments that demonstrably lessen their chances of survival, either by leading patients to reject effective treatment in favor of ineffective or even harmful treatments or, at the very least, to delay effective treatment until the patient realizes that the quackery chosen isn't preventing the growth and spread of his or her tumor. This can sometimes take a long time. I've seen women with breast cancer whose breasts were basically eaten away until there was nothing left but an ulcerated mass on their chest—more than that, a bleeding, rotting, malodorous ulcerated mass. Yes, it's an ugly picture, but I've seen it all too many times.

These sorts of cases are less common, though. Fortunately, relatively few are the women who reject conventional medicine altogether. Indeed, most women will accept surgery of some sort or another, either a lumpectomy or a mastectomy. Sometimes, they undergo an excisional biopsy, not realizing that that for smaller tumors an excisional biopsy can remove the whole tumor and in some cases be curative. No, far more common is the case where a woman accepts surgery but then refuses chemotherapy, hormonal therapy, and/or radiation, either altogether or in favor of some form of quackery. In doing so, such women, whether they simply refuse adjuvant therapy altogether for whatever reason or go beyond that and fall prey to quackery, fail to maximize their chances of surviving their breast cancer, sometimes by quite a bit, and that is something to be concerned about.

Indeed, these sorts of cases were one of the very first topics I ever wrote about on this blog and have remained a staple of the blog ever since, whether I was discussing Suzanne Somers, who had surgery and radiation but apparently refused Tamoxifen for her breast cancer and then later had what she thought to be a recurrence that almost certainly wasn't, other alternative breast cancer cure testimonials (like this one or this one), or even testimonials for other cancers where chemotherapy and/or radiation are used in addition to surgery.

The reason such alternative cancer cure testimonials are compelling is that most people don't understand the difference between the primary treatment for breast cancer and an adjuvant treatment. In the case of breast cancer, for instance (and colorectal cancer as well, among other solid tumors), surgery is the primary treatment and can be curative by itself. What chemotherapy, radiation therapy, and hormonal therapy can add to the treatment of, for example, breast cancer is to decrease the chance of its recurring after successful surgical excision, whether by mastectomy or lumpectomy. All a breast cancer patient does in refusing radiation therapy after successful breast conserving surgery is to accept a risk of recurrence in the breast of 30-40% instead of 5-8%. All a woman does by refusing recommended chemotherapy after surgery is to refuse a relative decrease in their risk of dying of a recurrence of breast cancer by 25-30%, a benefit that is, in absolute terms, much greater for more advanced but still curable breast cancers. However, many of these women who turn down adjuvant therapy in favor of quackery will still survive, thanks to the surgery, and the ones whose cancers recur rapidly disappear from the alternative cancer cure industry PR machine, never to be seen again.

Because adjuvant chemotherapy, targeted therapies, and hormonal therapies have contributed to a decline in mortality from breast cancer of 39% since 1989, it is important to determine why women refuse these treatments and fail to optimize their chances of long term survival. To a lesser, but still important extent, it's important to try to understand what motivates women to turn down effective adjuvant therapy, as that is the first step in developing strategies to persuade them. Recently, there was a relatively large study that addressed just this question.

Patient refusal of adjuvant therapy: A question of trust?

Earlier this month a number of news stories and press releases appeared about a study published in late September by investigators at Johns Hopkins Bloomberg School of Public Health, Columbia University, and Massachusetts General Hospital looking at trust—or, more specifically, a

lack of trust—as a key motivator in women refusing adjuvant therapy recommendations and opting for discordant care; i.e., care that doesn't conform to evidence-based care recommended by the patient's physicians. It's an issue that hasn't been studied as well as it should be, as the authors, Lorraine T. Dean, Shadiya L. Moss, Anne Marie McCarthy, and Katrina Armstrong point out in the introduction:

> Relatively little is currently known about the relationship between healthcare system distrust and cancer treatment. A previous study of distrust and adjuvant cancer treatment (3) found that distrust in medical institutions was associated with increased risk of not initiating adjuvant treatment in a sample of 258 early stage (Stage I and II) breast cancer patients from one urban area. However, that study did not include the following in their analysis: which treatments were recommended by the physician, the extent to which physician distrust mediated the relationship between healthcare system distrust and cancer treatment, and an assessment of those who may have initiated treatment but did not fully adhere to the treatment plan. Other studies of distrust among women with a history of breast cancer have focused on healthcare system distrust and: mental health or psychosocial outcomes (13), quality of care (14,15), greater emotional, physical, financial, and sexual problems after treatment (16), less comfort with the use of de-identified information from medical records for research (17), less endorsement of the necessity of adjuvant chemotherapy (18); and provider distrust and quality of care (19).
>
> The current study was designed to answer two related questions: Is healthcare system distrust associated with whether or not patients follow their physician's recommendations for adjuvant treatment after breast cancer; and does physician trust mediate the relationship between healthcare system distrust and receipt of adjuvant treatment? It expands on prior work by including a large population based sample in two different US states, Pennsylvania and Florida, based on physician recommendations for several adjuvant treatments with explicit testing of the potential mediating role of physician distrust, and assesses patients who did not complete the full treatment plan. To our knowledge, it is the largest study of healthcare system distrust among women with a history

of breast cancer and adds innovation of recruiting through a cancer registry to survey participants about healthcare system distrust.

To this end, the authors used Pennsylvania and Florida cancer registries, using data from a population from a study originally intended to assess the differences in breast cancer women associated with race. The inclusion criteria for the study included localized invasive breast cancer, age under 65 at the time of diagnosis, residency in either Pennsylvania or Florida at the time of diagnosis, and diagnosis between January 1, 2005 and December 31, 2007. Exclusion criteria included patients over 65, cognitive impairment, inability to speak English or Spanish, and metastatic disease at presentation. The overall response rate was very good for surveys of this type, 61%.

For purposes of the survey, cancer treatment discordance was defined as any difference in treatment that a patient reported receiving compared to the treatment the patient reported as having been recommended to her by the treating surgeon and/or oncologist. Now, I know what you're probably thinking: Is this accurate enough? It turns out that simple self-reporting like this is 90% accurate, particularly for yes/no questions about different kinds of therapy. Since the adjuvant therapies used after surgery for breast cancer include radiation therapy, chemotherapy, and hormonal therapy, the authors constructed a combined measure of treatment discordance based on how many of the three therapies patients accepted or declined. Of course, if a particular adjuvant therapy was not recommended for a patient, then not undergoing it couldn't be considered discordant. (For example, depending on the specific characteristics of the tumor, not all breast cancer patients are offered chemotherapy or hormonal therapy; and most patients—but by no means anywhere near all patients—undergoing mastectomy don't require radiation therapy.)

Patients were also assessed for their level of trust in the health care system and their physicians. Trust in the health care system was assessed using the 9-item Health Care System Distrust scale which measures of domains of values and competence distrust on a 5-point agreement scale (1 = strongly disagree, 5 = strongly agree), producing a score ranging from 9 to 45. The authors report that this measure has "acceptable construct validity and high internal consistency (α=0.84 in the current sample)." To measure trust in patients'

physicians, researchers used the 7-item Trust in Physician Scale, which uses a 7- point agreement scale (1=strongly disagree, 7=strongly agree), to produce a score ranging from 7 to 49. Information was also requested on socio-demographic factors, such as age, race, ethnicity, income, education, marital status, employment status, health insurance status, and state of residence at the time of diagnosis. They also went to the cancer registry databases to verify clinical treatment factors, such as stage, surgical removal of cancer, and recurrence.

So what did the authors find? There were 2,754 women included in the final analytic sample, of which 69.8% (n=1,922) reported always receiving the cancer treatments their surgeon or oncologist recommended, and 30.2% (n=832) reported not pursing at least one recommended treatment. I must admit that I was rather surprised that the percentage of discordant cases was so high, but maybe I shouldn't have been. In any case, in the total sample, 10% declined radiation treatment; 11% declined chemotherapy; and 18% declined hormone therapy. (Note that some women turned down more than one modality.) Looking at the numbers, though, some of this does appear to jibe with my clinical experience, in that I've encountered more women who have turned down hormonal therapy than who have turned down others. The reason is probably that hormonal therapy, although only a pill as opposed to chemotherapy, is administered for five or, in more recent recommendations, as many as ten years, and women who can tolerate the much more severe side effects of chemotherapy only have to endure them for a few months, whereas they have a harder time dealing with the side effects of Tamoxifen or aromatase inhibitors for five or ten years.

The authors found:

> The mean healthcare system distrust score was 28 (SD=3; range 9-40), while the mean physician trust score was 29 (SD=4; range 9-35). Bivariate models suggested that greater healthcare system distrust was significantly associated with older age, being Black, having attended some college, and being employed, while less healthcare system distrust was associated with greater physician trust, being married, having health insurance, and living in Pennsylvania. Only marital status, being employed, physician trust, and living in Pennsylvania were still

> associated with distrust in a fully adjusted model (Table 2). Participants reporting treatment discordance were significantly in the top tertile of healthcare system distrust (p=0.003) as well as being more likely to be older (p=0.04), be diagnosed at Stage 1 (p<0.001), and live in Florida (p=0.003). In contrast, physician trust was not a significant predictor of discordance (p=0.49). Although healthcare system distrust was significantly associated with discordance (p=0.03) and physician trust (p<0.001) (Figure 1), a mediation analysis (Table 3: Models A & B) suggested that physician trust was not a mediator of the relationship between healthcare system distrust and treatment discordance (total indirect OR=1.00 [1.00,1.01]). Thus, rather than treat physician trust as a mediator, it was included in the final model as a covariate.

Basically, those in the group with the highest distrust of the healthcare system were 22% more likely to have refused or fail to complete one or more adjuvant treatments. In other words, patients who had the most distrust of the healthcare system were more likely to be discordant in their adjuvant therapy; i.e., to refuse or fail to complete a recommended course of therapy. Interestingly, in this study, neither race nor socioeconomic status were significant drivers of discordance in this study, which is a good thing because these are not modifiable factors.

Physician trust versus a more generalized distrust

How could these results be? The authors note that attempts to increase physician trust as a strategy to reduce mistrust in the healthcare system have had results ranging from zero to very modest, which makes sense if patients view the two issues as separate. I like to make an analogy to Congress. Voters routinely express extreme distrust of Congress, but most voters actually like their own representative. Similarly, it’s not hard to envision how most patients might actually like and trust their own doctors, while simultaneously having a great deal of mistrust for the health care system as a whole.

As the authors note:

> The limited research to date about reducing distrust in healthcare has focused on increasing trust in physicians with null to modest (30-32) results. However, given that the relationship between distrust and treatment discordance was not mediated by physician trust, these results suggest that addressing healthcare system distrust may be an important and distinct effort from strategies focused on lack of physician trust. Rather than playing a mediating role, patients may view physician trust as independent of their trust in the healthcare system as an institution; that is, even if patients distrust the healthcare system, they may still have trust in their personal physicians. Patients may be able to exercise greater choice in physicians, but may not have the same breadth of choices in using the healthcare system. Addressing healthcare system distrust might be informed by strategies that have addressed distrust in other types of institutions, such as corporations (29), according to the values and competence domains. For example, addressing the subdomain of values might be achieved through expanded access to adjuvant care, while addressing the subdomain of competence might be achieved through expanded access to health professionals while deciding to start or continue adjuvant treatment. Of course, any intervention to reduce healthcare system distrust would first need to be tested before implementing wide-scale changes.

The authors also note a rather interesting potential wrinkle to the problem of patients refusing adjuvant therapy, namely that greater cancer treatment discordance will always lead to worse healthcare outcomes, noting that it is "possible that distrust could perform a function in course-correcting treatment that is overprescribed or too aggressive" and that such distrust "might lead to treatment discordance that was ultimately beneficial rather than detrimental." When I read that part, I had to concede that it is possible that this could be true, but unlikely. My own experience in quality improvement initiatives means that I've become fairly familiar with the literature on the relationship between concordance with evidence-based treatment guidelines and patient outcomes. That literature generally supports that better concordance results in better outcomes. So I couldn't help but smile as I continued to read and noted that, consistent with that, the authors examined a separate model of treatment discordance, looking at its association with cancer recurrence, and found that the model suggested a 40% increased risk of cancer recurrence for patients

who reported treatment discordance, after adjusting for adjusting for healthcare system and physician distrust and relevant racial and socioeconomic factors. This result suggests that that discordance due to distrust may lead to poorer health outcomes.

So what to do?

The authors note that improving trust in the healthcare system will require more than just trying to build trust in patients' physicians, noting:

> "If ordinary businesses can learn to increase trust in their brands, why not the same with health care institutions?" Dean says.

This is, of course, much easier said than done, and this study doesn't address how increasing trust in the healthcare system might be accomplished. That will be the task for the future. It is an important task, though, because, although I might be extrapolating more than the evidence supports (yet), I'd bet that such strategies could also help address the antivaccine movement as well. In any case, if we want to save as many savable lives of people with cancer as possible, this is where the healthcare system needs to pay more attention, and a salutary side effect would also be to make alternative cancer cure testimonials less common.

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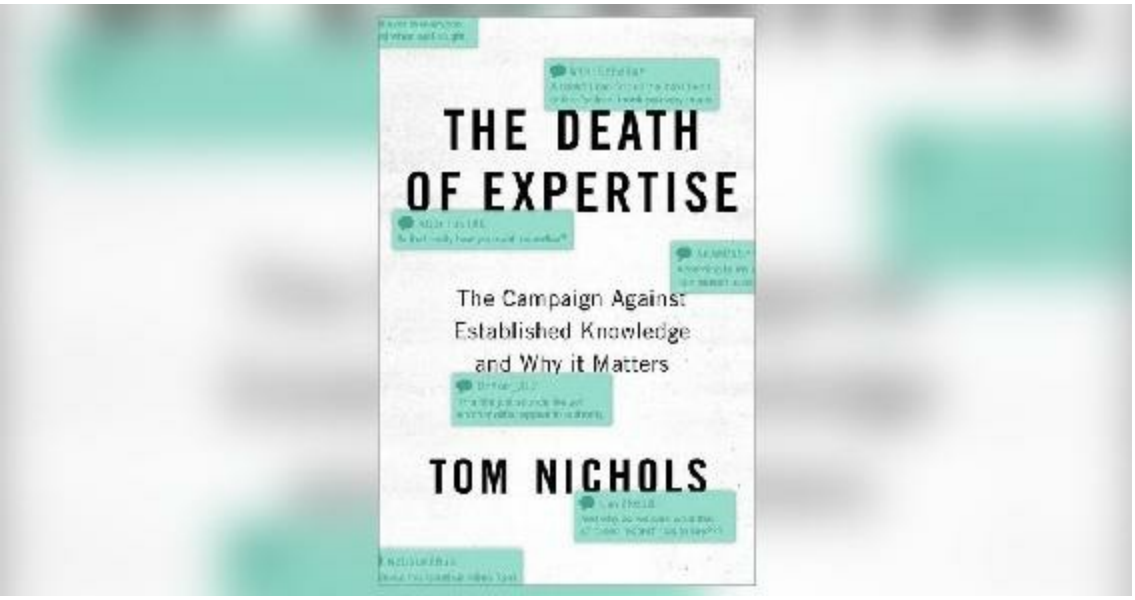
Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **The Death of Expertise** [周二, 21 11月 16:00]
  In Tom Nichols' new book, The Death of Expertise, he explains how a misguided intellectual egalitarianism is harming our ability to assess the truth and solve problems, and discusses some of the responsible factors and possible long-term consequences.
- **What is “integrative oncology”? Even the Society for Integrative Oncology doesn’t seem to know for sure** [周一, 20 11月 16:25]
  Last week, the Society for Integrative Oncology published an article attempting to define what "integrative oncology" is. The definition, when it isn't totally vague, ignores the pseudoscience at the heart of integrative oncology and medicine.
- **Hopelessly Devoted to Woo: TLC and Forbes Bring Us Yet Another Celebrity Healer** [周五, 17 11月 21:00]
  Endorsed by journalists and studied by academic medicine, bogus celebrity energy healer Charlie Goldsmith now has his own television program. In other words, it's just another day at Science-Based Medicine.

The Death of Expertise - Science-Based Medicine



Tom Nichols' new book *The Death of Expertise: The Campaign against Established Knowledge and Why It Matters* has direct relevance to many of the issues we are constantly grappling with on Science-Based Medicine. In a democracy, everyone has equal rights; and many people think that means they are equal to experts in knowledge and judgment. In medicine, as in most other areas of public discourse, we are faced with angry laymen who denounce intellectual achievement and scientific knowledge and who distrust experts.

People find ways to reject the evidence when it conflicts with their values and beliefs. When scientific evidence challenges their views, they doubt the science rather than themselves. New examples of this phenomenon can be found every day in the news and in the Comments sections of the Science-Based Medicine blog, and trying to set those people straight has proven a mostly futile exercise.

The failure of higher education

Students have become consumers. High school seniors tour college campuses with their parents looking for the one with the best dorms, cafeteria food, and extra-curricular activities, rather than the one that will challenge them and provide the best education. Nichols says colleges are not only failing to provide to their students the basic knowledge and skills that form expertise, they are failing to provide the ability to *recognize* expertise and to engage productively with experts and other professionals in daily life. They are not being taught "critical thinking: the ability to examine new information and competing ideas dispassionately, logically, and without emotional or personal preconceptions."

He says students are being treated as *clients* rather than students. "Many colleges have become hostages to students who demand that their feelings override every other consideration." Students "explode over imagined slights" and "build about themselves fortresses that no future teacher, expert, or intellectual will ever be able to breach." They want to be protected from ideas or language they find unpleasant. They are "demanding to run the school while at the same time insisting that they be treated as children."

The Internet

The Internet has provided people with an unprecedented abundance of information, but all too often it gives them the illusion of knowledge, encouraging them to believe they know as much as experts. They hear what they want to hear, and live in a bubble community of people with similar beliefs.

> People do not come to the Internet so that their bad information can be corrected or their cherished theories disproven. Rather, they ask the electronic oracle to confirm them in their ignorance.

Nichols says,

> …not only is the Internet making many of us dumber, it's making us meaner: alone behind their keyboards, people argue rather than discuss, and insult rather than listen.

People “power browse” rather than actually reading. We see this all the time on Science-Based Medicine, where commenters criticize an article they obviously have not read carefully or understood. Sometimes I suspect they may just have read the title and seized the opportunity to jump on their particular soap box.

Journalism

The dissemination of “fake news” is an ever more common reality. Most people are very poor at evaluating the reliability of a news source and the truth of what is reported. When a layperson challenges an expert by saying “I read it in the paper” or “I saw it on the news,” it may mean only “I saw something from a source I happen to like and it told me something I wanted to hear.” At that point, discussion has nowhere to go; the real issue is replaced by the effort to untangle which piece of misinformation is driving the conversation. People are constantly barraged with facts and knowledge, but they have become more resistant to facts and knowledge. How did we arrive at this state of affairs? Nichols says, “technology collided with capitalism and gave people what they wanted, even when it wasn’t good for them.”

When the experts are wrong

In our increasingly complex world, we can’t possibly know everything; we have no choice but to trust experts. But sometimes experts get things wrong. Most of the time, their errors are identified and counteracted by other experts. This works so well most of the time that we are shocked when we read about an exception; for instance, when we learn that an incompetent doctor has killed a patient or that a researcher has falsified data. Laymen get exasperated when science “changes its mind,” for instance telling the public eggs are bad for them and then saying no, they’re OK to eat. But that’s not a failure of science, but rather an example of how science works so well in the long run by following the evidence and discarding false provisional conclusions as the evidence improves.

When experts’ errors, fraud, and misconduct are revealed, a layperson naturally asks how we can trust studies in any field. Nichols says that’s the wrong question to ask, because “rarely does a single study make or break a

subject." Single studies are often wrong, but the aggregate of all research is trustworthy. The scientific enterprise as a whole is self-correcting and leads to a consensus of experts that approaches the truth as much as is humanly possible.

The impact on government

Science is essential to rational public policy; it can't make the decisions, but it provides reality-based information that can guide the decision-makers. Nichols says we have a President who sneers at experts and whose election was "one of the loudest trumpets announcing the impending death of expertise." He argues that Trump's campaign was "a one-man campaign against established knowledge." He provides examples: Trump's "birther" campaign against Obama, his quoting the *National Enquirer* approvingly as a source of news. Nichols says rather than being ashamed of his lack of knowledge, Trump exulted in it. "Worse, voters not only didn't care that Trump is ignorant or wrong, they likely were unable to recognize his ignorance or errors." He says the Dunning-Kruger effect was at work. It's not just the things we don't know (one in five adults think the sun revolves around the Earth), but the smug conviction that we don't need to know such things in the first place.

He warns,

> The relationship between experts and citizens, like almost all relationships in a democracy, is built on trust. When that trust collapses, experts and laypeople become warring factions. And when that happens, democracy itself can enter a death spiral that presents an immediate danger of decay either into rule by the mob or toward elitist technocracy. Both are authoritarian outcomes, and both threaten the United States today.

Conclusion: hope for the future?

He says Americans no longer understand that democracy only means political equality. They tend to think democracy is a state of actual equality in which everyone's opinion is as good as everyone else's, on every subject. Feelings are more important than facts: if people *think* vaccines are harmful, it is

considered “undemocratic” and “elitist” to contradict them.

He sees signs of hope. Experts are rebelling. He cites an angry doctor who asked patients, “Do you remember when you got polio? No, you don’t, because your parents got you [expletive] vaccinated.” He points out that without democracy and secular tolerance, nations have fallen prey to ideological, religious and populist attacks and have suffered terrible fates. But he ends on a hopeful note. He has faith in the American system and hopes that it will eventually establish new ground rules for productive engagement between the educated elite and the society they serve. I hope so too!

Longtime readers of Science-Based Medicine and my not-so-secret other blog probably know that I'm not a fan of the specialty known as "integrative oncology." My reasons are basically the same as the reasons why I detest "integrative medicine," only subspecialized (like oncology), so to speak. Basically, "integrative medicine" integrates quackery with medicine, and integrative oncology integrates quackery into oncology. Given that I'm a cancer surgeon, I tend to take an even dimmer view of the latter than of the former, if only because it hits me where I live. For instance, when "integrative oncology" starts appearing at symposia at major cancer meetings, with nary a skeptical word showing up in the panel discussions afterwards, I despair. Unfortunately, the credulity that allows modalities like acupuncture, reiki, intravenous high dose vitamin C, and various other unproven and disproven treatments to find their way into academic medical centers has spawned a related phenomenon, quackademic medicine, or the study and acceptance of quackery in academic medical centers. The most prominent example of this latter phenomenon occurred in September, when the University of California at Irvine accepted a $200 million gift from Susan and Henry Samueli to build and staff a college devoted to integrating quackery into its component departments and promoting "integrative medicine." Never mind the homeopathy.

Integrative oncology has become so established that it has its own professional society, the Society for Integrative Oncology (SIO). Not surprisingly, I'm not a fan of SIO, and SIO isn't exactly a fan of me, either. I've related the story before, but let's just say that the SIO was not pleased at my 2014 article in *Nature Reviews Cancer* discussing how integrative oncology is not evidence-based (to say the least), given its embrace of naturopathy. In brief, the SIO didn't like how much verbiage I devoted to homeopathy in the article, pointing out that homeopathy is indeed not evidence-based and that no integrative oncologist worth his or her salt would ever use it. I pointed out that you can't have naturopathy without homeopathy. After that, I asked how the SIO can reconcile its quite correct rejection of homeopathy with the fact that it admits naturopaths as members, that two of its recent past presidents have even been naturopaths, and that you can't have naturopathy without homeopathy. It's baked into the naturopathic

curriculum, and it's part of the naturopathic licensing exam. Moreover, one of the naturopaths who co-authored the SIO's breast cancer clinical guidelines ran a clinical trial on homeopathy. That same naturopath, by the way, was a co-author on the update to those guidelines published just this year. The SIO never learns.

This time around, though, the reason the SIO caught my attention was this Tweet by Dr. Sheila Garland, re-Tweeted by Dr. Jun J. Mao, immediate past president of the SIO (but still president at the time he re-Tweeted this):

> The beginning of a new era in evidence-informed integrative oncology research/practice that puts the person first #SIO2017 @Integrativeonc https://t.co/cmAMrCujjy
>
> — Dr. Sheila Garland (@SNGarlandPhD) November 13, 2017

This Tweet touted what is now the "official" definition" of "integrative oncology" recently laid down by the SIO:

> Official definition of Integrative Oncology! Spread the word! #SIO2017 We are research based! #cancerresearch pic.twitter.com/oeNsn9B1Jk
>
> — Jodi MacLeod (@write4wellness) November 13, 2017

It turns out that this definition had just been published by Witt et al in the November issue of *JNCI Monographs*, just in time for the SIO annual meeting last week. When I saw it, my first reaction was to e-mail my fellow SBM bloggers with a link and this image:

So let’s take a look.

The process of defining “integrative oncology”

My first reaction (besides possessiveness) when I saw the article by Witt et al, A Comprehensive Definition for Integrative Oncology was: What? The organization has existed for nearly 15 years, and in all that time it hasn’t yet managed to define what it’s about until now? My second reaction was: What on earth does this definition actually mean? It is about as boring, generic, and —shall we say?—vague a definition of anything as I’ve ever seen. Take a look:

> Integrative oncology is a patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments. Integrative oncology aims to optimize health, quality of life, and clinical outcomes across the cancer care

> continuum and to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment.

In actuality, I was more interested in what was left out of this definition than what was in it, but I'll get to that near the end of this post. First, I want to look at the process by which the authors developed this definition, as described in the article, which is open-access for those of you who want to read it yourselves. Before I get into the process, let's look at some of the authors, who are big names in the world of integrative oncology. The lead author, Dr. Claudia Witt, is Professor and Chair of the Institute for Complementary and Integrative Medicine at the University of Zurich and University Hospital Zurich, as well as part-time Professor of Primary Care and Community Medicine at the Center for Integrative Medicine University of Maryland School of Medicine. Dr. Jun J. Mao is, of course, president of the SIO and Chief of the Integrative Medicine Service at Memorial Sloan-Kettering Cancer Center. Dr. Lorenzo Cohen is someone whom we've met before, when he gave a talk at the American Society of Clinical Oncology (ASCO) meeting in 2014. He's the Director of the Integrative Medicine Program at The University of Texas MD Anderson Cancer Center. Linda Balneaves is a nurse and the current president of SIO, having succeeded Dr. Mao at the SIO annual meeting last week. I also can't help but note that one of the co-authors, Heather Greenlee, is a naturopath and has served as president of the SIO in the past as well.

In other words, these are indeed heavy hitters and the leadership of the SIO.

Let's look at their justification for seeking this definition. After regurgitating the usual "complementary and alternative medicine" (CAM) blather about how patients are just "looking for "additional interventions that may help improve the efficacy of conventional cancer treatments, increase their chance of survival, and/or reduce their symptom burden associated with cancer or treatments" and "improve their quality of life during and following treatment," Witt et al justify their search for a definition thusly:

> With the integration of interventions such as acupuncture, mindfulness and yoga, and lifestyle counseling into major cancer centers in North America (eg, MD Anderson and Memorial Sloan Kettering Cancer Center), the term "integrative oncology" has become increasingly used.

> “Integrative” better represents the process of care that is provided in centers where patients are receiving these types of interventions in addition to their conventional cancer treatments. With the establishment in 2003 of the Society of Integrative Oncology (SIO), a nonprofit multidisciplinary professional organization, the term “integrative oncology” was further legitimized and began to be widely used. However, the term “integrative” is also used in other contexts. An example is the Berlin School of Integrative Oncology at the Charité Medical School in Berlin (2), which is an initiative of the German federal and state governments that aims to educate young scientists and physicians in oncology in an interdisciplinary, translational research context. Although the term “integrative oncology” is rarely used in such an educational context, having totally different meanings for the same term can generate confusion. Adding to this complexity is the growing attention to the notion of integrated care programs in oncology, in which numerous cancer specialties (eg, medical oncology, radiation oncology, surgical oncology, genetics, plastic surgery) work together to provide comprehensive patient care (3).
>
> Furthermore, even in settings in which the term integrative oncology has been used to refer to the combination of complementary medicine therapies with conventional cancer treatments (4), the term has been defined in many different ways (5,6). Because of this lack of consensus, it has been difficult to communicate what is meant by “integrative oncology” to oncologists and other health professionals, as well as to key stakeholders, such as patients, administrators, and health policy makers. The aim of this project was to use a systematic approach to develop a comprehensive and acceptable definition for “integrative oncology.”

Actually, I’ve always rather suspected that this confusion is a feature, not a bug, related to the use of the word “integrative.” After all, integrative oncology, like integrative medicine, is a brand, not a specialty. It rebrands what should be considered perfectly fine science-based modalities, such as nutrition, lifestyle interventions, and the like, as somehow “alternative” or “integrative,” and then “integrates” quackery like acupuncture, reiki, functional medicine, and even homeopathy with them, to give the quackery

the appearance of scientific legitimacy. No, I don't think SIO is doing this intentionally; its leadership consists of true believers. But it is contributing to quackademic medicine and the integration of quackery into oncology. In any event, the word "integrative" is, as mentioned above, used to describe science-based endeavors, such as integrative biology. In this context, the word "integrative" connotes interdisciplinary study, a very different meaning than when the word "integrative" came to replace the term CAM to describe adding pseudoscience to medicine.

Indeed, use of the word "integrative" to describe medicine or the subspecialty of oncology connotes more than interdisciplinary patient care and research. It connotes the embrace of "alternative" treatment modalities as well. The term "CAM" still had the word "alternative" in it and the word "complementary" connoted that CAM was subsidiary to medicine, "complementary," the icing on the cake, if you will. In other words, it's not necessary, and science-based medicine is the real medicine. The adoption of the word "integrative" to rename CAM as "integrative medicine" was clearly intended to remove the implication that CAM was "complementary" and not as good as real medicine, in order to advance the narrative that integrative medicine is the "best of both worlds," while also borrowing from the cachet of various "integrative" scientific disciplines as being multidisciplinary. Again, I don't think SIO is out to deceive. Rather, the belief of the SIO leadership in the validity of integrative oncology has led them down this road, probably without even realizing it.

So how did Witt et al go about constructing their definition? Enter the mixed methods research design and Delphi method. This amused me, because it wasn't so long ago that naturopathic oncologists used this very method to try to define priorities in naturopathic oncology. If you want the details of how the Delphi method works I discussed them in deconstructing the nonsense that naturopaths laid down about their quack specialty using the Delphi method. The CliffsNotes version is that the Delphi method entails a using a group of experts to answer a question. The experts anonymously reply to questionnaires and subsequently receive feedback in the form of the statistical representation of the group response, after which the process repeats itself until something resembling a consensus is arrived at. The way Witt et al did this is described:

> A two-round Delphi process was then employed to further refine and gain consensus regarding the new definition. In the first round, the revised definition was distributed via an online survey (software SoSciSurvey [7]) to SIO board members as well as to a convenience sample of experts. The experts—oncologists, integrative oncology clinicians, and/or researchers from North America, Europe, and Asia—were contacted by the SIO board members. Based on first round feedback, the definition was revised and distributed again through an online survey to the full membership of SIO, with subsequent ratings and comments used to inform the final version of the definition. Data from both surveys were analyzed using descriptive statistics. Content analysis (8) was applied to the open-ended responses to identify any themes or concepts.

So, after this literature search and Delphi method, what did Witt et al find?

Defining “integrative oncology”

As a result of their literature search and two-round Delphi process, Witt et al found many definitions of “integrative medicine” and “integrative oncology” in the literature, which resulted in the following thematic suggestions:

- evidence-based/evidence-informed/evidence-guided/using best available evidence (14 of 20);
- accompanying conventional cancer treatment (18 of 20);
- addressing outcomes such as well-being, body, and mind-spirit, as well as physical, psychological, and spiritual quality of life (seven of 20);
- focused on health and not only on medicine (three of 20);
- provided by a team of health care providers/multidisciplinary/interdisciplinary (four of 20);
- patient-centered/personalized, individualized/whole person (two of 20).

The writing group, which consisted of “members with different professional/disciplinary backgrounds (ie, medical oncology, radiation

oncology, surgical oncology, nursing, patient advocacy, psychology, psycho-oncology, epidemiology, integrative medicine, health policy),” added these additional suggestions:

- type of interventions (mind-body therapies, natural products, lifestyle changes);
- beyond provision of health care (information, translation of evidence, identification of beliefs, values and preferences, empowerment).

The initial definition of integrative oncology developed by the group thus read:

> Integrative oncology is a patient-centered (theme 6), evidence-informed (theme 1) approach to health care (theme 4) that uses mind-body therapies, natural products, and lifestyle modification (theme 7) as adjunct to conventional cancer treatments (theme 2) and is ideally provided by a multidisciplinary team of care providers (theme 5). Integrative oncology aims to increase well-being of mind, body, and spirit (theme 3) and to provide patients with skills enabling them to help themselves during and beyond cancer treatment (theme 8).

After the two rounds of Delphi method, though, the group perceived that some changes were required:

> Overall, the comments on the second Delphi survey were positive, but the suggestions were quite heterogeneous. Two-thirds of suggestions focused on what were perceived to be missing interventions, and it became clear that therapies such as acupuncture and massage were not well represented in the definition. As a consequence, the definition was revised using the umbrella term “mind and body practices,” which is used by the National Center for Complementary and Integrative Health in the United States. This term includes mind-based techniques such as meditation and hypnosis, as well as manual techniques such as acupuncture and massage (9). One respondent mentioned that “health care” encompassed a broader area than integrative oncology, and the decision was made to be more focused and to use the term “cancer care” in the revised version. Another respondent also suggested that the phrase “approach to cancer care” could be misleading and not specific enough

> as a field of care or medical specialty. Integrative oncology is more than just an approach to overall cancer care; it has been the focus of a professional organization for more than 10 years and is an established field in its own right. During the review process, it was noted that cancer prevention was not included in the definition. Because the ultimate goal of many integrative oncology behaviors is cancer prevention and control, the definition was modified to include prevention.

I've discussed before how quackery like the theatrical placebo known as acupuncture has mysteriously been subsumed into "mind and body practices". Personally, I've always suspected that this was to hide the quackery of acupuncture with more benign modalities (such as massage) that, whether medically they can treat anything, generally do no harm, and can certainly feel good, thus improving quality of life. After all, given that the rationale in traditional Chinese medicine for acupuncture is that sticking the needles into specific "meridians" can redirect the flow of qi (life energy) for healing effect, acupuncture could easily be classified as a form of energy healing.

To the degree that integrative oncology sticks with science- and evidence-based tests and treatments, my main objection to it is that it's not necessary. Nutrition, exercise, and other lifestyle-based interventions are already a part of science-based medicine. I like to cite, for instance, evidence-based recommendations for the treatment of hypertension and type II diabetes, both of which emphasize, except for severe cases, dietary modifications, exercise, and weight loss as the first interventions to attempt before placing the patient on medications.

To paraphrase Harriet Hall, what is good about integrative oncology (or medicine) is not unique to it. Continuing the paraphrase, unfortunately, what is unique to integrative oncology is not good, and the SIO definition obscures or neglects to mention these unique (and not good) aspects.

What the SIO left out

If you read the full article, it should become very apparent that its authors

want desperately to convince the reader that integrative oncology is completely evidence-based. Sure, the SIO admits naturopaths and even elects them as the organization's president from time to time, never mind that all naturopaths are trained in The One Quackery To Rule Them All, homeopathy, and that the vast majority of naturopaths routinely prescribe homeopathic remedies, which, even the SIO concedes, are rooted in pseudoscience.

I was reminded of this on—where else?—Twitter. I came across a post on the University of Pennsylvania's OncoLink touting reiki in cancer care. Because the link was from 2011, I Tweeted a question to the OncoLink team. Here's the response:

> @gorskon, Reiki is a supportive therapy that can be used in conjunction with treatment. It is not promoted as an alternative to treatment
>
> — OncoLink Team (@OncoLinkTeam) November 2, 2017

If there is a challenger to homeopathy's title of The One Quackery To Rule Them All, reiki would be right up there. It is, as I have described many times before, a form of faith healing that substitutes Eastern religious beliefs for the Christian religious beliefs that usually undergird faith healing in the US.

But it's not just Penn. The Dana Farber Cancer Institute has also gone all in for nonsense:

> 7 Ways Integrative Therapies Help Cancer Patients: https://t.co/bRHYbqhrcy pic.twitter.com/0kVQ4FKW0o
>
> — Dana-Farber (@DanaFarber) August 26, 2017

The slideshow at the link above promotes reiki, reflexology, and acupuncture:

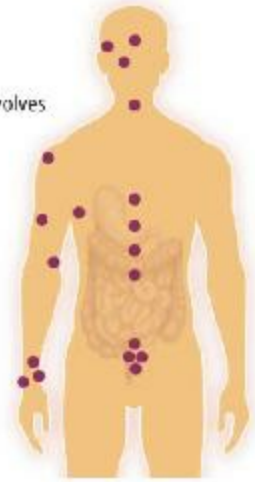
DANA-FARBER CANCER INSTITUTE
Discover. Care. Believe

7 WAYS INTEGRATIVE THERAPIES CAN HELP CANCER PATIENTS

1. ACUPUNCTURE

Acupuncture is a standard practice in Chinese medicine which involves gently inserting hair-thin needles into the skin at specific points. Acupuncture has been shown to:

- Reduce post-operative nausea and vomiting
- Decrease anxiety
- Treat pain and loss of nerve sensation
- Relieve joint pain
- Help relieve chronic pain



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Acupuncture is nothing more than a theatrical placebo, whose action has never been convincingly shown to be greater than that of placebo controls. Yet Dana Farber Cancer Center thinks acupuncture is science-based.

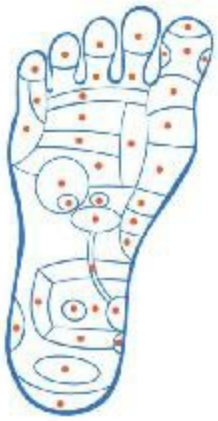
DANA-FARBER CANCER INSTITUTE
Discover. Care. Believe

7 WAYS INTEGRATIVE THERAPIES CAN HELP CANCER PATIENTS

3. REFLEXOLOGY

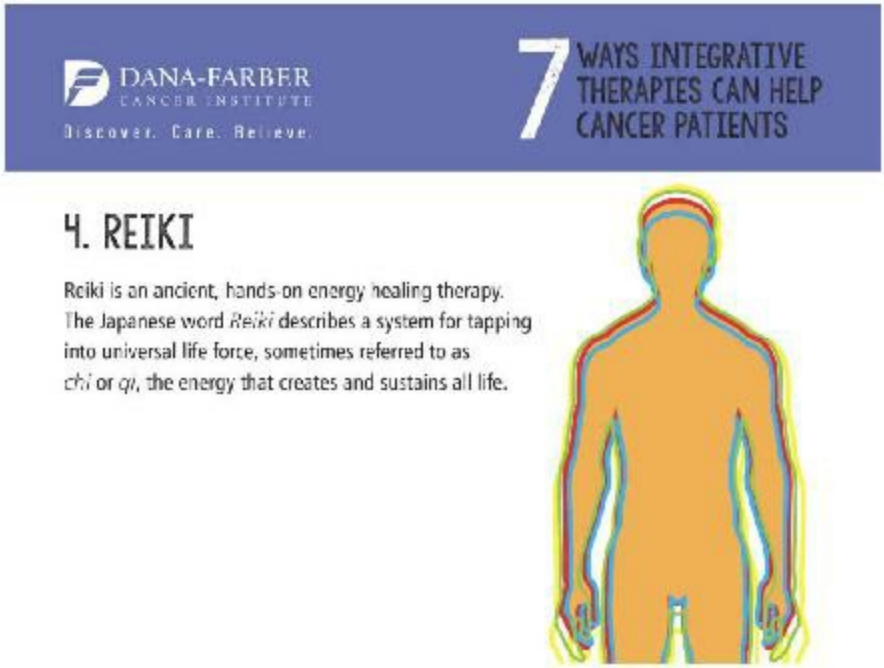
Reflexology is the application of pressure to areas on the feet, hands, and outer ears. The theory behind reflexology is that these areas correspond to organs and systems in the body. Patients have found that reflexology can:

- Promote relaxation and comfort
- Help with treatment symptoms like fatigue and nausea



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Reflexology posits the existence of physiologic or anatomic links between organs and body parts and areas on the soles of the feet and palms of the hand. Yet Dana Farber Cancer Center thinks this is science-based.



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Reiki masters claim to be able to heal by channeling energy into the patient from the "universal source." Replace "universal source" with "God" or "Jesus," and it becomes obvious that reiki is a form of faith healing that replaces Christian beliefs with Eastern mysticisms. Yet Dana Farber Cancer Center thinks it's science-based.

Of course, I've pointed out how oblivious the SIO is to the modalities that are really being "integrated" into oncology through integrative oncology just through the obliviousness of the SIO leadership to what naturopathy really is. As I've said before, if the SIO were really serious about being evidence-based, it would immediately purge itself of all naturopaths. It's not, though. Its leadership up in the ivory towers of medical academia can delude themselves into thinking integrative oncology is totally evidence based, because they manage to ignore the quackery that is "integrated" along with the lifestyle-, exercise-, nutrition-, and meditation-based modalities to which they love to point.

I can’t help but point out a few more examples of the quackery that goes along with integrative oncology. At UC-Irvine and the Cleveland Clinic, there’s homeopathy. At the University of Arizona Cancer Center, there was reiki, at least until a faculty member whose child developed cancer and was treated there made a stink. There’s also more energy medicine quackery, this time in the chemotherapy suite, at Georgetown University, as well as cupping, which is also pure quackery. There’s functional medicine at the Cleveland Clinic, George Washington University, University of Kansas, and, well, seemingly almost everywhere at any medical center with an integrative medicine program. If you want an idea of how bad functional medicine is, just check out this case report of functional medicine used for a patient with inflammatory breast cancer. This is what integrative oncology *really* involves.

It is also this quackery that the SIO definition of “integrative oncology” does its best to obscure or ignore. If the SIO is truly serious about being science- and evidence-based, it needs to speak out strongly and now against naturopathy and the various forms of quackery that have found their way into academic medical centers, of which, I assure you, the above is but a small sampling. It won’t, though. The quackery is why integrative medicine and oncology exist in the first place. Without the quackery, CAM (or integrative medicine or oncology) becomes completely unnecessary as a field.

In recognition of my 100th post on SBM, I was all set to write about some interesting updates on a few of my contributions over the years. But thanks to the machinations of the preternaturally cool Tim Caulfield, author of *The Cure for Everything* and *Is Gwyneth Paltrow Wrong About Everything?*, I was made aware of something that I just couldn't ignore: someone is wrong on the internet. That's right, yet another "energy healer" with bold claims of miracle cures is making the rounds. But this time will be different, apparently.

Remember Adam Dreamhealer? He was the teenage "intuitive healer" that could recognize and manipulate mysterious human energy fields to cure cancer and a whole host of other ailments, even over the phone or after only looking at a photograph of the patient. He claimed to have received his powers from a giant blackbird he met while hiking. Ring a bell? Well, it was a whole thing about a decade ago, just as I was starting my journey on the path of skepticism. Although he is still up to the same tricks as a "naturopathic oncologist", and he will always have a special place in my heart, Dreamhealer has some stiff competition for my favorite celebrity energy healer.

The new kid on the block is Australian energy healer Charlie Goldsmith, and technically he isn't all that new. Orac, who I believe is some kind of protocol droid, wrote about him back in 2015. Goldsmith was just dipping his toe in the water of widespread recognition at that time, getting some press in the form of credulous fluff pieces focusing on the fact that he is Olivia Newton John's nephew and on his involvement in a ridiculous study published in the *Journal of Alternative and Complementary Medicine*. Described as a "feasibility study", it is embarrassingly amateurish, really just a collection of cherry picked anecdotes that did not involve the slightest bit of blinding or control. The authors concluded what anyone remotely familiar with research like this would have expected.

What Caulfield alerted me to this week was the publication of yet another painfully credulous article, this time on the *Forbes Lifestyle* blog. In the piece, Forbes contributor and certified Holistic Health Coach Courtney Porkoláb asks the question "does energy healing work?" and invites readers

to decide for themselves. In a conversation with her on Twitter she was quick to remind me that hers wasn't a scientific article and to imply that she just wanted to "spark conversation." Yet in the article she provides only her gullible acceptance and a series of comments from Goldsmith and a few credentialed believers endorsing the benefits of energy healing and even proposing scientific explanations. There isn't even an attempt at token skepticism.

Porkoláb gushingly discusses Goldsmith as if he is a miracle worker:

> Goldsmith's success rates are undeniably high, having relieved people of all ages, with issues ranging from chronic pain to infections and auto-immune disorders, often in 60 seconds or less.

The article contains numerous absurd assumptions and laughably implausible claims, all in the service of promoting the fact that Goldsmith is now starring in a TLC program documenting his supposed abilities. It isn't alone, of course. This *Daily Mail* article is particularly informative as it provides a clip from the most recent episode. It shows Goldsmith taking advantage of the power of suggestion as he interrogates a 2-year-old child about his symptoms before going through the standard energy healing motions. The kid is adorable but it's pretty ridiculous, and what is really happening should be clear to anyone with a modicum of experience with toddler behavior. The deciphering of the child's unintelligible responses reminded me of how ghost hunters prime listeners when demonstrating EVP.

Orac, which I understand is some kind of prototype U.S. military robot that gained sentience and a powerful sense of skepticism after being struck by lightning, beat me to the punch and wrote an excellent discussion of Goldsmith and the *Forbes* article. Feel free to hop on over and read it. I'll provide a couple of the best quotes myself, however:

> Prior to the studies done in the public eye, Goldsmith spent years healing as many as he could, often those who had been failed by countless doctors and traditional medicine.

Regular readers of SBM know how unreliable claims such as this are. Unless Goldsmith was keeping meticulous records of his healing attempts and

following up to document long term outcomes, these kinds of statements are essentially meaningless. It's very easy with confirmation bias and motivated reasoning to look back over the years and come to the conclusion that you helped a lot of people. It's easy to discount the failures and focus on the apparent successes.

And patients can be "failed by traditional medicine" in numerous ways, many of which don't actually equate to what is being implied. Patients with vague or non-specific symptoms and certain world views often feel like conventional doctors have let them down when they aren't given a specific diagnosis, or when treatment recommendations consist of lifestyle changes or mental health assessments rather than confident assertions and a supposed cure. Often proponents of pseudomedicine convince people that their doctor has failed them by missing the diagnosis of a fictional malady, such as adrenal fatigue.

I found this quote from Goldsmith particularly interesting:

> To be honest, sometimes I'll work on something that—medically—is seemingly simple and not fix it. And something that is medically complex—something medically incurable, for example—that might be quite easy for me.

He chalks this up his healing powers not being an exact art. I see this as exactly what I would expect when all that is being offered is false hope and expectation, and one is counting on various placebo effects to give the appearance of benefit. But again, unless he has been keeping strict records of his encounters, his claims regarding past treatments can't really be assessed. I'm not just going to take his word for it that he has defied our fundamental understanding of human physiology.

The credentialed believers provide some of the most memorable contributions, which you can read about in the above linked post by Orac. These include demonstrations of a lack of understanding of how pain is assessed and treated as well as appeals to quantum physics and "bioenergy". There are also references to the time Gary Schwartz supposedly found a measurable differences in the magnetic fields surrounding the hands of energy healers and to a study on bio-photon emissions after energy healing.

Let’s do the science!

Goldsmith is on a mission to prove that what he does is legitimate and not just theatrical placebo by participating in clinical trials. I already mentioned the one published “study” he participated in above, and he claims to be involved with two more taking place at the same facility. It sounds like more of the same:

> The study presently underway is being undertaken at NYU Lutheran Hospital in New York and employs a qualitative methodology to help understand the experiences of patients who encounter Mr Goldsmith’s practices.

In other words, more anecdotes without proper controls or blinding. According to his website, this study has actually been completed. It’s being written and will be submitted for publication next year. We’ll see. He also claims to be participating in a prospective RCT, again at the same facility, that is currently going through the IRB approval process. Again, we shall see if this actually materializes.

I challenged Goldsmith during a lengthy discussion on Twitter, and he reassured me that his intentions are purely altruistic. He denies financial motivation and simply wants to prove to the world that his gift is real so that science might take the phenomenon seriously. He only wants to help reduce the pain and suffering of others. He has been treating patients for years and, according to Goldsmith, he only went public in order to help entice researchers to do the studies.

I am skeptical of his motivation. History has, time and time again, revealed that believers in highly implausible and unproven therapies don’t really care what the science says. Typically the studies end up having such poor methodology that a positive result is assured, and when proper studies fail to find a true effect, they are ignored. Regardless of the outcome, proponents can point to the fact that studies were even done in the first place as evidence of their pet remedy’s legitimacy.

It is abundantly clear that Goldsmith has already decided that he has the

ability to cure people through energy healing. He didn’t notice something odd and then look to science to determine if it was true. He noticed something was odd and then did it to people with real medical problems for years before agreeing to star in a television program highlighting it. In my opinion, the research angle is just marketing and I’m embarrassed for NYU.

Science Based Medicine

周三, 29 11月 2017

Science Based Medicine

[周三, 29 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Science Moms Fight Fears with Facts** [周二, 28 11月 16:00]
  A new documentary takes a novel approach. It features scientist moms who are just like other moms except that they understand the science. They set the record straight about GMOs, vaccines, and other subjects of interest to parents. They provide the facts to counteract unreasonable fears.
- **The integration of mysticism and pseudoscience with oncology continues apace in NCI-designated comprehensive cancer centers** [周一, 27 11月 16:32]
  Last week, I commented on the inability of the Society for Integrative Oncology to define what integrative oncology actually is. This week, I note the proliferation of the quackery of integrative oncology in places that should be rigorously science-based, namely NCI-designated comprehensive cancer centers.
- **And the server migration continues apace…but where are the comments?** [周六, 25 11月 10:15]
  SBM is changing servers again. Unfortunately, that means that there are problems with the comments.

At the recent conference of the Committee for Skeptical Inquiry (CSICON) in Las Vegas, on October 28, 2017, I had the great privilege and pleasure of being in the audience for the American premiere of a new documentary, *Science Moms*, as well as for the following live panel discussion by the women featured in the movie. In the documentary, a group of scientists and science communicators who are also moms address misperceptions created by misinformation in the media about GMOs, vaccines, and other issues important to parents. They point out that "moms whose opinions are formed by fear and hype are so loud. But they're the only people talking about it, the only resource people have." With this documentary, people now have another resource based on science, a resource that is easily digestible and compelling.

The film starts with a beautiful sunrise and a Gwyneth Paltrow quote: "The sun is the sun – how can it be bad for you? I don't think anything that's natural can be bad for you." The Moms answer:

"Wow! I could make a list for her."

"The sun causes cancer."

"Nature will kill you, really quickly."

"Sometimes I think she's trolling us."

Next, the Science Moms are introduced and talk about how they got interested in science. They are:

- Anastasia Bodnar, PhD, Plant Geneticist
- Alison Bernstein, PhD, Neuroscientist
- Layla Katiraee, PhD, Molecular Geneticist
- Jenny Splitter, Science Communicator and Storyteller
- Kavin Senapathy, Science Communicator

These women shatter the stereotypes of scientists as commonly portrayed in the media. They are normal, friendly, personable, attractive, well-groomed,

non-geeky, everyday people, just like other working moms except that their jobs happen to involve science. Moms viewing the film ought to be able to relate to them and listen to what they have to say just as they would listen to their friends.

Two of Science Moms were fans of *Buffy the Vampire Slayer* and were appalled to learn that the actress who played Buffy, Sarah Michelle Gellar, was speaking out against GMOs. They joined a group of 15 women scientists, bloggers, and educators to send a letter to Paltrow, Gellar, and other celebrities asking them not to co-opt motherhood and wield their fame to oppose beneficial technologies, but to use their influence responsibly and ensure that their advocacy is supported by facts, not fear.

The letter caught the attention of Natalie Newell, the host of "The Science Enthusiast" podcast. She contacted one of the letter's authors. One thing led to another, and the result was this documentary.

The Moms acknowledge that being a parent is scary. Parents desperately want to protect their children from any possible harm, and often they aren't sure how to best do that. Even they admit to having acted irrationally based on unrealistic fears for the welfare of their children. It's a great marketing technique: "If you can scare a parent, of course they're going to shell out for the alternative."

GMOs

People who don't know anything about GMOS may choose organic because they vaguely remember hearing that it was better for their kids. GMOs are presented in the media as inserting genes of one species into another species. But that's only one meaning. Genetic modification also means selective breeding, cross breeding, mutagenesis, genome editing, and other techniques.

When plants are cross-pollinated, a gene for disease resistance can spread to another species, but that's random. Why not use technology to put the desired gene into the plant? In reality, almost everything we eat was genetically engineered centuries ago by our ancestors' selective farming and breeding

practices.

The Moms point out these benefits of genetic modification:

- Drought resistance
- Pest resistance
- Disease resistance
- Increased crop yield
- Increased nutritional content
- Economic benefits
- Reduced pesticide usage
- Reduced greenhouse gas emissions

Vitamin A deficiency causes untold cases of blindness and death in developing countries. Golden rice was genetically modified to supply vitamin A, but thanks to anti-GMO ideology it hasn't reached those who need it most.

Some people fear that eating something genetically engineered will genetically engineer THEM. Not hardly! Despite widespread fears, GMOs have never harmed a single person's health in any way.

Fear of chemicals

The idea that "There is no safe amount of chemicals" is false. Everything is made of chemicals. They show a long list of all the scary-sounding chemicals in an all-natural blueberry. Pears naturally make formaldehyde.

The "most brilliant marketing move of the last ten years" was to convince everyone that organic is pesticide free. Copper sulfate is really bad for the environment, and it's allowed in organic farming.

Data doesn't support claims that organic is pesticide free, better for environment, or healthier.

There are no health benefits to be gained from organic. It's just more expensive.

Vaccines

We hear:

- Too many too soon
- Dangerous chemicals in vaccines
- I prefer to fight off disease naturally
- It's a Big Pharma conspiracy
- "These diseases aren't really that dangerous"

None of these are based on evidence or science. Unrealistic fears of vaccines have led to decreased herd immunity and disease outbreaks. Our grandparents aren't likely to fear vaccines, because they knew people who died of polio and other preventable diseases. It's ironic that people are afraid of harmless GMOs but don't fear the very real risks of vaccine preventable diseases.

Homeopathy

One Science Mom says, "I'm embarrassed to say I tried it. When I found out what it was, I thought 'Oh, that's why it didn't work.' I could have given the kids sugar water I made at home and saved a few bucks."

> I can't imagine parents reaching for something that is untested, unregulated, and has no active ingredients in it. It baffles me.

Perhaps it's because people want to do things on their own – homeopathy, homemade baby formula, anything that gives them the illusion of being in control.

Who's paying you??!!

The answer to this oft-repeated question is an emphatic "Nobody!" Kavin Senapathy says she has been called a fake mom, has gotten death threats, and has been told her name is made up (as if Monsanto would invent a name like

Kavin Senapathy!) She doesn't understand where the shill accusation comes from. The assumption seems to be that anyone who doesn't have the same world view as you, must be paid to have that view. It's hard to have your world view challenged, so it's easier to think they must be paid to disagree with you than to think your world view might be incorrect.

More

They explain that scientific consensus is not like a vote, it's the confluence of all the evidence coming together around a hypothesis.

When people ask if something is safe for their child, the best advice is to go to a real doctor (not a naturopath); and to buy real medicine (homeopathy is not real medicine).

Healthy diet? Eat lots of fruits and vegetables, buy whatever's cheaper, wash produce.

Some organizations are trying to scare people away from buying certain fruits and vegetables. That's CRAZY!

You might as well enjoy being a parent. "Basic safety stuff fits on half a page." Don't worry about minor details with no solid evidence, like when to introduce solid foods.

"When kids are 10-12, no one's talking about whether they were breast fed." The effects of stress on us and our kids are way worse than anything we're worrying about.

What's the real issue? If it's corporate control of our political system, that's a valid concern that many of us share. But GMOs aren't the cause of that. Focus on the real source of the anger rather than blaming a proxy.

Fear-based communities bring people together. The Science Moms are trying to create a new community based on science and reason; based on facts, not fear.

Conclusion: A lot of people really need to watch this documentary

Science Moms is short and to the point. The 30-minute film is scientifically accurate, persuasive, and well-designed, with good production values. It's available online for purchase at $4.99. I hope it will be more widely disseminated, because it offers important information that the general public needs to hear. People who have been exposed to anti-GMO or anti-vaccine propaganda are not likely to seek out, read, and understand the scientific evidence. But perhaps they will be willing to listen to moms who are just like them but who have the advantage of understanding the science.

Last week, I took note of how what is now a major medical society devoted to integrative oncology, the Society for Integrative Oncology (SIO), revealed itself to be unable to define, other than in platitudes and vague feel-good verbiage, just what the heck "integrative oncology" even is when it published a monograph in *JNCI*. What I didn't take note of last week was that the November issue in which the SIO's monograph defining what integrative oncology is (or what the SIO thinks it is) didn't contain just that one gem. In fact, like previous monographs published in years past, it's chock full of SIO propaganda for integrative oncology. Indeed, there's so much there that I could easily spend the next few weeks writing about each monograph in turn. I won't do that today, although I do reserve the right to discuss one or two more over the next couple of months if the urge takes me. What I do want to do is to discuss one monograph in particular, "Growth of Integrative Medicine at Leading Cancer Centers Between 2009 and 2016: A Systematic Analysis of NCI-Designated Comprehensive Cancer Center Websites," by Hyeongjun Yun, Lingyun Sun, and Jun J. Mao. I note that Dr. Mao is the immediate past president of SIO; this is coming from the top, so to speak.

I noted last week that I'm not a fan of the SIO, and it's not a fan of me. I won't repeat the story of my little discussion with them in which, in response to its umbrage taken in reaction to an article I published three years ago about integrative oncology, I tried to educate the leadership of the SIO that you can't have naturopathy without homeopathy. Reread last week's post if you want the details. My point is more that, as much as I don't like what SIO stands for, it has, unfortunately, been effective, and this survey provides yet another metric suggesting its effectiveness, along with that of all the other groups promoting the integration of pseudoscience and mysticism into medicine.

"Unmet needs"? Why would one need pseudoscience?

Yun et al. justify this survey with the usual tired tropes used to justify

“integrating” quackery with medicine, be it oncology or any other specialty. First, frame integrative oncology as an “unmet need”:

> Patients’ unmet needs in managing these symptoms coupled with their desire to use natural approaches to improve their health have created a demand for integrative medicine (3,4). According to the National Center for Complementary and Integrative Health (NCCIH), integrative medicine differs from complementary and alternative medicine (CAM) because it brings together conventional and complementary treatments in a coordinated way (5). Neither rejecting conventional therapies nor relying on alternative medicine, integrative medicine adopts only those complementary modalities supported by the highest evidence of safety and effectiveness (6). Numerous studies have evaluated the efficacy of utilizing integrative medicine modalities to treat the side effects of conventional cancer therapies. For instance, there is growing evidence that acupuncture may be effective in managing cancer therapy–related adverse effects such as fatigue (7–10), postoperative pain (11,12), vasomotor symptoms (13–16), and nausea and vomiting (17). Likewise, research supports the use of modalities such as massage (18,19) and mind-body therapies for symptom management and spiritual transformation; the latter remains a largely unmet need in the current health care system, yet directly impacts patients’ quality of life (4,20–23).

I can’t help but wonder how one quantitatively evaluates “spiritual transformation” in rigorous clinical trials, but that’s just me. In any case, I can’t help but note that some of the citations are articles discussed here and elsewhere before. For instance, reference 5 has been addressed before as “integrative health” being a rebranding of “complementary and alternative medicine” (CAM), which was a rebranding of alternative medicine. Other references, for instance, the ones supporting acupuncture, cite the usual low quality studies or studies that rebrand transcutaneous nerve stimulation (TENS) as “electroacupuncture.” Then there’s the whole framing of integrative oncology as an “unmet need.” It’s a very common framing of integrative medicine, be it through taking advantage of the opioid crisis to sell pseudoscience by claiming that nonpharmacologic management of pain must include CAM or by arguing that addressing unmet needs in symptom

management in cancer patients requires embracing pseudoscience. True, the latter argument isn't stated in those words, but when you strip away the "integrative" and CAM gobbledygook, that's the core of the argument you're left with: A false dichotomy that posits that, to treat the "whole patient" and to address "unmet needs," doctors must embrace the quackery in integrative medicine.

Next up, appeal to popularity:

> The use of integrative medicine is extensive among cancer survivors. Globally, up to 43% of patients with cancer have used integrative medicine therapies during their treatment, and the overall prevalence of integrative medicine use has increased noticeably over the past years (24–26). In the United States, cancer survivors use integrative medicine even more than individuals without cancer (27). Cancer survivors are more likely to use integrative medicine modalities for wellness, pain, and improving their immune functions. Interestingly, most of them started using integrative medicine because their conventional health providers recommended it to them (28).

Of course, as we've discussed before, this percentage is inflated by the broad definition of "integrative medicine." Basically, if you've ever had a massage or done art or music while being treated for cancer, by definition you've used integrative medicine. If you've ever meditated or prayed while being treated for cancer, you've used integrative medicine. If you've done Tai Chi, yoga, or Qi Gong (or even just exercise) while being treated for cancer, you've used "integrative medicine." You get the idea. When you look at the "hard core" quackery, such as homeopathy, you'll usually find that the number of patients using it is in low single digit percentages.

Integrative oncology and NCI-CCCs

The current survey is an update to a 2009 survey that found that 60% of National Cancer Institute (NCI)–designated comprehensive cancer centers (NCI-CCCs) provided information related to integrative therapies on their websites. Back in 2009, there were only 41 NCI-CCCs. Now there are 45. It's

worth looking at the old survey first, though, to see the sorts of modalities that were being offered at NCI-CCCs eight years ago and at what percentage of them:

Specific therapies listed did include some pure faith healing-related "energy medicine" quackery such as reiki (37% of websites), healing touch (29%). Not surprisingly, acupuncture showed up on 59% of websites, and dietary supplements, herbal medicine, and nutrition in one form or another showed up on between 42% and 56% of websites. To be honest, I was actually pleasantly surprised that only 60% of NCI-CCCs provided information on CAM. Indeed, it's kind of amusing to note the reaction of the authors to the perceived deficiencies of various NCI-CCCs with respect to CAM:

> Even with acknowledging these limitations, we still found that almost a third of leading U.S. cancer centers do not have functional websites related to CAM, and only a small proportion of the centers had websites independently judged to be excellent.

My reaction to that conclusion was: Gee, you say that as though it were a *bad* thing. I'm also happy that my cancer center's website would almost certainly have been in that one-third of cancer centers without information on CAM. Indeed, one of the things I've always liked about my cancer center is the relative paucity of integrative oncology options offered compared to other cancer centers, but I always fear that, sooner or later, we'll start to try to catch up.

So what's the situation now? Table 1 in the new study tells the tale. Mentions of quite a few modalities increased sharply. For instance, mentions of acupuncture increased by 30%, from 59% of NCI-CCCs to 89%. That's right. A whopping nine out of ten NCI-CCCs mention acupuncture credulously, and a full 73% offer it.

As a surrogate for just how much NCI-CCCs have abandoned science when it comes to integrative oncology, I like to examine the most implausible of treatments that fall under the mantle of "CAM" or integrative medicine. For example, mentions of healing touch, which is a form of "energy healing" (that doesn't actually involve touching) in which the practitioner claims to be able to detect and manipulate a patient's "life energy" field in order to heal

and/or relieve symptoms, increased from 29% to 58%, a doubling of the number, and 29% of NCI-CCCs actually offer this magical, mystical, "healing" touch. Mentions of reiki, which, as I've described many times before, is nothing more than faith healing that substitutes Asian mystical religious beliefs for Judeo-Christian beliefs as the basis for healing (replace the "universal source" from which reiki masters claim to derive the healing energy with God or Jesus, and you'll see what I mean), also increased markedly, from 37% of NCI-CCCs to more than half (53%) of NCI-CCCs, a more than 50% increase. Worse, 40% of NCI-CCCs actually offer reiki.

Not surprisingly, the "soft" parts of integrative medicine, the services that used to be offered for patient support and morale, such as art, music, massage, and various exercise programs but have, thanks to integrative medicine, become medicalized, appear on the vast majority of cancer center websites. One interesting finding is that, while exercise information is provided in 97.8% of cancer center websites, only 56% provide exercise/fitness services for their cancer patients. As much as it irks me that exercise and nutrition have been co-opted by integrative medicine and quacks like naturopaths, both can be science-based modalities for health promotion, particularly in cancer patients, although integrative medicine practitioners, particularly non-MD and non-dietician ones, often implement diet and exercise in non-evidence-based ways. (I'm talking to you, naturopaths, in particular.) Even so, we need to be doing better offering opportunities to help our patients exercise to improve their health and alleviate, for example, chemotherapy symptoms.

Overall, though, the authors are relatively happy with what they've found:

> Despite these limitations, we found that there has been substantial growth in the presence of integrative medicine on the websites of NCI-designated comprehensive cancer centers since 2009. In addition, the majority of the centers provide integrative medicine services within the same academic health systems in which they are located. As these centers lead the way in cancer research and clinical innovation, we need to ensure that integrative medicine can be cohesively incorporated into the continuum of cancer treatment and survivorship care using a financially sustainable structure. In addition, evidence-informed

> integrative medicine needs to expand beyond the walls of academic medical centers into community cancer centers and clinics to benefit patients from diverse socio-economic backgrounds.

The SIO even includes plans for world domination (OK, I mean the promotion of integrative oncology) around the world.

What the SIO left out: Most of the quackery

It's at this point that I can't resist mentioning what the SIO clearly left out. Remember, as I've pointed out many times, the SIO admits naturopaths. So where is naturopathy in this survey? Isn't naturopathy a part of "integrative oncology"? Certainly, the SIO seems to think so, given that it included presentations on naturopathic interventions in its recent annual meeting and even encourages naturopaths to join, listing them as equivalent to MDs. The SIO has even elevated two of them to the presidency of the organization! So why doesn't the SIO include a survey of which NCI-CCCs mention and offer naturopathy to their patients? Are they embarrassed? Trying to hide something? One wonders what Suzanna Zick, who was SIO President from 2015-2016, or Heather Greenlee, who was president from 2014-2015, think of this omission? Both are naturopaths.

I really can't help but suspect that, in its effort to persuade medical academia that integrative oncology is rigorously science- and evidence-based, whether intentionally or not, the SIO leadership is focusing all its attention on promoting the evidence-based modalities that have been "rebranded" as "integrative," such as diet, exercise, and the like, and the patient support modalities that have been medicalized into "integrative medicine," such as massage, art therapy, music therapy, and the like. Pay no attention to that quackery that integrative oncology and medicine lump together with the diet, exercise, and the like, the SIO seems to be saying by the absence of focus on naturopathy (and the homeopathy that nearly all naturopaths practice). Again, it can't be emphasized enough that, wherever you find naturopaths practicing, you will find homeopathy being practiced.

True, there are a couple of exceptions. The SIO does mention reiki and

therapeutic touch rather prominently in both surveys, both of which are obvious energy healing quackery. However, most people don't realize that. Most people view reiki and healing touch as a form of massage or hands-on healing, even though healing touch usually doesn't involve actually touching the patient. Either that, or they view them as some form of spirituality, which is actually not too far from the truth, but mystical claims such as what are made for reiki and healing touch do not belong in science- and evidence-based medicine. Yet there are NCI-CCCs that credulously promote energy healing. For instance, I've written about Georgetown University before. There's an NCI-CCC there, the Georgetown Lombardi Comprehensive Cancer Center. I've described Georgetown as a bastion of quackademic medicine before because of its "pioneering" efforts to "integrate" the teaching of pseudoscience into its medical school curriculum. Relevant to cancer, though, Georgetown published an article in its official magazine about reiki in the chemotherapy suite:

> For a long time Denise von Hengst had a secret she kept from friends and physicians alike. As she was undergoing treatment at Georgetown Lombardi Comprehensive Cancer Center for a particularly aggressive type of breast cancer—triple positive, HER2 positive—she was also regularly receiving Reiki, an ancient form of Japanese healing, to mitigate the debilitating anxiety and fear that accompanied her cancer diagnosis.
>
> "At first I told no one about the Reiki," says von Hengst. "Fear of the 'woo-woo' factor. People might think I'm nuts."

No, I don't think the patient is nuts. I think the cancer center is irresponsible for offering magic with its medicine, leavened with pseudo-skepticism:

> However, skepticism remains, not only in the general population, but also within the medical field. Recently, several clinical trials have emerged attempting to prove, or disprove, the effectiveness of Reiki. Many of these studies have been criticized for the trial. design, number of participants and reporting mechanisms. Results of the trials are often inconclusive.
>
> Yet as the anecdotal proof mounts and Reiki's popularity increases,

> prestigious medical centers around the country are taking note and offering the treatment to patients at their facilities. Reiki can be found at hospitals and medical centers such as Boston Children's Hospital, Dana Farber Cancer Institute, Stanford Health Care, Memorial Sloan Kettering Cancer Center, Duke University Health System and Cleveland Clinic, to name a few. Many academic medical centers such as Georgetown incorporate complementary therapies into their teaching curricula.

I have a question for the leadership of SIO: Is reiki evidence-based? Is it science-based? If it isn't, then why are you supportive of NCI-CCCs offering it?

Here's another example, the University of Arizona Cancer Center, which is an NCI-CCC. Take a look at its integrative medicine page. Look at what it offers: reiki (of course, even though a faculty member complained about it), reflexology (pure quackery that posits a nonexistent link between body parts and organs and specific areas on the soles of the feet and palms of the hands), craniosacral massage (which Mark Crislip drolly and correctly called a "SCAM of infinite jest"), healing touch (of course), and shiatsu (unproven).

Three years ago, the son of a professor in a humanities department at UA was treated for leukemia at the UA Cancer Center. He was appalled at all the quackery being offered to his son, including not just the above modalities, but distance healing, offered by a man named Frank Schuster:

Yes, as fantastic as it sounds, this was a web page hosted by the University of Arizona Cancer Center. It might be gone now, but it's not at all clear that the quack above is gone from UACC.

After this professor complained, Shuster's UA webpage was either removed or placed behind a login. However, I noticed something about UA's list of offerings for integrative medicine. First, none of the practitioners were listed by their full names any more. It's Jessica, Barb, Heidi, Michael, Denise, or Frank, the last of whom offers the reiki classes. Hmmm. I wonder if that's Frank Schuster, still there, still practicing energy healing. I bet it is, but haven't been able to verify it one way or the other.

I want to believe that the SIO wants to be scientifically rigorous. I really do.

I’m guessing that most of the SIO physician and scientific leadership believes that they are being scientifically rigorous and trying to lay down a framework in science and clinical evidence for “integrative oncology,” even if they have a hard time defining what, exactly, integrative oncology is. It’s just that, for whatever reason, physicians who drink the Kool Aid of integrative medicine tend to develop massive blindspots about all the quackery that comes as a package with all the parts of integrative medicine that they like, such as the emphasis on lifestyle, diet, exercise, and the treatment of the “whole” person. These blindspots extend to naturopathy in particular, which is a veritable cornucopia of quackery, including homeopathy. Until the SIO can eliminate its blindspots over all the quackery that is included in “integrative medicine,” its claims of being scientifically rigorous are just so much self-delusion.

And the server migration continues apace… but where are the comments? - Science-Based Medicine

As many of you noticed, there has been an issue with the comments that began last night. Here’s what happened. The Powers That Be decided to migrate the blog to a new server last night, and there were problems relinking Disqus to the new installation of WordPress. I am assured that the problem has been fixed, but also told that it could take 12 hours for all the old comments to redirect to our new location. So be patient, and the blog should be back to normal by tomorrow morning. There should be benefits to the new server as well, such as faster loading, less downtime, and the like. We’re sorry about the inconvenience today, but as one of our crew noted, for some reason migrations never seem to go as smoothly as we would like.

In any event, if after tomorrow there are still problems, let us know.

Science Based Medicine

周四, 09 11月 2017

Science Based Medicine

[周四, 09 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Risks of a Gluten-Free Diet** [周三, 08 11月 21:27]
  Non-Celiac Gluten Sensitivity does not seem to be a real entity according the current evidence, but this has not stopped the gluten-free fad, which may be causing real harm.
- **Update on ASEA, Protandim, and dōTERRA** [周二, 07 11月 16:00]
  Multilevel marketing distributors of dietary supplements and essential oils point to studies that they think constitute evidence that their products work. They don't understand why those studies are inadequate.
- **ORBITA: Another clinical trial demonstrating the need for sham controls in surgical trials** [周一, 06 11月 16:58]
  Last week, the results of ORBITA were published. This clinical trial tested coronary angioplasty and stunting versus optimal medical management in patients with single-vessel coronary artery disease. It was a resoundingly negative trial, meaning that adding stunting to drug management t didn't result in detectable clinical improvement. What was distinctive about this trial is that it used a sham procedure (i.e., placebo) control, which few trials testing surgery or a procedure use. The results of…

There is a simple reason we strongly promote science-based medicine – it results in the best outcomes for individuals. That is true by definition, since the SBM approach is to use the best evidence and science available in order to determine which interventions result in the best outcomes.

There are numerous ways in which relying upon poor-quality evidence or invalid methods for making health decisions cause potential harm. Often the list is unimaginatively limited to direct physical harm, but that is only the tip of the iceberg. There is financial harm, loss of opportunity to pursue more effective interventions, psychological harm from false hope and being deceived, and sacrifice of quality of life, time, and effort.

Even without direct physical harm, with inert treatments like homeopathy, there is tremendous potential harm from relying upon fake medicine and bad science. But often there is potential physical harm, and even if slight it is not justified if there is no real benefit. Medicine is a game of risk vs benefit – when the benefit is essentially zero, any risk is unacceptable.

The gluten-free fad

Even a small potential harm can be significantly magnified if it is marketed to the general public. The "clean eating" movement, in my opinion, clearly represents such a case. The best overall advice we can give the public regarding healthy eating is to eat a variety of food with plenty of fruits and vegetables and watch overall caloric intake. Unless you have special medical considerations, simply eating a good variety of different kinds of food will take care of most nutritional concerns. It will result in you getting enough of what you need and not too much of anything that can increase your risk.

Having a restricted or narrow diet is always tricky, and runs the risk that you will be getting too little of some key nutrients and may be getting exposed to too much of others. This is the key risk of so-called "fad" diets, because they are often premised on a simplistic notion that specific foods or categories of foods are inherently bad and should be avoided. Therefore any diet which

essentially consists of avoiding certain foods or heavily relying on others is likely to take you away from an optimal diet, and therefore be a net negative for your health.

The recent gluten-free fad is no exception.

As I discuss in detail here, gluten is a composite of two proteins found in wheat, rye, barley, spelt, and related grains. About 1% of the population has an autoimmune reaction to one of the components of gluten (usually gliadin) and eating gluten can cause serious illness (a condition known as celiac disease). For those with celiac disease, avoiding gluten is essential and even a small amount of gluten can cause serious symptoms.

There is a controversy, however, surrounding the alleged existence of so-called non-celiac gluten sensitivity (NCGS). This is a hypothetical condition in which people may have a sensitivity to gluten without forming antibodies to gliadin or meeting the diagnostic criteria for celiac disease. Discovering a new disease is always complex, and requires the identification of something definitive and discrete. We either need to identify a clear clinical syndrome, or some new specific pathology.

For NCGS there is no clear pathology. The entity's legitimacy currently relies on the alleged existence of individuals who do not have celiac disease but have a negative reaction to eating gluten. If, however, we are going to base a new disease purely on clinical history, we need to make sure that the history is accurate and that we are not simply overinterpreting non-specific symptoms or falling victim to confirmation bias.

For example, there are people who feel they have a specific syndrome of sensitivity to electromagnetic waves, despite the absence of any identifiable pathology. However, properly blinded studies show that self-identified sufferers of EM sensitivity cannot tell when they are being exposed to EM waves in a blinded condition.

For alleged NCGS the most salient evidence of its existence as a clinical entity are rechallenge studies. In these studies subjects are challenged with either gluten or placebo, then the gluten is removed, and then they are later rechallenged. If NCGS is a real entity then their symptoms should resolve

when gluten is removed and then return when rechallenged, at a higher frequency when the same is done with a placebo.

A recent systematic review of gluten rechallenge studies did not find significant evidence for NCGS. They conclude:

> The prevalence of NCGS after gluten re-challenge is low, and the percentage of relapse after a gluten or a placebo challenge is similar.

This is a pattern of evidence that is consistent with the null hypothesis, that NCGS does not exist – results are all over the place, with better-controlled studies tending not to show an effect, and on average there is only a tiny signal that does not reach statistical significance. The most parsimonious interpretation of available evidence, therefore, is that NCGS does not exist. Despite this fact, roughly one third of the population report that they are trying to avoid gluten.

What's the harm

What, then, is the potential harm from restricting gluten from the diet in the millions of people who do not have gluten sensitivity? Potentially, all of the things I listed above may contribute to harm.

For many people they have settled on gluten sensitivity to explain real symptoms they may be having. In this case they may be missing the real cause of their symptoms. There is therefore an opportunity cost of making a false diagnosis.

Perhaps most significantly, a gluten-free diet is very difficult. You have to eliminate all wheat and similar grains from the diet. This has become somewhat easier recently as industry is cashing in on the gluten-free fad, but it is still a significant inconvenience and expense and therefore drain on quality of life.

Further – a gluten free diet eliminates a major category of food from the diet. People on a low or gluten-free diet tend to also be low in whole grains. They risk being deficient in iron and folic acid. A recent study linked low-gluten

diets to a higher risk of type-II diabetes.

Avoidance of gluten may also result in a heavy reliance on rice as a staple grain, and this might increase the risk of heavy metal exposure. Again – having a varied diet spreads out exposure to contaminants and toxins as well as maximizing exposure to needed nutrients.

Science over marketing

If we take a scientific approach to the question of NCGS we find that there is no clear evidence that non-celiac gluten sensitivity is a real thing, and that gluten-free diets not only have no benefit for the general public they present health risks. Clearly, however, we need to do a better job of communicating this to the public.

Part of the challenge, however, is that nutritional gurus (who always seem to have something to sell) have a simple and appealing narrative to market. They tell the public that their problems are due to one bad food or type of food they just need to avoid. Or, they market of lifestyle of “clean eating” that is based on the appeal to nature and irrational fear of toxins and chemicals, rather than an even basic understanding of science and evidence.

The science-based position, however, takes time to emerge. It may take a decade or more to do the kinds of studies necessary to effective answer the question about whether or not a new hypothesized clinical entity exists. There are many types of evidence to be considered, and many sub-questions to be addressed. Over time a clear picture will tend to emerge, but in the meantime the health gurus can establish a market for their nonsense. Once their simplistic and marketable narrative gets into the public consciousness it is hard to correct.

I have written critiques of several dietary supplements sold through multilevel marketing (MLM) schemes, and they keep coming back to haunt me. I get testimonials from users who believe they have been cured of every ailment under the sun; and every time another study is done, I get e-mails from distributors who apparently think the new “evidence” will change my mind. Recently I received three more emails about ASEA, one about Protandim, and three about dōTERRA essential oils, asking me to reconsider. I thought this would be a good opportunity to explain why I have not changed my mind and to explain once again what constitutes evidence in science-based medicine.

ASEA

Recently an email from “The ASEA Team” asked us to delete the article I wrote about ASEA in 2012, based on their opinion that it “was not constructive” and “was not based on decent and verifiable facts.” They did not mention two other followup articles I wrote here and here. And they did not directly try to refute most of the points I made in my critique; I think they failed to understand what I was saying. They provided six attachments with

studies they said were “made to prove the effectiveness of ASEA” but those studies didn’t prove any such thing.

Last week Steven Novella answered them very effectively, calling ASEA snake oil and pointing out the deceptive marketing practices of the company, the pseudoscientific nature of their claims, and the worthlessness of the studies they cite.

The claims

The ASEA website currently makes these claims:

> As we age, and as stress and environmental toxins inundate our lives and weaken our defenses, normal cellular function declines, and with it, the body’s ability to produce and maintain a proper balance of redox signaling molecules. ASEA has developed the only technology that can create and stabilize active redox signaling molecules in a consumable form. No matter what your health concern may be, ASEA Redox Supplement can bring your cellular communication to optimal levels, improving the health of every system of your body.

Questions

This brings up several questions:

- How exactly does normal cellular function decline? How would improved cellular communication reverse the decline?
- What is a proper balance of redox signaling molecules? How do they know? How is it measured?
- What active redox molecules are in the product? (They won’t tell us. The label just lists salt and water. In my opinion, if there are redox molecules in ASEA, listing only salt and water constitutes false labeling.)
- What evidence do they have that the product improves health?

What redox molecules?

All they have is a statement from a lab, BioAgilytix, that indirectly measures "biomarkers" of redox levels in ASEA using a fluorescent indicator as a probe for unspecified highly reactive oxygen species. I don't know what that means. There is no direct evidence that redox molecules are present. No other lab has analyzed the product.

Safety

Their claim that the product is safe is based on a brief description of two unpublished studies. In the first study, 106 overweight women took ASEA or placebo for 12 weeks; they reported no adverse effects, (None?! In most studies, even the placebo group typically reports *some* symptoms.) and there were no changes in liver or kidney function tests or complete blood counts. In the second study, an *in vitro* study of cultured eukaryotic cells, the cells "did not register a significant toxic response as measured by a visual assessment of green dye that indicated "nuclear translocation." Based only on this flimsy subjective and *in vitro* evidence, they claimed "ASEA Redox Supplement, orally administered, does not manifest a toxic response or inflammation to exposed tissue." Such thin gruel does not constitute convincing evidence that the safety of the product has been established.

Studies

Before I accept that a treatment works, I want to see human studies published in peer reviewed journals. There are none on their website, but I was able to locate two articles in the *FASEB Journal* here and here.

It quickly became obvious why these are not featured on the company website: they are not full articles, but abstracts from a meeting that were published in a supplement to the journal. One is a human study, the other is in mice (the poor mice were gavaged with ASEA and then run to exhaustion). One of my correspondents claimed that these are peer-reviewed studies, but peer review is not possible when all that is available is an abstract.

As far as I could determine, there have been three studies in humans. One, a small study of 17 cyclists, has been deleted from the web. It was not placebo-controlled. There is an abstract of a similar study of 20 cyclists that did use a placebo control and was double-blinded. It was essentially *negative*: ASEA did not improve time trial performance. They found that it caused a significant shift (good or bad?) in 43 metabolites, but had no apparent influence on traditional biomarkers of inflammation, oxidative stress, or immunity.

The third, most recent human study is the one my true believer correspondents are currently crowing about. They refer to it as a "genetic" study. One of them snarkily commented "It's called science, u should look into it sometime." I did look into it, and I was not impressed. The title is "Initial Gene Study Showed ASEA REDOX Affected Important Signaling Pathway Genes." The company paid Tauret Labs to do the study. It has not been published in a peer-reviewed journal. It was an 8-week double-blind randomized placebo controlled study with 60 participants that measured changes in expression of 5 genes and found statistically significant changes of 20-31% with ASEA. They claim that "These genes are key in the health of the individual and play a vital role in five human health areas and dozens of pathways." Maybe, but they have not demonstrated that human health benefits in any way from these changes in gene expression. Their summary of results states "Effects are non-specific to race, sex or age, and were observed in all populations tested." This conclusion is not supported by their data. The only population tested was 60 individuals, 41% male, 92% Caucasian, average age 35 with age distribution not reported.

Conclusion

The evidence for their claims is indirect and inadequate. Half of all research studies turn out to be wrong. Changes in blood tests might be spurious; they have not been independently replicated. Changes may be statistically significant but not clinically significant. If they want us to believe ASEA causes objective, meaningful improvements in human health, they'll have to do better. They'll have to test directly for meaningful clinical outcomes. And if they want us to believe ASEA contains all those redox signaling molecules,

they'll have to prove it with a direct analysis by an independent lab and name those molecules.

As Steven Novella put it,

> Asea, however, is still a fantastical and unbelievable claim supported by nothing but hype, sales copy, and empty promises. It is salt water. The hand-waving nonsense about redox reactions is incoherent technobabble – the very essence of pseudoscience. What would be convincing is published, peer-reviewed, independent, rigorous scientific studies with clear results. These don't exist. No amount of distraction will change that fact.

Protandim

I have written about Protandim four times, here, here, here, and here.

What is it?

It is a mixture of five dietary supplements (Milk thistle, *Bacopa* extract, Ashwagandha, green tea extract, and turmeric extract) that allegedly stimulates the body to produce its own antioxidants. They claim it is "the only supplement clinically proven to reduce oxidative stress by 40%, slowing down the rate of cell aging to the level of a 20 year old [and they measured this how?]."

An email from a reader

> You really need to up date your studies on this product! There are thousands of people with improved health because of PROTANDIM. For example, my son in law with high blood pressure was able to cut his BP medication in half after only two months on it and after three months, he is off meds completely with normal blood pressure; my daughter suffered for a year with a horrible rash under her arm that

> looked like tree bark. After several visits to her doctor where he prescribed cortisone and antibiotics nothing worked. She finally went to a dermatologist who was shocked to see that she had Granular Parakeratosis a rare skin disease. My daughters case was only the second time she has seen it, and at a follow up visit was told that there is no cure, only palliative care. Three days later the crud came off in her washcloth in the shower, and she had been on PROTANDIM for about two months. See photos. On the after picture you can see a round sore which is from the biopsy. In addition, my husband who has cOPD and had bypass surgery last year, and myself have great, new energy. In addition, my nerve damaged feet and numbness in my right foot have improved by at least 80 per cent after only 5 weeks! For the first time in 15 years or so, I can now feel my right big toe and it is no longer cold, like a piece of granite, and our bad backs have greatly improved. I could go on and on and I don't need someone like you to tell me and thousands of others that it does not work! We are walking human studies for this amazing product! Check out the human studies for liver disease! I am proof it works so you should take another look: in fact go to You Tube PROTANDIM testimonials and see for yourself what this product does when it reduces oxidative stress!

My most recent article was in May 2017, and I'm not aware of any new studies requiring me to "update my studies" in the last six months. The evidence on the website is mainly about Nrf2 protein messengers in general, and studies of Protandim in cell culture (*in vitro*) and in mice. One 2006 human study found changes in lab tests such as TBARS but did not even attempt to look for any clinically meaningful improvement in health outcomes. A second human study in 2016 was negative: It concluded "Protandim® did not (1) alter 5-km running time, (2) lower TBARS at rest (3) raise antioxidant enzyme concentrations compared to placebo (with exception of SOD in those ≥ 35 years old) or, (4) affect quality of life compared to placebo." And another study of patients with alcohol use disorders was also negative. Not only negative but laughable.

Conclusion

Increasing levels of antioxidants could be beneficial or harmful. The only way to know if Protandim improves human health is to do properly designed, placebo-controlled human studies looking for meaningful clinical outcomes.

dōTERRA essential oils

I have written about dōTERRA twice before: here and here.

An email asked me to "Check with Johns Hopkins and the research published about dōTERRA oils. Dr. Nicole Parrish claims that dōTERRA oils have killed three super bugs that synthetics cannot. It is published and the medical world is learning more about essential oils in September." I asked her for links to that research; she never responded.

Another email chastised me for having a "complete scientific mindset." (I thought that was a *good* thing!) She said, "It really is worth looking further into to help people stay healthy." She provided all kinds of testimonials: her dentist and her real estate agent use it, her son and stepson carry the beadlets with them during allergy season, and when her husband got cancer, they used essential oils for diabetes, neuropathy, infections, and asthma. She also chastised me for not mentioning what the Bible says about oils and plants! She believes "science is here to prove God's existence and the Bible can be used for medicinal research." I didn't try to answer her.

An *in vitro* study was done on dog kidney cells infected with influenza virus. Based on their results, they speculated that essential oils *might* be useful in treating humans with influenza (or might not). In my article critiquing that study, I provided some guidelines on how to read research studies that claim to support a product.

A third email said I needed to visit the website again and review the 17 studies published in peer-reviewed journals. I found an *in vitro* study of frankincense and an *in vitro* study of Deep Blue, a mixture of essential oils. There was also an extensive bibliography which included a lot of irrelevant articles along with *in vitro* and animal studies. There were a lot of scattershot preliminary studies on individual oils, but these were seldom if ever followed

by replications or confirmations. My own PubMed search found a few studies supporting the use of an essential-oil-containing mouthrinse, reports of adverse effects of essential oils, some negative studies, and a couple of Cochrane reviews that pointed out the poor methodology of the few studies they found. A 2012 systematic review of aromatherapy concluded "the evidence is not sufficiently convincing that aromatherapy is an effective therapy for any condition."

My correspondent said, "In my opinion, there are too many confirmed reports of improved health & well-being (when using essential oils) to chalk it all up to "hysteria" or "ignorance" or even chance." Her opinion is misguided. The plural of anecdote is not data. Confirmed reports of improved health and well-being, no matter how numerous, are meaningless without a control group. Reports of failures are not systematically collected. Patients may improve for reasons other than the oils: suggestion, placebo effect, social factors, the natural course of the disease, regression to the mean, etc.

Essential oils can be very pleasant to use, and I have no problem with using them as "comfort" measures. And the company website is careful not to make any egregious disease-prevention or -treatment claims. But at their in-home presentations, the distributors feel free to claim that the oils can cure anything and everything, including cancer. These claims are not backed by any science but are illustrated by persuasive anecdotes, touching and heartwarming stories, testimonials from users that the attendees may know personally. Attendees are easily influenced to believe and to buy.

The published evidence for each of dōTERRA's many products is sparse to nonexistent. There *are* clinical studies to support *a few* of the recommended uses, but they are generally poorly designed, uncontrolled, unreplicated, and unconvincing. Research is difficult, because patients can't be blinded to the odors, and mental associations and relaxation could account for most of the observed effects. I remain skeptical of the claims for objective benefits in treating diseases.

Conclusion: No reason to change my mind

Testimonials are notoriously unreliable. These products are not supported by acceptable scientific evidence. I'm *not* saying they *don't* work. No one knows whether they work or not, because they have not been properly tested. I am simply asking for a single standard of evidence, the kind of evidence required to achieve a scientific consensus that any treatment is effective and safe. If they want us to buy their products, they should test them against placebo controls in human studies looking for objective, meaningful improvements in health; and they should get those studies published in reputable peer reviewed journals. In the pharmaceutical industry, only a small percentage of promising candidates survive testing. Considering the huge number of dietary supplement products like these on the market, the chance that any one of them will prove to be truly effective is vanishingly small.

We here at SBM devote a lot of discussion to unscientific and pseudoscientific treatment modalities, the vast majority of which can be best described as quackery. Sometimes, though, what's even more interesting are controversies in "conventional" science-based medicine. In particular, I'm a sucker for clinical trials that have the potential to upend what we think about a disease and how it's treated, particularly when the results seem to go against what we understand about the pathophysiology of a disease.

So it was that I started seeing news reports last week about ORBITA (Objective Randomised Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina). Basically, ORBITA is a double-blind, randomized controlled trial comparing percutaneous coronary intervention (PCI, or, as it's more commonly referred to colloquially, coronary angioplasty and/or stenting) versus a placebo procedure in patients with coronary artery disease. Indeed, the sham procedure is what makes this trial interesting and compelling, although the devil is in the details. What this trial and its results say about coronary artery angioplasty and stenting, placebo effects, and clinical trial ethics are worth exploring. Basically, ORBITA calls into doubt the efficacy and usefulness of PCI in a large subset of patients with stable angina (chest pain or discomfort due to constriction of one or more coronary arteries that most often occurs with fairly predictably with activity or emotional stress—that is, exertion).

Before I dig in, I can't resist mentioning that cardiac surgery was one of the very earliest forms of treatment in which the importance of a sham surgery control was shown to be very important. In 1939, an Italian surgeon named David Fieschi developed a technique in which he tied off (ligated) both internal mammary arteries through two small incisions, one on each side of the sternum. The idea was to "redirect" blood flow to the heart in order to overcome ischemic heart disease, in which the patient suffers pain, heart failure, or even death due to insufficient blood flow to the heart muscle caused by atherosclerotic narrowing of one or more of the coronary arteries. The results were striking, as three quarters of all patients on whom Dr. Fieschi did his procedure improved and as many as one third appeared to be cured. The procedure became very popular and appeared to work.

Nearly two decades later, in the late 1950s, the NIH funded a cardiologist in Seattle named Dr. Leonard Cobb to do a randomized controlled clinical trial of the Fieschi technique. He operated on 17 patients, of whom eight underwent the true Fieschi procedure, with both internal mammary arteries tied off, and nine underwent skin incisions in the appropriate location. In 1959, Dr. Cobb's results were published in the New England Journal of Medicine, where he reported that the results were the same for patients who underwent the "real" Fieschi operation or the sham procedure. This was the beginning of the end of internal mammary ligation as a treatment for angina and a landmark in the history of surgery. After this trial, understanding of the ethics of human subjects research changed, and including sham surgical procedures in clinical trial design became increasingly frowned upon.

ORBITA is one of several recent trials that use sham interventions that have been reported in recent years as that ethical understanding has shifted again in the face of increasing evidence that surgery can produces the most powerful placebo effects of all interventions. Another example is trials of vertebroplasty for vertebral fractures due to osteoporosis, which showed that vertebroplasty in this setting produced results indistinguishable from the sham procedure. Increasingly, it has been argued that more surgical trials should include a sham procedure group.

PCI: A brief history

Publication of the results of ORBITA were timed to coincide with the 40th anniversary of the development of PCI. Basically, coronary angioplasty was developed 40 years ago as a less invasive treatment than coronary artery bypass grafting (CABG) for coronary artery disease. In brief, in PCI a cardiologist will thread a catheter up a major blood vessel in the groin to the heart and into the coronary artery (or arteries) with blockages. At the end of the catheter is a balloon. The idea is to thread the end of the catheter under fluoroscopic guidance (fluoroscopy is a form of X-ray imaging with video) into the coronary artery and past the blockage, such that the balloon aligns with the atherosclerotic blockage. The balloon is then inflated to open up the blockage. That's the basic idea, although the methods have evolved markedly over the last forty years.

At this point I can't help but mention a bit of a personal note, as it involves the research I did as part of my PhD thesis, lo these many years ago. One of the huge problems with angioplasty early on was the high rate of restenosis (recurrent narrowing) of the blood vessel treated. The reason for this was that balloon angioplasty involved, in essence, injuring the vessel. As with any injury, there was an inflammatory reaction, and one consequence of the inflammatory reaction due to angioplasty is that the vascular smooth muscle cells in the media (the middle layer of the blood vessel) would be stimulated to proliferate and restenose the vessel. As part of my PhD thesis, I cloned and characterized a homeobox gene (yes, a homeobox gene, for you geeks out there) that inhibited the proliferation of vascular smooth muscle cells. The idea was to treat the area at the time of the procedure with this gene as a form of gene therapy to prevent restenosis.

I realize that those of you out there who might be cardiologists and who weren't practicing back in the 1990s probably think this was an insane idea, but here's why it wasn't so insane back then. Back then, coronary stents hadn't been perfected, much less the drug-eluting coronary stents that are commonly used now to prevent restenosis. Basically, after most angioplasty procedures now, cardiologists place a stent in the area of former blockage. To prevent cellular ingrowth into the holes of the stent and subsequent restenosis, the stent slowly elutes a drug that prevents the proliferation of vascular smooth muscle cells. (As an aside, one of the things about these stents that frequently causes problems to surgeons like me is that the patient needs to be on powerful anti-platelet drugs like Plavix for up to a year after stenting). In any case, with the development of drug-eluting stents, the idea of gene therapy to prevent restenosis disappeared into the dustbin of scientific history, for the most part.

Back when PCI was new and young, its indications were a lot more limited, but as time went on and cardiologists' confidence grew indications expanded to multivessel disease and other indications that used to mandate CABG, to the point that PCI for acute coronary syndromes has grown to predominate. As MedPageToday describes:

> In the early years of PCI it was widely believed that PCI to open a severely blocked artery would have long term cardiovascular benefits,

> even in stable patients. Angina patients, the thinking went, were at higher risk for CV events and death, and PCI or CABG lowered that risk by restoring flow through the blocked vessel and preventing a future MI. But doubts grew over time, as it became increasingly clear that MIs were more likely to occur at other, less obvious blockages. Coronary artery disease began to be seen more as a systemic condition and less as a focal plumbing problem. The positive role of medical therapy, including statins and aspirin, became increasingly recognized.
>
> Finally, a decade ago the COURAGE trial, despite widespread and fierce initial resistance in the interventional cardiology community, led to widespread agreement that in fact PCI in stable lesions did not produce long-term improvements in outcome when compared to optimal medical therapy (OMT).
>
> But PCI for stable angina maintained a strong clinical presence as a new consensus emerged in the cardiology community that PCI was superior to OMT in the relief of symptoms. The mantra was that patients would need a stent eventually so they might as well get it upfront. It is this reduction in symptoms that the ORBITA trial sought to test.

And it is this assumption or belief that ORBITA called into doubt, at least for one large subset of patients.

ORBITA

ORBIT has been published in the online first section of The Lancet; so let's dig in. The introduction tells the tale, and you don't even have to leave the abstract:

> Symptomatic relief is the primary goal of percutaneous coronary intervention (PCI) in stable angina and is commonly observed clinically. However, there is no evidence from blinded, placebo-controlled randomised trials to show its efficacy.

Or, in more detail in the introduction:

> Percutaneous coronary intervention (PCI) was originally introduced to treat stable angina.1 More than 500 000 PCI procedures are done annually worldwide for stable angina. The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial showed no difference in myocardial infarction and death rates between patients with stable coronary artery disease who underwent PCI and controls.[2] Meta-analyses have shown similar results.[3]
>
> Angina relief remains the primary reason for PCI in stable coronary artery disease.[4] Guidelines recommend antianginal medication as rst line therapy, with PCI reserved for the many patients who remain symptomatic.[5]
>
> Data from unblinded randomised trials have shown significant exercise time improvement, angina relief, and quality of life improvement from PCI.[6–8] However, symptomatic responses are subjective and include both a true therapeutic effect and a placebo effect.[9] Moreover, in an open trial, if patients randomised to no PCI have an expectation that PCI is advantageous, this might affect their reporting (and their physician's interpretation) of symptoms, artifactually increasing the rate of unplanned revascularisation in the control group.[4,10]

So the investigators who designed ORBITA sought to do a rigorous randomized, double-blind, sham-controlled clinical trial of PCI for patients in stable angina. One can argue that such a trial should have been done a long time ago, before PCI became such a popular procedure for stable angina, and you would be correct. However, it's been done now; so let's look at the design. First, the inclusion criteria:

- Age 18-85 years
- Stable angina/angina equivalent
- At least one angiographically significant lesion (≥70%) in a single vessel that was clinically appropriate for PCI

Exclusion criteria:

- Angiographic stenosis ≥50% in a nontarget vessel

- Acute coronary syndrome
- Previous coronary artery bypass graft surgery
- Left main stem coronary disease
- Contraindications to DES
- Chronic total coronary occlusion
- Severe valvular disease
- Severe left ventricular systolic impairment
- Moderate-to-severe pulmonary hypertension
- Life expectancy <2 years
- Inability to give consent

Other fedatures of the patient population studied:

- Previous PCI: 13%
- Left ventricular ejection fraction normal: 92%
- Canadian Cardiovascular Society angina severity grading class: I (3%), II (59%), III (39%)
- Angina duration: 9 months
- Vessel involved: left anterior descending (69%)
- Median area stenosis by quantitative coronary angiography: 85%
- Median baseline FFR value: 0.72; median post-PCI FFR value: 0.9

The primary endpoint to be assessed was improvement in exercise time. To determine if PCI patients with stable angina and evidence of severe single-vessel stenosis were randomized 1:1 to either PCI or a sham procedure. After enrollment, patients in both groups underwent six weeks of medical optimization. After that, they underwent either PCI or sham procedure with auditory isolation in which the subjects all wore headphones playing music throughout the procedure. During the procedure, patients' heart function (measurements known as fractional flow reserve (FFR) and instantaneous wave-free ratio (iFR)) was monitored using a research method, but operators were blinded to the physiology values and did not use them to guide treatment. Randomization occurred after this physiological assessment. For patients undergoing PCI, the operator used drug-eluting stents according to standard clinical guidelines with a mandate to achieve complete revascularization as determined by angiography. In the sham procedure group, subjects were kept sedated in the cath lab for at least `15 minutes, with

the coronary catheters withdrawn with no intervention having been done. Here's the summary of the timeline and allocation of the trial:

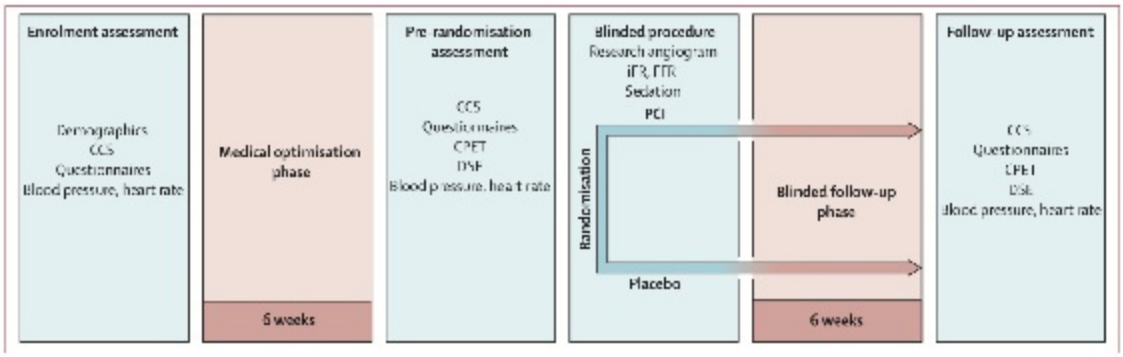


Figure 1: ORBITA study design
CCS=Canadian Cardiovascular Society angina severity grading. CPET=cardiopulmonary exercise testing. DSE=dobutamine stress echocardiography. iFR=instantaneous wave-free ratio. FFR=fractional flow reserve. PCI=percutaneous coronary intervention

Here's the trial outline:

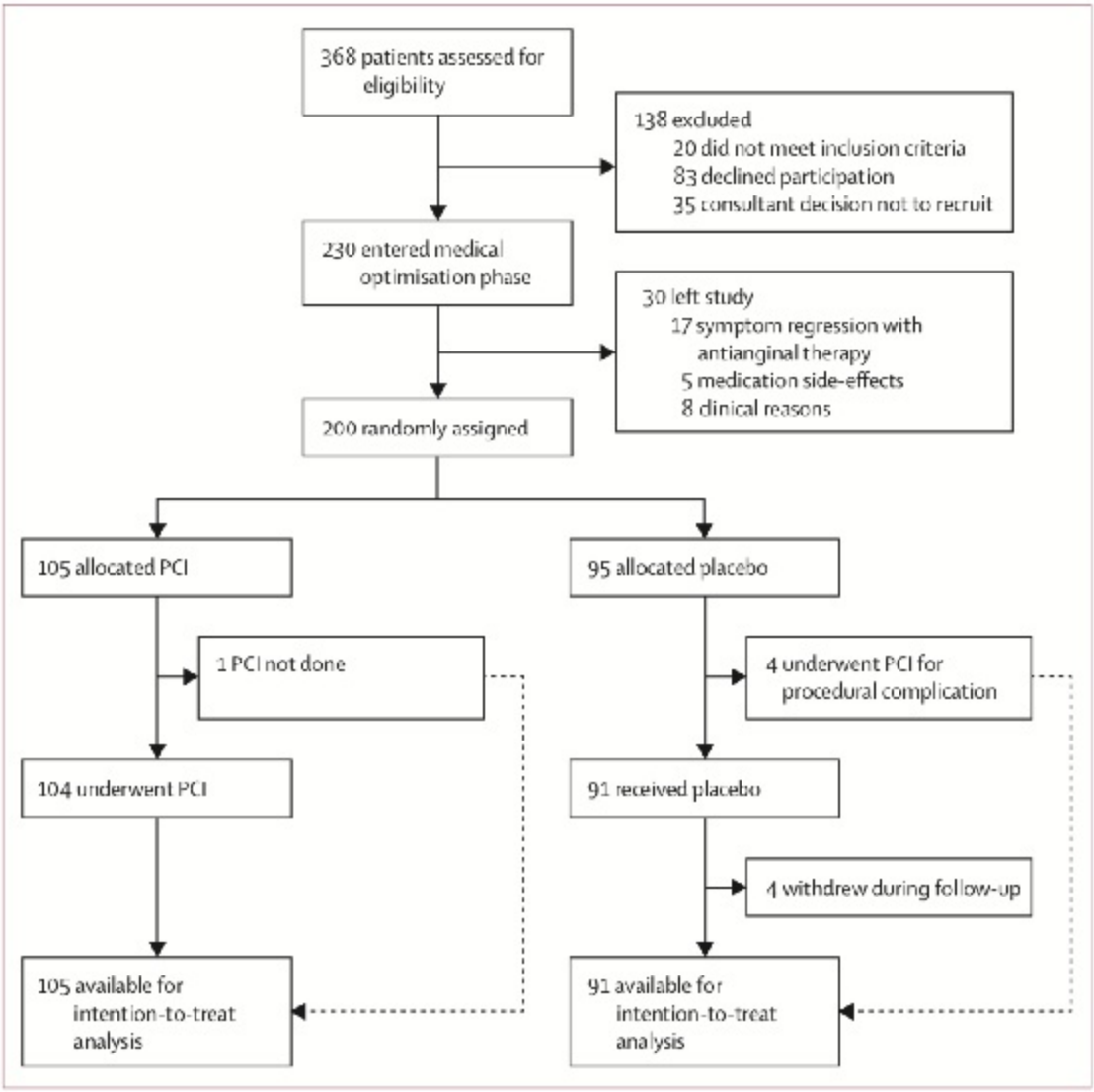


Figure 2: **Trial profile**
PCI=percutaneous coronary intervention.

Overall, there were 230 patients enrolled, of which after the medical optimization phase 200 were randomized, with 105 patients assigned to PCI and 95 assigned to sham procedure. And the results? They were what we call in the business a big nothingburger. The change in exercise time from baseline for PCI vs. sham, was 28.4 vs. 11.8 seconds, p = 0.2. Secondary outcomes were no better:

- Change in Seattle Angina Questionnaire (SAQ)-physical limitation from baseline: 7.4 vs. 5.0, p = 0.42
- Change in SAQ-angina frequency from baseline: 14.0 vs. 9.6, p = 0.26

- Change in Duke treadmill score from baseline: 1.22 vs. 0.1, p = 0.10

Also, at followup six weeks later, patients in both groups were receiving a mean of 2·9 medications; so PCI didn't decrease the need for cardiac medications. In other words, there was no statistically significant change in either the primary or secondary outcomes in patients with stable angina. The authors noted:

> In ORBITA, the first blinded, placebo-controlled trial of PCI for stable angina, PCI did not improve exercise time beyond the effect of the placebo. This was despite the patients having ischaemic symptoms, severe coronary stenosis both anatomically (84·4% area reduction) and haemodynamically (on-treatment FFR 0·69 and iFR 0·76), and objective relief of anatomical stenosis, invasive pressure, and non-invasive perfusion indices (FFR p<0·0001, iFR p<0·0001, stress wall motion score index p=0·0011). There was also no improvement beyond placebo in the other exercise and patient-centered effects with placebo effects. Forgetting this point, or denying it, causes overestimation of the physical effect.

In an accompanying editorial, David L. Brown and Rita F. Redberg commended the ORBITA investigators for "challenging the existing dogma around a procedure that has become routine, ingrained, and profitable," noting that ORBITA shows "(once again) why regulatory agencies, the medical profession, and the public must demand high-quality studies before the approval and adoption of new therapies" and characterizing PCI for stable angina as putting "PCI in the category of other abandoned therapies for cardiovascular disease, including percutaneous trans-myocardial laser revascularisation[10] and catheter-based radiofrequency renal artery sympathetic denervation[11]—procedures for which the initial apparent benefit was later shown in sham-controlled blinded studies to actually be due to the placebo effect." Noting that the short duration of followup actually would favor PCI because "any haemodynamic benefit from PCI occurs early and the benefits of medical therapy continue to accrue over years," Brown and Redberg conclude:

> The implications of ORBITA are profound and far-reaching. First and

> foremost, the results of ORBITA show unequivocally that there are no bene ts for PCI compared with medical therapy for stable angina, even when angina is refractory to medical therapy. Based on these data, all cardiology guidelines should be revised to downgrade the recommendation for PCI in patients with angina despite use of medical therapy. ORBITA highlights the importance of including sham controls and double blinding in a trial to avoid being fooled by illusory improvements due to the powerful placebo e ect of procedures such as PCI. Although sham-control procedures are associated with some adverse outcomes, those complications are dwarfed in magnitude by the rate of adverse events in the approximately 500 000 patients who undergo PCI for symptomatic relief of stable angina in the USA and Europe each year. These adverse events include death (0·65%), myocardial infarction (15%), renal injury (13%), stroke (0·2%), and vascular complications (2–6%).12 Health-care providers should focus their attention on treating patients with stable coronary artery disease with optimal medical therapy, which is very e ective, and on improving the lifestyle choices that represent a large proportion of modi able cardiovascular risk, including heart-healthy diets, regular physical activity, and abstention from smoking.

Based on the results of this trial, one can easily argue that PCI should rarely —if ever—be performed in patients with single vessel disease and stable angina.

The backlash

Not surprisingly, there was pushback. Cardiologists were not pleased by this result, even though it has been well known for a long time that in patients like those studied in ORBITA, PCI at least doesn’t improve survival or decrease progression to need revascularization more than OMT. For instance, in a on the study various cardiologists were quick to make excuses:

> Panelist Dr Martin Leon (Columbia University Medical Center, New York City) applauded the investigators efforts for a “remarkable study” but said it’s a much, much higher bar to achieve when the end points are

differences from baseline between two groups.

"Baseline data demonstrating that these patients had very good functional capacity, had infrequent angina, had very little ischemia, means that regardless of what you did to the coronary artery there was going to be very little you could demonstrate in terms of clinical therapeutic benefit. So I'm really glad that PCI had a statistically significant benefit in both echos and the stress tests," Leon said.

"The concern here is the results will be distorted and sensationalized to apply to other patient populations where this kind of outcome very likely would not occur," he added.

My counter to the argument that the patients included in this trial were not that sick is: Yes! That's the point. These are exactly the sorts of patients who too frequently are subjected to PCI for in essence no benefit over that which can be achieved by medical management.

Next up:

Commenting for theheart.org | Medscape Cardiology, Dr Roxana Mehran (Ichan School of Medicine at Mount Sinai, New York City) said, "To me actually this study shows angioplasty is quite effective in reducing ischemia, improving [fractional flow reserve] FFR, and in fact I'm actually very pleased with this. It's exactly what I want to do for my patients—improve their blood supply."

Asked whether this isn't just a positive spin on a negative study, Mehran quickly responded, "No," adding that whenever a primary end point is a change in a value, showing an important difference is very hard to do when baseline values are so good, especially with only 200 patients.

"I promise you, had she studied 400 patients this would be positive because everything was in the right direction," she said.

Actually, that's exactly what she's doing, trying to put a positive spin on a negative study. It's so blatantly obvious that that's what Dr. Mehran is doing that she should really be embarrassed to have said something like this to be

published for the public to read. In fairness, she does have a germ of a point in that the study was relatively small and potentially underpowered to detect some differences. On the other hand, it's rather interesting to note how some cardiologists totally twist the usual rationale and methodology used to determine if a therapy works. Here's what I mean.

Normally, when a new intervention is first tested, it's tested in small pilot trials. If a positive result is observed, that result justifies a larger trial to confirm efficacy and safety. If a positive result is not observed, then the treatment is generally abandoned or modified. before being tested again. Now, get a load this:

> During the press briefing Dr Robert Yeh (Beth Israel Deaconess Medical Center, Boston, MA) congratulated the authors on a courageous, bold, and well-executed trial but said the results reaffirm in many ways those from COURAGE.
>
> "To extrapolate that this means that elective PCI is not an indicated procedure is the furthest overreach that I can possibly imagine from a very small and I think hypothesis-generating trial with an interesting result," he said.

Let's grant Dr. Yeh his characterization of this study as "hypothesis-generating." When hypothesis-generating studies are negative, the hypothesis is usually considered to be not worth testing further, barring serious methodologic or design issues in the hypothesis-generating study. To demand another, much larger, much more expensive study to follow up on a result that, even if Dr. Yeh is correct, would likely be a very modest difference in an increase in exercise tolerance. Basically, much, although in fairness not all, of what these cardiologists are doing is to make excuses.

None of this is to say that ORBITA is bulletproof. It is, compared to other trials of PCI, relatively small. There was a trend towards improved exercise tolerance in the PCI group compared to the sham group that might have been significant with more patients. The question, of course, is whether it would be worth it to do another larger trial. After all, interventional cardiologists are utterly convinced that PCI is more effective than OMT and are unlikely to change practice (much) based on this trial:

> How will the results of ORBITA be viewed? It will be a combination of love and hate. ORBITA was rigorously designed and undertaken with great care and painstaking attention to detail using objective exercise and physiologic outcome measures before and after stabilization on OMT, combined with the use of well-validated quality of life metrics before and after randomization. Overall, the results were stunningly negative, which ORBITA supporters will cite. By contrast, it is very likely that many in the interventional community will be ready to pounce on and discredit this study — there certainly hasn't been an opportunity since COURAGE was published 10 years ago in 2007 to potentially discredit a trial that now confronts the sacred cow of PCI benefit for angina relief as the sole basis to justify PCI in stable CAD patients. They will likely cite the limitations of small numbers (only 200 patients), that the study was woefully underpowered, the potential ethical conundrum of subjecting subjects with significant flow-limiting CAD to a sham procedure (or deferred PCI for clinical need), that 28%-32% of randomized subjects had either normal FFR or IFR (and therefore didn't have a "physiologically significant," or flow-limiting stenosis, that PCI would otherwise benefit), that there was a low frequency of multivessel CAD, that the short duration of follow-up (only 6 weeks) was too brief to assess potential benefit (though this actually favored the PCI group) and, of course, who would have the time or patience to call patients three times/week to assess their response to intensifying medical therapy — "not real-world," just like the OMT used in COURAGE wasn't achievable in the real-world.

Despite these reactions, I do have some optimism. Interventional radiologists reacted very negatively to the trials showing that vertebroplasty for osteoporotic spinal fractures doesn't work. Eventually, they started to come around, and usage of vertebroplasty for this indication is declining, albeit not as fast as it should. Science- and evidence-based medicine is messy, and there is some truth to the old adage that old treatments don't ever quite disappear until the generation that learned them retires or dies off. But change does come in response to clinical trials.

In the meantime, whatever effect ORBITA has on clinical practice, it should serve as a wakeup call that in clinical trials of surgical or procedural

interventions examining endpoints with a degree of subjectivity (unlike, for instance, death or time to cancer recurrence), whenever possible, new interventions should be compared to sham procedures. Of course, this isn't always possible, either for ethical or practical reasons, but when it is practical sham procedures are just as essential as placebo controls in drug trials.

Science Based Medicine

周四, 16 11月 2017

Science Based Medicine

[周四, 16 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Placebo Myths Debunked** [周三, 15 11月 21:03]
  Placebo treatments are often sold as magical mind-over-matter healing effects, but they are mostly just illusions and non-specific effects.
- **Turpentine, the Fountain of Youth According to Dr. Jennifer Daniels** [周二, 14 11月 16:00]
  Jennifer Daniels says turpentine is the Fountain of Youth, able to cure many ailments, both real and imaginary. It isn't; it's a poison with no recognized benefits for human health.
- **Why do some women refuse treatments for their breast cancer?** [周一, 13 11月 16:14]
  Adjuvant therapy after surgery, such as chemotherapy, hormonal therapy, and radiation therapy, has contributed to a 39% decrease in breast cancer mortality since 1989. Unfortunately, a significant number of women decline evidence-based adjuvant therapy. A recent study suggests that distrust of the medical system plays a significant role in such refusal.

Placebo effects are largely misunderstood, even by professionals, and this leads to a lot of sloppy thinking about potential treatments. This problem has been exacerbated by the alternative medicine phenomenon.

Several decades ago, the proponents of so-called CAM promised that if only their preferred if unconventional treatments were properly tested medical science would discover how effective they are. “Effective” (or more precisely, “efficacy”) has a specific definition in medical science – it means that a treatment has been found to perform statistically significantly better than placebo in a blinded controlled trial. Several decades and thousands of studies later, the most popular CAM modalities (homeopathy, acupuncture, reiki, manipulation for medical indications, and more) have been shown to be no more effective than placebo. This means they don’t work.

Not to be deterred by reality, CAM proponents simply shifted the goal posts. Now many of them are saying that placebo effects are real, and therefore being as effective as placebo means that their treatments “work.” As part of this strategy they have promoted and amplified common myths about placebo effects. Let’s take a closer look at these myths and show why they are wrong.

Myth #1 – “The” placebo effect

The first and overriding myth about placebos is that there is one placebo effect (singular). This confusion is understandable, because scientists often refer to “the” placebo effect. However, they are referring to what is measured in the placebo arm of a clinical trial – that net effect (the difference between baseline or no treatment at all and a placebo treatment) is the placebo effect for that study.

There are multiple placebo effects contributing to that difference, however. Anything that might give the appearance of an improvement will contribute to the measured placebo effect. These placebo effects include: Regression to the mean – when symptoms flare, they are likely to return to baseline on their own. If you take any illness that fluctuates in severity, any treatment you take

when your symptoms are at their peak is likely by chance alone to be followed by a period of less intense symptoms.

Similar to this but distinct is the reality that many illnesses are self-limiting. If you have a cold, you will likely get better even if you do nothing – so anything you do will be followed by improvement. There is also bias in perceiving and reporting subjective symptoms. People want to feel better, they want to think that the treatment is working, and they may want to please the researcher or their physician. Further, researchers and doctors want their treatments to work.

There are also many possible non-specific effects just from the act of being treated. Hope can be a very positive emotion, and that alone may make people subjectively feel better. Subjects in a trial are also getting medical attention, and are likely paying more attention to their own health. They are likely to be more compliant with other treatments.

The treatment under study itself may have several components, some specific and some non-specific. Do people sometimes feel better after a session of reiki or acupuncture because they were laying down listening to music and smelling incense during the treatment? How much of a relaxation effect is at play? Does it matter if you actually stick the needles in alleged acupuncture points (the answer is no)?

Myth #2 – Placebo effects can cause healing

Because it is often believed that “the” placebo effect is one thing, that one thing is often believed to be a real mind-over-matter physical healing. There is no evidence to support this interpretation, however. In fact researchers looking for that real healing effect of placebos have only demonstrated that it doesn’t exist.

Part of the problem here is that the term “healing” is vague. It does not have a specific definition, but the implication is that biological repair is taking place. In practice researchers distinguish objective vs subjective markers of improvement. Subjective just means that the patient feels better in some way,

per their own report. They rate their own pain, for example. An objective outcome is something measurable, like blood pressure, survival, or tumor burden.

A systematic review of cancer research, for example, found that placebo interventions resulted in minor improvements in subjective symptoms, but no improvement in the cancer itself.

Placebo effects break down into several categories. One category is illusory – the misperception of improvement through regression to the mean or biased reporting. The second category is non-specific effects, such as emotional comfort from a practitioner, relaxation, or improved self-care or compliance. This third category is comprised of effects which can plausibly result from psychological interventions only. These relate mainly to stress, depression, anxiety, and the perception of pain and similar subjective symptoms. There is a mind-body connection – it's called the brain.

There is, however, no magical control of your brain over biological or physiological processes that are not networked with the brain through nerves or hormones.

Myth #3 – Animals and babies cannot have a placebo effect

This myth results from the false assumption that in order to have a placebo effect you need to believe that you are taking an active treatment. It is the belief that is causing the effect, and therefore it is a prerequisite. The logic then follows that animals and babies, who cannot know they are receiving a treatment, can therefore not have a placebo effect. Any improvement in this context, therefore, must be a physiological response to the treatment itself.

It should already be obvious, however, that these assumptions are incorrect. There are many sources of placebo effects that do not depend upon the subject knowing they are being treated, such as regression to the mean, the self-limiting nature of many ailments, and non-specific effects or benefits from simultaneous interventions.

Further, however, someone has to determine that the animal or baby has improved. That person is vulnerable to biased perception and reporting, and will also contribute to any measured effect.

This means that studies of treatments in animals or babies still need to be properly controlled, and whoever is assessing the outcome needs to be properly blinded to treatment allocation.

Myth #4 – Fanciful or alternative treatments yield better placebo effects

Desperate to salvage a role for their preferred but ineffective treatments, many alternative practitioners will argue that their real expertise is in maximizing placebo effects. OK, sure, the scientific evidence shows that my treatment is no better than placebo, but placebo effects are real, and I am very good at eliciting them. This is the “placebo medicine” gambit.

I have already debunked the first part of that claim. There is also no evidence for the second part, that alternative practitioners elicit more of a placebo effect. What the scientific evidence shows is that all interventions will produce some placebo effect, depending mainly on the outcome to be followed. The more subjective and amenable to variables such as mood, the larger the measured effect will be.

The existence of a placebo effect does not justify using inactive or pseudoscientific treatments. You can elicit the same effects from science-based interventions. Related to this is the notion of placebo effects without deception. This is certainly possible, if you include all the non-specific and statistical effects, but most patients would likely not be happy to be receiving a treatment that they were told was completely inert, just so it may bias their perception of their symptoms. All pseudoscientific treatments, even if they are justified through placebo effects, are given with a generous helping of deception, which violates patient autonomy.

The other variable that seems to be important, but requires further study, is the therapeutic relationship between practitioner and patient. Having a

positive relationship may enhance the measured placebo effect, but that may be just another measure of bias.

In any case, anything useful about placebo effects can be had with a positive therapeutic relationship, using science-based interventions, and following the ethical requirements of informed consent and patient autonomy.

Read the label. It doesn’t list any health benefits. It says harmful or fatal if swallowed.

Turpentine is a solvent and a poison, but some people are drinking it as a medicine.

Scott Gavura wrote about it

2 years ago and concluded, “There’s no reason to consume turpentine and multiple reasons to avoid it completely, with the primary reason being that

it’s a poison

.”

Scott’s article mentioned an MD who advocates turpentine to cure the fake illness chronic *Candida*, and who had been stripped of her license. That MD was Jennifer Daniels. It would be bad enough if she only recommended it for Candida, but she also claims to have discovered that turpentine is the Fountain of Youth, a miracle cure that reverses disease and aging and is good for pretty much whatever ails you. That’s ludicrous.

The facts

The *Natural Medicines Comprehensive Database* (which I consider to be the most reliable source) says, “There is insufficient reliable information” to evaluate its effectiveness for any medical use. It rates turpentine as “possibly safe” when used topically and appropriately, “possibly unsafe” when applied to large areas of skin, and “likely unsafe” when used orally for medicinal purposes; 2 ml/kg is toxic, and 120-180 ml is potentially lethal in adults.

The *NMCD* goes on to explain that turpentine is a central nervous system depressant, a pulmonary aspiration hazard, a skin irritant, and might cause abortions. It can have a decongestant effect when inhaled. Many adverse reactions are reported from ingestion, including headache, insomnia, coughing, vomiting, hematuria, albuminuria, urinary tract inflammation, coma, and death. Inhalation can cause inflammation and bronchial spasms. Applying it to the skin can lead to kidney and central nervous system damage.

A drug information website has an extensive monograph on turpentine. It says, “Turpentine has been used experimentally in a bath for the treatment of disseminated sclerosis and sexual dysfunction. It also has been studied for its antibacterial activity and inhibition of osteoclast activity. Turpentine is utilized in experimental models of inflammation to induce a systemic inflammatory immune response in animals.” It warns against using it during pregnancy and lactation, stresses that it is highly toxic (fatal poisonings have occurred with ingestion of as little as 15 mL, just 3 teaspoonsful) and has caused skin tumors in animals. It provides a bibliography with pertinent citations.

The discovery

Jennifer Daniels tells the story of her discovery in a radio interview. She asked her African-American patients if their slave ancestors had a miracle cure that cured everything and was cheap; several of them mentioned turpentine and sugar. So she tried it for herself. She put turpentine on 3 sugar cubes and washed them down. Right after ingesting it, she says:

> I think my IQ went up like 50 points, I could just feel it, all this mental energy and understanding and clarity, just like when I was 10 years old, everything was very clear and focused. I said WOW what a feeling. I did some math problems, I said this is pretty good.

She had heard that turpentine could cause seizures, so she figured out the maximum safe dose by stopping at a dose where she felt a little twitch, “even softer than a twitch.” Then she gave it to her mother, who began to feel better *in less than a minute* (!). It relieved pains that her mother had had for 30 years. Other family members served as guinea pigs and appeared to benefit. So with no further ado, Daniels started using it on all her patients.

The published evidence she relies on

In that same interview, Daniels talks about a review article from France with 100 references that supposedly support the use of turpentine for parasites,

cancer cells, pathogenic bacteria, fungus, yeast, rheumatism, MRSA, sciatica, nephritis, constipation, increasing membrane permeability, etc. It doesn't say what she thinks it says.

Using turpentine: The treatment plan

First you have to hydrate. Then you have to have three bowel movements a day, which you can supposedly achieve by taking her Vitality Capsules, which (unlike everything else on earth) contain "no chemicals." If you don't have three bowel movements a day, the *Candida* can't get out of your body and will "shift through your left hip to your right hip, your right hip to your stomach, and your stomach to your shoulder. It's gonna play musical chairs all over your body." Then you have to follow her diet instructions (organic, no GMOs, no "dead food," and many more restrictions). Only then can you do the Candida Cleanse.

She says you must avoid steroids, antibiotics, and chemotherapy, because they prevent cell repair and yeast will move in to eat up the dead cells. She advises patients to stop all their medications if they can (potentially dangerous advice).

She says in the last days of her practice, she stopped using antibiotics. She would not admit seriously ill patients with pneumonia to the hospital, but would dose them with turpentine and send them home. She thinks children with high fevers will recover in less than 24 hours if given turpentine. When her daughter badly injured her ankle, she gave her a teaspoon of turpentine and ¼ cup of castor oil. "She drank it, she pooped, all the pain was gone."

More strange and unsupported claims

- "Liver time is 1-3 AM; lung time is 3-5 AM."
- "Vitality Capsules clean out the bile ducts and the gall bladder system as well as the small intestine, large intestine, and it also promotes circulation."
- Children should start getting turpentine in castor oil when they reach 30

pounds, to prevent *Candida* and parasites.
- You should keep taking turpentine at least once a month for the rest of your life.
- Turpentine improves eyesight; users were able to throw away their reading glasses.
- "if I want thicker hair and less gray hair, then I'm gonna use minerals, small willow flower, and shou wu."
- Turpentine improves diabetes by healing the pancreas. It will allow Type I diabetics to lower their insulin dose.
- It resolves tinnitus.

To her credit, she does get a few things right; for instance, she realizes that "rope worms" are not actually worms. On the other hand, she is anti-vaccine: "There is no vaccine or injection Dr. Daniels recommends."

A spy troll is shocked

David McAfee infiltrated the closed 640-member Facebook group "Parasites cause all disease – turpentine cure" and was appalled at what he found. People were seeking support for the horrible side effects they were experiencing from turpentine. They were hoping to cure everything from scabies to herpes to "electromagnetic hypersensitivity."

One woman who was using turpentine and castor oil complained that when she did enemas a lot of red liquid came out. Another list member told her *not to worry* because it was probably just old and damaged intestine wall coming out!

Some of the comments following McAfee's exposé article were amusing:

- "Sometimes you just roll your eyes, mutter darwinism to yourself and move on."
- "I'm a believer in alternative medicine-trust me, these people aren't into alternative, they are idiots. Anyone with half a brain knows not to ingest a solvent. Dear god, where does this stupidity come from?"
- "There is in my family a story about the medical use of turpentine. It

dates from the time of my grand-father or great-grand-father. It was suggested as a topical treatment for hemorrhoids. It was not suggested in good faith. Folks could have a very crude sense of humor in those days too."

What about science?

Daniels is a graduate of Harvard and of the University of Pennsylvania School of Medicine. Surely she learned about science at those prestigious Ivy League schools. One can only wonder how she came to disregard science and go her own way. She says she reads research studies but does not believe them: "I'm not much of a fan of research because every research project I've been involved with, I've been asked to falsify data." That certainly is an unusual experience, and I can't help but wonder if she reported the fraud/misconduct. She could have had a great career as a whistleblower.

Her words and actions show that she does not think like a scientist. Here are just a few revelations from her *Confidential Underground Report: Top Secret; The Candida Cleanser*.

- She assumed the existence of some folk remedy that was a miracle cure that would cure everything. Considering all the many different causes of different illnesses, this is not a reasonable assumption.
- She experimented on herself and assumed that the dose that seemed to work for her would work for everyone. If that were true, drug companies could dispense with phase 2 trials and just give the drug to one person.
- She describes immediate results, too soon for a medication to be absorbed and have any effect; she doesn't recognize that this is almost certainly a placebo response.
- She doesn't put her belief that turpentine is effective to any kind of test.
- She wonders how long you could take it every day without experiencing side effects. So she takes it daily for a week, notices no adverse effects, and says "I decided that was long enough for the purposes of science." Wow! Wouldn't Big Pharma love to hear that all they needed to do to demonstrate the safety of their drugs to the FDA was to have one person take a drug for a week and say they hadn't noticed any symptoms?

- Without any further testing, she immediately moves on to treating other people with turpentine.
- She makes all kinds of claims unsupported by any evidence, for instance:
    - Breads, meats and dairy are all full of parasites.
    - “Trail mix is an abomination and has destroyed the health of many a health nut.”
    - “It has been *my observation* [emphasis added] that one should be having at least three bowel movements a day.”
    - “There is no medication that turpentine interacts with.”
    - “Censorship is so severe that it is difficult to find information on turpentine in print.”
- She makes dangerous recommendations: laxatives and daily enemas, stopping prescription medications, avoiding immunizations, and many more.

No longer practicing, but…

On her website, it says “Dr. Daniels is a former medical doctor who had her medical license suspended due to not prescribing enough drugs and truly healing her patients.” I don’t believe that; no medical board has ever suspended a doctor’s license for healing their patients or for “not prescribing enough drugs.” According to the New York medical board website, she surrendered her license less than 6 years after it was granted. Apparently she was uncooperative, refusing to share her patient records with the board, and from her comments online it seems she was deliberately trying to hide her many questionable treatment methods from the authorities. By voluntarily surrendering her license, she avoided any further investigation or board actions.

No longer able to practice medicine, Daniels has moved to Panama, where she is making a living producing books, radio shows, CDs, and videos; selling supplements; and advising clients as a health coach. She is available for “Holistic Mentoring Consultations;” you can schedule a consultation online and will be able to speak to the doctor directly. What she is doing may not be illegal, but she is still in a position to harm people with bad advice.

Conclusion: not recommended

Not only is turpentine not the Fountain of Youth, it has not been proven effective for any health condition. Jennifer Daniels is not a reliable source of health information. She fails to understand the need for scientific testing, relies on testimonials and beliefs instead of facts, and demonstrates poor judgment. She makes claims that are bald assertions not supported by any evidence. She is offering dangerous advice, not just about turpentine but about vaccines and other things.

I write about alternative cancer treatments a lot, in particular the lack of evidence for such practices, many of which are at best pseudoscientific and at worst pure mystical nonsense. The reason, of course, is simple. I'm a breast cancer surgeon, and I hate seeing people who might be saved from death due to cancer falling prey to treatments that demonstrably lessen their chances of survival, either by leading patients to reject effective treatment in favor of ineffective or even harmful treatments or, at the very least, to delay effective treatment until the patient realizes that the quackery chosen isn't preventing the growth and spread of his or her tumor. This can sometimes take a long time. I've seen women with breast cancer whose breasts were basically eaten away until there was nothing left but an ulcerated mass on their chest—more than that, a bleeding, rotting, malodorous ulcerated mass. Yes, it's an ugly picture, but I've seen it all too many times.

These sorts of cases are less common, though. Fortunately, relatively few are the women who reject conventional medicine altogether. Indeed, most women will accept surgery of some sort or another, either a lumpectomy or a mastectomy. Sometimes, they undergo an excisional biopsy, not realizing that that for smaller tumors an excisional biopsy can remove the whole tumor and in some cases be curative. No, far more common is the case where a woman accepts surgery but then refuses chemotherapy, hormonal therapy, and/or radiation, either altogether or in favor of some form of quackery. In doing so, such women, whether they simply refuse adjuvant therapy altogether for whatever reason or go beyond that and fall prey to quackery, fail to maximize their chances of surviving their breast cancer, sometimes by quite a bit, and that is something to be concerned about.

Indeed, these sorts of cases were one of the very first topics I ever wrote about on this blog and have remained a staple of the blog ever since, whether I was discussing Suzanne Somers, who had surgery and radiation but apparently refused Tamoxifen for her breast cancer and then later had what she thought to be a recurrence that almost certainly wasn't, other alternative breast cancer cure testimonials (like this one or this one), or even testimonials for other cancers where chemotherapy and/or radiation are used in addition to surgery.

The reason such alternative cancer cure testimonials are compelling is that most people don't understand the difference between the primary treatment for breast cancer and an adjuvant treatment. In the case of breast cancer, for instance (and colorectal cancer as well, among other solid tumors), surgery is the primary treatment and can be curative by itself. What chemotherapy, radiation therapy, and hormonal therapy can add to the treatment of, for example, breast cancer is to decrease the chance of its recurring after successful surgical excision, whether by mastectomy or lumpectomy. All a breast cancer patient does in refusing radiation therapy after successful breast conserving surgery is to accept a risk of recurrence in the breast of 30-40% instead of 5-8%. All a woman does by refusing recommended chemotherapy after surgery is to refuse a relative decrease in their risk of dying of a recurrence of breast cancer by 25-30%, a benefit that is, in absolute terms, much greater for more advanced but still curable breast cancers. However, many of these women who turn down adjuvant therapy in favor of quackery will still survive, thanks to the surgery, and the ones whose cancers recur rapidly disappear from the alternative cancer cure industry PR machine, never to be seen again.

Because adjuvant chemotherapy, targeted therapies, and hormonal therapies have contributed to a decline in mortality from breast cancer of 39% since 1989, it is important to determine why women refuse these treatments and fail to optimize their chances of long term survival. To a lesser, but still important extent, it's important to try to understand what motivates women to turn down effective adjuvant therapy, as that is the first step in developing strategies to persuade them. Recently, there was a relatively large study that addressed just this question.

Patient refusal of adjuvant therapy: A question of trust?

Earlier this month a number of news stories and press releases appeared about a study published in late September by investigators at Johns Hopkins Bloomberg School of Public Health, Columbia University, and Massachusetts General Hospital looking at trust—or, more specifically, a

lack of trust—as a key motivator in women refusing adjuvant therapy recommendations and opting for discordant care; i.e., care that doesn't conform to evidence-based care recommended by the patient's physicians. It's an issue that hasn't been studied as well as it should be, as the authors, Lorraine T. Dean, Shadiya L. Moss, Anne Marie McCarthy, and Katrina Armstrong point out in the introduction:

> Relatively little is currently known about the relationship between healthcare system distrust and cancer treatment. A previous study of distrust and adjuvant cancer treatment (3) found that distrust in medical institutions was associated with increased risk of not initiating adjuvant treatment in a sample of 258 early stage (Stage I and II) breast cancer patients from one urban area. However, that study did not include the following in their analysis: which treatments were recommended by the physician, the extent to which physician distrust mediated the relationship between healthcare system distrust and cancer treatment, and an assessment of those who may have initiated treatment but did not fully adhere to the treatment plan. Other studies of distrust among women with a history of breast cancer have focused on healthcare system distrust and: mental health or psychosocial outcomes (13), quality of care (14,15), greater emotional, physical, financial, and sexual problems after treatment (16), less comfort with the use of de-identified information from medical records for research (17), less endorsement of the necessity of adjuvant chemotherapy (18); and provider distrust and quality of care (19).
>
> The current study was designed to answer two related questions: Is healthcare system distrust associated with whether or not patients follow their physician's recommendations for adjuvant treatment after breast cancer; and does physician trust mediate the relationship between healthcare system distrust and receipt of adjuvant treatment? It expands on prior work by including a large population based sample in two different US states, Pennsylvania and Florida, based on physician recommendations for several adjuvant treatments with explicit testing of the potential mediating role of physician distrust, and assesses patients who did not complete the full treatment plan. To our knowledge, it is the largest study of healthcare system distrust among women with a history

of breast cancer and adds innovation of recruiting through a cancer registry to survey participants about healthcare system distrust.

To this end, the authors used Pennsylvania and Florida cancer registries, using data from a population from a study originally intended to assess the differences in breast cancer women associated with race. The inclusion criteria for the study included localized invasive breast cancer, age under 65 at the time of diagnosis, residency in either Pennsylvania or Florida at the time of diagnosis, and diagnosis between January 1, 2005 and December 31, 2007. Exclusion criteria included patients over 65, cognitive impairment, inability to speak English or Spanish, and metastatic disease at presentation. The overall response rate was very good for surveys of this type, 61%.

For purposes of the survey, cancer treatment discordance was defined as any difference in treatment that a patient reported receiving compared to the treatment the patient reported as having been recommended to her by the treating surgeon and/or oncologist. Now, I know what you're probably thinking: Is this accurate enough? It turns out that simple self-reporting like this is 90% accurate, particularly for yes/no questions about different kinds of therapy. Since the adjuvant therapies used after surgery for breast cancer include radiation therapy, chemotherapy, and hormonal therapy, the authors constructed a combined measure of treatment discordance based on how many of the three therapies patients accepted or declined. Of course, if a particular adjuvant therapy was not recommended for a patient, then not undergoing it couldn't be considered discordant. (For example, depending on the specific characteristics of the tumor, not all breast cancer patients are offered chemotherapy or hormonal therapy; and most patients—but by no means anywhere near all patients—undergoing mastectomy don't require radiation therapy.)

Patients were also assessed for their level of trust in the health care system and their physicians. Trust in the health care system was assessed using the 9-item Health Care System Distrust scale which measures of domains of values and competence distrust on a 5-point agreement scale (1 = strongly disagree, 5 = strongly agree), producing a score ranging from 9 to 45. The authors report that this measure has "acceptable construct validity and high internal consistency (α=0.84 in the current sample)." To measure trust in patients'

physicians, researchers used the 7-item Trust in Physician Scale, which uses a 7- point agreement scale (1=strongly disagree, 7=strongly agree), to produce a score ranging from 7 to 49. Information was also requested on socio-demographic factors, such as age, race, ethnicity, income, education, marital status, employment status, health insurance status, and state of residence at the time of diagnosis. They also went to the cancer registry databases to verify clinical treatment factors, such as stage, surgical removal of cancer, and recurrence.

So what did the authors find? There were 2,754 women included in the final analytic sample, of which 69.8% (n=1,922) reported always receiving the cancer treatments their surgeon or oncologist recommended, and 30.2% (n=832) reported not pursing at least one recommended treatment. I must admit that I was rather surprised that the percentage of discordant cases was so high, but maybe I shouldn't have been. In any case, in the total sample, 10% declined radiation treatment; 11% declined chemotherapy; and 18% declined hormone therapy. (Note that some women turned down more than one modality.) Looking at the numbers, though, some of this does appear to jibe with my clinical experience, in that I've encountered more women who have turned down hormonal therapy than who have turned down others. The reason is probably that hormonal therapy, although only a pill as opposed to chemotherapy, is administered for five or, in more recent recommendations, as many as ten years, and women who can tolerate the much more severe side effects of chemotherapy only have to endure them for a few months, whereas they have a harder time dealing with the side effects of Tamoxifen or aromatase inhibitors for five or ten years.

The authors found:

> The mean healthcare system distrust score was 28 (SD=3; range 9-40), while the mean physician trust score was 29 (SD=4; range 9-35). Bivariate models suggested that greater healthcare system distrust was significantly associated with older age, being Black, having attended some college, and being employed, while less healthcare system distrust was associated with greater physician trust, being married, having health insurance, and living in Pennsylvania. Only marital status, being employed, physician trust, and living in Pennsylvania were still

> associated with distrust in a fully adjusted model (Table 2). Participants reporting treatment discordance were significantly in the top tertile of healthcare system distrust (p=0.003) as well as being more likely to be older (p=0.04), be diagnosed at Stage 1 (p<0.001), and live in Florida (p=0.003). In contrast, physician trust was not a significant predictor of discordance (p=0.49). Although healthcare system distrust was significantly associated with discordance (p=0.03) and physician trust (p<0.001) (Figure 1), a mediation analysis (Table 3: Models A & B) suggested that physician trust was not a mediator of the relationship between healthcare system distrust and treatment discordance (total indirect OR=1.00 [1.00,1.01]). Thus, rather than treat physician trust as a mediator, it was included in the final model as a covariate.

Basically, those in the group with the highest distrust of the healthcare system were 22% more likely to have refused or fail to complete one or more adjuvant treatments. In other words, patients who had the most distrust of the healthcare system were more likely to be discordant in their adjuvant therapy; i.e., to refuse or fail to complete a recommended course of therapy. Interestingly, in this study, neither race nor socioeconomic status were significant drivers of discordance in this study, which is a good thing because these are not modifiable factors.

Physician trust versus a more generalized distrust

How could these results be? The authors note that attempts to increase physician trust as a strategy to reduce mistrust in the healthcare system have had results ranging from zero to very modest, which makes sense if patients view the two issues as separate. I like to make an analogy to Congress. Voters routinely express extreme distrust of Congress, but most voters actually like their own representative. Similarly, it’s not hard to envision how most patients might actually like and trust their own doctors, while simultaneously having a great deal of mistrust for the health care system as a whole.

As the authors note:

> The limited research to date about reducing distrust in healthcare has focused on increasing trust in physicians with null to modest (30-32) results. However, given that the relationship between distrust and treatment discordance was not mediated by physician trust, these results suggest that addressing healthcare system distrust may be an important and distinct effort from strategies focused on lack of physician trust. Rather than playing a mediating role, patients may view physician trust as independent of their trust in the healthcare system as an institution; that is, even if patients distrust the healthcare system, they may still have trust in their personal physicians. Patients may be able to exercise greater choice in physicians, but may not have the same breadth of choices in using the healthcare system. Addressing healthcare system distrust might be informed by strategies that have addressed distrust in other types of institutions, such as corporations (29), according to the values and competence domains. For example, addressing the subdomain of values might be achieved through expanded access to adjuvant care, while addressing the subdomain of competence might be achieved through expanded access to health professionals while deciding to start or continue adjuvant treatment. Of course, any intervention to reduce healthcare system distrust would first need to be tested before implementing wide-scale changes.

The authors also note a rather interesting potential wrinkle to the problem of patients refusing adjuvant therapy, namely that greater cancer treatment discordance will always lead to worse healthcare outcomes, noting that it is "possible that distrust could perform a function in course-correcting treatment that is overprescribed or too aggressive" and that such distrust "might lead to treatment discordance that was ultimately beneficial rather than detrimental." When I read that part, I had to concede that it is possible that this could be true, but unlikely. My own experience in quality improvement initiatives means that I've become fairly familiar with the literature on the relationship between concordance with evidence-based treatment guidelines and patient outcomes. That literature generally supports that better concordance results in better outcomes. So I couldn't help but smile as I continued to read and noted that, consistent with that, the authors examined a separate model of treatment discordance, looking at its association with cancer recurrence, and found that the model suggested a 40% increased risk of cancer recurrence for patients

who reported treatment discordance, after adjusting for adjusting for healthcare system and physician distrust and relevant racial and socioeconomic factors. This result suggests that that discordance due to distrust may lead to poorer health outcomes.

So what to do?

The authors note that improving trust in the healthcare system will require more than just trying to build trust in patients' physicians, noting:

> "If ordinary businesses can learn to increase trust in their brands, why not the same with health care institutions?" Dean says.

This is, of course, much easier said than done, and this study doesn't address how increasing trust in the healthcare system might be accomplished. That will be the task for the future. It is an important task, though, because, although I might be extrapolating more than the evidence supports (yet), I'd bet that such strategies could also help address the antivaccine movement as well. In any case, if we want to save as many savable lives of people with cancer as possible, this is where the healthcare system needs to pay more attention, and a salutary side effect would also be to make alternative cancer cure testimonials less common.

Science Based Medicine

周四, 23 11月 2017

Science Based Medicine

[周四, 23 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **New Tools Against Antibiotic Resistance** [周三, 22 11月 20:24]
  Antibiotic resistance is a serious problem that may lead to a post-antibiotic era. However, there are potential solutions that deserve research priority.
- **The Death of Expertise** [周二, 21 11月 16:00]
  In Tom Nichols' new book, The Death of Expertise, he explains how a misguided intellectual egalitarianism is harming our ability to assess the truth and solve problems, and discusses some of the responsible factors and possible long-term consequences.
- **What is “integrative oncology”? Even the Society for Integrative Oncology doesn’t seem to know for sure** [周一, 20 11月 16:25]
  Last week, the Society for Integrative Oncology published an article attempting to define what "integrative oncology" is. The definition, when it isn't totally vague, ignores the pseudoscience at the heart of integrative oncology and medicine.

New Tools Against Antibiotic Resistance - Science-Based Medicine

Scientists are often placed in the role of Cassandra – because of their expertise and knowledge they may see potential serious problems on the horizon, but may also find it challenging to convince the general public. Sometimes they are working uphill against vested interests. Often scientists will warn against possible problems that they then work to prevent, and when successful it seems like their warnings were unwarranted. Or they may simply be calling for preparation for a possible event, like an epidemic, that still probably won't occur but you should be prepared ahead of time in case it does.

Also, as science communicators we don't want to overhype potential problems. It can be a delicate balance. With all that in mind, it is probably difficult to overstate the potential risk of antibiotic resistance. This is one of those looming issues that I genuinely worry about, but gets too little attention, if anything, in the media. It is also a manageable problem – there are things we can do to mitigate antibiotic resistance, if we take the issue seriously enough.

The World Health Organization summarizes the problem in stark terms:

> Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. A growing list of infections – such as pneumonia, tuberculosis, blood poisoning, gonorrhoea, and foodborne diseases – are becoming harder, and sometimes impossible, to treat as antibiotics become less effective.
>
> Where antibiotics can be bought for human or animal use without a prescription, the emergence and spread of resistance is made worse. Similarly, in countries without standard treatment guidelines, antibiotics are often over-prescribed by health workers and veterinarians and over-

> used by the public.
>
> Without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill.

I don't think they are overstating the problem.

The cause of antibiotic resistance is fairly easy to understand. Bacteria reproduce very quickly in large numbers. When someone takes an antibiotic, that provides a selective pressure towards resistance. If any individual bacterium has a gene which provides resistance to the mechanism of that antibiotic it will tend to survive the treatment and then reproduce a new generation of resistant bacteria.

Bacteria also have the ability to swap genes, so that are not just passed from parent to offspring, but horizontally to other bacteria in a process called conjugation. Bacteria may contain plasmids, which are loops of DNA. Those plasmids can be copied from one bacterium to another. A plasmid may contain one or even multiple genes that confer resistance – and so in one conjugation event a bacterium may receive resistance to multiple antibiotics.

The existence of bacterial plasmids with multiple resistant genes is a problem, because if they are exposed to one of the antibiotics to which they are resistant, that will favor the proliferation of the bacteria with plasmids that confer multiple resistance.

There is one potential bright spot in all this. Genes that confer antibiotic resistance often come at a price. They may make it more difficult for the bacteria to reproduce, or force them to expend more energy. That is why they don't have the feature in the first place. The selective pressure of antibiotics is necessary to favor the more costly feature. The hope is that in the absence of selective pressure from antibiotic, the resistant features will tend to fade away.

However, a new study suggests that this may not always be the case. Researchers looked at costly antibiotic resistance features in various strains of *E. coli*. They followed them for over a month and found that strains were able to maintain even costly antibiotic resistance in the absence of antibiotics if

they contained plasmids. The key is the conjugation rate – how frequently do bacteria exchange plasmids? The research found that, at least in these strains, the rate was high enough to maintain antibiotic resistance even in the absence of antibiotics.

This research suggests that limiting antibiotic use may not be enough to reverse existing antibiotic resistance. Of course, limiting use is essential to slowing the development and spread of resistance. This is the primary mechanism by which the medical community is trying to combat resistance, but even here we are not doing enough. Antibiotics are still massively overprescribed. Some countries allow for over-the-counter antibiotic use, and it is common for the public to take them for viral illnesses. Antibiotics are also heavily used in the farming industry.

Even if we achieved our goal to properly limit antibiotic use, and educated practitioners to optimally prescribe antibiotics, the current research suggests this may not be enough to reverse some types of resistance. However, the same research suggests there may be more active interventions that will.

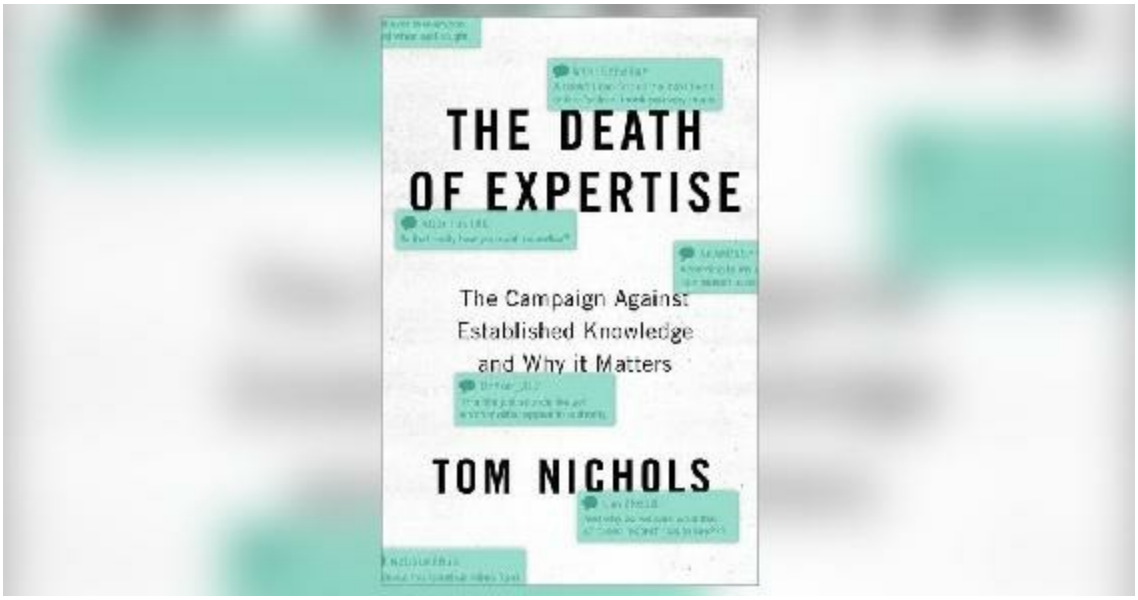
There are potential drugs that can limit conjugation or induce bacteria to lose their plasmids. For example, a 2015 study identified features of synthetic fatty acids that were effective conjugation inhibitors. This would limit the horizontal spread of plasmids among bacteria, and therefore limit the spread of resistance.

Another approach is to prevent plasmid replication. Researchers are looking at ways to exploit the existing compatibility system in bacteria toward this end. Since bacteria are so promiscuous with their genes, they need mechanisms to know when plasmids are incompatible with their other DNA. You could essentially trick a bacterium into thinking its plasmid is incompatible, and therefore when the bacteria reproduces it will not replicate the plasmid. The plasmid will therefore be lost to the next generation. These treatments would not just limit the spread of resistance, but cause a population of bacteria to lose their resistance.

What all of this research suggests is that we should not only be researching novel antibiotic mechanisms, we should be investing in research into drugs that inhibit plasmid conjugation and induce plasmid loss. These treatments

can reduce the spread of resistance, and even potentially reverse resistance. Such treatments could be given alongside antibiotic regimens, or used in farming or similar contexts to limit the development of resistance.

My hope is that this type of research will eventually lead to a situation in which all those scientists and science-communicators who warned about the coming post-antibiotic era will look like Cassandras. Rather than getting the credit for identifying and then preventing a major problem, people will either forget them or falsely think the warnings were overhyped to begin with. But I will take that fate if it means avoiding a post-antibiotic era.



Tom Nichols' new book *The Death of Expertise: The Campaign against Established Knowledge and Why It Matters* has direct relevance to many of the issues we are constantly grappling with on Science-Based Medicine. In a democracy, everyone has equal rights. Many people think that means they are equal to experts in knowledge and judgment. In medicine, as in most other areas of public discourse, we are faced with angry laymen who denounce intellectual achievement and scientific knowledge and who distrust experts.

People find ways to reject the evidence when it conflicts with their values and beliefs. When scientific evidence challenges their views, they doubt the science rather than themselves. New examples of this phenomenon can be found every day in the news and in the comments sections of the Science-Based Medicine blog, and trying to set those people straight has proven a mostly futile exercise.

The failure of higher education

Students have become consumers. High school seniors tour college campuses with their parents looking for the one with the best dorms, cafeteria food, and extra-curricular activities, rather than the one that will challenge them and provide the best education. Nichols says colleges are not only failing to

provide to their students the basic knowledge and skills that form expertise, they are failing to provide the ability to *recognize* expertise and to engage productively with experts and other professionals in daily life. They are not being taught "critical thinking: the ability to examine new information and competing ideas dispassionately, logically, and without emotional or personal preconceptions."

He says students are being treated as *clients* rather than students. "Many colleges have become hostages to students who demand that their feelings override every other consideration." Students "explode over imagined slights" and "build about themselves fortresses that no future teacher, expert, or intellectual will ever be able to breach." They want to be protected from ideas or language they find unpleasant. They are "demanding to run the school while at the same time insisting that they be treated as children."

The internet

The Internet has provided people with an unprecedented abundance of information, but all too often it gives them the illusion of knowledge, encouraging them to believe they know as much as experts. They hear what they want to hear, and live in a bubble community of people with similar beliefs.

> People do not come to the Internet so that their bad information can be corrected or their cherished theories disproven. Rather, they ask the electronic oracle to confirm them in their ignorance.

Nichols says,

> …not only is the Internet making many of us dumber, it's making us meaner: alone behind their keyboards, people argue rather than discuss, and insult rather than listen.

People "power browse" rather than actually reading. We see this all the time on Science-Based Medicine, where commenters criticize an article they obviously have not read carefully or understood. Sometimes I suspect they may just have read the title and seized the opportunity to jump on their

particular soap box.

Journalism

The dissemination of “fake news” is an ever more common reality. Most people are very poor at evaluating the reliability of a news source and the truth of what is reported. When a layperson challenges an expert by saying “I read it in the paper” or “I saw it on the news,” it may mean only “I saw something from a source I happen to like and it told me something I wanted to hear.” At that point, discussion has nowhere to go; the real issue is replaced by the effort to untangle which piece of misinformation is driving the conversation. People are constantly barraged with facts and knowledge, but they have become more resistant to facts and knowledge. How did we arrive at this state of affairs? Nichols says, “technology collided with capitalism and gave people what they wanted, even when it wasn’t good for them.”

When the experts are wrong

In our increasingly complex world, we can’t possibly know everything; we have no choice but to trust experts. But sometimes experts get things wrong. Most of the time, their errors are identified and counteracted by other experts. This works so well most of the time that we are shocked when we read about an exception; for instance, when we learn that an incompetent doctor has killed a patient or that a researcher has falsified data. Laymen get exasperated when science “changes its mind,” for instance telling the public eggs are bad for them and then saying no, they’re OK to eat. But that’s not a failure of science, but rather an example of how science works so well in the long run by following the evidence and discarding false provisional conclusions as the evidence improves.

When experts’ errors, fraud, and misconduct are revealed, a layperson naturally asks how we can trust studies in any field. Nichols says that’s the wrong question to ask, because “rarely does a single study make or break a subject.” Single studies are often wrong, but the aggregate of all research is

trustworthy. The scientific enterprise as a whole is self-correcting and leads to a consensus of experts that approaches the truth as much as is humanly possible.

The impact on government

Science is essential to rational public policy; it can't make the decisions, but it provides reality-based information that can guide the decision-makers. Nichols says we have a President who sneers at experts and whose election was "one of the loudest trumpets announcing the impending death of expertise." He argues that Trump's campaign was "a one-man campaign against established knowledge." He provides examples: Trump's "birther" campaign against Obama, his quoting the *National Enquirer* approvingly as a source of news. Nichols says rather than being ashamed of his lack of knowledge, Trump exulted in it. "Worse, voters not only didn't care that Trump is ignorant or wrong, they likely were unable to recognize his ignorance or errors." He says the Dunning-Kruger effect was at work. It's not just the things we don't know (one in five adults think the sun revolves around the Earth), but the smug conviction that we don't need to know such things in the first place.

He warns,

> The relationship between experts and citizens, like almost all relationships in a democracy, is built on trust. When that trust collapses, experts and laypeople become warring factions. And when that happens, democracy itself can enter a death spiral that presents an immediate danger of decay either into rule by the mob or toward elitist technocracy. Both are authoritarian outcomes, and both threaten the United States today.

Conclusion: Hope for the future?

He says Americans no longer understand that democracy only means political equality. They tend to think democracy is a state of actual equality in which

everyone’s opinion is as good as everyone else’s, on every subject. Feelings are more important than facts: if people *think* vaccines are harmful, it is considered “undemocratic” and “elitist” to contradict them.

He sees signs of hope. Experts are rebelling. He cites an angry doctor who asked patients, “Do you remember when you got polio? No, you don’t, because your parents got you [expletive] vaccinated.” He points out that without democracy and secular tolerance, nations have fallen prey to ideological, religious and populist attacks and have suffered terrible fates. But he ends on a hopeful note. He has faith in the American system and hopes that it will eventually establish new ground rules for productive engagement between the educated elite and the society they serve. I hope so too!

Longtime readers of Science-Based Medicine and my not-so-secret other blog probably know that I'm not a fan of the specialty known as "integrative oncology." My reasons are basically the same as the reasons why I detest "integrative medicine," only subspecialized (like oncology), so to speak. Basically, "integrative medicine" integrates quackery with medicine, and integrative oncology integrates quackery into oncology. Given that I'm a cancer surgeon, I tend to take an even dimmer view of the latter than of the former, if only because it hits me where I live. For instance, when "integrative oncology" starts appearing at symposia at major cancer meetings, with nary a skeptical word showing up in the panel discussions afterwards, I despair. Unfortunately, the credulity that allows modalities like acupuncture, reiki, intravenous high dose vitamin C, and various other unproven and disproven treatments to find their way into academic medical centers has spawned a related phenomenon, quackademic medicine, or the study and acceptance of quackery in academic medical centers. The most prominent example of this latter phenomenon occurred in September, when the University of California at Irvine accepted a $200 million gift from Susan and Henry Samueli to build and staff a college devoted to integrating quackery into its component departments and promoting "integrative medicine." Never mind the homeopathy.

Integrative oncology has become so established that it has its own professional society, the Society for Integrative Oncology (SIO). Not surprisingly, I'm not a fan of SIO, and SIO isn't exactly a fan of me, either. I've related the story before, but let's just say that the SIO was not pleased at my 2014 article in *Nature Reviews Cancer* discussing how integrative oncology is not evidence-based (to say the least), given its embrace of naturopathy. In brief, the SIO didn't like how much verbiage I devoted to homeopathy in the article, pointing out that homeopathy is indeed not evidence-based and that no integrative oncologist worth his or her salt would ever use it. I pointed out that you can't have naturopathy without homeopathy. After that, I asked how the SIO can reconcile its quite correct rejection of homeopathy with the fact that it admits naturopaths as members, that two of its recent past presidents have even been naturopaths, and that you can't have naturopathy without homeopathy. It's baked into the naturopathic

curriculum, and it's part of the naturopathic licensing exam. Moreover, one of the naturopaths who co-authored the SIO's breast cancer clinical guidelines ran a clinical trial on homeopathy. That same naturopath, by the way, was a co-author on the update to those guidelines published just this year. The SIO never learns.

This time around, though, the reason the SIO caught my attention was this Tweet by Dr. Sheila Garland, re-Tweeted by Dr. Jun J. Mao, immediate past president of the SIO (but still president at the time he re-Tweeted this):

> The beginning of a new era in evidence-informed integrative oncology research/practice that puts the person first #SIO2017 @Integrativeonc https://t.co/cmAMrCujjy
>
> — Dr. Sheila Garland (@SNGarlandPhD) November 13, 2017

This Tweet touted what is now the "official" definition" of "integrative oncology" recently laid down by the SIO:

> Official definition of Integrative Oncology! Spread the word! #SIO2017 We are research based! #cancerresearch pic.twitter.com/oeNsn9B1Jk
>
> — Jodi MacLeod (@write4wellness) November 13, 2017

It turns out that this definition had just been published by Witt et al in the November issue of *JNCI Monographs*, just in time for the SIO annual meeting last week. When I saw it, my first reaction was to e-mail my fellow SBM bloggers with a link and this image:

So let’s take a look.

The process of defining “integrative oncology”

My first reaction (besides possessiveness) when I saw the article by Witt et al, A Comprehensive Definition for Integrative Oncology was: What? The organization has existed for nearly 15 years, and in all that time it hasn’t yet managed to define what it’s about until now? My second reaction was: What on earth does this definition actually mean? It is about as boring, generic, and —shall we say?—vague a definition of anything as I’ve ever seen. Take a look:

> Integrative oncology is a patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments. Integrative oncology aims to optimize health, quality of life, and clinical outcomes across the cancer care

> continuum and to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment.

In actuality, I was more interested in what was left out of this definition than what was in it, but I'll get to that near the end of this post. First, I want to look at the process by which the authors developed this definition, as described in the article, which is open-access for those of you who want to read it yourselves. Before I get into the process, let's look at some of the authors, who are big names in the world of integrative oncology. The lead author, Dr. Claudia Witt, is Professor and Chair of the Institute for Complementary and Integrative Medicine at the University of Zurich and University Hospital Zurich, as well as part-time Professor of Primary Care and Community Medicine at the Center for Integrative Medicine University of Maryland School of Medicine. Dr. Jun J. Mao is, of course, president of the SIO and Chief of the Integrative Medicine Service at Memorial Sloan-Kettering Cancer Center. Dr. Lorenzo Cohen is someone whom we've met before, when he gave a talk at the American Society of Clinical Oncology (ASCO) meeting in 2014. He's the Director of the Integrative Medicine Program at The University of Texas MD Anderson Cancer Center. Linda Balneaves is a nurse and the current president of SIO, having succeeded Dr. Mao at the SIO annual meeting last week. I also can't help but note that one of the co-authors, Heather Greenlee, is a naturopath and has served as president of the SIO in the past as well.

In other words, these are indeed heavy hitters and the leadership of the SIO.

Let's look at their justification for seeking this definition. After regurgitating the usual "complementary and alternative medicine" (CAM) blather about how patients are just "looking for "additional interventions that may help improve the efficacy of conventional cancer treatments, increase their chance of survival, and/or reduce their symptom burden associated with cancer or treatments" and "improve their quality of life during and following treatment," Witt et al justify their search for a definition thusly:

> With the integration of interventions such as acupuncture, mindfulness and yoga, and lifestyle counseling into major cancer centers in North America (eg, MD Anderson and Memorial Sloan Kettering Cancer Center), the term "integrative oncology" has become increasingly used.

> “Integrative” better represents the process of care that is provided in centers where patients are receiving these types of interventions in addition to their conventional cancer treatments. With the establishment in 2003 of the Society of Integrative Oncology (SIO), a nonprofit multidisciplinary professional organization, the term “integrative oncology” was further legitimized and began to be widely used. However, the term “integrative” is also used in other contexts. An example is the Berlin School of Integrative Oncology at the Charité Medical School in Berlin (2), which is an initiative of the German federal and state governments that aims to educate young scientists and physicians in oncology in an interdisciplinary, translational research context. Although the term “integrative oncology” is rarely used in such an educational context, having totally different meanings for the same term can generate confusion. Adding to this complexity is the growing attention to the notion of integrated care programs in oncology, in which numerous cancer specialties (eg, medical oncology, radiation oncology, surgical oncology, genetics, plastic surgery) work together to provide comprehensive patient care (3).
>
> Furthermore, even in settings in which the term integrative oncology has been used to refer to the combination of complementary medicine therapies with conventional cancer treatments (4), the term has been defined in many different ways (5,6). Because of this lack of consensus, it has been difficult to communicate what is meant by “integrative oncology” to oncologists and other health professionals, as well as to key stakeholders, such as patients, administrators, and health policy makers. The aim of this project was to use a systematic approach to develop a comprehensive and acceptable definition for “integrative oncology.”

Actually, I’ve always rather suspected that this confusion is a feature, not a bug, related to the use of the word “integrative.” After all, integrative oncology, like integrative medicine, is a brand, not a specialty. It rebrands what should be considered perfectly fine science-based modalities, such as nutrition, lifestyle interventions, and the like, as somehow “alternative” or “integrative,” and then “integrates” quackery like acupuncture, reiki, functional medicine, and even homeopathy with them, to give the quackery

the appearance of scientific legitimacy. No, I don't think SIO is doing this intentionally; its leadership consists of true believers. But it is contributing to quackademic medicine and the integration of quackery into oncology. In any event, the word "integrative" is, as mentioned above, used to describe science-based endeavors, such as integrative biology. In this context, the word "integrative" connotes interdisciplinary study, a very different meaning than when the word "integrative" came to replace the term CAM to describe adding pseudoscience to medicine.

Indeed, use of the word "integrative" to describe medicine or the subspecialty of oncology connotes more than interdisciplinary patient care and research. It connotes the embrace of "alternative" treatment modalities as well. The term "CAM" still had the word "alternative" in it and the word "complementary" connoted that CAM was subsidiary to medicine, "complementary," the icing on the cake, if you will. In other words, it's not necessary, and science-based medicine is the real medicine. The adoption of the word "integrative" to rename CAM as "integrative medicine" was clearly intended to remove the implication that CAM was "complementary" and not as good as real medicine, in order to advance the narrative that integrative medicine is the "best of both worlds," while also borrowing from the cachet of various "integrative" scientific disciplines as being multidisciplinary. Again, I don't think SIO is out to deceive. Rather, the belief of the SIO leadership in the validity of integrative oncology has led them down this road, probably without even realizing it.

So how did Witt et al go about constructing their definition? Enter the mixed methods research design and Delphi method. This amused me, because it wasn't so long ago that naturopathic oncologists used this very method to try to define priorities in naturopathic oncology. If you want the details of how the Delphi method works I discussed them in deconstructing the nonsense that naturopaths laid down about their quack specialty using the Delphi method. The CliffsNotes version is that the Delphi method entails a using a group of experts to answer a question. The experts anonymously reply to questionnaires and subsequently receive feedback in the form of the statistical representation of the group response, after which the process repeats itself until something resembling a consensus is arrived at. The way Witt et al did this is described:

> A two-round Delphi process was then employed to further refine and gain consensus regarding the new definition. In the first round, the revised definition was distributed via an online survey (software SoSciSurvey [7]) to SIO board members as well as to a convenience sample of experts. The experts—oncologists, integrative oncology clinicians, and/or researchers from North America, Europe, and Asia—were contacted by the SIO board members. Based on first round feedback, the definition was revised and distributed again through an online survey to the full membership of SIO, with subsequent ratings and comments used to inform the final version of the definition. Data from both surveys were analyzed using descriptive statistics. Content analysis (8) was applied to the open-ended responses to identify any themes or concepts.

So, after this literature search and Delphi method, what did Witt et al find?

Defining “integrative oncology”

As a result of their literature search and two-round Delphi process, Witt et al found many definitions of “integrative medicine” and “integrative oncology” in the literature, which resulted in the following thematic suggestions:

- evidence-based/evidence-informed/evidence-guided/using best available evidence (14 of 20);
- accompanying conventional cancer treatment (18 of 20);
- addressing outcomes such as well-being, body, and mind-spirit, as well as physical, psychological, and spiritual quality of life (seven of 20);
- focused on health and not only on medicine (three of 20);
- provided by a team of health care providers/multidisciplinary/interdisciplinary (four of 20);
- patient-centered/personalized, individualized/whole person (two of 20).

The writing group, which consisted of “members with different professional/disciplinary backgrounds (ie, medical oncology, radiation

oncology, surgical oncology, nursing, patient advocacy, psychology, psycho-oncology, epidemiology, integrative medicine, health policy),” added these additional suggestions:

- type of interventions (mind-body therapies, natural products, lifestyle changes);
- beyond provision of health care (information, translation of evidence, identification of beliefs, values and preferences, empowerment).

The initial definition of integrative oncology developed by the group thus read:

> Integrative oncology is a patient-centered (theme 6), evidence-informed (theme 1) approach to health care (theme 4) that uses mind-body therapies, natural products, and lifestyle modification (theme 7) as adjunct to conventional cancer treatments (theme 2) and is ideally provided by a multidisciplinary team of care providers (theme 5). Integrative oncology aims to increase well-being of mind, body, and spirit (theme 3) and to provide patients with skills enabling them to help themselves during and beyond cancer treatment (theme 8).

After the two rounds of Delphi method, though, the group perceived that some changes were required:

> Overall, the comments on the second Delphi survey were positive, but the suggestions were quite heterogeneous. Two-thirds of suggestions focused on what were perceived to be missing interventions, and it became clear that therapies such as acupuncture and massage were not well represented in the definition. As a consequence, the definition was revised using the umbrella term “mind and body practices,” which is used by the National Center for Complementary and Integrative Health in the United States. This term includes mind-based techniques such as meditation and hypnosis, as well as manual techniques such as acupuncture and massage (9). One respondent mentioned that “health care” encompassed a broader area than integrative oncology, and the decision was made to be more focused and to use the term “cancer care” in the revised version. Another respondent also suggested that the phrase “approach to cancer care” could be misleading and not specific enough

> as a field of care or medical specialty. Integrative oncology is more than just an approach to overall cancer care; it has been the focus of a professional organization for more than 10 years and is an established field in its own right. During the review process, it was noted that cancer prevention was not included in the definition. Because the ultimate goal of many integrative oncology behaviors is cancer prevention and control, the definition was modified to include prevention.

I've discussed before how quackery like the theatrical placebo known as acupuncture has mysteriously been subsumed into "mind and body practices". Personally, I've always suspected that this was to hide the quackery of acupuncture with more benign modalities (such as massage) that, whether medically they can treat anything, generally do no harm, and can certainly feel good, thus improving quality of life. After all, given that the rationale in traditional Chinese medicine for acupuncture is that sticking the needles into specific "meridians" can redirect the flow of qi (life energy) for healing effect, acupuncture could easily be classified as a form of energy healing.

To the degree that integrative oncology sticks with science- and evidence-based tests and treatments, my main objection to it is that it's not necessary. Nutrition, exercise, and other lifestyle-based interventions are already a part of science-based medicine. I like to cite, for instance, evidence-based recommendations for the treatment of hypertension and type II diabetes, both of which emphasize, except for severe cases, dietary modifications, exercise, and weight loss as the first interventions to attempt before placing the patient on medications.

To paraphrase Harriet Hall, what is good about integrative oncology (or medicine) is not unique to it. Continuing the paraphrase, unfortunately, what is unique to integrative oncology is not good, and the SIO definition obscures or neglects to mention these unique (and not good) aspects.

What the SIO left out

If you read the full article, it should become very apparent that its authors

want desperately to convince the reader that integrative oncology is completely evidence-based. Sure, the SIO admits naturopaths and even elects them as the organization's president from time to time, never mind that all naturopaths are trained in The One Quackery To Rule Them All, homeopathy, and that the vast majority of naturopaths routinely prescribe homeopathic remedies, which, even the SIO concedes, are rooted in pseudoscience.

I was reminded of this on—where else?—Twitter. I came across a post on the University of Pennsylvania's OncoLink touting reiki in cancer care. Because the link was from 2011, I Tweeted a question to the OncoLink team. Here's the response:

> @gorskon, Reiki is a supportive therapy that can be used in conjunction with treatment. It is not promoted as an alternative to treatment
>
> — OncoLink Team (@OncoLinkTeam) November 2, 2017

If there is a challenger to homeopathy's title of The One Quackery To Rule Them All, reiki would be right up there. It is, as I have described many times before, a form of faith healing that substitutes Eastern religious beliefs for the Christian religious beliefs that usually undergird faith healing in the US.

But it's not just Penn. The Dana Farber Cancer Institute has also gone all in for nonsense:

> 7 Ways Integrative Therapies Help Cancer Patients: https://t.co/bRHYbqhrcy pic.twitter.com/0kVQ4FKW0o
>
> — Dana-Farber (@DanaFarber) August 26, 2017

The slideshow at the link above promotes reiki, reflexology, and acupuncture:

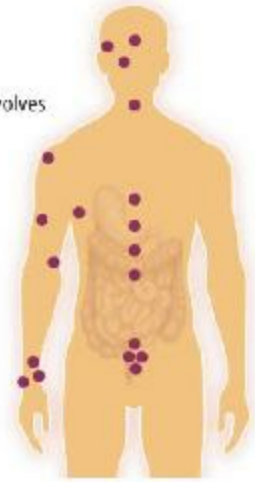
DANA-FARBER CANCER INSTITUTE
Discover. Care. Believe

7 WAYS INTEGRATIVE THERAPIES CAN HELP CANCER PATIENTS

1. ACUPUNCTURE

Acupuncture is a standard practice in Chinese medicine which involves gently inserting hair-thin needles into the skin at specific points. Acupuncture has been shown to:

- Reduce post-operative nausea and vomiting
- Decrease anxiety
- Treat pain and loss of nerve sensation
- Relieve joint pain
- Help relieve chronic pain



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Acupuncture is nothing more than a theatrical placebo, whose action has never been convincingly shown to be greater than that of placebo controls. Yet Dana Farber Cancer Center thinks acupuncture is science-based.

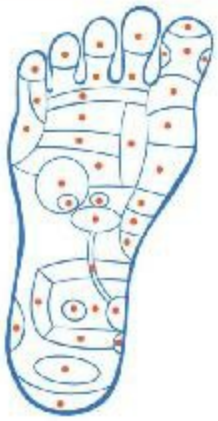
DANA-FARBER CANCER INSTITUTE
Discover. Care. Believe

7 WAYS INTEGRATIVE THERAPIES CAN HELP CANCER PATIENTS

3. REFLEXOLOGY

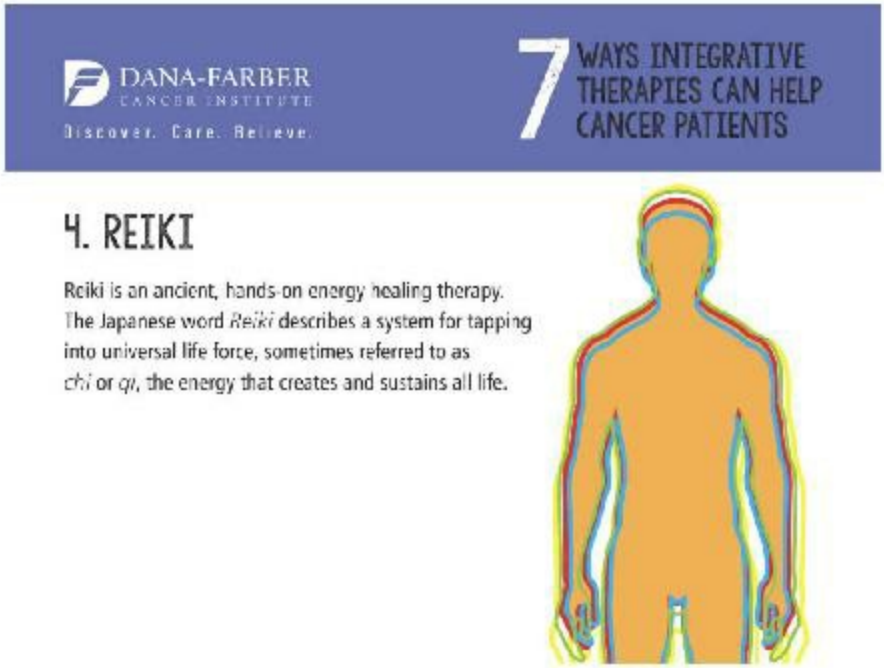
Reflexology is the application of pressure to areas on the feet, hands, and outer ears. The theory behind reflexology is that these areas correspond to organs and systems in the body. Patients have found that reflexology can:

- Promote relaxation and comfort
- Help with treatment symptoms like fatigue and nausea



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Reflexology posits the existence of physiologic or anatomic links between organs and body parts and areas on the soles of the feet and palms of the hand. Yet Dana Farber Cancer Center thinks this is science-based.



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Reiki masters claim to be able to heal by channeling energy into the patient from the "universal source." Replace "universal source" with "God" or "Jesus," and it becomes obvious that reiki is a form of faith healing that replaces Christian beliefs with Eastern mysticisms. Yet Dana Farber Cancer Center thinks it's science-based.

Of course, I've pointed out how oblivious the SIO is to the modalities that are really being "integrated" into oncology through integrative oncology just through the obliviousness of the SIO leadership to what naturopathy really is. As I've said before, if the SIO were really serious about being evidence-based, it would immediately purge itself of all naturopaths. It's not, though. Its leadership up in the ivory towers of medical academia can delude themselves into thinking integrative oncology is totally evidence based, because they manage to ignore the quackery that is "integrated" along with the lifestyle-, exercise-, nutrition-, and meditation-based modalities to which they love to point.

I can’t help but point out a few more examples of the quackery that goes along with integrative oncology. At UC-Irvine and the Cleveland Clinic, there’s homeopathy. At the University of Arizona Cancer Center, there was reiki, at least until a faculty member whose child developed cancer and was treated there made a stink. There’s also more energy medicine quackery, this time in the chemotherapy suite, at Georgetown University, as well as cupping, which is also pure quackery. There’s functional medicine at the Cleveland Clinic, George Washington University, University of Kansas, and, well, seemingly almost everywhere at any medical center with an integrative medicine program. If you want an idea of how bad functional medicine is, just check out this case report of functional medicine used for a patient with inflammatory breast cancer. This is what integrative oncology *really* involves.

It is also this quackery that the SIO definition of “integrative oncology” does its best to obscure or ignore. If the SIO is truly serious about being science- and evidence-based, it needs to speak out strongly and now against naturopathy and the various forms of quackery that have found their way into academic medical centers, of which, I assure you, the above is but a small sampling. It won’t, though. The quackery is why integrative medicine and oncology exist in the first place. Without the quackery, CAM (or integrative medicine or oncology) becomes completely unnecessary as a field.

Science Based Medicine

周四, 30 11月 2017

Science Based Medicine

[周四, 30 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **SBM Progress Report** [周三, 29 11月 20:29]
  Science-Based Medicine has been operating for a decade. While we have been successful by many measures, the challenges we face remain great. Here is a look at the mission of SBM, and a call for support to our readers.
- **Science Moms Fight Fears with Facts** [周二, 28 11月 16:00]
  A new documentary takes a novel approach. It features scientist moms who are just like other moms except that they understand the science. They set the record straight about GMOs, vaccines, and other subjects of interest to parents. They provide the facts to counteract unreasonable fears.
- **The integration of mysticism and pseudoscience with oncology continues apace in NCI-designated comprehensive cancer centers** [周一, 27 11月 16:32]
  Last week, I commented on the inability of the Society for Integrative Oncology to define what integrative oncology actually is. This week, I note the proliferation of the quackery of integrative oncology in places that should be rigorously science-based, namely NCI-designated comprehensive cancer centers.
- **And the server migration continues apace…but where are the comments?** [周六, 25 11月 10:15]
  SBM is changing servers again. Unfortunately, that means that there are problems with the comments.

In a month SBM will have been operating for a decade – 10 years and over 3,000 posts. How has the SBM project been faring in the last decade, and where do we go from here?

As a blog, SBM has been reasonably successful. Just surviving for 10 years is a milestone for any social media project, and SBM has done more than just survive. We have built a fantastic audience and have established ourselves as a premiere site for medical information, analysis, and commentary. We have drawn the attention of the media, the NIH, and regulatory agencies who have sought our opinions and input. We have also drawn the attention of quacks, which means we are doing our job. And I have noticed that the term, Science-Based Medicine, coined by this very blog, has come into common use in the conversation about the science and medicine.

SBM has also spawned the Society for Science-Based Medicine (SfSBM), a membership organization which is still building but doing well. We have also sponsored several SBM conferences, attached to the NECSS conference held in New York.

How effective has SBM been at stemming the tide of pseudoscience in the medical profession? That is an impossible question to answer, because we can't know what the world would have been like had SBM not existed. But we can take a look at what has been happening and we can speculate about what we need to do going forward.

Help support SBM

SBM is a project of the New England Skeptical Society, which is a 501(c) non-profit organization. We receive no corporate backing and have no major sponsors. SBM is supported mostly by donations. We have experimented with online ads to help pay for bandwidth and technical support, which is substantial for a blog with the traffic of SBM. However, you may notice that with a recent update we have removed ads from the site. Essentially we concluded, after several tries, that there were no ad services that were

compatible with our editorial policy. So we decided to just get rid of the ads, despite the fact that they were a significant source of revenue, and rely entirely on donations for support.

This means that SBM needs the support of its readers, and anyone who thinks that medical care should be safe and effective as determined by the best scientific evidence available. There is a Donate button in the upper right of the page, through which you can make one-time or recurring donations to SBM. We greatly appreciate any amount of support you can give. The more support we can get, the more we can do to further our mission.

It is an unfortunate reality that the forces we are up against are extremely well-funded. Quackery, fraud, and snake-oil are highly profitable. The billions of dollars generated by the supplement industry, homeopathy, and countless worthless health services and products have been funding several decades' worth of concerted efforts to infiltrate pseudoscience into medical schools. These funds have been used to lobby state and federal governments for quack-friendly laws. They have been used to market a narrative of medical pseudoscience to the public, fostering a distrust of genuine expertise, and promoting conspiracy theories and blatant misinformation.

They have literally millions of times more funding than we do. There is no profit in defending science and critical thinking, in medicine or elsewhere. All of the SBM editors and contributors are volunteers. We actually sacrifice time we could be expending more profitably elsewhere to promote SBM. But we have learned how to accomplish a lot with a little.

There are actually several ways you can support SBM. Of course, ultimately we need to keep the lights on, so please consider financial support. But we also need people to help spread the word. Link and share articles on SBM. Be the voice of reason in your job and in your social group. Write your representatives about bad laws, and file complaints when you confront health fraud. Even just giving your personal health care providers feedback about your desire to be treated with science-based medicine will help push back against pseudoscience.

Our mission

SBM is operating on several fronts simultaneously. Mostly we are engaged in a public conversation about the proper relationship between science, evidence, and the practice of medicine. This discussion is with professionals, regulators, the media, and the public at the same time. In the last decade we have actually learned quite a bit about the nature and extent of the problem of pseudoscience in medicine. A decade ago I had never heard of p-hacking, of researcher degrees of freedom, or the Dunning-Kruger effect. In that time we have also learned about the seriousness of the replication problem in biomedical research, and the statistical effects of prior plausibility.

There have been some improvements – journals rethinking the role of the p-value, publishing only registered clinical trials, retracting bad systematic reviews of alternative medicine, and a greater awareness of Bayesian analysis.

Assaults on the quality of science in medicine continue, however. We have had to face the challenge of open access journals, many of which are predatory, publishing any nonsense for a fee. But they have also been exposed.

Much of what we do feels like an endless game of whack-a-mole (to use that now overused metaphor). But if we didn't, the "moles" would breed and spread unchecked.

Perhaps our biggest regulatory victory was with homeopathy – the FTC has updated their policy, strengthening their regulation of these entirely worthless fake medicines. The FDA is still, apparently, reviewing their regulation but the current political environment may have put that on pause.

Going forward, in addition to continuing to do what we have been doing, I would like to see SBM expand our pool of regular contributors. Above all else, we are an intellectual trust of health care professionals who have developed an expertise in pseudoscience in medicine, regulation, science communication, and the application of critical thinking and skepticism to medicine. The more we can nurture other professionals with these same skills the better.

I do think we need to become more active in the regulatory sphere. This is a

little difficult as a poor non-profit, mostly run by people with day-jobs, but if we are able to expand our resources that would be one place I think we need to expand our efforts. I also think we need to become more active in mainstream academic circles. Too many of our academic colleagues do not recognize the problem of pseudoscience invading our profession. We need to get the word out, before they are bribed to turn the other way while nonsense is “integrated” into our profession.

There is endless work to be done. But we have a powerful message that we have also been forging over decades. Science-based medicine is where the medical profession needs to go. Despite our many challenges, I am optimistic about the next ten years.

At the recent conference of the Committee for Skeptical Inquiry (CSICON) in Las Vegas, on October 28, 2017, I had the great privilege and pleasure of being in the audience for the American premiere of a new documentary, *Science Moms*, as well as for the following live panel discussion by the women featured in the movie. In the documentary, a group of scientists and science communicators who are also moms address misperceptions created by misinformation in the media about GMOs, vaccines, and other issues important to parents. They point out that "moms whose opinions are formed by fear and hype are so loud. But they're the only people talking about it, the only resource people have." With this documentary, people now have another resource based on science, a resource that is easily digestible and compelling.

The film starts with a beautiful sunrise and a Gwyneth Paltrow quote: "The sun is the sun – how can it be bad for you? I don't think anything that's natural can be bad for you." The Moms answer:

"Wow! I could make a list for her."

"The sun causes cancer."

"Nature will kill you, really quickly."

"Sometimes I think she's trolling us."

Next, the Science Moms are introduced and talk about how they got interested in science. They are:

- Anastasia Bodnar, PhD, Plant Geneticist
- Alison Bernstein, PhD, Neuroscientist
- Layla Katiraee, PhD, Molecular Geneticist
- Jenny Splitter, Science Communicator and Storyteller
- Kavin Senapathy, Science Communicator

These women shatter the stereotypes of scientists as commonly portrayed in the media. They are normal, friendly, personable, attractive, well-groomed,

non-geeky, everyday people, just like other working moms except that their jobs happen to involve science. Moms viewing the film ought to be able to relate to them and listen to what they have to say just as they would listen to their friends.

Two of Science Moms were fans of *Buffy the Vampire Slayer* and were appalled to learn that the actress who played Buffy, Sarah Michelle Gellar, was speaking out against GMOs. They joined a group of 15 women scientists, bloggers, and educators to send a letter to Paltrow, Gellar, and other celebrities asking them not to co-opt motherhood and wield their fame to oppose beneficial technologies, but to use their influence responsibly and ensure that their advocacy is supported by facts, not fear.

The letter caught the attention of Natalie Newell, the host of "The Science Enthusiast" podcast. She contacted one of the letter's authors. One thing led to another, and the result was this documentary.

The Moms acknowledge that being a parent is scary. Parents desperately want to protect their children from any possible harm, and often they aren't sure how to best do that. Even they admit to having acted irrationally based on unrealistic fears for the welfare of their children. It's a great marketing technique: "If you can scare a parent, of course they're going to shell out for the alternative."

GMOs

People who don't know anything about GMOS may choose organic because they vaguely remember hearing that it was better for their kids. GMOs are presented in the media as inserting genes of one species into another species. But that's only one meaning. Genetic modification also means selective breeding, cross breeding, mutagenesis, genome editing, and other techniques.

When plants are cross-pollinated, a gene for disease resistance can spread to another species, but that's random. Why not use technology to put the desired gene into the plant? In reality, almost everything we eat was genetically engineered centuries ago by our ancestors' selective farming and breeding

practices.

The Moms point out these benefits of genetic modification:

- Drought resistance
- Pest resistance
- Disease resistance
- Increased crop yield
- Increased nutritional content
- Economic benefits
- Reduced pesticide usage
- Reduced greenhouse gas emissions

Vitamin A deficiency causes untold cases of blindness and death in developing countries. Golden rice was genetically modified to supply vitamin A, but thanks to anti-GMO ideology it hasn't reached those who need it most.

Some people fear that eating something genetically engineered will genetically engineer THEM. Not hardly! Despite widespread fears, GMOs have never harmed a single person's health in any way.

Fear of chemicals

The idea that "There is no safe amount of chemicals" is false. Everything is made of chemicals. They show a long list of all the scary-sounding chemicals in an all-natural blueberry. Pears naturally make formaldehyde.

The "most brilliant marketing move of the last ten years" was to convince everyone that organic is pesticide free. Copper sulfate is really bad for the environment, and it's allowed in organic farming.

Data doesn't support claims that organic is pesticide free, better for environment, or healthier.

There are no health benefits to be gained from organic. It's just more expensive.

Vaccines

We hear:

- Too many too soon
- Dangerous chemicals in vaccines
- I prefer to fight off disease naturally
- It's a Big Pharma conspiracy
- "These diseases aren't really that dangerous"

None of these are based on evidence or science. Unrealistic fears of vaccines have led to decreased herd immunity and disease outbreaks. Our grandparents aren't likely to fear vaccines, because they knew people who died of polio and other preventable diseases. It's ironic that people are afraid of harmless GMOs but don't fear the very real risks of vaccine preventable diseases.

Homeopathy

One Science Mom says, "I'm embarrassed to say I tried it. When I found out what it was, I thought 'Oh, that's why it didn't work.' I could have given the kids sugar water I made at home and saved a few bucks."

> I can't imagine parents reaching for something that is untested, unregulated, and has no active ingredients in it. It baffles me.

Perhaps it's because people want to do things on their own – homeopathy, homemade baby formula, anything that gives them the illusion of being in control.

Who's paying you??!!

The answer to this oft-repeated question is an emphatic "Nobody!" Kavin Senapathy says she has been called a fake mom, has gotten death threats, and has been told her name is made up (as if Monsanto would invent a name like

Kavin Senapathy!) She doesn't understand where the shill accusation comes from. The assumption seems to be that anyone who doesn't have the same world view as you, must be paid to have that view. It's hard to have your world view challenged, so it's easier to think they must be paid to disagree with you than to think your world view might be incorrect.

More

They explain that scientific consensus is not like a vote, it's the confluence of all the evidence coming together around a hypothesis.

When people ask if something is safe for their child, the best advice is to go to a real doctor (not a naturopath); and to buy real medicine (homeopathy is not real medicine).

Healthy diet? Eat lots of fruits and vegetables, buy whatever's cheaper, wash produce.

Some organizations are trying to scare people away from buying certain fruits and vegetables. That's CRAZY!

You might as well enjoy being a parent. "Basic safety stuff fits on half a page." Don't worry about minor details with no solid evidence, like when to introduce solid foods.

"When kids are 10-12, no one's talking about whether they were breast fed." The effects of stress on us and our kids are way worse than anything we're worrying about.

What's the real issue? If it's corporate control of our political system, that's a valid concern that many of us share. But GMOs aren't the cause of that. Focus on the real source of the anger rather than blaming a proxy.

Fear-based communities bring people together. The Science Moms are trying to create a new community based on science and reason; based on facts, not fear.

Conclusion: A lot of people really need to watch this documentary

Science Moms is short and to the point. The 30-minute film is scientifically accurate, persuasive, and well-designed, with good production values. It's available online for purchase at $4.99. I hope it will be more widely disseminated, because it offers important information that the general public needs to hear. People who have been exposed to anti-GMO or anti-vaccine propaganda are not likely to seek out, read, and understand the scientific evidence. But perhaps they will be willing to listen to moms who are just like them but who have the advantage of understanding the science.

Last week, I took note of how what is now a major medical society devoted to integrative oncology, the Society for Integrative Oncology (SIO), revealed itself to be unable to define, other than in platitudes and vague feel-good verbiage, just what the heck "integrative oncology" even is when it published a monograph in *JNCI*. What I didn't take note of last week was that the November issue in which the SIO's monograph defining what integrative oncology is (or what the SIO thinks it is) didn't contain just that one gem. In fact, like previous monographs published in years past, it's chock full of SIO propaganda for integrative oncology. Indeed, there's so much there that I could easily spend the next few weeks writing about each monograph in turn. I won't do that today, although I do reserve the right to discuss one or two more over the next couple of months if the urge takes me. What I do want to do is to discuss one monograph in particular, "Growth of Integrative Medicine at Leading Cancer Centers Between 2009 and 2016: A Systematic Analysis of NCI-Designated Comprehensive Cancer Center Websites," by Hyeongjun Yun, Lingyun Sun, and Jun J. Mao. I note that Dr. Mao is the immediate past president of SIO; this is coming from the top, so to speak.

I noted last week that I'm not a fan of the SIO, and it's not a fan of me. I won't repeat the story of my little discussion with them in which, in response to its umbrage taken in reaction to an article I published three years ago about integrative oncology, I tried to educate the leadership of the SIO that you can't have naturopathy without homeopathy. Reread last week's post if you want the details. My point is more that, as much as I don't like what SIO stands for, it has, unfortunately, been effective, and this survey provides yet another metric suggesting its effectiveness, along with that of all the other groups promoting the integration of pseudoscience and mysticism into medicine.

"Unmet needs"? Why would one need pseudoscience?

Yun et al. justify this survey with the usual tired tropes used to justify

“integrating” quackery with medicine, be it oncology or any other specialty. First, frame integrative oncology as an “unmet need”:

> Patients’ unmet needs in managing these symptoms coupled with their desire to use natural approaches to improve their health have created a demand for integrative medicine (3,4). According to the National Center for Complementary and Integrative Health (NCCIH), integrative medicine differs from complementary and alternative medicine (CAM) because it brings together conventional and complementary treatments in a coordinated way (5). Neither rejecting conventional therapies nor relying on alternative medicine, integrative medicine adopts only those complementary modalities supported by the highest evidence of safety and effectiveness (6). Numerous studies have evaluated the efficacy of utilizing integrative medicine modalities to treat the side effects of conventional cancer therapies. For instance, there is growing evidence that acupuncture may be effective in managing cancer therapy–related adverse effects such as fatigue (7–10), postoperative pain (11,12), vasomotor symptoms (13–16), and nausea and vomiting (17). Likewise, research supports the use of modalities such as massage (18,19) and mind-body therapies for symptom management and spiritual transformation; the latter remains a largely unmet need in the current health care system, yet directly impacts patients’ quality of life (4,20–23).

I can’t help but wonder how one quantitatively evaluates “spiritual transformation” in rigorous clinical trials, but that’s just me. In any case, I can’t help but note that some of the citations are articles discussed here and elsewhere before. For instance, reference 5 has been addressed before as “integrative health” being a rebranding of “complementary and alternative medicine” (CAM), which was a rebranding of alternative medicine. Other references, for instance, the ones supporting acupuncture, cite the usual low quality studies or studies that rebrand transcutaneous nerve stimulation (TENS) as “electroacupuncture.” Then there’s the whole framing of integrative oncology as an “unmet need.” It’s a very common framing of integrative medicine, be it through taking advantage of the opioid crisis to sell pseudoscience by claiming that nonpharmacologic management of pain must include CAM or by arguing that addressing unmet needs in symptom

management in cancer patients requires embracing pseudoscience. True, the latter argument isn't stated in those words, but when you strip away the "integrative" and CAM gobbledygook, that's the core of the argument you're left with: A false dichotomy that posits that, to treat the "whole patient" and to address "unmet needs," doctors must embrace the quackery in integrative medicine.

Next up, appeal to popularity:

> The use of integrative medicine is extensive among cancer survivors. Globally, up to 43% of patients with cancer have used integrative medicine therapies during their treatment, and the overall prevalence of integrative medicine use has increased noticeably over the past years (24–26). In the United States, cancer survivors use integrative medicine even more than individuals without cancer (27). Cancer survivors are more likely to use integrative medicine modalities for wellness, pain, and improving their immune functions. Interestingly, most of them started using integrative medicine because their conventional health providers recommended it to them (28).

Of course, as we've discussed before, this percentage is inflated by the broad definition of "integrative medicine." Basically, if you've ever had a massage or done art or music while being treated for cancer, by definition you've used integrative medicine. If you've ever meditated or prayed while being treated for cancer, you've used integrative medicine. If you've done Tai Chi, yoga, or Qi Gong (or even just exercise) while being treated for cancer, you've used "integrative medicine." You get the idea. When you look at the "hard core" quackery, such as homeopathy, you'll usually find that the number of patients using it is in low single digit percentages.

Integrative oncology and NCI-CCCs

The current survey is an update to a 2009 survey that found that 60% of National Cancer Institute (NCI)–designated comprehensive cancer centers (NCI-CCCs) provided information related to integrative therapies on their websites. Back in 2009, there were only 41 NCI-CCCs. Now there are 45. It's

worth looking at the old survey first, though, to see the sorts of modalities that were being offered at NCI-CCCs eight years ago and at what percentage of them:

Specific therapies listed did include some pure faith healing-related "energy medicine" quackery such as reiki (37% of websites), healing touch (29%). Not surprisingly, acupuncture showed up on 59% of websites, and dietary supplements, herbal medicine, and nutrition in one form or another showed up on between 42% and 56% of websites. To be honest, I was actually pleasantly surprised that only 60% of NCI-CCCs provided information on CAM. Indeed, it's kind of amusing to note the reaction of the authors to the perceived deficiencies of various NCI-CCCs with respect to CAM:

> Even with acknowledging these limitations, we still found that almost a third of leading U.S. cancer centers do not have functional websites related to CAM, and only a small proportion of the centers had websites independently judged to be excellent.

My reaction to that conclusion was: Gee, you say that as though it were a *bad* thing. I'm also happy that my cancer center's website would almost certainly have been in that one-third of cancer centers without information on CAM. Indeed, one of the things I've always liked about my cancer center is the relative paucity of integrative oncology options offered compared to other cancer centers, but I always fear that, sooner or later, we'll start to try to catch up.

So what's the situation now? Table 1 in the new study tells the tale. Mentions of quite a few modalities increased sharply. For instance, mentions of acupuncture increased by 30%, from 59% of NCI-CCCs to 89%. That's right. A whopping nine out of ten NCI-CCCs mention acupuncture credulously, and a full 73% offer it.

As a surrogate for just how much NCI-CCCs have abandoned science when it comes to integrative oncology, I like to examine the most implausible of treatments that fall under the mantle of "CAM" or integrative medicine. For example, mentions of healing touch, which is a form of "energy healing" (that doesn't actually involve touching) in which the practitioner claims to be able to detect and manipulate a patient's "life energy" field in order to heal

and/or relieve symptoms, increased from 29% to 58%, a doubling of the number, and 29% of NCI-CCCs actually offer this magical, mystical, "healing" touch. Mentions of reiki, which, as I've described many times before, is nothing more than faith healing that substitutes Asian mystical religious beliefs for Judeo-Christian beliefs as the basis for healing (replace the "universal source" from which reiki masters claim to derive the healing energy with God or Jesus, and you'll see what I mean), also increased markedly, from 37% of NCI-CCCs to more than half (53%) of NCI-CCCs, a more than 50% increase. Worse, 40% of NCI-CCCs actually offer reiki.

Not surprisingly, the "soft" parts of integrative medicine, the services that used to be offered for patient support and morale, such as art, music, massage, and various exercise programs but have, thanks to integrative medicine, become medicalized, appear on the vast majority of cancer center websites. One interesting finding is that, while exercise information is provided in 97.8% of cancer center websites, only 56% provide exercise/fitness services for their cancer patients. As much as it irks me that exercise and nutrition have been co-opted by integrative medicine and quacks like naturopaths, both can be science-based modalities for health promotion, particularly in cancer patients, although integrative medicine practitioners, particularly non-MD and non-dietician ones, often implement diet and exercise in non-evidence-based ways. (I'm talking to you, naturopaths, in particular.) Even so, we need to be doing better offering opportunities to help our patients exercise to improve their health and alleviate, for example, chemotherapy symptoms.

Overall, though, the authors are relatively happy with what they've found:

> Despite these limitations, we found that there has been substantial growth in the presence of integrative medicine on the websites of NCI-designated comprehensive cancer centers since 2009. In addition, the majority of the centers provide integrative medicine services within the same academic health systems in which they are located. As these centers lead the way in cancer research and clinical innovation, we need to ensure that integrative medicine can be cohesively incorporated into the continuum of cancer treatment and survivorship care using a financially sustainable structure. In addition, evidence-informed

> integrative medicine needs to expand beyond the walls of academic medical centers into community cancer centers and clinics to benefit patients from diverse socio-economic backgrounds.

The SIO even includes plans for world domination (OK, I mean the promotion of integrative oncology) around the world.

What the SIO left out: Most of the quackery

It's at this point that I can't resist mentioning what the SIO clearly left out. Remember, as I've pointed out many times, the SIO admits naturopaths. So where is naturopathy in this survey? Isn't naturopathy a part of "integrative oncology"? Certainly, the SIO seems to think so, given that it included presentations on naturopathic interventions in its recent annual meeting and even encourages naturopaths to join, listing them as equivalent to MDs. The SIO has even elevated two of them to the presidency of the organization! So why doesn't the SIO include a survey of which NCI-CCCs mention and offer naturopathy to their patients? Are they embarrassed? Trying to hide something? One wonders what Suzanna Zick, who was SIO President from 2015-2016, or Heather Greenlee, who was president from 2014-2015, think of this omission? Both are naturopaths.

I really can't help but suspect that, in its effort to persuade medical academia that integrative oncology is rigorously science- and evidence-based, whether intentionally or not, the SIO leadership is focusing all its attention on promoting the evidence-based modalities that have been "rebranded" as "integrative," such as diet, exercise, and the like, and the patient support modalities that have been medicalized into "integrative medicine," such as massage, art therapy, music therapy, and the like. Pay no attention to that quackery that integrative oncology and medicine lump together with the diet, exercise, and the like, the SIO seems to be saying by the absence of focus on naturopathy (and the homeopathy that nearly all naturopaths practice). Again, it can't be emphasized enough that, wherever you find naturopaths practicing, you will find homeopathy being practiced.

True, there are a couple of exceptions. The SIO does mention reiki and

therapeutic touch rather prominently in both surveys, both of which are obvious energy healing quackery. However, most people don't realize that. Most people view reiki and healing touch as a form of massage or hands-on healing, even though healing touch usually doesn't involve actually touching the patient. Either that, or they view them as some form of spirituality, which is actually not too far from the truth, but mystical claims such as what are made for reiki and healing touch do not belong in science- and evidence-based medicine. Yet there are NCI-CCCs that credulously promote energy healing. For instance, I've written about Georgetown University before. There's an NCI-CCC there, the Georgetown Lombardi Comprehensive Cancer Center. I've described Georgetown as a bastion of quackademic medicine before because of its "pioneering" efforts to "integrate" the teaching of pseudoscience into its medical school curriculum. Relevant to cancer, though, Georgetown published an article in its official magazine about reiki in the chemotherapy suite:

> For a long time Denise von Hengst had a secret she kept from friends and physicians alike. As she was undergoing treatment at Georgetown Lombardi Comprehensive Cancer Center for a particularly aggressive type of breast cancer—triple positive, HER2 positive—she was also regularly receiving Reiki, an ancient form of Japanese healing, to mitigate the debilitating anxiety and fear that accompanied her cancer diagnosis.
>
> "At first I told no one about the Reiki," says von Hengst. "Fear of the 'woo-woo' factor. People might think I'm nuts."

No, I don't think the patient is nuts. I think the cancer center is irresponsible for offering magic with its medicine, leavened with pseudo-skepticism:

> However, skepticism remains, not only in the general population, but also within the medical field. Recently, several clinical trials have emerged attempting to prove, or disprove, the effectiveness of Reiki. Many of these studies have been criticized for the trial. design, number of participants and reporting mechanisms. Results of the trials are often inconclusive.
>
> Yet as the anecdotal proof mounts and Reiki's popularity increases,

> prestigious medical centers around the country are taking note and offering the treatment to patients at their facilities. Reiki can be found at hospitals and medical centers such as Boston Children's Hospital, Dana Farber Cancer Institute, Stanford Health Care, Memorial Sloan Kettering Cancer Center, Duke University Health System and Cleveland Clinic, to name a few. Many academic medical centers such as Georgetown incorporate complementary therapies into their teaching curricula.

I have a question for the leadership of SIO: Is reiki evidence-based? Is it science-based? If it isn't, then why are you supportive of NCI-CCCs offering it?

Here's another example, the University of Arizona Cancer Center, which is an NCI-CCC. Take a look at its integrative medicine page. Look at what it offers: reiki (of course, even though a faculty member complained about it), reflexology (pure quackery that posits a nonexistent link between body parts and organs and specific areas on the soles of the feet and palms of the hands), craniosacral massage (which Mark Crislip drolly and correctly called a "SCAM of infinite jest"), healing touch (of course), and shiatsu (unproven).

Three years ago, the son of a professor in a humanities department at UA was treated for leukemia at the UA Cancer Center. He was appalled at all the quackery being offered to his son, including not just the above modalities, but distance healing, offered by a man named Frank Schuster:

Yes, as fantastic as it sounds, this was a web page hosted by the University of Arizona Cancer Center. It might be gone now, but it's not at all clear that the quack above is gone from UACC.

After this professor complained, Shuster's UA webpage was either removed or placed behind a login. However, I noticed something about UA's list of offerings for integrative medicine. First, none of the practitioners were listed by their full names any more. It's Jessica, Barb, Heidi, Michael, Denise, or Frank, the last of whom offers the reiki classes. Hmmm. I wonder if that's Frank Schuster, still there, still practicing energy healing. I bet it is, but haven't been able to verify it one way or the other.

I want to believe that the SIO wants to be scientifically rigorous. I really do.

I’m guessing that most of the SIO physician and scientific leadership believes that they are being scientifically rigorous and trying to lay down a framework in science and clinical evidence for “integrative oncology,” even if they have a hard time defining what, exactly, integrative oncology is. It’s just that, for whatever reason, physicians who drink the Kool Aid of integrative medicine tend to develop massive blindspots about all the quackery that comes as a package with all the parts of integrative medicine that they like, such as the emphasis on lifestyle, diet, exercise, and the treatment of the “whole” person. These blindspots extend to naturopathy in particular, which is a veritable cornucopia of quackery, including homeopathy. Until the SIO can eliminate its blindspots over all the quackery that is included in “integrative medicine,” its claims of being scientifically rigorous are just so much self-delusion.

And the server migration continues apace… but where are the comments? - Science-Based Medicine

As many of you noticed, there has been an issue with the comments that began last night. Here’s what happened. The Powers That Be decided to migrate the blog to a new server last night, and there were problems relinking Disqus to the new installation of WordPress. I am assured that the problem has been fixed, but also told that it could take 12 hours for all the old comments to redirect to our new location. So be patient, and the blog should be back to normal by tomorrow morning. There should be benefits to the new server as well, such as faster loading, less downtime, and the like. We’re sorry about the inconvenience today, but as one of our crew noted, for some reason migrations never seem to go as smoothly as we would like.

In any event, if after tomorrow there are still problems, let us know.

Science Based Medicine

周五, 10 11月 2017

Science Based Medicine

[周五, 10 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Another “Chronic Lyme” VIP disciplined by NY medical authorities: Bernard Raxlen** [周四, 09 11月 14:00]
  Another "Lyme literate" NY physician is on probation and under orders to clean up his act. Will other physicians treating "chronic Lyme" take note?
- **Risks of a Gluten-Free Diet** [周三, 08 11月 21:27]
  Non-Celiac Gluten Sensitivity does not seem to be a real entity according the current evidence, but this has not stopped the gluten-free fad, which may be causing real harm.
- **Update on ASEA, Protandim, and dōTERRA** [周二, 07 11月 16:00]
  Multilevel marketing distributors of dietary supplements and essential oils point to studies that they think constitute evidence that their products work. They don't understand why those studies are inadequate.
- **ORBITA: Another clinical trial demonstrating the need for sham controls in surgical trials** [周一, 06 11月 16:58]
  Last week, the results of ORBITA were published. This clinical trial tested coronary angioplasty and stenting versus optimal medical management in patients with single-vessel coronary artery disease. It was a resoundingly negative trial, meaning that adding stenting to drug management didn't result in detectable clinical improvement. What was distinctive about this trial is that it used a sham procedure (i.e., placebo) control, which few trials testing surgery or a procedure use. The results of O…

Bernard Raxlen, MD, who devotes more than 90% of his practice to the treatment of so-called “chronic Lyme” disease, is on a three-year probation imposed by the New York State Board for Professional Medical Conduct (BPMC). Raxlen agreed to probation and a lengthy list of practice requirements last month following allegations, filed in September, of negligence, incompetence, gross negligence, gross incompetence, and failure to maintain adequate patient records. In doing so, he becomes the second “Lyme literate” VIP disciplined by the NY medical authorities this year. Based on similar charges of professional misconduct, David Cameron, MD, was also put on probation with numerous practice restrictions in June.

Who is Bernard Raxlen, MD?

Raxlen is a psychiatrist and solo “chronic Lyme” practitioner in New York City who says he’s “successfully treated” over 3,500 cases of tick-borne disease in the past 15 years. (He named his practice “Lyme Resource Medical of New York.”) He touts a “total comprehensive treatment program which

utilizes both oral and intravenous (IV) antibiotic treatment." It doesn't come cheap, either. An initial visit with Raxlen costs $1,200 with follow-up visits between $600 and $700. A PICC-line insertion (presumably for long-term antibiotics) is $750 and a "nutritional IV" is $150. He does not accept public or private insurance.

Raxlen has a history of disciplinary actions against him in two states stretching back almost 20 years. In Connecticut, where he was formerly licensed, he was reprimanded and paid a total of $35,000 in civil penalties in two cases arising out of his refusal to provide patient records to the Health Department and insurance companies, even though patients had signed releases. He was also disciplined for inappropriate prescribing and failing to maintain malpractice insurance. Because these infractions constituted professional misconduct in New York as well, he was subject to two disciplinary actions in that state, resulting in censure, reprimand and a $2,500 fine.

According to the *Chicago Tribune*, Raxlen had other professional misconduct charges brought against him by Connecticut authorities but they were ultimately dropped. The *Tribune* reported that, in one case, Raxlen was charged with telling a patient with Lou Gehrig's disease (ALS) that she had Lyme disease and treating her with an illegal drug from Germany. He told the reporter that the relationship between ALS and Lyme was "unclear," even though ALS experts concluded that there was no evidence of a connection.

Per his New York State Department of Health physician profile (just type his name into the search engine), Raxlen completed residency training in psychiatry and lists his specialty as psychiatry, but he is not board certified in any specialty. He did not train in internal medicine, family medicine or pediatrics (although he treats pediatric patients), specialties that normally treat routine Lyme infections. Nor did he train in infectious diseases, experts to whom patients with more complicated cases of Lyme would normally be referred by other practitioners.

Yet, he is described by the International Lyme and Associated Disease Society (ILADS) as a "leader in Lyme disease treatment and research." In fact, he is a founding member of ILADS, former Secretary of the Board, and has taught a number of ILADS courses. He was a co-author of the original

ILADS guidelines for the treatment of tick-borne diseases. Despite their troubling disciplinary status, both he and David Cameron are scheduled to speak at the ILADS Annual Scientific Conference, which starts today in Boston.

How can this be? How can one be a leading light in ILADS with a disciplinary history like Raxlen's and no graduate medical education in infectious diseases?

"Lyme literate" physicians like Raxlen consider "chronic Lyme" a real disease and treat it with long-term antibiotics, sometimes for months to years. Board-certified infectious diseases doctors and other "conventional" physicians do not. These experts agree that "chronic Lyme" is not a real disease and rely on well-conducted trials showing that long-term antibiotics do not substantially improve the outcome for patients diagnosed with so-called "chronic Lyme." Long-term antibiotics can, in fact, result in serious harm, including death, a subject our good friend Orac covered recently over on Respectful Insolence. Orac's post nicely summarizes the differences between real Lyme disease and "chronic Lyme," "a prototypical fake medical diagnosis," and the dangers of long-term antibiotics, as have posts on SBM, here, here, here, and here.

The CDC, the Infectious Diseases Society of America (IDSA), the American Academy of Pediatrics, the American College of Physicians, the *Medical Letter* and the American Academy of Neurology all reject the notion that "chronic Lyme" exists and that long-term antibiotics are an appropriate treatment. There is something called "post-treatment Lyme disease syndrome," but responsible medical authorities do not equate this syndrome with the nebulous symptoms and unvalidated lab tests of "chronic Lyme" and specifically reject the utility long-term antibiotic treatment based on well-conducted clinical trials.

None of this stopped "Lyme literate" doctors from banding together to form ILADS and issuing their own guidelines for the diagnosis and treatment of "chronic Lyme," guidelines based on very low levels of evidence that are accepted only by themselves and, in contrast to the IDSA guidelines, no other professional medical organization. ILADS teaches physicians and other practitioners how to become "Lyme literate." ILADS, again in contrast to

IDSA, is not an ACCME-accredited provider of continuing medical education although, for some inexplicable reason, the Westchester [County, NY] Medical Society has teamed up with ILADS and is using its accrediting authority to grant CME credit for some of the talks (also here) at the ILADS Scientific Conference.

Despite the lack of evidence that "chronic Lyme" is a real disease, and the lack of efficacy as well as the risks of long-term antibiotic treatment, ILADS healthcare providers currently treat more than 100,000 patients with "chronic Lyme" and tick-borne diseases in the USA and around the world. Given media reports that patients can spend $10,000 to $35,000 for treatment, "Lyme literacy" translates into millions of dollars for practitioners.

While it may be profitable, "Lyme literate" doctors risk running afoul of state medical boards. Raxlen is just one among ILADS-trained, "Lyme literate" physicians who have had their medical practices questioned by their peers, up to and including discipline imposed by state authorities (also, here and here).

With that background, let's look at the allegations against Raxlen and the terms of his probation.

The BPMC v. Raxlen

New York's medical misconduct procedures do not require the physician charged to stipulate to any particular acts of misconduct as a condition of settling his case. The physician can, as Raxlen did here, simply state he is unable to "successfully defend against at least one of the acts of misconduct alleged" and agree to the imposition of sanctions. This means the allegations in the state's Statement of Charges were never proven, as it was unnecessary to reach a decision on the factual issues once Raxlen agreed to a settlement. However, per the Office of Professional Medical Conduct's (OPMC) standard procedures, the allegations were based on expert review of Raxlen's patients' records and they remain uncontested by him.

The allegations of misconduct arise out of Raxlen's care of eight patients. As is typical of "chronic Lyme" diagnosis and treatment, patients (whose

identities are protected) presented with a variety of disparate symptoms, such as:

- Patient A: freezing, burning, air hunger, weakness, fatigue, neck pain and intestinal pain.
- Patient E: fatigue, migraines, neck pain, joint pain, numbness and tingling, irritability, sound, light and temperature sensitivity and nonrestorative sleep.
- Patient G: back pain, abdominal pain, feet pain, extremity weakness, anxiety, depression and mood swings.
- Patient H (who got the Hickman catheter and numerous antibiotics mentioned below): mouth, teeth and jaw pain, confusion, forgetfulness, irritability and mood swings.

Diagnosis and treatment of "chronic Lyme" is never mentioned, a wise decision on the part of the BPMC prosecutors in light of the ill-conceived New York law protecting "Lyme literate" doctors from prosecution

> based solely upon the recommendation or provision of a treatment modality by a licensee that is not universally accepted by the medical profession, including but not limited to, varying modalities used in the treatment of lyme disease and other tick-borne diseases.

Instead, the BPMC focused on the fact that Raxlen had failed in the most basic tenets of good medical care, although the fingerprints of "chronic Lyme" diagnosis and treatment, such as failure to consider alternative diagnoses, prescribing IV antibiotics and using a Hickman catheter, are all over the charges. The charges included:

- Repeatedly failing to perform or note in the patient's chart a comprehensive history and appropriate physical exam, including (despite his being a psychiatrist) a psychiatric history, neuropsychological testing and mental health status exam.
- Failing to construct a differential diagnosis and pursue a thorough diagnostic evaluation prior to instituting a treatment plan.
- Inappropriate prescribing, including prescribing Rifampin for a patient on Tamoxifen and prescribing addictive medications prior to a making a diagnosis and without considering non-addictive treatment.

- Inappropriately relying on Applied Kinesiology (which is quackery) to formulate a diagnosis.
- Placement of a Hickman catheter without medical necessity.
- Inappropriately administering antibiotics, including intravenous Invanz, Clindamycin, Flagyl, Rifampin, Minocycline, Mepron, Plaquenil and Bactrim, all of these for *one patient*.
- Failure to present or note in the patient's chart potential risks, benefits, side effects and safe use of prescribed medications.
- Failure to appropriately identify, address, and/or follow-up on potential side effects.
- Treating inappropriately with an ongoing and/or escalating medication regimen without appropriate physical exams and clinical reassessment for consideration of alternative diagnoses and treatment.
- Poor record-keeping.

These allegations resulted in charges of negligence, incompetence, gross negligence, gross incompetence, and failure to maintain adequate patient records. As noted, Raxlen agreed to a three-year probation in addition to the imposition of conditions on his practice. He must, among other things:

- Communicate to patients the nature of his medical role, whether it be a primary care physician responsible for the patient's general medical condition, or for a defined or limited purpose, and/or as a practitioner of a particular medical specialty.
- Obtain written informed consent addressing all aspects of treatment and document same, including documentation of all discussions with the patient about the nature and scope of his evaluation and treatment and the patient's need to pursue "conventional medical care elsewhere."
- Document all histories and physicals.
- Refer patients to primary care physicians, specialists or consultants for further evaluation and/or treatment where medically warranted and provide these physicians with all relevant patient information.
- Cooperate fully with the state in enforcing the Consent Order and timely respond to all state requests for written periodic verification of his compliance and all documents.

What now?

Based on a birthdate of 1938 in his state physician profile, Raxlen is either already, or soon will be, 79 years old. One wonders whether he will continue his practice in face of these new sanctions, although his website is still trying to attract patients.

Sadly, the chronic Lyme lobby responsible for passing the law protecting "Lyme literate" doctors has its sights set on even greater rewards. Several bills are pending in the NY legislature which would force insurers to cover "chronic Lyme" treatment (Assembly Bill 114, Senate Bill 4713, Senate Bill 670). Other bills give them the opportunity to argue in yet another venue for insurance coverage. (Assembly Bill 4863, Senate Bill 2168, Assembly Bill 6927).

In any event, it is commendable that the Board for Professional Medical Conduct has not let New York's unfortunate law get in the way of its prosecuting physicians who take advantage of patients with a diagnosis of "chronic Lyme," no matter how they frame the specific charges. With two leading NY "Lyme literate" physicians now on probation and under strict orders to clean up their acts, it remains to be seen what effect this might have on other "Lyme literate" doctors in the state.

There is a simple reason we strongly promote science-based medicine – it results in the best outcomes for individuals. That is true by definition, since the SBM approach is to use the best evidence and science available in order to determine which interventions result in the best outcomes.

There are numerous ways in which relying upon poor-quality evidence or invalid methods for making health decisions cause potential harm. Often the list is unimaginatively limited to direct physical harm, but that is only the tip of the iceberg. There is financial harm, loss of opportunity to pursue more effective interventions, psychological harm from false hope and being deceived, and sacrifice of quality of life, time, and effort.

Even without direct physical harm, with inert treatments like homeopathy, there is tremendous potential harm from relying upon fake medicine and bad science. But often there is potential physical harm, and even if slight it is not justified if there is no real benefit. Medicine is a game of risk vs benefit – when the benefit is essentially zero, any risk is unacceptable.

The gluten-free fad

Even a small potential harm can be significantly magnified if it is marketed to the general public. The "clean eating" movement, in my opinion, clearly represents such a case. The best overall advice we can give the public regarding healthy eating is to eat a variety of food with plenty of fruits and vegetables and watch overall caloric intake. Unless you have special medical considerations, simply eating a good variety of different kinds of food will take care of most nutritional concerns. It will result in you getting enough of what you need and not too much of anything that can increase your risk.

Having a restricted or narrow diet is always tricky, and runs the risk that you will be getting too little of some key nutrients and may be getting exposed to too much of others. This is the key risk of so-called "fad" diets, because they are often premised on a simplistic notion that specific foods or categories of foods are inherently bad and should be avoided. Therefore any diet which

essentially consists of avoiding certain foods or heavily relying on others is likely to take you away from an optimal diet, and therefore be a net negative for your health.

The recent gluten-free fad is no exception.

As I discuss in detail here, gluten is a composite of two proteins found in wheat, rye, barley, spelt, and related grains. About 1% of the population has an autoimmune reaction to one of the components of gluten (usually gliadin) and eating gluten can cause serious illness (a condition known as celiac disease). For those with celiac disease, avoiding gluten is essential and even a small amount of gluten can cause serious symptoms.

There is a controversy, however, surrounding the alleged existence of so-called non-celiac gluten sensitivity (NCGS). This is a hypothetical condition in which people may have a sensitivity to gluten without forming antibodies to gliadin or meeting the diagnostic criteria for celiac disease. Discovering a new disease is always complex, and requires the identification of something definitive and discrete. We either need to identify a clear clinical syndrome, or some new specific pathology.

For NCGS there is no clear pathology. The entity's legitimacy currently relies on the alleged existence of individuals who do not have celiac disease but have a negative reaction to eating gluten. If, however, we are going to base a new disease purely on clinical history, we need to make sure that the history is accurate and that we are not simply overinterpreting non-specific symptoms or falling victim to confirmation bias.

For example, there are people who feel they have a specific syndrome of sensitivity to electromagnetic waves, despite the absence of any identifiable pathology. However, properly blinded studies show that self-identified sufferers of EM sensitivity cannot tell when they are being exposed to EM waves in a blinded condition.

For alleged NCGS the most salient evidence of its existence as a clinical entity are rechallenge studies. In these studies subjects are challenged with either gluten or placebo, then the gluten is removed, and then they are later rechallenged. If NCGS is a real entity then their symptoms should resolve

when gluten is removed and then return when rechallenged, at a higher frequency when the same is done with a placebo.

A recent systematic review of gluten rechallenge studies did not find significant evidence for NCGS. They conclude:

> The prevalence of NCGS after gluten re-challenge is low, and the percentage of relapse after a gluten or a placebo challenge is similar.

This is a pattern of evidence that is consistent with the null hypothesis, that NCGS does not exist – results are all over the place, with better-controlled studies tending not to show an effect, and on average there is only a tiny signal that does not reach statistical significance. The most parsimonious interpretation of available evidence, therefore, is that NCGS does not exist. Despite this fact, roughly one third of the population report that they are trying to avoid gluten.

What's the harm

What, then, is the potential harm from restricting gluten from the diet in the millions of people who do not have gluten sensitivity? Potentially, all of the things I listed above may contribute to harm.

For many people they have settled on gluten sensitivity to explain real symptoms they may be having. In this case they may be missing the real cause of their symptoms. There is therefore an opportunity cost of making a false diagnosis.

Perhaps most significantly, a gluten-free diet is very difficult. You have to eliminate all wheat and similar grains from the diet. This has become somewhat easier recently as industry is cashing in on the gluten-free fad, but it is still a significant inconvenience and expense and therefore drain on quality of life.

Further – a gluten free diet eliminates a major category of food from the diet. People on a low or gluten-free diet tend to also be low in whole grains. They risk being deficient in iron and folic acid. A recent study linked low-gluten

diets to a higher risk of type-II diabetes.

Avoidance of gluten may also result in a heavy reliance on rice as a staple grain, and this might increase the risk of heavy metal exposure. Again – having a varied diet spreads out exposure to contaminants and toxins as well as maximizing exposure to needed nutrients.

Science over marketing

If we take a scientific approach to the question of NCGS we find that there is no clear evidence that non-celiac gluten sensitivity is a real thing, and that gluten-free diets not only have no benefit for the general public they present health risks. Clearly, however, we need to do a better job of communicating this to the public.

Part of the challenge, however, is that nutritional gurus (who always seem to have something to sell) have a simple and appealing narrative to market. They tell the public that their problems are due to one bad food or type of food they just need to avoid. Or, they market of lifestyle of “clean eating” that is based on the appeal to nature and irrational fear of toxins and chemicals, rather than an even basic understanding of science and evidence.

The science-based position, however, takes time to emerge. It may take a decade or more to do the kinds of studies necessary to effective answer the question about whether or not a new hypothesized clinical entity exists. There are many types of evidence to be considered, and many sub-questions to be addressed. Over time a clear picture will tend to emerge, but in the meantime the health gurus can establish a market for their nonsense. Once their simplistic and marketable narrative gets into the public consciousness it is hard to correct.

I have written critiques of several dietary supplements sold through multilevel marketing (MLM) schemes, and they keep coming back to haunt me. I get testimonials from users who believe they have been cured of every ailment under the sun; and every time another study is done, I get e-mails from distributors who apparently think the new “evidence” will change my mind. Recently I received three more emails about ASEA, one about Protandim, and three about dōTERRA essential oils, asking me to reconsider. I thought this would be a good opportunity to explain why I have not changed my mind and to explain once again what constitutes evidence in science-based medicine.

ASEA

Recently an email from “The ASEA Team” asked us to delete the article I wrote about ASEA in 2012, based on their opinion that it “was not constructive” and “was not based on decent and verifiable facts.” They did not mention two other followup articles I wrote here and here. And they did not directly try to refute most of the points I made in my critique; I think they failed to understand what I was saying. They provided six attachments with

studies they said were “made to prove the effectiveness of ASEA” but those studies didn’t prove any such thing.

Last week Steven Novella answered them very effectively, calling ASEA snake oil and pointing out the deceptive marketing practices of the company, the pseudoscientific nature of their claims, and the worthlessness of the studies they cite.

The claims

The ASEA website currently makes these claims:

> As we age, and as stress and environmental toxins inundate our lives and weaken our defenses, normal cellular function declines, and with it, the body’s ability to produce and maintain a proper balance of redox signaling molecules. ASEA has developed the only technology that can create and stabilize active redox signaling molecules in a consumable form. No matter what your health concern may be, ASEA Redox Supplement can bring your cellular communication to optimal levels, improving the health of every system of your body.

Questions

This brings up several questions:

- How exactly does normal cellular function decline? How would improved cellular communication reverse the decline?
- What is a proper balance of redox signaling molecules? How do they know? How is it measured?
- What active redox molecules are in the product? (They won’t tell us. The label just lists salt and water. In my opinion, if there are redox molecules in ASEA, listing only salt and water constitutes false labeling.)
- What evidence do they have that the product improves health?

What redox molecules?

All they have is a statement from a lab, BioAgilytix, that indirectly measures "biomarkers" of redox levels in ASEA using a fluorescent indicator as a probe for unspecified highly reactive oxygen species. I don't know what that means. There is no direct evidence that redox molecules are present. No other lab has analyzed the product.

Safety

Their claim that the product is safe is based on a brief description of two unpublished studies. In the first study, 106 overweight women took ASEA or placebo for 12 weeks; they reported no adverse effects, (None?! In most studies, even the placebo group typically reports *some* symptoms.) and there were no changes in liver or kidney function tests or complete blood counts. In the second study, an *in vitro* study of cultured eukaryotic cells, the cells "did not register a significant toxic response as measured by a visual assessment of green dye that indicated "nuclear translocation." Based only on this flimsy subjective and *in vitro* evidence, they claimed "ASEA Redox Supplement, orally administered, does not manifest a toxic response or inflammation to exposed tissue." Such thin gruel does not constitute convincing evidence that the safety of the product has been established.

Studies

Before I accept that a treatment works, I want to see human studies published in peer reviewed journals. There are none on their website, but I was able to locate two articles in the *FASEB Journal* here and here.

It quickly became obvious why these are not featured on the company website: they are not full articles, but abstracts from a meeting that were published in a supplement to the journal. One is a human study, the other is in mice (the poor mice were gavaged with ASEA and then run to exhaustion). One of my correspondents claimed that these are peer-reviewed studies, but peer review is not possible when all that is available is an abstract.

As far as I could determine, there have been three studies in humans. One, a small study of 17 cyclists, has been deleted from the web. It was not placebo-controlled. There is an abstract of a similar study of 20 cyclists that did use a placebo control and was double-blinded. It was essentially *negative*: ASEA did not improve time trial performance. They found that it caused a significant shift (good or bad?) in 43 metabolites, but had no apparent influence on traditional biomarkers of inflammation, oxidative stress, or immunity.

The third, most recent human study is the one my true believer correspondents are currently crowing about. They refer to it as a "genetic" study. One of them snarkily commented "It's called science, u should look into it sometime." I did look into it, and I was not impressed. The title is "Initial Gene Study Showed ASEA REDOX Affected Important Signaling Pathway Genes." The company paid Tauret Labs to do the study. It has not been published in a peer-reviewed journal. It was an 8-week double-blind randomized placebo controlled study with 60 participants that measured changes in expression of 5 genes and found statistically significant changes of 20-31% with ASEA. They claim that "These genes are key in the health of the individual and play a vital role in five human health areas and dozens of pathways." Maybe, but they have not demonstrated that human health benefits in any way from these changes in gene expression. Their summary of results states "Effects are non-specific to race, sex or age, and were observed in all populations tested." This conclusion is not supported by their data. The only population tested was 60 individuals, 41% male, 92% Caucasian, average age 35 with age distribution not reported.

Conclusion

The evidence for their claims is indirect and inadequate. Half of all research studies turn out to be wrong. Changes in blood tests might be spurious; they have not been independently replicated. Changes may be statistically significant but not clinically significant. If they want us to believe ASEA causes objective, meaningful improvements in human health, they'll have to do better. They'll have to test directly for meaningful clinical outcomes. And if they want us to believe ASEA contains all those redox signaling molecules,

they'll have to prove it with a direct analysis by an independent lab and name those molecules.

As Steven Novella put it,

> Asea, however, is still a fantastical and unbelievable claim supported by nothing but hype, sales copy, and empty promises. It is salt water. The hand-waving nonsense about redox reactions is incoherent technobabble – the very essence of pseudoscience. What would be convincing is published, peer-reviewed, independent, rigorous scientific studies with clear results. These don't exist. No amount of distraction will change that fact.

Protandim

I have written about Protandim four times, here, here, here, and here.

What is it?

It is a mixture of five dietary supplements (Milk thistle, *Bacopa* extract, Ashwagandha, green tea extract, and turmeric extract) that allegedly stimulates the body to produce its own antioxidants. They claim it is "the only supplement clinically proven to reduce oxidative stress by 40%, slowing down the rate of cell aging to the level of a 20 year old [and they measured this how?]."

An email from a reader

> You really need to up date your studies on this product! There are thousands of people with improved health because of PROTANDIM. For example, my son in law with high blood pressure was able to cut his BP medication in half after only two months on it and after three months, he is off meds completely with normal blood pressure; my daughter suffered for a year with a horrible rash under her arm that

> looked like tree bark. After several visits to her doctor where he prescribed cortisone and antibiotics nothing worked. She finally went to a dermatologist who was shocked to see that she had Granular Parakeratosis a rare skin disease. My daughters case was only the second time she has seen it, and at a follow up visit was told that there is no cure, only palliative care. Three days later the crud came off in her washcloth in the shower, and she had been on PROTANDIM for about two months. See photos. On the after picture you can see a round sore which is from the biopsy. In addition, my husband who has cOPD and had bypass surgery last year, and myself have great, new energy. In addition, my nerve damaged feet and numbness in my right foot have improved by at least 80 per cent after only 5 weeks! For the first time in 15 years or so, I can now feel my right big toe and it is no longer cold, like a piece of granite, and our bad backs have greatly improved. I could go on and on and I don't need someone like you to tell me and thousands of others that it does not work! We are walking human studies for this amazing product! Check out the human studies for liver disease! I am proof it works so you should take another look: in fact go to You Tube PROTANDIM testimonials and see for yourself what this product does when it reduces oxidative stress!

My most recent article was in May 2017, and I'm not aware of any new studies requiring me to "update my studies" in the last six months. The evidence on the website is mainly about Nrf2 protein messengers in general, and studies of Protandim in cell culture (*in vitro*) and in mice. One 2006 human study found changes in lab tests such as TBARS but did not even attempt to look for any clinically meaningful improvement in health outcomes. A second human study in 2016 was negative: It concluded "Protandim® did not (1) alter 5-km running time, (2) lower TBARS at rest (3) raise antioxidant enzyme concentrations compared to placebo (with exception of SOD in those ≥ 35 years old) or, (4) affect quality of life compared to placebo." And another study of patients with alcohol use disorders was also negative. Not only negative but laughable.

Conclusion

Increasing levels of antioxidants could be beneficial or harmful. The only way to know if Protandim improves human health is to do properly designed, placebo-controlled human studies looking for meaningful clinical outcomes.

dōTERRA essential oils

I have written about dōTERRA twice before: here and here.

An email asked me to "Check with Johns Hopkins and the research published about dōTERRA oils. Dr. Nicole Parrish claims that dōTERRA oils have killed three super bugs that synthetics cannot. It is published and the medical world is learning more about essential oils in September." I asked her for links to that research; she never responded.

Another email chastised me for having a "complete scientific mindset." (I thought that was a *good* thing!) She said, "It really is worth looking further into to help people stay healthy." She provided all kinds of testimonials: her dentist and her real estate agent use it, her son and stepson carry the beadlets with them during allergy season, and when her husband got cancer, they used essential oils for diabetes, neuropathy, infections, and asthma. She also chastised me for not mentioning what the Bible says about oils and plants! She believes "science is here to prove God's existence and the Bible can be used for medicinal research." I didn't try to answer her.

An *in vitro* study was done on dog kidney cells infected with influenza virus. Based on their results, they speculated that essential oils *might* be useful in treating humans with influenza (or might not). In my article critiquing that study, I provided some guidelines on how to read research studies that claim to support a product.

A third email said I needed to visit the website again and review the 17 studies published in peer-reviewed journals. I found an *in vitro* study of frankincense and an *in vitro* study of Deep Blue, a mixture of essential oils. There was also an extensive bibliography which included a lot of irrelevant articles along with *in vitro* and animal studies. There were a lot of scattershot preliminary studies on individual oils, but these were seldom if ever followed

by replications or confirmations. My own PubMed search found a few studies supporting the use of an essential-oil-containing mouthrinse, reports of adverse effects of essential oils, some negative studies, and a couple of Cochrane reviews that pointed out the poor methodology of the few studies they found. A 2012 systematic review of aromatherapy concluded "the evidence is not sufficiently convincing that aromatherapy is an effective therapy for any condition."

My correspondent said, "In my opinion, there are too many confirmed reports of improved health & well-being (when using essential oils) to chalk it all up to "hysteria" or "ignorance" or even chance." Her opinion is misguided. The plural of anecdote is not data. Confirmed reports of improved health and well-being, no matter how numerous, are meaningless without a control group. Reports of failures are not systematically collected. Patients may improve for reasons other than the oils: suggestion, placebo effect, social factors, the natural course of the disease, regression to the mean, etc.

Essential oils can be very pleasant to use, and I have no problem with using them as "comfort" measures. And the company website is careful not to make any egregious disease-prevention or -treatment claims. But at their in-home presentations, the distributors feel free to claim that the oils can cure anything and everything, including cancer. These claims are not backed by any science but are illustrated by persuasive anecdotes, touching and heartwarming stories, testimonials from users that the attendees may know personally. Attendees are easily influenced to believe and to buy.

The published evidence for each of dōTERRA's many products is sparse to nonexistent. There *are* clinical studies to support *a few* of the recommended uses, but they are generally poorly designed, uncontrolled, unreplicated, and unconvincing. Research is difficult, because patients can't be blinded to the odors, and mental associations and relaxation could account for most of the observed effects. I remain skeptical of the claims for objective benefits in treating diseases.

Conclusion: No reason to change my mind

Testimonials are notoriously unreliable. These products are not supported by acceptable scientific evidence. I'm *not* saying they *don't* work. No one knows whether they work or not, because they have not been properly tested. I am simply asking for a single standard of evidence, the kind of evidence required to achieve a scientific consensus that any treatment is effective and safe. If they want us to buy their products, they should test them against placebo controls in human studies looking for objective, meaningful improvements in health; and they should get those studies published in reputable peer reviewed journals. In the pharmaceutical industry, only a small percentage of promising candidates survive testing. Considering the huge number of dietary supplement products like these on the market, the chance that any one of them will prove to be truly effective is vanishingly small.

We here at SBM devote a lot of discussion to unscientific and pseudoscientific treatment modalities, the vast majority of which can be best described as quackery. Sometimes, though, what's even more interesting are controversies in "conventional" science-based medicine. In particular, I'm a sucker for clinical trials that have the potential to upend what we think about a disease and how it's treated, particularly when the results seem to go against what we understand about the pathophysiology of a disease.

So it was that I started seeing news reports last week about ORBITA (Objective Randomised Blinded Investigation With Optimal Medical Therapy of Angioplasty in Stable Angina). Basically, ORBITA is a double-blind, randomized controlled trial comparing percutaneous coronary intervention (PCI, or, as it's more commonly referred to colloquially, coronary angioplasty and/or stenting) versus a placebo procedure in patients with coronary artery disease. Indeed, the sham procedure is what makes this trial interesting and compelling, although the devil is in the details. What this trial and its results say about coronary artery angioplasty and stenting, placebo effects, and clinical trial ethics are worth exploring. Basically, ORBITA calls into doubt the efficacy and usefulness of PCI in a large subset of patients with stable angina (chest pain or discomfort due to constriction of one or more coronary arteries that most often occurs with fairly predictably with activity or emotional stress—that is, exertion).

Before I dig in, I can't resist mentioning that cardiac surgery was one of the very earliest forms of treatment in which the importance of a sham surgery control was shown to be very important. In 1939, an Italian surgeon named David Fieschi developed a technique in which he tied off (ligated) both internal mammary arteries through two small incisions, one on each side of the sternum. The idea was to "redirect" blood flow to the heart in order to overcome ischemic heart disease, in which the patient suffers pain, heart failure, or even death due to insufficient blood flow to the heart muscle caused by atherosclerotic narrowing of one or more of the coronary arteries. The results were striking, as three quarters of all patients on whom Dr. Fieschi did his procedure improved and as many as one third appeared to be cured. The procedure became very popular and appeared to work.

Nearly two decades later, in the late 1950s, the NIH funded a cardiologist in Seattle named Dr. Leonard Cobb to do a randomized controlled clinical trial of the Fieschi technique. He operated on 17 patients, of whom eight underwent the true Fieschi procedure, with both internal mammary arteries tied off, and nine underwent skin incisions in the appropriate location. In 1959, Dr. Cobb's results were published in the *New England Journal of Medicine*, where he reported that the results were the same for patients who underwent the "real" Fieschi operation or the sham procedure. This was the beginning of the end of internal mammary ligation as a treatment for angina and a landmark in the history of surgery. After this trial, understanding of the ethics of human subjects research changed, and including sham surgical procedures in clinical trial design became increasingly frowned upon.

ORBITA is one of several recent trials that use sham interventions that have been reported in recent years as that ethical understanding has shifted again in the face of increasing evidence that surgery can produce the most powerful placebo effects of all interventions. Another example is trials of vertebroplasty for vertebral fractures due to osteoporosis, which showed that vertebroplasty in this setting produced results indistinguishable from the sham procedure. Increasingly, it has been argued that more surgical trials should include a sham procedure group.

PCI: A brief history

Publication of the results of ORBITA were timed to coincide with the 40th anniversary of the development of PCI. Basically, coronary angioplasty was developed 40 years ago as a less invasive treatment than coronary artery bypass grafting (CABG) for coronary artery disease. In brief, in PCI a cardiologist will thread a catheter up a major blood vessel in the groin to the heart and into the coronary artery (or arteries) with blockages. At the end of the catheter is a balloon. The idea is to thread the end of the catheter under fluoroscopic guidance (fluoroscopy is a form of X-ray imaging with video) into the coronary artery and past the blockage, such that the balloon aligns with the atherosclerotic blockage. The balloon is then inflated to open up the blockage. That's the basic idea, although the methods have evolved markedly over the last forty years.

At this point I can't help but mention a bit of a personal note, as it involves the research I did as part of my PhD thesis, lo these many years ago. One of the huge problems with angioplasty early on was the high rate of restenosis (recurrent narrowing) of the blood vessel treated. The reason for this was that balloon angioplasty involved, in essence, injuring the vessel. As with any injury, there was an inflammatory reaction, and one consequence of the inflammatory reaction due to angioplasty is that the vascular smooth muscle cells in the media (the middle layer of the blood vessel) would be stimulated to proliferate and restenose the vessel. As part of my PhD thesis, I cloned and characterized a homeobox gene (yes, a homeobox gene, for you geeks out there) that inhibited the proliferation of vascular smooth muscle cells. The idea was to treat the area at the time of the procedure with this gene as a form of gene therapy to prevent restenosis.

I realize that those of you out there who might be cardiologists and who weren't practicing back in the 1990s probably think this was an insane idea, but here's why it wasn't so insane back then. In those days, coronary stents hadn't been perfected, much less the drug-eluting coronary stents that are commonly used now to prevent restenosis. Basically, after most angioplasty procedures now, cardiologists place a stent in the area of former blockage. To prevent cellular ingrowth into the holes of the stent and subsequent restenosis, the stent slowly elutes a drug that prevents the proliferation of vascular smooth muscle cells. (As an aside, one of the things about these stents that frequently causes problems to surgeons like me is that the patient needs to be on powerful anti-platelet drugs like Plavix for up to a year after stenting). In any case, with the development of drug-eluting stents, the idea of gene therapy to prevent restenosis disappeared into the dustbin of scientific history, for the most part.

Back when PCI was new and young, its indications were a lot more limited, but as time went on and cardiologists' confidence grew indications expanded to multivessel disease and other indications that used to mandate CABG, to the point that PCI for acute coronary syndromes has grown to predominate. As MedPageToday describes:

> In the early years of PCI it was widely believed that PCI to open a severely blocked artery would have long term cardiovascular benefits,

> even in stable patients. Angina patients, the thinking went, were at higher risk for CV events and death, and PCI or CABG lowered that risk by restoring flow through the blocked vessel and preventing a future MI. But doubts grew over time, as it became increasingly clear that MIs were more likely to occur at other, less obvious blockages. Coronary artery disease began to be seen more as a systemic condition and less as a focal plumbing problem. The positive role of medical therapy, including statins and aspirin, became increasingly recognized.
>
> Finally, a decade ago the COURAGE trial, despite widespread and fierce initial resistance in the interventional cardiology community, led to widespread agreement that in fact PCI in stable lesions did not produce long-term improvements in outcome when compared to optimal medical therapy (OMT).
>
> But PCI for stable angina maintained a strong clinical presence as a new consensus emerged in the cardiology community that PCI was superior to OMT in the relief of symptoms. The mantra was that patients would need a stent eventually so they might as well get it upfront. It is this reduction in symptoms that the ORBITA trial sought to test.

And it is this assumption or belief that ORBITA called into doubt, at least for one large subset of patients.

ORBITA

ORBIT has been published in the online first section of *The Lancet*; so let's dig in. The introduction tells the tale, and you don't even have to leave the abstract:

> Symptomatic relief is the primary goal of percutaneous coronary intervention (PCI) in stable angina and is commonly observed clinically. However, there is no evidence from blinded, placebo-controlled randomised trials to show its efficacy.

Or, in more detail in the introduction:

> Percutaneous coronary intervention (PCI) was originally introduced to treat stable angina.[1] More than 500 000 PCI procedures are done annually worldwide for stable angina. The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial showed no difference in myocardial infarction and death rates between patients with stable coronary artery disease who underwent PCI and controls.[2] Meta-analyses have shown similar results.[3]
>
> Angina relief remains the primary reason for PCI in stable coronary artery disease.[4] Guidelines recommend antianginal medication as rst line therapy, with PCI reserved for the many patients who remain symptomatic.[5]
>
> Data from unblinded randomised trials have shown significant exercise time improvement, angina relief, and quality of life improvement from PCI.[6–8] However, symptomatic responses are subjective and include both a true therapeutic effect and a placebo effect.[9] Moreover, in an open trial, if patients randomised to no PCI have an expectation that PCI is advantageous, this might affect their reporting (and their physician's interpretation) of symptoms, artifactually increasing the rate of unplanned revascularisation in the control group.[4,10]

So the investigators who designed ORBITA sought to do a rigorous randomized, double-blind, sham-controlled clinical trial of PCI for patients in stable angina. One can argue that such a trial should have been done a long time ago, before PCI became such a popular procedure for stable angina, and you would be correct. However, it's been done now; so let's look at the design. First, the inclusion criteria:

- Age 18-85 years
- Stable angina/angina equivalent
- At least one angiographically significant lesion (≥70%) in a single vessel that was clinically appropriate for PCI

Exclusion criteria:

- Angiographic stenosis ≥50% in a nontarget vessel

- Acute coronary syndrome
- Previous coronary artery bypass graft surgery
- Left main stem coronary disease
- Contraindications to DES
- Chronic total coronary occlusion
- Severe valvular disease
- Severe left ventricular systolic impairment
- Moderate-to-severe pulmonary hypertension
- Life expectancy <2 years
- Inability to give consent

Other features of the patient population studied:

- Previous PCI: 13%
- Left ventricular ejection fraction normal: 92%
- Canadian Cardiovascular Society angina severity grading class: I (3%), II (59%), III (39%)
- Angina duration: 9 months
- Vessel involved: left anterior descending (69%)
- Median area stenosis by quantitative coronary angiography: 85%
- Median baseline FFR value: 0.72; median post-PCI FFR value: 0.9

The primary endpoint to be assessed was improvement in exercise time. Patients with stable angina and evidence of severe single-vessel stenosis were randomized 1:1 to either PCI or a sham procedure. After enrollment, patients in both groups underwent six weeks of medical optimization. After that, they underwent either PCI or sham procedure with auditory isolation in which the subjects all wore headphones playing music throughout the procedure. During the procedure, patients' heart function (measurements known as fractional flow reserve (FFR) and instantaneous wave-free ratio (iFR)) was monitored using a research method, but operators were blinded to the physiology values and did not use them to guide treatment. Randomization occurred after this physiological assessment. For patients undergoing PCI, the operator used drug-eluting stents according to standard clinical guidelines with a mandate to achieve complete revascularization as determined by angiography. In the sham procedure group, subjects were kept sedated in the cath lab for at least 15 minutes, with the coronary catheters withdrawn with

no intervention having been done. Here’s the summary of the timeline and allocation of the trial:

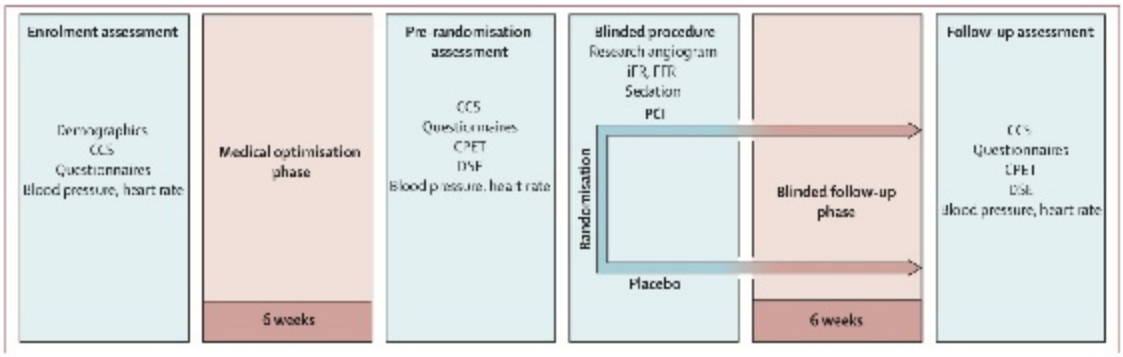


Figure 1: ORBITA study design
CCS=Canadian Cardiovascular Society angina severity grading. CPET=cardiopulmonary exercise testing. DSE=dobutamine stress echocardiography. iFR=instantaneous wave-free ratio. FFR=fractional flow reserve. PCI=percutaneous coronary intervention

Here’s the trial outline:

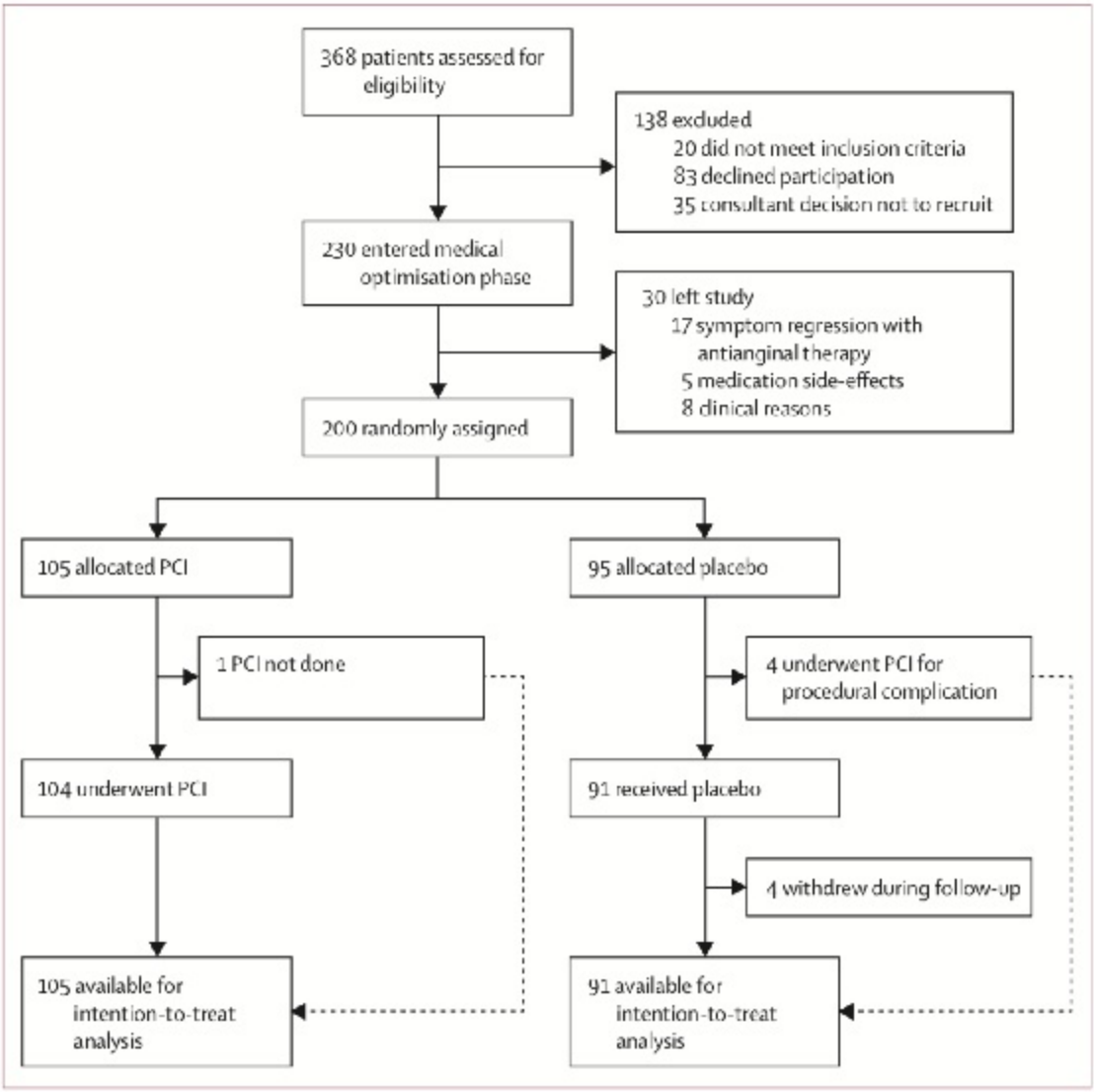


Figure 2: **Trial profile**
PCI=percutaneous coronary intervention.

Overall, there were 230 patients enrolled, of which after the medical optimization phase 200 were randomized, with 105 patients assigned to PCI and 95 assigned to sham procedure. And the results? They were what we call in the business a big nothingburger. The change in exercise time from baseline for PCI vs. sham, was 28.4 vs. 11.8 seconds, p = 0.2. Secondary outcomes were no better:

- Change in Seattle Angina Questionnaire (SAQ)-physical limitation from baseline: 7.4 vs. 5.0, p = 0.42
- Change in SAQ-angina frequency from baseline: 14.0 vs. 9.6, p = 0.26

- Change in Duke treadmill score from baseline: 1.22 vs. 0.1, p = 0.10

Also, at followup six weeks later, patients in both groups were receiving a mean of 2·9 medications; so PCI didn't decrease the need for cardiac medications. In other words, there was no statistically significant change in either the primary or secondary outcomes in patients with stable angina. The authors noted:

> In ORBITA, the first blinded, placebo-controlled trial of PCI for stable angina, PCI did not improve exercise time beyond the effect of the placebo. This was despite the patients having ischaemic symptoms, severe coronary stenosis both anatomically (84·4% area reduction) and haemodynamically (on-treatment FFR 0·69 and iFR 0·76), and objective relief of anatomical stenosis, invasive pressure, and non-invasive perfusion indices (FFR p<0·0001, iFR p<0·0001, stress wall motion score index p=0·0011). There was also no improvement beyond placebo in the other exercise and patient-centered effects with placebo effects. Forgetting this point, or denying it, causes overestimation of the physical effect.

In an accompanying editorial, David L. Brown and Rita F. Redberg commended the ORBITA investigators for "challenging the existing dogma around a procedure that has become routine, ingrained, and profitable," noting that ORBITA shows "(once again) why regulatory agencies, the medical profession, and the public must demand high-quality studies before the approval and adoption of new therapies" and characterizing PCI for stable angina as putting "PCI in the category of other abandoned therapies for cardiovascular disease, including percutaneous trans-myocardial laser revascularisation[10] and catheter-based radiofrequency renal artery sympathetic denervation[11]—procedures for which the initial apparent benefit was later shown in sham-controlled blinded studies to actually be due to the placebo effect." Noting that the short duration of followup actually would favor PCI because "any haemodynamic benefit from PCI occurs early and the benefits of medical therapy continue to accrue over years," Brown and Redberg conclude:

> The implications of ORBITA are profound and far-reaching. First and

> foremost, the results of ORBITA show unequivocally that there are no benefits for PCI compared with medical therapy for stable angina, even when angina is refractory to medical therapy. Based on these data, all cardiology guidelines should be revised to downgrade the recommendation for PCI in patients with angina despite use of medical therapy. ORBITA highlights the importance of including sham controls and double blinding in a trial to avoid being fooled by illusory improvements due to the powerful placebo effect of procedures such as PCI. Although sham-control procedures are associated with some adverse outcomes, those complications are dwarfed in magnitude by the rate of adverse events in the approximately 500 000 patients who undergo PCI for symptomatic relief of stable angina in the USA and Europe each year. These adverse events include death (0·65%), myocardial infarction (15%), renal injury (13%), stroke (0·2%), and vascular complications (2–6%).12 Health-care providers should focus their attention on treating patients with stable coronary artery disease with optimal medical therapy, which is very effective, and on improving the lifestyle choices that represent a large proportion of modifiable cardiovascular risk, including heart-healthy diets, regular physical activity, and abstention from smoking.

Based on the results of this trial, one can easily argue that PCI should rarely —if ever—be performed in patients with single vessel disease and stable angina.

The backlash

Not surprisingly, there was pushback. Cardiologists were not pleased by this result, even though it has been well known for a long time that in patients like those studied in ORBITA, PCI at least doesn't improve survival or decrease progression to need revascularization more than OMT. For instance, in a comment on the study various cardiologists were quick to make excuses:

> Panelist Dr Martin Leon (Columbia University Medical Center, New York City) applauded the investigators efforts for a "remarkable study" but said it's a much, much higher bar to achieve when the end points are

differences from baseline between two groups.

"Baseline data demonstrating that these patients had very good functional capacity, had infrequent angina, had very little ischemia, means that regardless of what you did to the coronary artery there was going to be very little you could demonstrate in terms of clinical therapeutic benefit. So I'm really glad that PCI had a statistically significant benefit in both echos and the stress tests," Leon said.

"The concern here is the results will be distorted and sensationalized to apply to other patient populations where this kind of outcome very likely would not occur," he added.

My counter to the argument that the patients included in this trial were not that sick is: Yes! That's the point. These are exactly the sorts of patients who too frequently are subjected to PCI for in essence no benefit over that which can be achieved by medical management.

Next up:

Commenting for *theheart.org* | *Medscape Cardiology*, Dr Roxana Mehran (Ichan [*sic*] School of Medicine at Mount Sinai, New York City) said, "To me actually this study shows angioplasty is quite effective in reducing ischemia, improving [fractional flow reserve] FFR, and in fact I'm actually very pleased with this. It's exactly what I want to do for my patients—improve their blood supply."

Asked whether this isn't just a positive spin on a negative study, Mehran quickly responded, "No," adding that whenever a primary end point is a change in a value, showing an important difference is very hard to do when baseline values are so good, especially with only 200 patients.

"I promise you, had she studied 400 patients this would be positive because everything was in the right direction," she said.

Actually, that's exactly what she's doing, trying to put a positive spin on a negative study. It's so blatantly obvious that that's what Dr. Mehran is doing that she should really be embarrassed to have said something like this to be

published for the public to read. In fairness, she does have a germ of a point in that the study was relatively small and potentially underpowered to detect some differences. On the other hand, it's rather interesting to note how some cardiologists totally twist the usual rationale and methodology used to determine if a therapy works. Here's what I mean.

Normally, when a new intervention is first tested, it's tested in small pilot trials. If a positive result is observed, that result justifies a larger trial to confirm efficacy and safety. If a positive result is not observed, then the treatment is generally abandoned or modified before being tested again. Now, get a load this:

> During the press briefing Dr Robert Yeh (Beth Israel Deaconess Medical Center, Boston, MA) congratulated the authors on a courageous, bold, and well-executed trial but said the results reaffirm in many ways those from COURAGE.
>
> "To extrapolate that this means that elective PCI is not an indicated procedure is the furthest overreach that I can possibly imagine from a very small and I think hypothesis-generating trial with an interesting result," he said.

Let's grant Dr. Yeh his characterization of this study as "hypothesis-generating." When hypothesis-generating studies are negative, the hypothesis is usually considered to be not worth testing further, barring serious methodologic or design issues in the hypothesis-generating study. To demand another, much larger, much more expensive study to follow up on a result that, even if Dr. Yeh is correct, would likely be a very modest difference in an increase in exercise tolerance. Basically, much, although in fairness not all, of what these cardiologists are doing is to make excuses.

None of this is to say that ORBITA is bulletproof. It is, compared to other trials of PCI, relatively small. There was a trend towards improved exercise tolerance in the PCI group compared to the sham group that might have been significant with more patients. The question, of course, is whether it would be worth it to do another larger trial. After all, interventional cardiologists are utterly convinced that PCI is more effective than OMT and are unlikely to change practice (much) based on this trial:

> How will the results of ORBITA be viewed? It will be a combination of love and hate. ORBITA was rigorously designed and undertaken with great care and painstaking attention to detail using objective exercise and physiologic outcome measures before and after stabilization on OMT, combined with the use of well-validated quality of life metrics before and after randomization. Overall, the results were stunningly negative, which ORBITA supporters will cite. By contrast, it is very likely that many in the interventional community will be ready to pounce on and discredit this study — there certainly hasn't been an opportunity since COURAGE was published 10 years ago in 2007 to potentially discredit a trial that now confronts the sacred cow of PCI benefit for angina relief as the sole basis to justify PCI in stable CAD patients. They will likely cite the limitations of small numbers (only 200 patients), that the study was woefully underpowered, the potential ethical conundrum of subjecting subjects with significant flow-limiting CAD to a sham procedure (or deferred PCI for clinical need), that 28%-32% of randomized subjects had either normal FFR or IFR (and therefore didn't have a "physiologically significant," or flow-limiting stenosis, that PCI would otherwise benefit), that there was a low frequency of multivessel CAD, that the short duration of follow-up (only 6 weeks) was too brief to assess potential benefit (though this actually favored the PCI group) and, of course, who would have the time or patience to call patients three times/week to assess their response to intensifying medical therapy — "not real-world," just like the OMT used in COURAGE wasn't achievable in the real-world.

Despite these reactions, I do have some optimism. Interventional radiologists reacted very negatively to the trials showing that vertebroplasty for osteoporotic spinal fractures doesn't work. Eventually, they started to come around, and usage of vertebroplasty for this indication is declining, albeit not as fast as it should. Science- and evidence-based medicine is messy, and there is some truth to the old adage that old treatments don't ever quite disappear until the generation that learned them retires or dies off. But change does come in response to clinical trials.

In the meantime, whatever effect ORBITA has on clinical practice, it should serve as a wakeup call that in clinical trials of surgical or procedural

interventions examining endpoints with a degree of subjectivity (unlike, for instance, death or time to cancer recurrence), whenever possible, new interventions should be compared to sham procedures. Of course, this isn't always possible, either for ethical or practical reasons, but when it is practical sham procedures are just as essential as placebo controls in drug trials.

Science Based Medicine

周五, 17 11月 2017

Science Based Medicine

[周五, 17 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **CAM use leads to delays in appropriate, effective arthritis therapy** [周四, 16 11月 22:00]
  A preference to use CAM before seeking medical advice may be harming patients with inflammatory arthritis.
- **Placebo Myths Debunked** [周三, 15 11月 21:03]
  Placebo treatments are often sold as magical mind-over-matter healing effects, but they are mostly just illusions and non-specific effects.
- **Turpentine, the Fountain of Youth According to Dr. Jennifer Daniels** [周二, 14 11月 16:00]
  Jennifer Daniels says turpentine is the Fountain of Youth, able to cure many ailments, both real and imaginary. It isn't; it's a poison with no recognized benefits for human health.
- **Why do some women refuse treatments for their breast cancer?** [周一, 13 11月 16:14]
  Adjuvant therapy after surgery, such as chemotherapy, hormonal therapy, and radiation therapy, has contributed to a 39% decrease in breast cancer mortality since 1989. Unfortunately, a significant number of women decline evidence-based adjuvant therapy. A recent study suggests that distrust of the medical system plays a significant role in such refusal.

Several weeks ago I summarized the evidence that demonstrates that when you delay cancer chemotherapy and substitute alternative medicine, you die sooner. Thank you to the tireless Edzard Ernst, who identified non-cancer evidence that demonstrates how choosing complementary and alternative medicine (CAM) instead of real medicine, can cause harm. In this case, the example is early inflammatory arthritis (EIA), and what was studied was the relationship between CAM use, and the delay to initiation of medical therapy. Time is of the essence with inflammatory arthritis, as there are medications that can reduce the risk of permanent joint damage. This new paper adds to the accumulated evidence to show that CAM, while it is commonly thought to be harmless, can indeed harm – not only from direct effects, but also from delaying the initiation of proper, effective medical treatment.

What is inflammatory arthritis?

Inflammatory arthritis is a term that describes inflammation of the joints (and other tissues). Inflammatory arthritis can include rheumatoid arthritis, and several other conditions. These are often autoimmune conditions, where your immune system treats its own tissues as foreign, and attacks it. Pain, swelling and tenderness are typical with inflammatory arthritis, and a diagnosis is usually based on a physical examination and laboratory tests. There are now many medications that can treat arthritis, ranging from the non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen and ibuprofen, to disease-modifying anti-rheumatic drugs which include biologic drugs that can be very effective and even put the disease into remission. While inflammation can be treated, joint destruction from arthritis can be permanent, so starting appropriate therapy, quickly, is important to reduce the risk of long-term damage. Today, aggressive treatment early in the course of the disease is considered to be the standard of care, so it is important for new cases to be recognized and referred for specialist assessment as quickly as possible. Barriers to early treatment include patient delays, but also system delays like wait times for referrals. Understanding why patients may not seek treatment is a question that led to this most recent study.

Studying CAM and inflammatory arthritis

Complementary and alternative medicine (CAM) is commonly used in different cultures, including Asian cultures, where traditional Chinese medicine may even be government-endorsed, despite the lack of evidence to show it is an effective system of medicine. When a group of researchers identified that many patients with a new diagnosis of arthritis had tried CAM prior to seeking medical treatment, they hypothesized that CAM may be delaying referral and medical therapy.

This paper is from Manjari Lahiri and colleagues and was published in the *International Journal of Rheumatic Diseases*. Entitled "Use of complementary and alternative medicines is associated with delay to initiation of disease-modifying anti-rheumatic drug therapy in early inflammatory arthritis", this was a prospective survey of patients with EIA. All patients seen at one of two hospitals in Singapore where they were invited to participate. Patients were included if they had a self-reported symptom of EIA, which was defined as inflammation of two or more joints, not caused by trauma. Patients were assessed at 3, 6, and 12 months, then annually for 3 years. All participants completed a nurse-administered questionnaire on demographic, health and lifestyle factors including CAM use. In this study, CAM was defined as the ingestion of tablets, herbs, powders or drinks purported to have medicinal properties. They could be prescribed (e.g., by a practitioner in traditional Chinese medicine) or purchase over the counter. Acupuncture, therapeutic massage and cupping, when used for the purpose of a therapeutic effect where included in the definition of CAM, while exercise (including yoga and tai chi), physiotherapy, and occupational therapy were not considered CAM. (This is among the more accurate delineations of CAM/non-CAM I've seen in a study.)

CAM users delay treatment

For this study, only the baseline (time=0) results were used. Overall, 180 patients were included. The median time from diagnosis to recruitment was 3 weeks. The median age was 51, and 71% of the participants were women.

When stratified by CAM use, Chinese patients more commonly used CAM, and oral tablets/powders and acupuncture were the most common forms of CAM. Full details are in Table 1:

Table 1 Baseline characteristics

Characteristic	Proportion (%) or median (IQR)			P-value
	Overall (n = 180)	CAM users (n = 71)	CAM non users (n = 105)	
Age at diagnosis, years, median (IQR)	51.1 (40.9–59.8)	53.9 (43.8–60.7)	47.3 (40.2–58.3)	0.05
Bottom tertile, 22.3–44.3 years	33.5	25.7	39.0	0.14
Middle tertile, 44.4–57.4 years	33.5	35.1	32.1	
Top tertile, 57.5–81.4 years	33.0	39.2	28.5	
Female	70.5	68.9	71.4	0.72
Race				
Chinese	58.3	82.4	40.9	< 0.001
Malay	18.3	5.4	27.5	
Indian	16.7	8.1	22.9	
Others	6.7	4.0	8.5	
Body mass index	24.3 (21.2–27.6)	24.0 (20.3–26.4)	24.9 (21.3–28.2)	0.25
Non-English speaking	30.2	50.0	16.4	< 0.001
Level of education				
None or primary	21.2	20.3	22.1	0.15
Secondary or vocational	46.1	51.0	40.1	
Diploma or degree	32.4	25.7	37.5	
Ever smokers	26.8	35.1	20.9	0.03
Diagnosis				
Rheumatoid arthritis	83.0	83.8	83.8	0.92
Psoriatic arthritis	12.8	13.5	12.4	
Undifferentiated arthritis	3.3	2.7	3.8	
Symptom duration, weeks‡	16.5 (9.2–26.6)	20.8 (13.1–30.1)	13.7 (8.7–21.8)	0.004
Disease duration, weeks§	3 (0–16.9)	3.2 (0–18)	4 (0–16)	0.25
Sero-positive¶	57.0	62.9	52.9	0.20
RF positive	50.3	55.5	46	0.12
ACPA positive	52.7	55.9	50.0	0.70
DAS28, median (IQR)	4.30 (2.84–5.71)	4.56 (3.15–5.78)	3.86 (2.47–5.58)	0.02
Low disease activity, DAS28 < 3.2	30.3	20.8	37.2	0.07
Moderate disease activity, DAS28 ≥ 3.2 to < 5.1	38.9	43.1	35.3	
High disease activity, DAS28 ≥ 5.1	30.9	35.1	27.4	
mHAQ, median (IQR)	0.37 (0–0.87)	0.37 (0.12–0.87)	0.37 (0–1)	0.92
mHAQ ≥ 1 (vs. < 1)	24.5	21.6	26.7	0.41

P-value for comparison between CAM users versus non-users using Chi-squared test or Mann–Whitney U-test. ‡From symptom onset to first rheumatologist review. §From time of diagnosis to recruitment to the Singapore Early Arthritis Cohort. ¶Either RF or ACPA positive. IDR, interquartile range; CAM, complementary and alternative medicines; ACPA, anti-citrullinated peptide antibody; DAS28, Disease Activity Score in 28 joints; mHAQ, modified Health Assessment Questionnaire; IQR, Interquartile range; RF, rheumatoid factor

Table 1: Baseline Characteristics

The CAM stratification also shows some additional differences between the groups. There are race, language, and smoking histories that are quite different. Note that the duration of symptoms (until rheumatologist review) was 13.7 weeks among non-users and 20.8 weeks among CAM users. That is, CAM users waited almost twice as long to see a specialist, compared to non-users. Not surprisingly, this meant a delay to the initiation of disease-modifying anti-rheumatic drugs (DMARDs). Figure 1 shows the overall difference between CAM users and non-users:

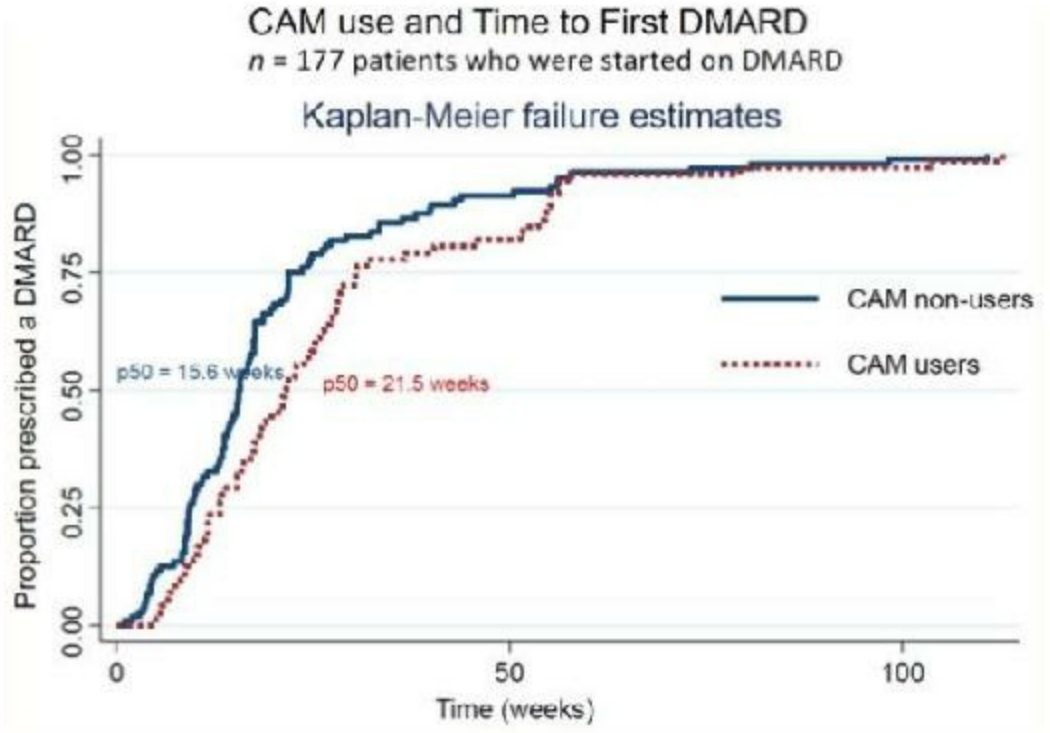


Figure 1 Kaplan–Meier plot of time to disease-modifying anti-rheumatic drugs (DMARDs) for complementary and alternative medicines (CAM) users versus non-users.

Only CAM use was significantly associated with the time to first DMARD initiation.

CAM use delays effective arthritis therapy

This small study illustrates what appears to be an unfortunate consequence of CAM use: It may be contributing to delays in seeking effective therapies, which may have additional negative consequences. While this study does not show direct harms from CAM use, the relationship between earlier therapy and positive disease outcomes is well established. The authors conclude that patient and public education programs to raise awareness about EIA, and the importance of early treatment, are essential. I would add that continuing to

raise awareness of the limitations of CAM, and the consequences of its use, need just as much awareness.

Placebo effects are largely misunderstood, even by professionals, and this leads to a lot of sloppy thinking about potential treatments. This problem has been exacerbated by the alternative medicine phenomenon.

Several decades ago, the proponents of so-called CAM promised that if only their preferred if unconventional treatments were properly tested medical science would discover how effective they are. “Effective” (or more precisely, “efficacy”) has a specific definition in medical science – it means that a treatment has been found to perform statistically significantly better than placebo in a blinded controlled trial. Several decades and thousands of studies later, the most popular CAM modalities (homeopathy, acupuncture, reiki, manipulation for medical indications, and more) have been shown to be no more effective than placebo. This means they don’t work.

Not to be deterred by reality, CAM proponents simply shifted the goal posts. Now many of them are saying that placebo effects are real, and therefore being as effective as placebo means that their treatments “work.” As part of this strategy they have promoted and amplified common myths about placebo effects. Let’s take a closer look at these myths and show why they are wrong.

Myth #1 – “The” placebo effect

The first and overriding myth about placebos is that there is one placebo effect (singular). This confusion is understandable, because scientists often refer to “the” placebo effect. However, they are referring to what is measured in the placebo arm of a clinical trial – that net effect (the difference between baseline or no treatment at all and a placebo treatment) is the placebo effect for that study.

There are multiple placebo effects contributing to that difference, however. Anything that might give the appearance of an improvement will contribute to the measured placebo effect. These placebo effects include: Regression to the mean – when symptoms flare, they are likely to return to baseline on their own. If you take any illness that fluctuates in severity, any treatment you take

when your symptoms are at their peak is likely by chance alone to be followed by a period of less intense symptoms.

Similar to this but distinct is the reality that many illnesses are self-limiting. If you have a cold, you will likely get better even if you do nothing – so anything you do will be followed by improvement. There is also bias in perceiving and reporting subjective symptoms. People want to feel better, they want to think that the treatment is working, and they may want to please the researcher or their physician. Further, researchers and doctors want their treatments to work.

There are also many possible non-specific effects just from the act of being treated. Hope can be a very positive emotion, and that alone may make people subjectively feel better. Subjects in a trial are also getting medical attention, and are likely paying more attention to their own health. They are likely to be more compliant with other treatments.

The treatment under study itself may have several components, some specific and some non-specific. Do people sometimes feel better after a session of reiki or acupuncture because they were laying down listening to music and smelling incense during the treatment? How much of a relaxation effect is at play? Does it matter if you actually stick the needles in alleged acupuncture points (the answer is no)?

Myth #2 – Placebo effects can cause healing

Because it is often believed that “the” placebo effect is one thing, that one thing is often believed to be a real mind-over-matter physical healing. There is no evidence to support this interpretation, however. In fact researchers looking for that real healing effect of placebos have only demonstrated that it doesn’t exist.

Part of the problem here is that the term “healing” is vague. It does not have a specific definition, but the implication is that biological repair is taking place. In practice researchers distinguish objective vs subjective markers of improvement. Subjective just means that the patient feels better in some way,

per their own report. They rate their own pain, for example. An objective outcome is something measurable, like blood pressure, survival, or tumor burden.

A systematic review of cancer research, for example, found that placebo interventions resulted in minor improvements in subjective symptoms, but no improvement in the cancer itself.

Placebo effects break down into several categories. One category is illusory – the misperception of improvement through regression to the mean or biased reporting. The second category is non-specific effects, such as emotional comfort from a practitioner, relaxation, or improved self-care or compliance. This third category is comprised of effects which can plausibly result from psychological interventions only. These relate mainly to stress, depression, anxiety, and the perception of pain and similar subjective symptoms. There is a mind-body connection – it's called the brain.

There is, however, no magical control of your brain over biological or physiological processes that are not networked with the brain through nerves or hormones.

Myth #3 – Animals and babies cannot have a placebo effect

This myth results from the false assumption that in order to have a placebo effect you need to believe that you are taking an active treatment. It is the belief that is causing the effect, and therefore it is a prerequisite. The logic then follows that animals and babies, who cannot know they are receiving a treatment, can therefore not have a placebo effect. Any improvement in this context, therefore, must be a physiological response to the treatment itself.

It should already be obvious, however, that these assumptions are incorrect. There are many sources of placebo effects that do not depend upon the subject knowing they are being treated, such as regression to the mean, the self-limiting nature of many ailments, and non-specific effects or benefits from simultaneous interventions.

Further, however, someone has to determine that the animal or baby has improved. That person is vulnerable to biased perception and reporting, and will also contribute to any measured effect.

This means that studies of treatments in animals or babies still need to be properly controlled, and whoever is assessing the outcome needs to be properly blinded to treatment allocation.

Myth #4 – Fanciful or alternative treatments yield better placebo effects

Desperate to salvage a role for their preferred but ineffective treatments, many alternative practitioners will argue that their real expertise is in maximizing placebo effects. OK, sure, the scientific evidence shows that my treatment is no better than placebo, but placebo effects are real, and I am very good at eliciting them. This is the “placebo medicine” gambit.

I have already debunked the first part of that claim. There is also no evidence for the second part, that alternative practitioners elicit more of a placebo effect. What the scientific evidence shows is that all interventions will produce some placebo effect, depending mainly on the outcome to be followed. The more subjective and amenable to variables such as mood, the larger the measured effect will be.

The existence of a placebo effect does not justify using inactive or pseudoscientific treatments. You can elicit the same effects from science-based interventions. Related to this is the notion of placebo effects without deception. This is certainly possible, if you include all the non-specific and statistical effects, but most patients would likely not be happy to be receiving a treatment that they were told was completely inert, just so it may bias their perception of their symptoms. All pseudoscientific treatments, even if they are justified through placebo effects, are given with a generous helping of deception, which violates patient autonomy.

The other variable that seems to be important, but requires further study, is the therapeutic relationship between practitioner and patient. Having a

positive relationship may enhance the measured placebo effect, but that may be just another measure of bias.

In any case, anything useful about placebo effects can be had with a positive therapeutic relationship, using science-based interventions, and following the ethical requirements of informed consent and patient autonomy.

Read the label. It doesn’t list any health benefits. It says harmful or fatal if swallowed.

Turpentine is a solvent and a poison, but some people are drinking it as a medicine.

Scott Gavura wrote about it

2 years ago and concluded, “There’s no reason to consume turpentine and multiple reasons to avoid it completely, with the primary reason being that

it’s a poison

.”

Scott’s article mentioned an MD who advocates turpentine to cure the fake illness chronic *Candida*, and who had been stripped of her license. That MD was Jennifer Daniels. It would be bad enough if she only recommended it for Candida, but she also claims to have discovered that turpentine is the Fountain of Youth, a miracle cure that reverses disease and aging and is good for pretty much whatever ails you. That’s ludicrous.

The facts

The *Natural Medicines Comprehensive Database* (which I consider to be the most reliable source) says, “There is insufficient reliable information” to evaluate its effectiveness for any medical use. It rates turpentine as “possibly safe” when used topically and appropriately, “possibly unsafe” when applied to large areas of skin, and “likely unsafe” when used orally for medicinal purposes; 2 ml/kg is toxic, and 120-180 ml is potentially lethal in adults.

The *NMCD* goes on to explain that turpentine is a central nervous system depressant, a pulmonary aspiration hazard, a skin irritant, and might cause abortions. It can have a decongestant effect when inhaled. Many adverse reactions are reported from ingestion, including headache, insomnia, coughing, vomiting, hematuria, albuminuria, urinary tract inflammation, coma, and death. Inhalation can cause inflammation and bronchial spasms. Applying it to the skin can lead to kidney and central nervous system damage.

A drug information website has an extensive monograph on turpentine. It says, “Turpentine has been used experimentally in a bath for the treatment of disseminated sclerosis and sexual dysfunction. It also has been studied for its antibacterial activity and inhibition of osteoclast activity. Turpentine is utilized in experimental models of inflammation to induce a systemic inflammatory immune response in animals.” It warns against using it during pregnancy and lactation, stresses that it is highly toxic (fatal poisonings have occurred with ingestion of as little as 15 mL, just 3 teaspoonsful) and has caused skin tumors in animals. It provides a bibliography with pertinent citations.

The discovery

Jennifer Daniels tells the story of her discovery in a radio interview. She asked her African-American patients if their slave ancestors had a miracle cure that cured everything and was cheap; several of them mentioned turpentine and sugar. So she tried it for herself. She put turpentine on 3 sugar cubes and washed them down. Right after ingesting it, she says:

> I think my IQ went up like 50 points, I could just feel it, all this mental energy and understanding and clarity, just like when I was 10 years old, everything was very clear and focused. I said WOW what a feeling. I did some math problems, I said this is pretty good.

She had heard that turpentine could cause seizures, so she figured out the maximum safe dose by stopping at a dose where she felt a little twitch, “even softer than a twitch.” Then she gave it to her mother, who began to feel better *in less than a minute* (!). It relieved pains that her mother had had for 30 years. Other family members served as guinea pigs and appeared to benefit. So with no further ado, Daniels started using it on all her patients.

The published evidence she relies on

In that same interview, Daniels talks about a review article from France with 100 references that supposedly support the use of turpentine for parasites,

cancer cells, pathogenic bacteria, fungus, yeast, rheumatism, MRSA, sciatica, nephritis, constipation, increasing membrane permeability, etc. It doesn't say what she thinks it says.

Using turpentine: The treatment plan

First you have to hydrate. Then you have to have three bowel movements a day, which you can supposedly achieve by taking her Vitality Capsules, which (unlike everything else on earth) contain "no chemicals." If you don't have three bowel movements a day, the *Candida* can't get out of your body and will "shift through your left hip to your right hip, your right hip to your stomach, and your stomach to your shoulder. It's gonna play musical chairs all over your body." Then you have to follow her diet instructions (organic, no GMOs, no "dead food," and many more restrictions). Only then can you do the Candida Cleanse.

She says you must avoid steroids, antibiotics, and chemotherapy, because they prevent cell repair and yeast will move in to eat up the dead cells. She advises patients to stop all their medications if they can (potentially dangerous advice).

She says in the last days of her practice, she stopped using antibiotics. She would not admit seriously ill patients with pneumonia to the hospital, but would dose them with turpentine and send them home. She thinks children with high fevers will recover in less than 24 hours if given turpentine. When her daughter badly injured her ankle, she gave her a teaspoon of turpentine and ¼ cup of castor oil. "She drank it, she pooped, all the pain was gone."

More strange and unsupported claims

- "Liver time is 1-3 AM; lung time is 3-5 AM."
- "Vitality Capsules clean out the bile ducts and the gall bladder system as well as the small intestine, large intestine, and it also promotes circulation."
- Children should start getting turpentine in castor oil when they reach 30

pounds, to prevent *Candida* and parasites.
- You should keep taking turpentine at least once a month for the rest of your life.
- Turpentine improves eyesight; users were able to throw away their reading glasses.
- "if I want thicker hair and less gray hair, then I'm gonna use minerals, small willow flower, and shou wu."
- Turpentine improves diabetes by healing the pancreas. It will allow Type I diabetics to lower their insulin dose.
- It resolves tinnitus.

To her credit, she does get a few things right; for instance, she realizes that "rope worms" are not actually worms. On the other hand, she is anti-vaccine: "There is no vaccine or injection Dr. Daniels recommends."

A spy troll is shocked

David McAfee infiltrated the closed 640-member Facebook group "Parasites cause all disease – turpentine cure" and was appalled at what he found. People were seeking support for the horrible side effects they were experiencing from turpentine. They were hoping to cure everything from scabies to herpes to "electromagnetic hypersensitivity."

One woman who was using turpentine and castor oil complained that when she did enemas a lot of red liquid came out. Another list member told her *not to worry* because it was probably just old and damaged intestine wall coming out!

Some of the comments following McAfee's exposé article were amusing:

- "Sometimes you just roll your eyes, mutter darwinism to yourself and move on."
- "I'm a believer in alternative medicine-trust me, these people aren't into alternative, they are idiots. Anyone with half a brain knows not to ingest a solvent. Dear god, where does this stupidity come from?"
- "There is in my family a story about the medical use of turpentine. It

dates from the time of my grand-father or great-grand-father. It was suggested as a topical treatment for hemorrhoids. It was not suggested in good faith. Folks could have a very crude sense of humor in those days too."

What about science?

Daniels is a graduate of Harvard and of the University of Pennsylvania School of Medicine. Surely she learned about science at those prestigious Ivy League schools. One can only wonder how she came to disregard science and go her own way. She says she reads research studies but does not believe them: "I'm not much of a fan of research because every research project I've been involved with, I've been asked to falsify data." That certainly is an unusual experience, and I can't help but wonder if she reported the fraud/misconduct. She could have had a great career as a whistleblower.

Her words and actions show that she does not think like a scientist. Here are just a few revelations from her *Confidential Underground Report: Top Secret; The Candida Cleanser*.

- She assumed the existence of some folk remedy that was a miracle cure that would cure everything. Considering all the many different causes of different illnesses, this is not a reasonable assumption.
- She experimented on herself and assumed that the dose that seemed to work for her would work for everyone. If that were true, drug companies could dispense with phase 2 trials and just give the drug to one person.
- She describes immediate results, too soon for a medication to be absorbed and have any effect; she doesn't recognize that this is almost certainly a placebo response.
- She doesn't put her belief that turpentine is effective to any kind of test.
- She wonders how long you could take it every day without experiencing side effects. So she takes it daily for a week, notices no adverse effects, and says "I decided that was long enough for the purposes of science." Wow! Wouldn't Big Pharma love to hear that all they needed to do to demonstrate the safety of their drugs to the FDA was to have one person take a drug for a week and say they hadn't noticed any symptoms?

- Without any further testing, she immediately moves on to treating other people with turpentine.
- She makes all kinds of claims unsupported by any evidence, for instance:
    - Breads, meats and dairy are all full of parasites.
    - “Trail mix is an abomination and has destroyed the health of many a health nut.”
    - “It has been *my observation* [emphasis added] that one should be having at least three bowel movements a day.”
    - “There is no medication that turpentine interacts with.”
    - “Censorship is so severe that it is difficult to find information on turpentine in print.”
- She makes dangerous recommendations: laxatives and daily enemas, stopping prescription medications, avoiding immunizations, and many more.

No longer practicing, but…

On her website, it says “Dr. Daniels is a former medical doctor who had her medical license suspended due to not prescribing enough drugs and truly healing her patients.” I don’t believe that; no medical board has ever suspended a doctor’s license for healing their patients or for “not prescribing enough drugs.” According to the New York medical board website, she surrendered her license less than 6 years after it was granted. Apparently she was uncooperative, refusing to share her patient records with the board, and from her comments online it seems she was deliberately trying to hide her many questionable treatment methods from the authorities. By voluntarily surrendering her license, she avoided any further investigation or board actions.

No longer able to practice medicine, Daniels has moved to Panama, where she is making a living producing books, radio shows, CDs, and videos; selling supplements; and advising clients as a health coach. She is available for “Holistic Mentoring Consultations;” you can schedule a consultation online and will be able to speak to the doctor directly. What she is doing may not be illegal, but she is still in a position to harm people with bad advice.

Conclusion: not recommended

Not only is turpentine not the Fountain of Youth, it has not been proven effective for any health condition. Jennifer Daniels is not a reliable source of health information. She fails to understand the need for scientific testing, relies on testimonials and beliefs instead of facts, and demonstrates poor judgment. She makes claims that are bald assertions not supported by any evidence. She is offering dangerous advice, not just about turpentine but about vaccines and other things.

I write about alternative cancer treatments a lot, in particular the lack of evidence for such practices, many of which are at best pseudoscientific and at worst pure mystical nonsense. The reason, of course, is simple. I'm a breast cancer surgeon, and I hate seeing people who might be saved from death due to cancer falling prey to treatments that demonstrably lessen their chances of survival, either by leading patients to reject effective treatment in favor of ineffective or even harmful treatments or, at the very least, to delay effective treatment until the patient realizes that the quackery chosen isn't preventing the growth and spread of his or her tumor. This can sometimes take a long time. I've seen women with breast cancer whose breasts were basically eaten away until there was nothing left but an ulcerated mass on their chest—more than that, a bleeding, rotting, malodorous ulcerated mass. Yes, it's an ugly picture, but I've seen it all too many times.

These sorts of cases are less common, though. Fortunately, relatively few are the women who reject conventional medicine altogether. Indeed, most women will accept surgery of some sort or another, either a lumpectomy or a mastectomy. Sometimes, they undergo an excisional biopsy, not realizing that that for smaller tumors an excisional biopsy can remove the whole tumor and in some cases be curative. No, far more common is the case where a woman accepts surgery but then refuses chemotherapy, hormonal therapy, and/or radiation, either altogether or in favor of some form of quackery. In doing so, such women, whether they simply refuse adjuvant therapy altogether for whatever reason or go beyond that and fall prey to quackery, fail to maximize their chances of surviving their breast cancer, sometimes by quite a bit, and that is something to be concerned about.

Indeed, these sorts of cases were one of the very first topics I ever wrote about on this blog and have remained a staple of the blog ever since, whether I was discussing Suzanne Somers, who had surgery and radiation but apparently refused Tamoxifen for her breast cancer and then later had what she thought to be a recurrence that almost certainly wasn't, other alternative breast cancer cure testimonials (like this one or this one), or even testimonials for other cancers where chemotherapy and/or radiation are used in addition to surgery.

The reason such alternative cancer cure testimonials are compelling is that most people don't understand the difference between the primary treatment for breast cancer and an adjuvant treatment. In the case of breast cancer, for instance (and colorectal cancer as well, among other solid tumors), surgery is the primary treatment and can be curative by itself. What chemotherapy, radiation therapy, and hormonal therapy can add to the treatment of, for example, breast cancer is to decrease the chance of its recurring after successful surgical excision, whether by mastectomy or lumpectomy. All a breast cancer patient does in refusing radiation therapy after successful breast conserving surgery is to accept a risk of recurrence in the breast of 30-40% instead of 5-8%. All a woman does by refusing recommended chemotherapy after surgery is to refuse a relative decrease in their risk of dying of a recurrence of breast cancer by 25-30%, a benefit that is, in absolute terms, much greater for more advanced but still curable breast cancers. However, many of these women who turn down adjuvant therapy in favor of quackery will still survive, thanks to the surgery, and the ones whose cancers recur rapidly disappear from the alternative cancer cure industry PR machine, never to be seen again.

Because adjuvant chemotherapy, targeted therapies, and hormonal therapies have contributed to a decline in mortality from breast cancer of 39% since 1989, it is important to determine why women refuse these treatments and fail to optimize their chances of long term survival. To a lesser, but still important extent, it's important to try to understand what motivates women to turn down effective adjuvant therapy, as that is the first step in developing strategies to persuade them. Recently, there was a relatively large study that addressed just this question.

Patient refusal of adjuvant therapy: A question of trust?

Earlier this month a number of news stories and press releases appeared about a study published in late September by investigators at Johns Hopkins Bloomberg School of Public Health, Columbia University, and Massachusetts General Hospital looking at trust—or, more specifically, a

lack of trust—as a key motivator in women refusing adjuvant therapy recommendations and opting for discordant care; i.e., care that doesn't conform to evidence-based care recommended by the patient's physicians. It's an issue that hasn't been studied as well as it should be, as the authors, Lorraine T. Dean, Shadiya L. Moss, Anne Marie McCarthy, and Katrina Armstrong point out in the introduction:

> Relatively little is currently known about the relationship between healthcare system distrust and cancer treatment. A previous study of distrust and adjuvant cancer treatment (3) found that distrust in medical institutions was associated with increased risk of not initiating adjuvant treatment in a sample of 258 early stage (Stage I and II) breast cancer patients from one urban area. However, that study did not include the following in their analysis: which treatments were recommended by the physician, the extent to which physician distrust mediated the relationship between healthcare system distrust and cancer treatment, and an assessment of those who may have initiated treatment but did not fully adhere to the treatment plan. Other studies of distrust among women with a history of breast cancer have focused on healthcare system distrust and: mental health or psychosocial outcomes (13), quality of care (14,15), greater emotional, physical, financial, and sexual problems after treatment (16), less comfort with the use of de-identified information from medical records for research (17), less endorsement of the necessity of adjuvant chemotherapy (18); and provider distrust and quality of care (19).
>
> The current study was designed to answer two related questions: Is healthcare system distrust associated with whether or not patients follow their physician's recommendations for adjuvant treatment after breast cancer; and does physician trust mediate the relationship between healthcare system distrust and receipt of adjuvant treatment? It expands on prior work by including a large population based sample in two different US states, Pennsylvania and Florida, based on physician recommendations for several adjuvant treatments with explicit testing of the potential mediating role of physician distrust, and assesses patients who did not complete the full treatment plan. To our knowledge, it is the largest study of healthcare system distrust among women with a history

of breast cancer and adds innovation of recruiting through a cancer registry to survey participants about healthcare system distrust.

To this end, the authors used Pennsylvania and Florida cancer registries, using data from a population from a study originally intended to assess the differences in breast cancer women associated with race. The inclusion criteria for the study included localized invasive breast cancer, age under 65 at the time of diagnosis, residency in either Pennsylvania or Florida at the time of diagnosis, and diagnosis between January 1, 2005 and December 31, 2007. Exclusion criteria included patients over 65, cognitive impairment, inability to speak English or Spanish, and metastatic disease at presentation. The overall response rate was very good for surveys of this type, 61%.

For purposes of the survey, cancer treatment discordance was defined as any difference in treatment that a patient reported receiving compared to the treatment the patient reported as having been recommended to her by the treating surgeon and/or oncologist. Now, I know what you're probably thinking: Is this accurate enough? It turns out that simple self-reporting like this is 90% accurate, particularly for yes/no questions about different kinds of therapy. Since the adjuvant therapies used after surgery for breast cancer include radiation therapy, chemotherapy, and hormonal therapy, the authors constructed a combined measure of treatment discordance based on how many of the three therapies patients accepted or declined. Of course, if a particular adjuvant therapy was not recommended for a patient, then not undergoing it couldn't be considered discordant. (For example, depending on the specific characteristics of the tumor, not all breast cancer patients are offered chemotherapy or hormonal therapy; and most patients—but by no means anywhere near all patients—undergoing mastectomy don't require radiation therapy.)

Patients were also assessed for their level of trust in the health care system and their physicians. Trust in the health care system was assessed using the 9-item Health Care System Distrust scale which measures of domains of values and competence distrust on a 5-point agreement scale (1 = strongly disagree, 5 = strongly agree), producing a score ranging from 9 to 45. The authors report that this measure has "acceptable construct validity and high internal consistency (α=0.84 in the current sample)." To measure trust in patients'

physicians, researchers used the 7-item Trust in Physician Scale, which uses a 7- point agreement scale (1=strongly disagree, 7=strongly agree), to produce a score ranging from 7 to 49. Information was also requested on socio-demographic factors, such as age, race, ethnicity, income, education, marital status, employment status, health insurance status, and state of residence at the time of diagnosis. They also went to the cancer registry databases to verify clinical treatment factors, such as stage, surgical removal of cancer, and recurrence.

So what did the authors find? There were 2,754 women included in the final analytic sample, of which 69.8% (n=1,922) reported always receiving the cancer treatments their surgeon or oncologist recommended, and 30.2% (n=832) reported not pursing at least one recommended treatment. I must admit that I was rather surprised that the percentage of discordant cases was so high, but maybe I shouldn't have been. In any case, in the total sample, 10% declined radiation treatment; 11% declined chemotherapy; and 18% declined hormone therapy. (Note that some women turned down more than one modality.) Looking at the numbers, though, some of this does appear to jibe with my clinical experience, in that I've encountered more women who have turned down hormonal therapy than who have turned down others. The reason is probably that hormonal therapy, although only a pill as opposed to chemotherapy, is administered for five or, in more recent recommendations, as many as ten years, and women who can tolerate the much more severe side effects of chemotherapy only have to endure them for a few months, whereas they have a harder time dealing with the side effects of Tamoxifen or aromatase inhibitors for five or ten years.

The authors found:

> The mean healthcare system distrust score was 28 (SD=3; range 9-40), while the mean physician trust score was 29 (SD=4; range 9-35). Bivariate models suggested that greater healthcare system distrust was significantly associated with older age, being Black, having attended some college, and being employed, while less healthcare system distrust was associated with greater physician trust, being married, having health insurance, and living in Pennsylvania. Only marital status, being employed, physician trust, and living in Pennsylvania were still

> associated with distrust in a fully adjusted model (Table 2). Participants reporting treatment discordance were significantly in the top tertile of healthcare system distrust (p=0.003) as well as being more likely to be older (p=0.04), be diagnosed at Stage 1 (p<0.001), and live in Florida (p=0.003). In contrast, physician trust was not a significant predictor of discordance (p=0.49). Although healthcare system distrust was significantly associated with discordance (p=0.03) and physician trust (p<0.001) (Figure 1), a mediation analysis (Table 3: Models A & B) suggested that physician trust was not a mediator of the relationship between healthcare system distrust and treatment discordance (total indirect OR=1.00 [1.00,1.01]). Thus, rather than treat physician trust as a mediator, it was included in the final model as a covariate.

Basically, those in the group with the highest distrust of the healthcare system were 22% more likely to have refused or fail to complete one or more adjuvant treatments. In other words, patients who had the most distrust of the healthcare system were more likely to be discordant in their adjuvant therapy; i.e., to refuse or fail to complete a recommended course of therapy. Interestingly, in this study, neither race nor socioeconomic status were significant drivers of discordance in this study, which is a good thing because these are not modifiable factors.

Physician trust versus a more generalized distrust

How could these results be? The authors note that attempts to increase physician trust as a strategy to reduce mistrust in the healthcare system have had results ranging from zero to very modest, which makes sense if patients view the two issues as separate. I like to make an analogy to Congress. Voters routinely express extreme distrust of Congress, but most voters actually like their own representative. Similarly, it’s not hard to envision how most patients might actually like and trust their own doctors, while simultaneously having a great deal of mistrust for the health care system as a whole.

As the authors note:

> The limited research to date about reducing distrust in healthcare has focused on increasing trust in physicians with null to modest (30-32) results. However, given that the relationship between distrust and treatment discordance was not mediated by physician trust, these results suggest that addressing healthcare system distrust may be an important and distinct effort from strategies focused on lack of physician trust. Rather than playing a mediating role, patients may view physician trust as independent of their trust in the healthcare system as an institution; that is, even if patients distrust the healthcare system, they may still have trust in their personal physicians. Patients may be able to exercise greater choice in physicians, but may not have the same breadth of choices in using the healthcare system. Addressing healthcare system distrust might be informed by strategies that have addressed distrust in other types of institutions, such as corporations (29), according to the values and competence domains. For example, addressing the subdomain of values might be achieved through expanded access to adjuvant care, while addressing the subdomain of competence might be achieved through expanded access to health professionals while deciding to start or continue adjuvant treatment. Of course, any intervention to reduce healthcare system distrust would first need to be tested before implementing wide-scale changes.

The authors also note a rather interesting potential wrinkle to the problem of patients refusing adjuvant therapy, namely that greater cancer treatment discordance will always lead to worse healthcare outcomes, noting that it is "possible that distrust could perform a function in course-correcting treatment that is overprescribed or too aggressive" and that such distrust "might lead to treatment discordance that was ultimately beneficial rather than detrimental." When I read that part, I had to concede that it is possible that this could be true, but unlikely. My own experience in quality improvement initiatives means that I've become fairly familiar with the literature on the relationship between concordance with evidence-based treatment guidelines and patient outcomes. That literature generally supports that better concordance results in better outcomes. So I couldn't help but smile as I continued to read and noted that, consistent with that, the authors examined a separate model of treatment discordance, looking at its association with cancer recurrence, and found that the model suggested a 40% increased risk of cancer recurrence for patients

who reported treatment discordance, after adjusting for adjusting for healthcare system and physician distrust and relevant racial and socioeconomic factors. This result suggests that that discordance due to distrust may lead to poorer health outcomes.

So what to do?

The authors note that improving trust in the healthcare system will require more than just trying to build trust in patients' physicians, noting:

> "If ordinary businesses can learn to increase trust in their brands, why not the same with health care institutions?" Dean says.

This is, of course, much easier said than done, and this study doesn't address how increasing trust in the healthcare system might be accomplished. That will be the task for the future. It is an important task, though, because, although I might be extrapolating more than the evidence supports (yet), I'd bet that such strategies could also help address the antivaccine movement as well. In any case, if we want to save as many savable lives of people with cancer as possible, this is where the healthcare system needs to pay more attention, and a salutary side effect would also be to make alternative cancer cure testimonials less common.

Science Based Medicine

周五, 24 11月 2017

Science Based Medicine

[周五, 24 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Happy Thanksgiving!** [周四, 23 11月 14:00]
  Happy Thanksgiving to our American readers, and to everyone else- have a great Thursday in November!
- **New Tools Against Antibiotic Resistance** [周三, 22 11月 20:24]
  Antibiotic resistance is a serious problem that may lead to a post-antibiotic era. However, there are potential solutions that deserve research priority.
- **The Death of Expertise** [周二, 21 11月 16:00]
  In Tom Nichols' new book, The Death of Expertise, he explains how a misguided intellectual egalitarianism is harming our ability to assess the truth and solve problems, and discusses some of the responsible factors and possible long-term consequences.
- **What is “integrative oncology”? Even the Society for Integrative Oncology doesn’t seem to know for sure** [周一, 20 11月 16:25]
  Last week, the Society for Integrative Oncology published an article attempting to define what "integrative oncology" is. The definition, when it isn't totally vague, ignores the pseudoscience at the heart of integrative oncology and medicine.

Happy Thanksgiving! - Science-Based Medicine

We celebrate Thanksgiving today in the U.S. and SBM is taking the day off. We are thankful for all of our readers and commenters and wish you a Happy Thanksgiving.

New Tools Against Antibiotic Resistance - Science-Based Medicine

Scientists are often placed in the role of Cassandra – because of their expertise and knowledge they may see potential serious problems on the horizon, but may also find it challenging to convince the general public. Sometimes they are working uphill against vested interests. Often scientists will warn against possible problems that they then work to prevent, and when successful it seems like their warnings were unwarranted. Or they may simply be calling for preparation for a possible event, like an epidemic, that still probably won't occur but you should be prepared ahead of time in case it does.

Also, as science communicators we don't want to overhype potential problems. It can be a delicate balance. With all that in mind, it is probably difficult to overstate the potential risk of antibiotic resistance. This is one of those looming issues that I genuinely worry about, but gets too little attention, if anything, in the media. It is also a manageable problem – there are things we can do to mitigate antibiotic resistance, if we take the issue seriously enough.

The World Health Organization summarizes the problem in stark terms:

> Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. A growing list of infections – such as pneumonia, tuberculosis, blood poisoning, gonorrhoea, and foodborne diseases – are becoming harder, and sometimes impossible, to treat as antibiotics become less effective.
>
> Where antibiotics can be bought for human or animal use without a prescription, the emergence and spread of resistance is made worse. Similarly, in countries without standard treatment guidelines, antibiotics are often over-prescribed by health workers and veterinarians and over-

> used by the public.
>
> Without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill.

I don't think they are overstating the problem.

The cause of antibiotic resistance is fairly easy to understand. Bacteria reproduce very quickly in large numbers. When someone takes an antibiotic, that provides a selective pressure towards resistance. If any individual bacterium has a gene which provides resistance to the mechanism of that antibiotic it will tend to survive the treatment and then reproduce a new generation of resistant bacteria.

Bacteria also have the ability to swap genes, so that are not just passed from parent to offspring, but horizontally to other bacteria in a process called conjugation. Bacteria may contain plasmids, which are loops of DNA. Those plasmids can be copied from one bacterium to another. A plasmid may contain one or even multiple genes that confer resistance – and so in one conjugation event a bacterium may receive resistance to multiple antibiotics.

The existence of bacterial plasmids with multiple resistant genes is a problem, because if they are exposed to one of the antibiotics to which they are resistant, that will favor the proliferation of the bacteria with plasmids that confer multiple resistance.

There is one potential bright spot in all this. Genes that confer antibiotic resistance often come at a price. They may make it more difficult for the bacteria to reproduce, or force them to expend more energy. That is why they don't have the feature in the first place. The selective pressure of antibiotics is necessary to favor the more costly feature. The hope is that in the absence of selective pressure from antibiotic, the resistant features will tend to fade away.

However, a new study suggests that this may not always be the case. Researchers looked at costly antibiotic resistance features in various strains of *E. coli*. They followed them for over a month and found that strains were able to maintain even costly antibiotic resistance in the absence of antibiotics if

they contained plasmids. The key is the conjugation rate – how frequently do bacteria exchange plasmids? The research found that, at least in these strains, the rate was high enough to maintain antibiotic resistance even in the absence of antibiotics.

This research suggests that limiting antibiotic use may not be enough to reverse existing antibiotic resistance. Of course, limiting use is essential to slowing the development and spread of resistance. This is the primary mechanism by which the medical community is trying to combat resistance, but even here we are not doing enough. Antibiotics are still massively overprescribed. Some countries allow for over-the-counter antibiotic use, and it is common for the public to take them for viral illnesses. Antibiotics are also heavily used in the farming industry.

Even if we achieved our goal to properly limit antibiotic use, and educated practitioners to optimally prescribe antibiotics, the current research suggests this may not be enough to reverse some types of resistance. However, the same research suggests there may be more active interventions that will.

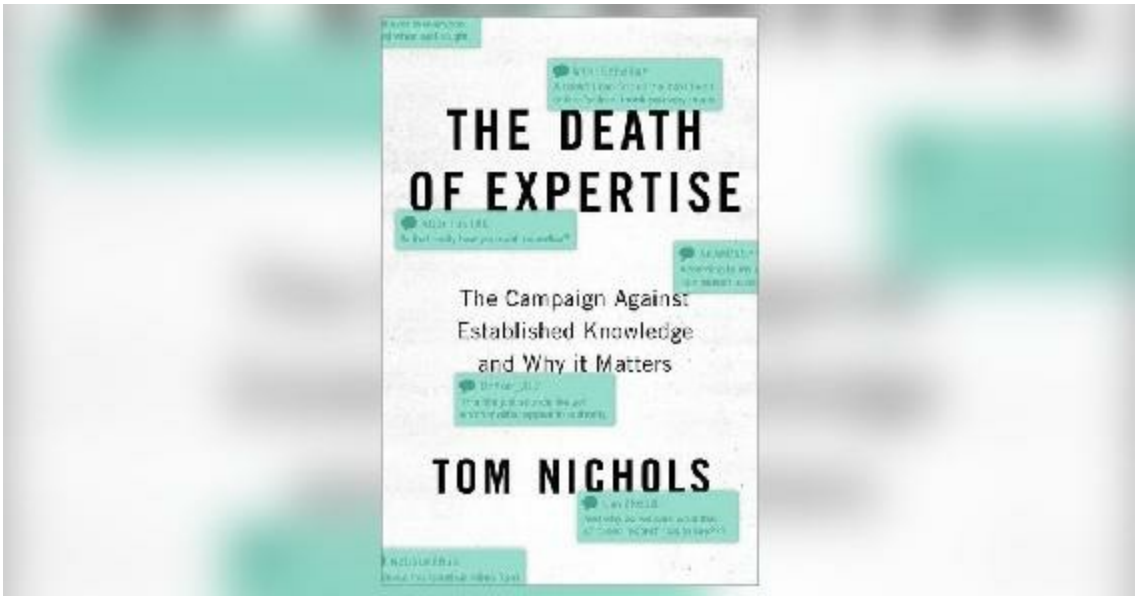
There are potential drugs that can limit conjugation or induce bacteria to lose their plasmids. For example, a 2015 study identified features of synthetic fatty acids that were effective conjugation inhibitors. This would limit the horizontal spread of plasmids among bacteria, and therefore limit the spread of resistance.

Another approach is to prevent plasmid replication. Researchers are looking at ways to exploit the existing compatibility system in bacteria toward this end. Since bacteria are so promiscuous with their genes, they need mechanisms to know when plasmids are incompatible with their other DNA. You could essentially trick a bacterium into thinking its plasmid is incompatible, and therefore when the bacteria reproduces it will not replicate the plasmid. The plasmid will therefore be lost to the next generation. These treatments would not just limit the spread of resistance, but cause a population of bacteria to lose their resistance.

What all of this research suggests is that we should not only be researching novel antibiotic mechanisms, we should be investing in research into drugs that inhibit plasmid conjugation and induce plasmid loss. These treatments

can reduce the spread of resistance, and even potentially reverse resistance. Such treatments could be given alongside antibiotic regimens, or used in farming or similar contexts to limit the development of resistance.

My hope is that this type of research will eventually lead to a situation in which all those scientists and science-communicators who warned about the coming post-antibiotic era will look like Cassandras. Rather than getting the credit for identifying and then preventing a major problem, people will either forget them or falsely think the warnings were overhyped to begin with. But I will take that fate if it means avoiding a post-antibiotic era.



Tom Nichols' new book *The Death of Expertise: The Campaign against Established Knowledge and Why It Matters* has direct relevance to many of the issues we are constantly grappling with on Science-Based Medicine. In a democracy, everyone has equal rights. Many people think that means they are equal to experts in knowledge and judgment. In medicine, as in most other areas of public discourse, we are faced with angry laymen who denounce intellectual achievement and scientific knowledge and who distrust experts.

People find ways to reject the evidence when it conflicts with their values and beliefs. When scientific evidence challenges their views, they doubt the science rather than themselves. New examples of this phenomenon can be found every day in the news and in the comments sections of the Science-Based Medicine blog, and trying to set those people straight has proven a mostly futile exercise.

The failure of higher education

Students have become consumers. High school seniors tour college campuses with their parents looking for the one with the best dorms, cafeteria food, and extra-curricular activities, rather than the one that will challenge them and provide the best education. Nichols says colleges are not only failing to

provide to their students the basic knowledge and skills that form expertise, they are failing to provide the ability to *recognize* expertise and to engage productively with experts and other professionals in daily life. They are not being taught "critical thinking: the ability to examine new information and competing ideas dispassionately, logically, and without emotional or personal preconceptions."

He says students are being treated as *clients* rather than students. "Many colleges have become hostages to students who demand that their feelings override every other consideration." Students "explode over imagined slights" and "build about themselves fortresses that no future teacher, expert, or intellectual will ever be able to breach." They want to be protected from ideas or language they find unpleasant. They are "demanding to run the school while at the same time insisting that they be treated as children."

The internet

The Internet has provided people with an unprecedented abundance of information, but all too often it gives them the illusion of knowledge, encouraging them to believe they know as much as experts. They hear what they want to hear, and live in a bubble community of people with similar beliefs.

> People do not come to the Internet so that their bad information can be corrected or their cherished theories disproven. Rather, they ask the electronic oracle to confirm them in their ignorance.

Nichols says,

> …not only is the Internet making many of us dumber, it's making us meaner: alone behind their keyboards, people argue rather than discuss, and insult rather than listen.

People "power browse" rather than actually reading. We see this all the time on Science-Based Medicine, where commenters criticize an article they obviously have not read carefully or understood. Sometimes I suspect they may just have read the title and seized the opportunity to jump on their

particular soap box.

Journalism

The dissemination of “fake news” is an ever more common reality. Most people are very poor at evaluating the reliability of a news source and the truth of what is reported. When a layperson challenges an expert by saying “I read it in the paper” or “I saw it on the news,” it may mean only “I saw something from a source I happen to like and it told me something I wanted to hear.” At that point, discussion has nowhere to go; the real issue is replaced by the effort to untangle which piece of misinformation is driving the conversation. People are constantly barraged with facts and knowledge, but they have become more resistant to facts and knowledge. How did we arrive at this state of affairs? Nichols says, “technology collided with capitalism and gave people what they wanted, even when it wasn’t good for them.”

When the experts are wrong

In our increasingly complex world, we can’t possibly know everything; we have no choice but to trust experts. But sometimes experts get things wrong. Most of the time, their errors are identified and counteracted by other experts. This works so well most of the time that we are shocked when we read about an exception; for instance, when we learn that an incompetent doctor has killed a patient or that a researcher has falsified data. Laymen get exasperated when science “changes its mind,” for instance telling the public eggs are bad for them and then saying no, they’re OK to eat. But that’s not a failure of science, but rather an example of how science works so well in the long run by following the evidence and discarding false provisional conclusions as the evidence improves.

When experts’ errors, fraud, and misconduct are revealed, a layperson naturally asks how we can trust studies in any field. Nichols says that’s the wrong question to ask, because “rarely does a single study make or break a subject.” Single studies are often wrong, but the aggregate of all research is

trustworthy. The scientific enterprise as a whole is self-correcting and leads to a consensus of experts that approaches the truth as much as is humanly possible.

The impact on government

Science is essential to rational public policy; it can't make the decisions, but it provides reality-based information that can guide the decision-makers. Nichols says we have a President who sneers at experts and whose election was "one of the loudest trumpets announcing the impending death of expertise." He argues that Trump's campaign was "a one-man campaign against established knowledge." He provides examples: Trump's "birther" campaign against Obama, his quoting the *National Enquirer* approvingly as a source of news. Nichols says rather than being ashamed of his lack of knowledge, Trump exulted in it. "Worse, voters not only didn't care that Trump is ignorant or wrong, they likely were unable to recognize his ignorance or errors." He says the Dunning-Kruger effect was at work. It's not just the things we don't know (one in five adults think the sun revolves around the Earth), but the smug conviction that we don't need to know such things in the first place.

He warns,

> The relationship between experts and citizens, like almost all relationships in a democracy, is built on trust. When that trust collapses, experts and laypeople become warring factions. And when that happens, democracy itself can enter a death spiral that presents an immediate danger of decay either into rule by the mob or toward elitist technocracy. Both are authoritarian outcomes, and both threaten the United States today.

Conclusion: Hope for the future?

He says Americans no longer understand that democracy only means political equality. They tend to think democracy is a state of actual equality in which

everyone’s opinion is as good as everyone else’s, on every subject. Feelings are more important than facts: if people *think* vaccines are harmful, it is considered “undemocratic” and “elitist” to contradict them.

He sees signs of hope. Experts are rebelling. He cites an angry doctor who asked patients, “Do you remember when you got polio? No, you don’t, because your parents got you [expletive] vaccinated.” He points out that without democracy and secular tolerance, nations have fallen prey to ideological, religious and populist attacks and have suffered terrible fates. But he ends on a hopeful note. He has faith in the American system and hopes that it will eventually establish new ground rules for productive engagement between the educated elite and the society they serve. I hope so too!

Longtime readers of Science-Based Medicine and my not-so-secret other blog probably know that I'm not a fan of the specialty known as "integrative oncology." My reasons are basically the same as the reasons why I detest "integrative medicine," only subspecialized (like oncology), so to speak. Basically, "integrative medicine" integrates quackery with medicine, and integrative oncology integrates quackery into oncology. Given that I'm a cancer surgeon, I tend to take an even dimmer view of the latter than of the former, if only because it hits me where I live. For instance, when "integrative oncology" starts appearing at symposia at major cancer meetings, with nary a skeptical word showing up in the panel discussions afterwards, I despair. Unfortunately, the credulity that allows modalities like acupuncture, reiki, intravenous high dose vitamin C, and various other unproven and disproven treatments to find their way into academic medical centers has spawned a related phenomenon, quackademic medicine, or the study and acceptance of quackery in academic medical centers. The most prominent example of this latter phenomenon occurred in September, when the University of California at Irvine accepted a $200 million gift from Susan and Henry Samueli to build and staff a college devoted to integrating quackery into its component departments and promoting "integrative medicine." Never mind the homeopathy.

Integrative oncology has become so established that it has its own professional society, the Society for Integrative Oncology (SIO). Not surprisingly, I'm not a fan of SIO, and SIO isn't exactly a fan of me, either. I've related the story before, but let's just say that the SIO was not pleased at my 2014 article in *Nature Reviews Cancer* discussing how integrative oncology is not evidence-based (to say the least), given its embrace of naturopathy. In brief, the SIO didn't like how much verbiage I devoted to homeopathy in the article, pointing out that homeopathy is indeed not evidence-based and that no integrative oncologist worth his or her salt would ever use it. I pointed out that you can't have naturopathy without homeopathy. After that, I asked how the SIO can reconcile its quite correct rejection of homeopathy with the fact that it admits naturopaths as members, that two of its recent past presidents have even been naturopaths, and that you can't have naturopathy without homeopathy. It's baked into the naturopathic

curriculum, and it's part of the naturopathic licensing exam. Moreover, one of the naturopaths who co-authored the SIO's breast cancer clinical guidelines ran a clinical trial on homeopathy. That same naturopath, by the way, was a co-author on the update to those guidelines published just this year. The SIO never learns.

This time around, though, the reason the SIO caught my attention was this Tweet by Dr. Sheila Garland, re-Tweeted by Dr. Jun J. Mao, immediate past president of the SIO (but still president at the time he re-Tweeted this):

> The beginning of a new era in evidence-informed integrative oncology research/practice that puts the person first #SIO2017 @Integrativeonc https://t.co/cmAMrCujjy
>
> — Dr. Sheila Garland (@SNGarlandPhD) November 13, 2017

This Tweet touted what is now the "official" definition" of "integrative oncology" recently laid down by the SIO:

> Official definition of Integrative Oncology! Spread the word! #SIO2017 We are research based! #cancerresearch pic.twitter.com/oeNsn9B1Jk
>
> — Jodi MacLeod (@write4wellness) November 13, 2017

It turns out that this definition had just been published by Witt et al in the November issue of *JNCI Monographs*, just in time for the SIO annual meeting last week. When I saw it, my first reaction was to e-mail my fellow SBM bloggers with a link and this image:

So let’s take a look.

The process of defining “integrative oncology”

My first reaction (besides possessiveness) when I saw the article by Witt et al, A Comprehensive Definition for Integrative Oncology was: What? The organization has existed for nearly 15 years, and in all that time it hasn’t yet managed to define what it’s about until now? My second reaction was: What on earth does this definition actually mean? It is about as boring, generic, and —shall we say?—vague a definition of anything as I’ve ever seen. Take a look:

> Integrative oncology is a patient-centered, evidence-informed field of cancer care that utilizes mind and body practices, natural products, and/or lifestyle modifications from different traditions alongside conventional cancer treatments. Integrative oncology aims to optimize health, quality of life, and clinical outcomes across the cancer care

> continuum and to empower people to prevent cancer and become active participants before, during, and beyond cancer treatment.

In actuality, I was more interested in what was left out of this definition than what was in it, but I'll get to that near the end of this post. First, I want to look at the process by which the authors developed this definition, as described in the article, which is open-access for those of you who want to read it yourselves. Before I get into the process, let's look at some of the authors, who are big names in the world of integrative oncology. The lead author, Dr. Claudia Witt, is Professor and Chair of the Institute for Complementary and Integrative Medicine at the University of Zurich and University Hospital Zurich, as well as part-time Professor of Primary Care and Community Medicine at the Center for Integrative Medicine University of Maryland School of Medicine. Dr. Jun J. Mao is, of course, president of the SIO and Chief of the Integrative Medicine Service at Memorial Sloan-Kettering Cancer Center. Dr. Lorenzo Cohen is someone whom we've met before, when he gave a talk at the American Society of Clinical Oncology (ASCO) meeting in 2014. He's the Director of the Integrative Medicine Program at The University of Texas MD Anderson Cancer Center. Linda Balneaves is a nurse and the current president of SIO, having succeeded Dr. Mao at the SIO annual meeting last week. I also can't help but note that one of the co-authors, Heather Greenlee, is a naturopath and has served as president of the SIO in the past as well.

In other words, these are indeed heavy hitters and the leadership of the SIO.

Let's look at their justification for seeking this definition. After regurgitating the usual "complementary and alternative medicine" (CAM) blather about how patients are just "looking for "additional interventions that may help improve the efficacy of conventional cancer treatments, increase their chance of survival, and/or reduce their symptom burden associated with cancer or treatments" and "improve their quality of life during and following treatment," Witt et al justify their search for a definition thusly:

> With the integration of interventions such as acupuncture, mindfulness and yoga, and lifestyle counseling into major cancer centers in North America (eg, MD Anderson and Memorial Sloan Kettering Cancer Center), the term "integrative oncology" has become increasingly used.

> “Integrative” better represents the process of care that is provided in centers where patients are receiving these types of interventions in addition to their conventional cancer treatments. With the establishment in 2003 of the Society of Integrative Oncology (SIO), a nonprofit multidisciplinary professional organization, the term “integrative oncology” was further legitimized and began to be widely used. However, the term “integrative” is also used in other contexts. An example is the Berlin School of Integrative Oncology at the Charité Medical School in Berlin (2), which is an initiative of the German federal and state governments that aims to educate young scientists and physicians in oncology in an interdisciplinary, translational research context. Although the term “integrative oncology” is rarely used in such an educational context, having totally different meanings for the same term can generate confusion. Adding to this complexity is the growing attention to the notion of integrated care programs in oncology, in which numerous cancer specialties (eg, medical oncology, radiation oncology, surgical oncology, genetics, plastic surgery) work together to provide comprehensive patient care (3).
>
> Furthermore, even in settings in which the term integrative oncology has been used to refer to the combination of complementary medicine therapies with conventional cancer treatments (4), the term has been defined in many different ways (5,6). Because of this lack of consensus, it has been difficult to communicate what is meant by “integrative oncology” to oncologists and other health professionals, as well as to key stakeholders, such as patients, administrators, and health policy makers. The aim of this project was to use a systematic approach to develop a comprehensive and acceptable definition for “integrative oncology.”

Actually, I’ve always rather suspected that this confusion is a feature, not a bug, related to the use of the word “integrative.” After all, integrative oncology, like integrative medicine, is a brand, not a specialty. It rebrands what should be considered perfectly fine science-based modalities, such as nutrition, lifestyle interventions, and the like, as somehow “alternative” or “integrative,” and then “integrates” quackery like acupuncture, reiki, functional medicine, and even homeopathy with them, to give the quackery

the appearance of scientific legitimacy. No, I don't think SIO is doing this intentionally; its leadership consists of true believers. But it is contributing to quackademic medicine and the integration of quackery into oncology. In any event, the word "integrative" is, as mentioned above, used to describe science-based endeavors, such as integrative biology. In this context, the word "integrative" connotes interdisciplinary study, a very different meaning than when the word "integrative" came to replace the term CAM to describe adding pseudoscience to medicine.

Indeed, use of the word "integrative" to describe medicine or the subspecialty of oncology connotes more than interdisciplinary patient care and research. It connotes the embrace of "alternative" treatment modalities as well. The term "CAM" still had the word "alternative" in it and the word "complementary" connoted that CAM was subsidiary to medicine, "complementary," the icing on the cake, if you will. In other words, it's not necessary, and science-based medicine is the real medicine. The adoption of the word "integrative" to rename CAM as "integrative medicine" was clearly intended to remove the implication that CAM was "complementary" and not as good as real medicine, in order to advance the narrative that integrative medicine is the "best of both worlds," while also borrowing from the cachet of various "integrative" scientific disciplines as being multidisciplinary. Again, I don't think SIO is out to deceive. Rather, the belief of the SIO leadership in the validity of integrative oncology has led them down this road, probably without even realizing it.

So how did Witt et al go about constructing their definition? Enter the mixed methods research design and Delphi method. This amused me, because it wasn't so long ago that naturopathic oncologists used this very method to try to define priorities in naturopathic oncology. If you want the details of how the Delphi method works I discussed them in deconstructing the nonsense that naturopaths laid down about their quack specialty using the Delphi method. The CliffsNotes version is that the Delphi method entails a using a group of experts to answer a question. The experts anonymously reply to questionnaires and subsequently receive feedback in the form of the statistical representation of the group response, after which the process repeats itself until something resembling a consensus is arrived at. The way Witt et al did this is described:

> A two-round Delphi process was then employed to further refine and gain consensus regarding the new definition. In the first round, the revised definition was distributed via an online survey (software SoSciSurvey [7]) to SIO board members as well as to a convenience sample of experts. The experts—oncologists, integrative oncology clinicians, and/or researchers from North America, Europe, and Asia—were contacted by the SIO board members. Based on first round feedback, the definition was revised and distributed again through an online survey to the full membership of SIO, with subsequent ratings and comments used to inform the final version of the definition. Data from both surveys were analyzed using descriptive statistics. Content analysis (8) was applied to the open-ended responses to identify any themes or concepts.

So, after this literature search and Delphi method, what did Witt et al find?

Defining “integrative oncology”

As a result of their literature search and two-round Delphi process, Witt et al found many definitions of “integrative medicine” and “integrative oncology” in the literature, which resulted in the following thematic suggestions:

- evidence-based/evidence-informed/evidence-guided/using best available evidence (14 of 20);
- accompanying conventional cancer treatment (18 of 20);
- addressing outcomes such as well-being, body, and mind-spirit, as well as physical, psychological, and spiritual quality of life (seven of 20);
- focused on health and not only on medicine (three of 20);
- provided by a team of health care providers/multidisciplinary/interdisciplinary (four of 20);
- patient-centered/personalized, individualized/whole person (two of 20).

The writing group, which consisted of “members with different professional/disciplinary backgrounds (ie, medical oncology, radiation

oncology, surgical oncology, nursing, patient advocacy, psychology, psycho-oncology, epidemiology, integrative medicine, health policy),” added these additional suggestions:

- type of interventions (mind-body therapies, natural products, lifestyle changes);
- beyond provision of health care (information, translation of evidence, identification of beliefs, values and preferences, empowerment).

The initial definition of integrative oncology developed by the group thus read:

> Integrative oncology is a patient-centered (theme 6), evidence-informed (theme 1) approach to health care (theme 4) that uses mind-body therapies, natural products, and lifestyle modification (theme 7) as adjunct to conventional cancer treatments (theme 2) and is ideally provided by a multidisciplinary team of care providers (theme 5). Integrative oncology aims to increase well-being of mind, body, and spirit (theme 3) and to provide patients with skills enabling them to help themselves during and beyond cancer treatment (theme 8).

After the two rounds of Delphi method, though, the group perceived that some changes were required:

> Overall, the comments on the second Delphi survey were positive, but the suggestions were quite heterogeneous. Two-thirds of suggestions focused on what were perceived to be missing interventions, and it became clear that therapies such as acupuncture and massage were not well represented in the definition. As a consequence, the definition was revised using the umbrella term “mind and body practices,” which is used by the National Center for Complementary and Integrative Health in the United States. This term includes mind-based techniques such as meditation and hypnosis, as well as manual techniques such as acupuncture and massage (9). One respondent mentioned that “health care” encompassed a broader area than integrative oncology, and the decision was made to be more focused and to use the term “cancer care” in the revised version. Another respondent also suggested that the phrase “approach to cancer care” could be misleading and not specific enough

> as a field of care or medical specialty. Integrative oncology is more than just an approach to overall cancer care; it has been the focus of a professional organization for more than 10 years and is an established field in its own right. During the review process, it was noted that cancer prevention was not included in the definition. Because the ultimate goal of many integrative oncology behaviors is cancer prevention and control, the definition was modified to include prevention.

I've discussed before how quackery like the theatrical placebo known as acupuncture has mysteriously been subsumed into "mind and body practices". Personally, I've always suspected that this was to hide the quackery of acupuncture with more benign modalities (such as massage) that, whether medically they can treat anything, generally do no harm, and can certainly feel good, thus improving quality of life. After all, given that the rationale in traditional Chinese medicine for acupuncture is that sticking the needles into specific "meridians" can redirect the flow of qi (life energy) for healing effect, acupuncture could easily be classified as a form of energy healing.

To the degree that integrative oncology sticks with science- and evidence-based tests and treatments, my main objection to it is that it's not necessary. Nutrition, exercise, and other lifestyle-based interventions are already a part of science-based medicine. I like to cite, for instance, evidence-based recommendations for the treatment of hypertension and type II diabetes, both of which emphasize, except for severe cases, dietary modifications, exercise, and weight loss as the first interventions to attempt before placing the patient on medications.

To paraphrase Harriet Hall, what is good about integrative oncology (or medicine) is not unique to it. Continuing the paraphrase, unfortunately, what is unique to integrative oncology is not good, and the SIO definition obscures or neglects to mention these unique (and not good) aspects.

What the SIO left out

If you read the full article, it should become very apparent that its authors

want desperately to convince the reader that integrative oncology is completely evidence-based. Sure, the SIO admits naturopaths and even elects them as the organization's president from time to time, never mind that all naturopaths are trained in The One Quackery To Rule Them All, homeopathy, and that the vast majority of naturopaths routinely prescribe homeopathic remedies, which, even the SIO concedes, are rooted in pseudoscience.

I was reminded of this on—where else?—Twitter. I came across a post on the University of Pennsylvania's OncoLink touting reiki in cancer care. Because the link was from 2011, I Tweeted a question to the OncoLink team. Here's the response:

> @gorskon, Reiki is a supportive therapy that can be used in conjunction with treatment. It is not promoted as an alternative to treatment
>
> — OncoLink Team (@OncoLinkTeam) November 2, 2017

If there is a challenger to homeopathy's title of The One Quackery To Rule Them All, reiki would be right up there. It is, as I have described many times before, a form of faith healing that substitutes Eastern religious beliefs for the Christian religious beliefs that usually undergird faith healing in the US.

But it's not just Penn. The Dana Farber Cancer Institute has also gone all in for nonsense:

> 7 Ways Integrative Therapies Help Cancer Patients: https://t.co/bRHYbqhrcy pic.twitter.com/0kVQ4FKW0o
>
> — Dana-Farber (@DanaFarber) August 26, 2017

The slideshow at the link above promotes reiki, reflexology, and acupuncture:

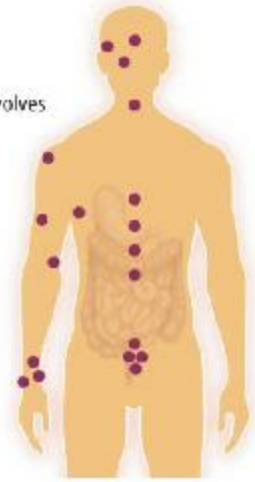
DANA-FARBER CANCER INSTITUTE
Discover. Care. Believe

7 WAYS INTEGRATIVE THERAPIES CAN HELP CANCER PATIENTS

1. ACUPUNCTURE

Acupuncture is a standard practice in Chinese medicine which involves gently inserting hair-thin needles into the skin at specific points. Acupuncture has been shown to:

- Reduce post-operative nausea and vomiting
- Decrease anxiety
- Treat pain and loss of nerve sensation
- Relieve joint pain
- Help relieve chronic pain



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Acupuncture is nothing more than a theatrical placebo, whose action has never been convincingly shown to be greater than that of placebo controls. Yet Dana Farber Cancer Center thinks acupuncture is science-based.

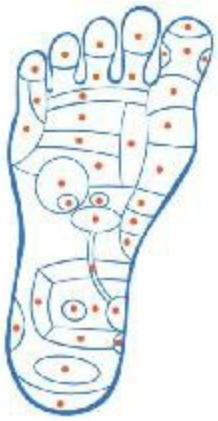
DANA-FARBER CANCER INSTITUTE
Discover. Care. Believe

7 WAYS INTEGRATIVE THERAPIES CAN HELP CANCER PATIENTS

3. REFLEXOLOGY

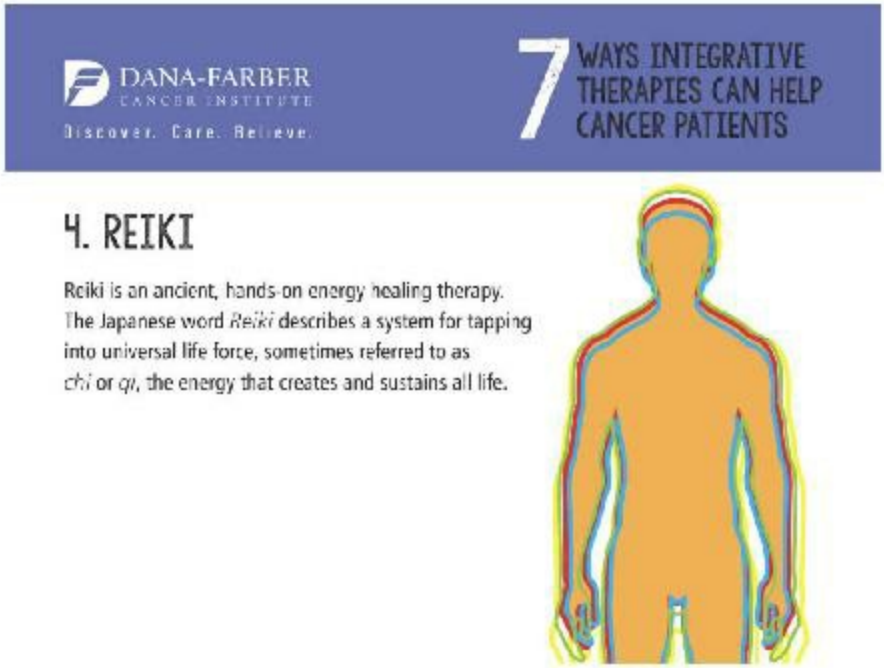
Reflexology is the application of pressure to areas on the feet, hands, and outer ears. The theory behind reflexology is that these areas correspond to organs and systems in the body. Patients have found that reflexology can:

- Promote relaxation and comfort
- Help with treatment symptoms like fatigue and nausea



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Reflexology posits the existence of physiologic or anatomic links between organs and body parts and areas on the soles of the feet and palms of the hand. Yet Dana Farber Cancer Center thinks this is science-based.



Visit the Zakim Center for Integrative Therapies website for more information on integrative therapies.

Reiki masters claim to be able to heal by channeling energy into the patient from the "universal source." Replace "universal source" with "God" or "Jesus," and it becomes obvious that reiki is a form of faith healing that replaces Christian beliefs with Eastern mysticisms. Yet Dana Farber Cancer Center thinks it's science-based.

Of course, I've pointed out how oblivious the SIO is to the modalities that are really being "integrated" into oncology through integrative oncology just through the obliviousness of the SIO leadership to what naturopathy really is. As I've said before, if the SIO were really serious about being evidence-based, it would immediately purge itself of all naturopaths. It's not, though. Its leadership up in the ivory towers of medical academia can delude themselves into thinking integrative oncology is totally evidence based, because they manage to ignore the quackery that is "integrated" along with the lifestyle-, exercise-, nutrition-, and meditation-based modalities to which they love to point.

I can’t help but point out a few more examples of the quackery that goes along with integrative oncology. At UC-Irvine and the Cleveland Clinic, there’s homeopathy. At the University of Arizona Cancer Center, there was reiki, at least until a faculty member whose child developed cancer and was treated there made a stink. There’s also more energy medicine quackery, this time in the chemotherapy suite, at Georgetown University, as well as cupping, which is also pure quackery. There’s functional medicine at the Cleveland Clinic, George Washington University, University of Kansas, and, well, seemingly almost everywhere at any medical center with an integrative medicine program. If you want an idea of how bad functional medicine is, just check out this case report of functional medicine used for a patient with inflammatory breast cancer. This is what integrative oncology *really* involves.

It is also this quackery that the SIO definition of “integrative oncology” does its best to obscure or ignore. If the SIO is truly serious about being science- and evidence-based, it needs to speak out strongly and now against naturopathy and the various forms of quackery that have found their way into academic medical centers, of which, I assure you, the above is but a small sampling. It won’t, though. The quackery is why integrative medicine and oncology exist in the first place. Without the quackery, CAM (or integrative medicine or oncology) becomes completely unnecessary as a field.

Science Based Medicine

周一, 06 11月 2017

Science Based Medicine

[周一, 06 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **The American Chiropractic Association Answers Crislip's Call, Joins the Choosing Wisely Campaign** [周五, 03 11月 20:00]
  The Choosing Wisely campaign has invited the largest chiropractic organization in the United States to publish a list of interventions to avoid. The results, while not entirely without merit, consist of redundant or unnecessary recommendations. And there is a glaring absence of recommendations to avoid any of the blatant pseudoscience commonly practiced by chiropractors.
- **Liver cancer, naturally** [周四, 02 11月 19:30]
  Aristolochic acid, a highly toxic substance naturally found in some traditional herbal medicines, may be a significant cause of liver cancer.
- **ASEA – Still Selling Snake Oil** [周三, 01 11月 20:49]
  ASEAs marketing practices, in my opinion, are clearly deceptive. They use a lot of pseudoscientific claims representing the epitome of supplement industry misdirection and obfuscation. They use science as a marketing tool, not as a method for legitimately advancing our knowledge or answering questions about the efficacy of specific interventions.

Three years ago, Mark Crislip closed a post discussing the ABIM Foundation's Choosing Wisely initiative with the following thought:

> I wonder if a chiropractor could come up with five standards treatments in chiropractic to be avoided…

Well, now they've finally gone and done it, with results that, while not entirely without merit, are a bit off the mark in my opinion.

Choosing Wisely and chiropractic

For the sake of further discussion, let's all just agree to ignore the fact, also pointed out by Dr. Crislip in his post, that chiropractic as a profession doesn't exactly stand up to the scrutiny of the campaign's criteria:

> *Choosing Wisely* aims to promote conversations between clinicians and patients by helping patients choose care that is:
>
> - Supported by evidence
> - Not duplicative of other tests or procedures already received
> - Free from harm
> - Truly necessary

Of course to be fair, no medical intervention is completely "free from harm", but I assume that what the ABIM Foundation actually means is that interventions should have a favorable risk to benefit assessment. This is arguably not the case when assessing chiropractic as a whole. While not all of the treatments I prescribe are based on robust randomized controlled trials, they are "supported by evidence" in the vast majority of cases, and often by very good evidence. Chiropractic doesn't really bring anything original to the table that passes this test.

There are similar issues with the phrase "truly necessary", whatever that means. Many medical interventions aren't "truly necessary" in my opinion. Other Choosing Wisely lists cover a number of these, but there are also tests

and treatments that may have value while perhaps not meeting this criterion absolutely depending on who is assessing the scene. But again, being charitable, I assume that the ABIM Foundation is focusing on common interventions for common human ailments that don't tend to improve objective outcomes.

Specific treatments provided by a chiropractor might provide some objective benefit for a small sliver of musculoskeletal complaints, with those unique to chiropractic being the least helpful. But whatever improvement that can be attributed to visiting a chiropractor isn't better than more conventional approaches, such as physical therapy or recommendations from a patient's primary care provider for exercise, stretching, massage, etc. These approaches come with considerably less baggage and aren't as likely to be accompanied by pseudoscience or anti-vaccine propaganda.

The Choosing Wisely lists published by participating organizations aren't meant to serve as treatment guidelines, of course. Instead, they are intended to encourage a conversation around whether or not the listed interventions are a good idea, or if they may put patients at risk of more harm than benefit. Unfortunately, in my opinion, they have largely gone unnoticed by medical providers and the general public. I am confident that the list of questionable chiropractic interventions will be similarly ignored by practitioners.

The ACA's list

The list in question, released in August, comes from the American Chiropractic Association (ACA). The ACA claims 15,000 members, which is less than a quarter of practicing chiropractors, and recognizes 11 specialty areas, such as chiropractic acupuncture, pediatrics, diagnosis and management of internal disorders, and forensic sciences. It describes itself with typical grandeur:

> The American Chiropractic Association (ACA) is the largest professional chiropractic organization in the United States. ACA attracts the most principled and accomplished chiropractors, who understand that it takes more to be called an ACA chiropractor.

> We are leading our profession in the most constructive and far-reaching ways — by working hand in hand with other health care professionals, by lobbying for pro-chiropractic legislation and policies, by supporting meaningful research and by using that research to inform our treatment practices.
>
> We also provide professional and educational opportunities for all our members and are committed to being a positive and unifying force for the practice of modern chiropractic.

What does it take to called "an ACA chiropractor"? Membership requirements consist of being a licensed chiropractor in the United States and paying yearly dues. The ACA even goes so far as to state that they do not deny membership to anyone meeting the above qualifications as long as what they do in their practice isn't illegal. In that way, they are similar to the American Academy of Pediatrics, which even allows pediatricians who are blatantly anti-vaccine to be members in good standing.

Here are the five things that chiropractors and their patients should question according to the ACA:

Do not obtain spinal imaging for patients with acute low-back pain during the six (6) weeks after onset in the absence of red flags.

What red flags, you ask? The ACA mentions "history of cancer, fracture or suspected fracture based on clinical history, progressive neurologic symptoms and infection, as well as conditions that potentially preclude a dynamic thrust to the spine, such as osteopenia, osteoporosis, axial spondyloarthritis and tumors". I would argue that if you have any of these red flags, you should not be under the care of a chiropractor. There isn't any evidence to support superiority of chiropractic care to conventional approaches for acute low-back pain anyway.

Do not perform repeat imaging to monitor patients'

progress.

They list idiopathic scoliosis as an exception, despite the fact that their own research shows no good evidence to support chiropractic management of this condition. I agree with this recommendation, and the reasoning of the ACA in this case is sound. I'm just not holding my breath while waiting to see if this will change anything, however.

Avoid protracted use of passive or palliative physical therapeutic modalities for low-back pain disorders unless they support the goal(s) of an active treatment plan.

In other words, commonly recommended interventions like heat, ultrasound, and electrical stimulation, shouldn't be used in isolation because they don't provide much benefit. The absolute worst thing you can do to prevent or treat lower back pain, which virtually all humans will experience at some point in their lifetime thanks to evolution, is nothing. General physical activity and back specific exercises are key, and in no way unique to chiropractic.

I don't think you will find many chiropractors not recommending an exercise regimen for lower back pain disorders, so this item is a bit odd. You also won't find many that won't provide some kind of spinal manipulation, because that's their thing that they do. In this section, the ACA writes that physical activity and back exercises "may lead to better outcomes when combined with spinal manipulation." In reality, spinal manipulation is more like multiplying by one. It changes nothing for the long term outcome.

Do not provide long-term pain management without a psychosocial screening or assessment.

Chronic pain disorders often have a psychosocial component. Chronic pain can cause or be caused/exacerbated by anxiety and depression, for example.

Some patients are at risk for the development of chronic pain because of a variety of psychosocial factors and chiropractors are not trained to evaluate or manage them. The ACA recommends that chiropractors use a screening tool and refer when necessary because the ACA imagines chiropractors to be primary care providers.

Do not prescribe lumbar supports or braces for the long-term treatment or prevention of low-back pain.

Another odd inclusion. Chiropractors simply aren't out there putting people in back braces for long periods of time for treatment or prevention of back pain. I was easily able to find that this recommendation is already widely accepted. Meanwhile, the ACA is inviting speakers to their conferences to promote nonsense like the Activator Method.

The ACA press release announcing their participation in Choosing Wisely is interesting. They point out that multiple other organizations already participating have included recommendations to avoid spinal imaging for acute lower back pain. It's a solid recommendation, but instead of actually attempting to show a commitment to change by pointing out some of the abject nonsense they have supported sans evidence, they went the safe route. And in the press release they essentially give their members enough wiggle room that they can continue obtaining frequent spinal films without losing any sleep.

My favorite quote involves the practice of "defensive medicine":

> As with many of our colleagues in the health care professions, we have learned from experience to practice "defensive medicine." This perspective may be even more deeply ingrained within the chiropractic profession based on our prior experiences with bias and/or lack of understanding regarding chiropractic care. As an example, just look how long it took before Choosing Wisely® was even willing to consider a chiropractic list!

So do chiropractors practice defensively, which implies a concern for facing a malpractice suit, or not? It would appear that the latter is the case when you consider how often they point out how undeniably safe chiropractic is. Often this is done in the context of attacking conventional medical care. It's also unclear to me how the medical community's lack of "understanding regarding chiropractic care" encourages defensive practice.

Conclusion: The ABIM did not Choose Wisely

How does the ACA describe chiropractic on the Choosing Wisely website? Just as you would expect them to, of course. Remember though that this is an organization that is fighting for chiropractors to be considered primary care physicians complete with the right to prescribe medications.

> Chiropractors focus on disorders of the musculoskeletal system and the nervous system, and the effects of these disorders on general health and function. Chiropractic services are used most often to treat conditions such as back pain, neck pain, pain in the joints of the arms or legs, and headaches. Widely known for their expertise in spinal manipulation, chiropractors practice a hands-on, drug-free approach to health care that includes patient examination, diagnosis and treatment.

The ABIM Foundation is very likely completely ignorant of both the history and the current reality of the chiropractic profession. Frankly I think it's ridiculous that a chiropractic organization was invited to participate. We certainly have come a long way from Wilk v. AMA, haven't we?

This is just another example, in a very long line, of the undeserved legitimization of alternative medicine that will serve as more of a marketing purpose than as a means of improving chiropractic practice. All that the ACA has done is provide a list of redundant or unnecessary recommendations. And the few chiropractors who already avoid excessive spinal imaging will continue to do so, while the vast majority will compartmentalize these "suggestions" and carry on as is.

Extras

- Here is a response to the ACA Choosing Wisely list from the International Chiropractic Association.
- Here is an ACA video describing the benefits of pediatric chiropractic. In March of 2017, the ACA reaffirmed its public policy on chiropractors as primary care providers. This policy includes the following:

> Doctors of chiropractic also recommend and manage dietary changes, nutritional interventions, botanical medicines, homeopathic medicines, acupuncture and other services when indicated.

The ACA, while not overtly anti-vaccine in policy, supports conscience waivers.

Not all cancers affect all populations equally. Liver cancer is the fifth-most common cancer worldwide, but the prevalence varies widely. Liver cancer cases skew heavily to less developed regions of the world, where 83% of cases are found – it's over six times more common there than in Northern Europe, for example. In Asia, the high rates of liver cancer have been linked to hepatitis B and C, which is widespread, and a proven cause of cancer. And liver cancer continues to strike Asian American and Pacific Islanders more than any other American ethnic group as well, where hepatitis continues to circulate in the population. Now there's new evidence to suggest that a substance found in some traditional Chinese medicines may also be causing liver cancer. They're called aristolochic acids, and they illustrate, with a substantial body count, that what's natural isn't necessarily healthy or good.

What are Aristolochic acids?

In the early 1990's a strange cluster of acute, end-stage renal disease appeared in women in Belgium. It was determined that all had been exposed to the chemical aristolochic acid (AA) at a weight loss clinic, due to the consumption of Chinese herbs which contained natural AA. Approximately one third of the more than 300 cases have subsequently required a kidney transplant, and cancers of the urothelial tract in this group have also been widespread. In the Balkans, low level exposure to AA via flour consumption that contains seeds from *Aristolochia clematitis* is believed to be responsible for what is now called Balkan-endemic nephropathy. Subsequent study that was initiated after the Belgian case identified that that AA is responsible for tumour development and for activating destructive fibrotic changes in the kidney. For over a decade now it has been well established that AA is a nephrotoxin and a powerful carcinogen with a short "latency period", in that it causes permanently damage, quickly. What's remarkable is that none of this was known until the 1990s despite "thousands of years" of use as a traditional medicine. As Steven Novella noted in a past post on aristolochic acid and urinary tract cancer:

> This example just highlights the fact that widespread use of an herbal

> product, or any treatment, is not sufficient to ensure that it is safe, or even that it is effective. Common use may be enough to detect immediate or obvious effects, but not increased risk of developing disease over time. That requires careful epidemiology or specific clinical studies. We know about the risks of prescription drugs only because they are studied, and then tracked once they are on the market. Without similar study and tracking there is simply no way to know about the risks of herbal products. Relying upon "generally recognized as safe" is folly.

While herbal remedies that contain AA are now banned in many countries, AA-induced kidney damage and related cancers continues to appear worldwide. As AA's cancer-causing effects have now been widely studied, the distinct way that they damage cells has been described as a sort of "signature" that is easily identifiable in tumour samples. This brings us to this new study of liver cancers attributed to AA, which have been less closely associated with AA. This study used that unique "signature" to look for AA exposure.

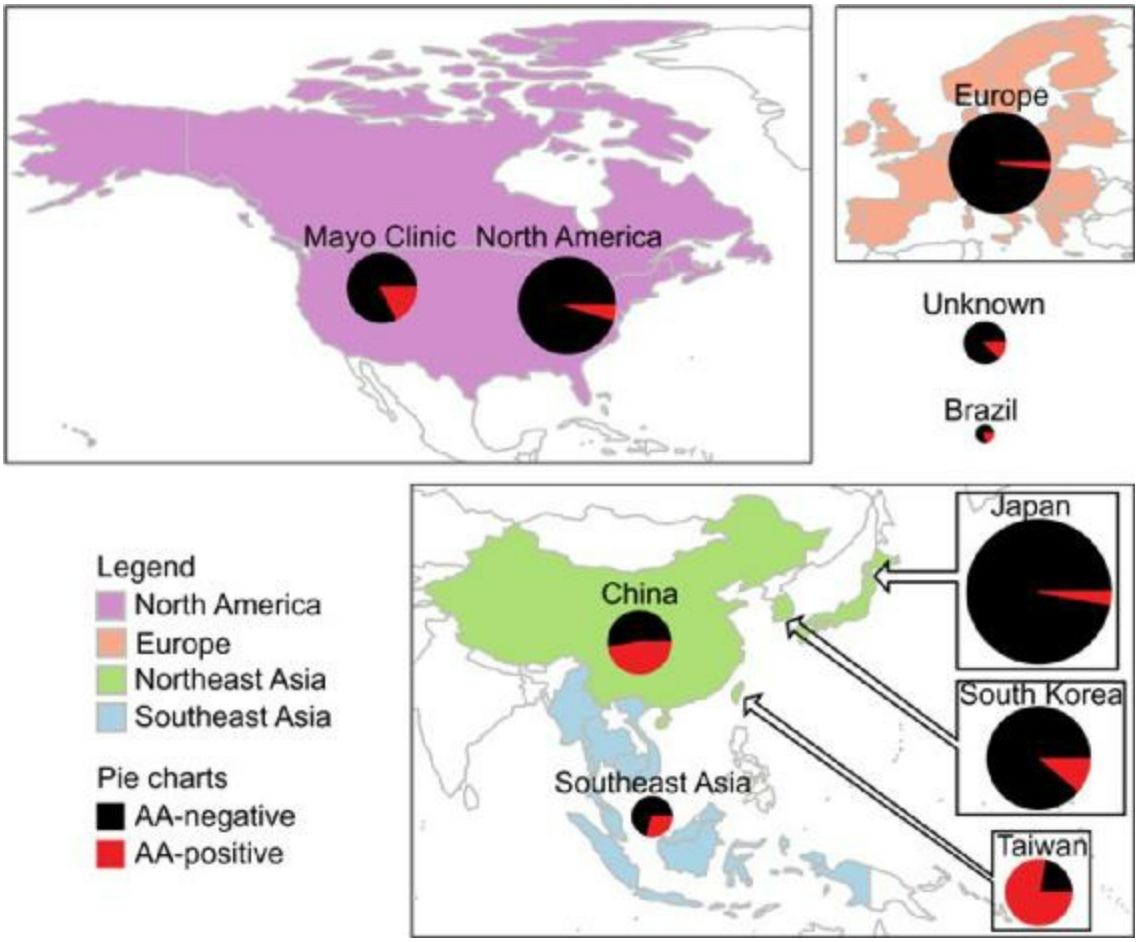
Aristolochic acids and liver cancers

There is good evidence to show that the consumption of AA-containing products in Taiwan has been widespread through the use of prescribed herbal medicines. The paper is entitled "Aristolochic acids and their derivatives are widely implicated in liver cancers in Taiwan and throughout Asia" and it's from Alvin Ng and associates, published in *Science Translational Medicine* in October, 2017. This was a retrospective analysis of hepatocellular carcinomas (HCC, liver cancer in lay terms) and patients were included if they (1) had true HCC (2) there was sufficient DNA available from a sample of the tumour. 98 HCCs from Taiwan hospitals were studied based on whole-exome sequencing and mutation identification. They looked for the distinctive way in which AA causes mutations. The researchers subsequently examined 1,400 HCCs from other regions in the world. The final analysis was as follows:

- Taiwan: 78% of tumours had evidence of AA exposure

- China: 47% of tumours had evidence of AA exposure
- Southeast Asia: 29% of tumours had evidence of AA exposure
- Korea: 13% of tumours had evidence of AA exposure
- Japan: 2.7% of tumours had evidence of AA exposure
- North America: 4.8% of tumours (in one hospital, 22% of 87 patients, all of Asian ancestry, had evidence of AA exposure)
- Europe: 1.7% of tumours had evidence of AA exposure

Here is the global breakdown, with the red portion illustrating the proportion of tumours that were linked to AA exposure:



Global distribution of mutagenesis associated with aristolochic acid and derivatives in liver cancer.

Reducing your risk of kidney and liver

cancer

Herbal remedies are popular worldwide. In China and other countries in Asia, there is strong support for, and belief in “traditional” Chinese medicine despite the fact that it is neither truly traditional (as it is now promoted), nor particularly effective. This new analysis shows that the use of (or exposure to) AA is widespread in some parts of the world, and appears to be be a cause in a substantial numbers of liver cancers. The authors noted that the presence of AA-associated cancer does not appear to be declining in Taiwan, despite the banning of some AA-containing herbs in 2003. This may be due to a lag effect (like cancer and smoking) but may also be due to continued exposure to, or consumption of, AA-containing products.

If you’re a user of traditional Chinese medicine, avoiding AA is easier said than done, unless you have impeccable knowledge of herbs, their origins, and the supply chains you’re getting your products from. I’ve blogged before about TCM, noting that contamination is common. Mislabelling of products also appears to be widespread, suggesting that rigorous and credible testing of final products may be the only way consumers can be assured they’re avoiding AA in the products they buy. The linkage of AA to kidney damage, and the evolving story of its cancer-causing potential illustrates that even widespread use of a product for hundreds (or thousands) of years give no automatic assurance of safety. If it were not for the Belgian weight loss clinic kidney failure cluster, the widespread toxicity of AA may not even be known today.

ASEA - Still Selling Snake Oil - Science-Based Medicine

We often examine the claims made by companies or individuals for their health products, especially those we feel are making dubious claims based on questionable science. In 2012 Harriet Hall wrote an excellent review of one multi-level marketing company, ASEA, who are basically selling salt water with a load of dubious pseudoscientific claims. ASEA is just about a perfect example of everything we try to warn consumers about when it comes to dubious supplements and the inadequacies of current regulations.

When we post such reviews it is not uncommon for the company to give us push back, and it is much more likely if that company sells through multi-level marketing (which is a scam unto itself). We recently received an e-mail from the "ASEA Team" who were not happy about Harriet's review. They asked us to revisit our review (be careful what you wish for), concluding:

> Bottom Line for our part:
>
> The criticism of ASEA made by Mr. Hall [*sic*] is not constructive and Author's points of view are not based on decent and verifiable facts. On the contrary, we have provided you with reliable information that is proven by the documentation. So, the article is misleading and deceives your website's auditory and our potential and current customers. We are sure that after a deep consideration you will come to a conclusion and agree with us that it would be best to delete the article. Thank you.
>
> Respectfully,
>
> ASEA team.

After deep consideration, and re-review of the ASEA current website, I have come to the personal conclusion (and hope they will agree) that ASEA is selling quackery and nonsense with misleading claims designed to defraud

both their customers and their sales agents (who often overlap). I suspect there is a combination of (financially) motivated reasoning and scientific illiteracy on their part, so I will explain again why I have come to this conclusion.

Let's take their points in the ASEA team e-mail to SBM. They begin by objecting to Harriet's (who they refer to as male throughout their letter) listing of the claims they were making on their website at the time:

> ASEA allegedly:
>
> - Promotes enhanced immune function
> - Supports the vital activity of cellular communication
> - Provides superior "support" to athletes
> - Boosts efficiency of the body's own antioxidants by 500%
> - Protects against free radical damage

Their "counterpoint":

> This information is out of date and does not correspond to reality, you can not even find these statements up on our website anymore. We have changed the formula, carefully tested it out and conducted several studies that proved that ASEA products have been shown to signal the activation of genetic pathways or affect genes that:
>
> Improve immune system health;
>
> Help maintain a healthy inflammatory response;
>
> Help maintain cardiovascular health and support arterial elasticity;
>
> Improve gut health and digestive enzyme production;
>
> Modulate hormone balance to support vitality and wellness.

I see, they swapped out one list of dubious claims for a slightly tweaked list of dubious claims. "Promotes enhanced immune function" became "Improve immune system health." And of course if you go to their website the old claims are still there, maybe not in the same location and jot list, but deeper

in the copy or the linked “studies.” They are still claiming it improves cell signaling and increasing the body’s own anti-oxidants.

As a side point, we do not maintain and update every article. That is not standard or practical, nor is it expected, nor do we claim to. Articles are clearly dated, and it should be obvious they are only as current as the date they were posted. We will make corrections if they are pointed out to us or we discover them, and we use our own discretion in deciding whether or not to write an addendum or an updated article.

Their next point was so clueless it gave me the impression that we were dealing with low-level sales people who are not only scientifically illiterate, but had no backing from anyone with legal experience. In response to Harriet pointing out that ASEA is not making disease claims, because they can’t, they responded:

> This statement doesn’t make any sense. As it was correctly noticed, we can’t legally and we actually don’t claim that ASEA is effective for any disease, so there is no point in writing more about this and even mentioning this. There is no information up on our website that says that ASEA would cure cancer or other diseases, however we do say that ASEA improves immune system health as well as has some other beneficial effects for a human being, and as we pinpointed that before, the effects have been verified by several laboratory tests. This statement made by Mr. Hall is far-fetched and offensive and shows that the Author tends to make things up and base his article on assumptions rather than on the facts.

Where do I begin? Here is the very salient point that Harriet was making, and that we make frequently on SBM. The current US regulations allow companies to make “structure-function” claims for their “supplements” without FDA oversight. Products with disease claims are, by definition, drugs and subject to FDA regulation. So what do many supplement companies do? They make structure-function claims that sound as if they may be beneficial for health, and combine those legally allowed claims with other statements about diseases, hoping their potential customers will connect the dots. They are skirting the spirit of the law in order to imply, without directly making, unsupported health claims.

On ASEA's website they make the following claims:

- Decline of cell signaling causes cellular breakdown, which in turn causes a long list of common diseases including autoimmune and cardiovascular disease.
- ASEA improves cell-signaling which decreases cellular breakdown.
- Here is some (not peer-reviewed) science showing that ASEA alters markers which we will choose to interpret as "improving" some aspect of cell signaling or function.

So they do not directly say that ASEA cures any disease, because they know that it is not legal under current regulation, but they do imply that it does through the above chain of claims. That is standard procedure in the dubious corners of the supplement industry (i.e. most of the supplement industry).

Let's get to the scientific studies they use to support their claims. In response to Harriet's review they wrote:

> The studies that Mr. Hall is referring to are old and no longer available on the ASEA website. Instead, we have conducted other studies that proved the effect of the ASEA products as well as their safety.

So, were those previous studies not valid? Science is cumulative. We don't just scrub "old" studies from the record and replace them with new studies. In my opinion that reveals the marketing mentality of the "ASEA team". Studies are not used to determine if their product works, but to support their marketing claims that it does work.

As Harriet pointed out, their studies are not being performed by academic scientists and published in peer-reviewed journals. They are being outsourced to third party research companies for hire. There is no paper-trail of research that would lead an honest scientist to the conclusions that ASEA is now selling. They appear to have started with their product and are backfilling in essentially worthless studies (as far as clinical claims go) to support their marketing.

Perhaps the biggest problem with ASEA's "research" is that they don't actually address their implied clinical claims. In other words – there are no

studies that directly show that ASEA will improve your health – let alone multiple independently replicated rigorous studies published in peer-reviewed journals.

Their current marketing focuses heavily on the claim that ASEA increases natural antioxidants in the body. Antioxidants are currently very popular, having been given a health halo by two decades of heavy marketing. However, the real science tells a different story. In their scientific summary they write:

> Oxidative damage has been implicated in aging and agedependent diseases, including cardiovascular disease, cancer, neurodegenerative disorders, and other chronic conditions. If the generation of free radicals exceeds the protective effects of antioxidants and some co-factors, this can cause oxidative damage.

That is the simplistic story that the anti-oxidant industry is selling, but it is nonsense. Essentially they are assuming that increasing antioxidant activity (even assuming that ASEA does so, which I doubt) must be a good thing. This turns out to be a naive assumption. A homeostatic balance between oxygen free radicals and antioxidants evolved to optimality, unless adversely affected by a disease state such as a genetic mutation. There is no reason to think that artificially disrupting this natural homeostasis would be a good thing. In fact, the evidence has shown that actual antioxidants taken in large amounts are bad for your health. Our bodies use free radicals as part of the immune system, to kill invading cells, and as important signaling molecules. Blocking free radicals in a healthy person can actual cause harm.

The same is true of immune function, which naturally exists in a carefully-balanced state. ASEA marketing naively assumes that increasing any arbitrary marker of immune function equals “improving” immune function. If you have an auto-immune disease, increasing immune function would be a bad thing.

This is the core fallacy of the entire supplement industry, which assumes that you can “improve” the function of an evolved homeostatic system by simply pushing it in one direction. This often leads to contradictory claims, such as some supplements claiming to increase oxygen while others claim to be anti-

oxidants.

Finally, Harriet appropriately asked what was in ASEA anyway. It appears to be just salt and water, and ASEA makes the pseudoscientific claim that the salt water molecules have been arranged somehow into these redox signaling molecules. They respond:

> As for what the components are, this is a confidential information. We have spent a lot of time and resources coming up with the idea as well as setting it all in motion.

Sorry, but science requires transparency. You cannot pretend to be scientific and then simultaneously state that your core claim is a secret. This is especially true when that core claim makes no scientific sense. It is not an extrapolation of existing scientific research or established principles. In fact, their core claim sounds like utter nonsense, so simply saying that it is a secret does not inspire confidence.

Far from taking down Harriet's original review of ASEA and their claims, her assessment deserves to be updated and amplified. ASEAs marketing practices, in my opinion, are clearly deceptive. They use a lot of pseudoscientific claims representing the epitome of supplement industry misdirection and obfuscation. They use science as a marketing tool, not as a method for legitimately advancing our knowledge or answering questions about the efficacy of specific interventions.

I am amused that they chose to e-mail us with their juvenile analysis and requests. That may suggest they are more naïve than calculating, but it really doesn't matter. They are selling a product with health claims. They have the responsibility not to deceive their customers, and I do not feel as if they have met their burden for due diligence. They may have from a regulatory perspective, but only because current regulations are horrifically inadequate. But they certainly haven't from a moral or scientific perspective.

Science Based Medicine

周一, 13 11月 2017

Science Based Medicine

[周一, 13 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Another “Chronic Lyme” VIP disciplined by NY medical authorities: Bernard Raxlen** [周四, 09 11月 14:00]
  Another "Lyme literate" NY physician is on probation and under orders to clean up his act. Will other physicians treating "chronic Lyme" take note?
- **Risks of a Gluten-Free Diet** [周三, 08 11月 21:27]
  Non-Celiac Gluten Sensitivity does not seem to be a real entity according the current evidence, but this has not stopped the gluten-free fad, which may be causing real harm.

Bernard Raxlen, MD, who devotes more than 90% of his practice to the treatment of so-called “chronic Lyme” disease, is on a three-year probation imposed by the New York State Board for Professional Medical Conduct (BPMC). Raxlen agreed to probation and a lengthy list of practice requirements last month following allegations, filed in September, of negligence, incompetence, gross negligence, gross incompetence, and failure to maintain adequate patient records. In doing so, he becomes the second “Lyme literate” VIP disciplined by the NY medical authorities this year. Based on similar charges of professional misconduct, David Cameron, MD, was also put on probation with numerous practice restrictions in June.

Who is Bernard Raxlen, MD?

Raxlen is a psychiatrist and solo “chronic Lyme” practitioner in New York City who says he’s “successfully treated” over 3,500 cases of tick-borne disease in the past 15 years. (He named his practice “Lyme Resource Medical of New York.”) He touts a “total comprehensive treatment program which

utilizes both oral and intravenous (IV) antibiotic treatment." It doesn't come cheap, either. An initial visit with Raxlen costs $1,200 with follow-up visits between $600 and $700. A PICC-line insertion (presumably for long-term antibiotics) is $750 and a "nutritional IV" is $150. He does not accept public or private insurance.

Raxlen has a history of disciplinary actions against him in two states stretching back almost 20 years. In Connecticut, where he was formerly licensed, he was reprimanded and paid a total of $35,000 in civil penalties in two cases arising out of his refusal to provide patient records to the Health Department and insurance companies, even though patients had signed releases. He was also disciplined for inappropriate prescribing and failing to maintain malpractice insurance. Because these infractions constituted professional misconduct in New York as well, he was subject to two disciplinary actions in that state, resulting in censure, reprimand and a $2,500 fine.

According to the *Chicago Tribune*, Raxlen had other professional misconduct charges brought against him by Connecticut authorities but they were ultimately dropped. The *Tribune* reported that, in one case, Raxlen was charged with telling a patient with Lou Gehrig's disease (ALS) that she had Lyme disease and treating her with an illegal drug from Germany. He told the reporter that the relationship between ALS and Lyme was "unclear," even though ALS experts concluded that there was no evidence of a connection.

Per his New York State Department of Health physician profile (just type his name into the search engine), Raxlen completed residency training in psychiatry and lists his specialty as psychiatry, but he is not board certified in any specialty. He did not train in internal medicine, family medicine or pediatrics (although he treats pediatric patients), specialties that normally treat routine Lyme infections. Nor did he train in infectious diseases, experts to whom patients with more complicated cases of Lyme would normally be referred by other practitioners.

Yet, he is described by the International Lyme and Associated Disease Society (ILADS) as a "leader in Lyme disease treatment and research." In fact, he is a founding member of ILADS, former Secretary of the Board, and has taught a number of ILADS courses. He was a co-author of the original

ILADS guidelines for the treatment of tick-borne diseases. Despite their troubling disciplinary status, both he and David Cameron are scheduled to speak at the ILADS Annual Scientific Conference, which starts today in Boston.

How can this be? How can one be a leading light in ILADS with a disciplinary history like Raxlen's and no graduate medical education in infectious diseases?

"Lyme literate" physicians like Raxlen have fabricated a disease they call "chronic Lyme," which they regularly "diagnose" and treat with long-term antibiotics, sometimes for months to years. Board-certified infectious diseases doctors and other "conventional" physicians all agree that "chronic Lyme" is *not* a valid diagnosis and rely on well-conducted trials showing that long-term antibiotics do not substantially improve the outcome for patients diagnosed with so-called "chronic Lyme." Long-term antibiotics can, in fact, result in serious harm, including death, a subject our good friend Orac covered recently over on Respectful Insolence. Orac's post nicely summarizes the differences between real Lyme disease and "chronic Lyme," "a prototypical fake medical diagnosis," and the dangers of long-term antibiotics, as have posts on SBM, here, here, here, and here.

The CDC, the Infectious Diseases Society of America (IDSA), the American Academy of Pediatrics, the American College of Physicians, the *Medical Letter* and the American Academy of Neurology all reject the notion that "chronic Lyme" exists and that long-term antibiotics are an appropriate treatment. There is something called "post-treatment Lyme disease syndrome," but responsible medical authorities do not equate this syndrome with the nebulous symptoms and unvalidated lab tests of "chronic Lyme" and specifically reject the utility long-term antibiotic treatment based on well-conducted clinical trials. None of this is to say that patients who've been told they have "chronic Lyme" are not truly suffering, a fact that makes "Lyme literate" practices all the more reprehensible.

None of this stopped "Lyme literate" doctors from banding together to form ILADS and issuing their own guidelines for the diagnosis and treatment of "chronic Lyme," guidelines based on very low levels of evidence that are accepted only by themselves and, in contrast to the IDSA guidelines, no other

professional medical organization. ILADS teaches physicians and other practitioners how to become "Lyme literate." ILADS, again in contrast to IDSA, is not an ACCME-accredited provider of continuing medical education although, for some inexplicable reason, the Westchester [County, NY] Medical Society has teamed up with ILADS and is using its accrediting authority to grant CME credit for some of the talks (also here) at the ILADS Scientific Conference.

Despite the lack of evidence that "chronic Lyme" is a valid diagnosis, and the lack of efficacy as well as the risks of long-term antibiotic treatment, ILADS healthcare providers currently treat more than 100,000 patients with "chronic Lyme" and tick-borne diseases in the USA and around the world. Given media reports that patients can spend $10,000 to $35,000 for treatment, "Lyme literacy" translates into millions of dollars for practitioners.

While it may be profitable, "Lyme literate" doctors risk running afoul of state medical boards. Raxlen is just one among ILADS-trained, "Lyme literate" physicians who have had their medical practices questioned by their peers, up to and including discipline imposed by state authorities (also, here and here).

With that background, let's look at the allegations against Raxlen and the terms of his probation.

The BPMC v. Raxlen

New York's medical misconduct procedures do not require the physician charged to stipulate to any particular acts of misconduct as a condition of settling his case. The physician can, as Raxlen did here, simply state he is unable to "successfully defend against at least one of the acts of misconduct alleged" and agree to the imposition of sanctions. This means the allegations in the state's Statement of Charges were never proven, as it was unnecessary to reach a decision on the factual issues once Raxlen agreed to a settlement. However, per the Office of Professional Medical Conduct's (OPMC) standard procedures, the allegations were based on expert review of Raxlen's patients' records and they remain uncontested by him.

The allegations of misconduct arise out of Raxlen's care of eight patients. As is typical of "chronic Lyme" diagnosis and treatment, patients (whose identities are protected) presented with a variety of disparate symptoms, such as:

- Patient A: freezing, burning, air hunger, weakness, fatigue, neck pain and intestinal pain.
- Patient E: fatigue, migraines, neck pain, joint pain, numbness and tingling, irritability, sound, light and temperature sensitivity and nonrestorative sleep.
- Patient G: back pain, abdominal pain, feet pain, extremity weakness, anxiety, depression and mood swings.
- Patient H (who got the Hickman catheter and numerous antibiotics mentioned below): mouth, teeth and jaw pain, confusion, forgetfulness, irritability and mood swings.

Diagnosis and treatment of "chronic Lyme" is never mentioned, a wise decision on the part of the BPMC prosecutors in light of the ill-conceived New York law protecting "Lyme literate" doctors from prosecution

> based solely upon the recommendation or provision of a treatment modality by a licensee that is not universally accepted by the medical profession, including but not limited to, varying modalities used in the treatment of lyme disease and other tick-borne diseases.

Instead, the BPMC focused on the fact that Raxlen had failed in the most basic tenets of good medical care, although the fingerprints of "chronic Lyme" diagnosis and treatment, such as failure to consider alternative diagnoses, prescribing IV antibiotics and using a Hickman catheter, are all over the charges. The charges included:

- Repeatedly failing to perform or note in the patient's chart a comprehensive history and appropriate physical exam, including (despite his being a psychiatrist) a psychiatric history, neuropsychological testing and mental health status exam.
- Failing to construct a differential diagnosis and pursue a thorough diagnostic evaluation prior to instituting a treatment plan.
- Inappropriate prescribing, including prescribing Rifampin for a patient

on Tamoxifen and prescribing addictive medications prior to a making a diagnosis and without considering non-addictive treatment.
- Inappropriately relying on Applied Kinesiology (which is quackery) to formulate a diagnosis.
- Placement of a Hickman catheter without medical necessity.
- Inappropriately administering antibiotics, including intravenous Invanz, Clindamycin, Flagyl, Rifampin, Minocycline, Mepron, Plaquenil and Bactrim, all of these for *one patient*.
- Failure to present or note in the patient's chart potential risks, benefits, side effects and safe use of prescribed medications.
- Failure to appropriately identify, address, and/or follow-up on potential side effects.
- Treating inappropriately with an ongoing and/or escalating medication regimen without appropriate physical exams and clinical reassessment for consideration of alternative diagnoses and treatment.
- Poor record-keeping.

These allegations resulted in charges of negligence, incompetence, gross negligence, gross incompetence, and failure to maintain adequate patient records. As noted, Raxlen agreed to a three-year probation in addition to the imposition of conditions on his practice. He must, among other things:

- Communicate to patients the nature of his medical role, whether it be a primary care physician responsible for the patient's general medical condition, or for a defined or limited purpose, and/or as a practitioner of a particular medical specialty.
- Obtain written informed consent addressing all aspects of treatment and document same, including documentation of all discussions with the patient about the nature and scope of his evaluation and treatment and the patient's need to pursue "conventional medical care elsewhere."
- Document all histories and physicals.
- Refer patients to primary care physicians, specialists or consultants for further evaluation and/or treatment where medically warranted and provide these physicians with all relevant patient information.
- Cooperate fully with the state in enforcing the Consent Order and timely respond to all state requests for written periodic verification of his compliance and all documents.

What now?

Based on a birthdate of 1938 in his state physician profile, Raxlen is either already, or soon will be, 79 years old. One wonders whether he will continue his practice in face of these new sanctions, although his website is still trying to attract patients.

Sadly, the “chronic Lyme” lobby responsible for passing the law protecting “Lyme literate” doctors has its sights set on even greater rewards. Several bills are pending in the NY legislature which would force insurers to cover “chronic Lyme” treatment (Assembly Bill 114, Senate Bill 4713, Senate Bill 670). Other bills give them the opportunity to argue in yet another venue for insurance coverage. (Assembly Bill 4863, Senate Bill 2168, Assembly Bill 6927).

In any event, it is commendable that the Board for Professional Medical Conduct has not let New York’s unfortunate law get in the way of its prosecuting physicians who take advantage of patients with a diagnosis of “chronic Lyme,” no matter how they frame the specific charges. With two leading NY “Lyme literate” physicians now on probation and under strict orders to clean up their acts, it remains to be seen what effect this might have on other “Lyme literate” doctors in the state.

There is a simple reason we strongly promote science-based medicine – it results in the best outcomes for individuals. That is true by definition, since the SBM approach is to use the best evidence and science available in order to determine which interventions result in the best outcomes.

There are numerous ways in which relying upon poor-quality evidence or invalid methods for making health decisions cause potential harm. Often the list is unimaginatively limited to direct physical harm, but that is only the tip of the iceberg. There is financial harm, loss of opportunity to pursue more effective interventions, psychological harm from false hope and being deceived, and sacrifice of quality of life, time, and effort.

Even without direct physical harm, with inert treatments like homeopathy, there is tremendous potential harm from relying upon fake medicine and bad science. But often there is potential physical harm, and even if slight it is not justified if there is no real benefit. Medicine is a game of risk vs benefit – when the benefit is essentially zero, any risk is unacceptable.

The gluten-free fad

Even a small potential harm can be significantly magnified if it is marketed to the general public. The "clean eating" movement, in my opinion, clearly represents such a case. The best overall advice we can give the public regarding healthy eating is to eat a variety of food with plenty of fruits and vegetables and watch overall caloric intake. Unless you have special medical considerations, simply eating a good variety of different kinds of food will take care of most nutritional concerns. It will result in you getting enough of what you need and not too much of anything that can increase your risk.

Having a restricted or narrow diet is always tricky, and runs the risk that you will be getting too little of some key nutrients and may be getting exposed to too much of others. This is the key risk of so-called "fad" diets, because they are often premised on a simplistic notion that specific foods or categories of foods are inherently bad and should be avoided. Therefore any diet which

essentially consists of avoiding certain foods or heavily relying on others is likely to take you away from an optimal diet, and therefore be a net negative for your health.

The recent gluten-free fad is no exception.

As I discuss in detail here, gluten is a composite of two proteins found in wheat, rye, barley, spelt, and related grains. About 1% of the population has an autoimmune reaction to one of the components of gluten (usually gliadin) and eating gluten can cause serious illness (a condition known as celiac disease). For those with celiac disease, avoiding gluten is essential and even a small amount of gluten can cause serious symptoms.

There is a controversy, however, surrounding the alleged existence of so-called non-celiac gluten sensitivity (NCGS). This is a hypothetical condition in which people may have a sensitivity to gluten without forming antibodies to gliadin or meeting the diagnostic criteria for celiac disease. Discovering a new disease is always complex, and requires the identification of something definitive and discrete. We either need to identify a clear clinical syndrome, or some new specific pathology.

For NCGS there is no clear pathology. The entity's legitimacy currently relies on the alleged existence of individuals who do not have celiac disease but have a negative reaction to eating gluten. If, however, we are going to base a new disease purely on clinical history, we need to make sure that the history is accurate and that we are not simply overinterpreting non-specific symptoms or falling victim to confirmation bias.

For example, there are people who feel they have a specific syndrome of sensitivity to electromagnetic waves, despite the absence of any identifiable pathology. However, properly blinded studies show that self-identified sufferers of EM sensitivity cannot tell when they are being exposed to EM waves in a blinded condition.

For alleged NCGS the most salient evidence of its existence as a clinical entity are rechallenge studies. In these studies subjects are challenged with either gluten or placebo, then the gluten is removed, and then they are later rechallenged. If NCGS is a real entity then their symptoms should resolve

when gluten is removed and then return when rechallenged, at a higher frequency when the same is done with a placebo.

A recent systematic review of gluten rechallenge studies did not find significant evidence for NCGS. They conclude:

> The prevalence of NCGS after gluten re-challenge is low, and the percentage of relapse after a gluten or a placebo challenge is similar.

This is a pattern of evidence that is consistent with the null hypothesis, that NCGS does not exist – results are all over the place, with better-controlled studies tending not to show an effect, and on average there is only a tiny signal that does not reach statistical significance. The most parsimonious interpretation of available evidence, therefore, is that NCGS does not exist. Despite this fact, roughly one third of the population report that they are trying to avoid gluten.

What's the harm

What, then, is the potential harm from restricting gluten from the diet in the millions of people who do not have gluten sensitivity? Potentially, all of the things I listed above may contribute to harm.

For many people they have settled on gluten sensitivity to explain real symptoms they may be having. In this case they may be missing the real cause of their symptoms. There is therefore an opportunity cost of making a false diagnosis.

Perhaps most significantly, a gluten-free diet is very difficult. You have to eliminate all wheat and similar grains from the diet. This has become somewhat easier recently as industry is cashing in on the gluten-free fad, but it is still a significant inconvenience and expense and therefore drain on quality of life.

Further – a gluten free diet eliminates a major category of food from the diet. People on a low or gluten-free diet tend to also be low in whole grains. They risk being deficient in iron and folic acid. A recent study linked low-gluten

diets to a higher risk of type-II diabetes.

Avoidance of gluten may also result in a heavy reliance on rice as a staple grain, and this might increase the risk of heavy metal exposure. Again – having a varied diet spreads out exposure to contaminants and toxins as well as maximizing exposure to needed nutrients.

Science over marketing

If we take a scientific approach to the question of NCGS we find that there is no clear evidence that non-celiac gluten sensitivity is a real thing, and that gluten-free diets not only have no benefit for the general public they present health risks. Clearly, however, we need to do a better job of communicating this to the public.

Part of the challenge, however, is that nutritional gurus (who always seem to have something to sell) have a simple and appealing narrative to market. They tell the public that their problems are due to one bad food or type of food they just need to avoid. Or, they market of lifestyle of “clean eating” that is based on the appeal to nature and irrational fear of toxins and chemicals, rather than an even basic understanding of science and evidence.

The science-based position, however, takes time to emerge. It may take a decade or more to do the kinds of studies necessary to effective answer the question about whether or not a new hypothesized clinical entity exists. There are many types of evidence to be considered, and many sub-questions to be addressed. Over time a clear picture will tend to emerge, but in the meantime the health gurus can establish a market for their nonsense. Once their simplistic and marketable narrative gets into the public consciousness it is hard to correct.

Science Based Medicine

周一, 20 11月 2017

Science Based Medicine

[周一, 20 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **Hopelessly Devoted to Woo: TLC and Forbes Bring Us Yet Another Celebrity Healer** [周五, 17 11月 21:00]
  Endorsed by journalists and studied by academic medicine, bogus celebrity energy healer Charlie Goldsmith now has his own television program. In other words, it's just another day at Science-Based Medicine.
- **CAM use leads to delays in appropriate, effective arthritis therapy** [周四, 16 11月 22:00]
  A preference to use CAM before seeking medical advice may be harming patients with inflammatory arthritis.
- **Placebo Myths Debunked** [周三, 15 11月 21:03]
  Placebo treatments are often sold as magical mind-over-matter healing effects, but they are mostly just illusions and non-specific effects.

In recognition of my 100th post on SBM, I was all set to write about some interesting updates on a few of my contributions over the years. But thanks to the machinations of the preternaturally cool Tim Caulfield, author of *The Cure for Everything* and *Is Gwyneth Paltrow Wrong About Everything?*, I was made aware of something that I just couldn't ignore: someone is wrong on the internet. That's right, yet another "energy healer" with bold claims of miracle cures is making the rounds. But this time will be different, apparently.

Remember Adam Dreamhealer? He was the teenage "intuitive healer" that could recognize and manipulate mysterious human energy fields to cure cancer and a whole host of other ailments, even over the phone or after only looking at a photograph of the patient. He claimed to have received his powers from a giant blackbird he met while hiking. Ring a bell? Well, it was a whole thing about a decade ago, just as I was starting my journey on the path of skepticism. Although he is still up to the same tricks as a "naturopathic oncologist", and he will always have a special place in my heart, Dreamhealer has some stiff competition for my favorite celebrity energy healer.

The new kid on the block is Australian energy healer Charlie Goldsmith, and technically he isn't all that new. Orac, who I believe is some kind of protocol droid, wrote about him back in 2015. Goldsmith was just dipping his toe in the water of widespread recognition at that time, getting some press in the form of credulous fluff pieces focusing on the fact that he is Olivia Newton John's nephew and on his involvement in a ridiculous study published in the *Journal of Alternative and Complementary Medicine*. Described as a "feasibility study", it is embarrassingly amateurish, really just a collection of cherry picked anecdotes that did not involve the slightest bit of blinding or control. The authors concluded what anyone remotely familiar with research like this would have expected.

What Caulfield alerted me to this week was the publication of yet another painfully credulous article, this time on the *Forbes Lifestyle* blog. In the piece, Forbes contributor and certified Holistic Health Coach Courtney Porkoláb asks the question "does energy healing work?" and invites readers

to decide for themselves. In a conversation with her on Twitter she was quick to remind me that hers wasn't a scientific article and to imply that she just wanted to "spark conversation." Yet in the article she provides only her gullible acceptance and a series of comments from Goldsmith and a few credentialed believers endorsing the benefits of energy healing and even proposing scientific explanations. There isn't even an attempt at token skepticism.

Porkoláb gushingly discusses Goldsmith as if he is a miracle worker:

> Goldsmith's success rates are undeniably high, having relieved people of all ages, with issues ranging from chronic pain to infections and auto-immune disorders, often in 60 seconds or less.

The article contains numerous absurd assumptions and laughably implausible claims, all in the service of promoting the fact that Goldsmith is now starring in a TLC program documenting his supposed abilities. It isn't alone, of course. This *Daily Mail* article is particularly informative as it provides a clip from the most recent episode. It shows Goldsmith taking advantage of the power of suggestion as he interrogates a 2-year-old child about his symptoms before going through the standard energy healing motions. The kid is adorable but it's pretty ridiculous, and what is really happening should be clear to anyone with a modicum of experience with toddler behavior. The deciphering of the child's unintelligible responses reminded me of how ghost hunters prime listeners when demonstrating EVP.

Orac, which I understand is some kind of prototype U.S. military robot that gained sentience and a powerful sense of skepticism after being struck by lightning, beat me to the punch and wrote an excellent discussion of Goldsmith and the *Forbes* article. Feel free to hop on over and read it. I'll provide a couple of the best quotes myself, however:

> Prior to the studies done in the public eye, Goldsmith spent years healing as many as he could, often those who had been failed by countless doctors and traditional medicine.

Regular readers of SBM know how unreliable claims such as this are. Unless Goldsmith was keeping meticulous records of his healing attempts and

following up to document long term outcomes, these kinds of statements are essentially meaningless. It's very easy with confirmation bias and motivated reasoning to look back over the years and come to the conclusion that you helped a lot of people. It's easy to discount the failures and focus on the apparent successes.

And patients can be "failed by traditional medicine" in numerous ways, many of which don't actually equate to what is being implied. Patients with vague or non-specific symptoms and certain world views often feel like conventional doctors have let them down when they aren't given a specific diagnosis, or when treatment recommendations consist of lifestyle changes or mental health assessments rather than confident assertions and a supposed cure. Often proponents of pseudomedicine convince people that their doctor has failed them by missing the diagnosis of a fictional malady, such as adrenal fatigue.

I found this quote from Goldsmith particularly interesting:

> To be honest, sometimes I'll work on something that—medically—is seemingly simple and not fix it. And something that is medically complex—something medically incurable, for example—that might be quite easy for me.

He chalks this up his healing powers not being an exact art. I see this as exactly what I would expect when all that is being offered is false hope and expectation, and one is counting on various placebo effects to give the appearance of benefit. But again, unless he has been keeping strict records of his encounters, his claims regarding past treatments can't really be assessed. I'm not just going to take his word for it that he has defied our fundamental understanding of human physiology.

The credentialed believers provide some of the most memorable contributions, which you can read about in the above linked post by Orac. These include demonstrations of a lack of understanding of how pain is assessed and treated as well as appeals to quantum physics and "bioenergy". There are also references to the time Gary Schwartz supposedly found a measurable differences in the magnetic fields surrounding the hands of energy healers and to a study on bio-photon emissions after energy healing.

Let’s do the science!

Goldsmith is on a mission to prove that what he does is legitimate and not just theatrical placebo by participating in clinical trials. I already mentioned the one published “study” he participated in above, and he claims to be involved with two more taking place at the same facility. It sounds like more of the same:

> The study presently underway is being undertaken at NYU Lutheran Hospital in New York and employs a qualitative methodology to help understand the experiences of patients who encounter Mr Goldsmith’s practices.

In other words, more anecdotes without proper controls or blinding. According to his website, this study has actually been completed. It’s being written and will be submitted for publication next year. We’ll see. He also claims to be participating in a prospective RCT, again at the same facility, that is currently going through the IRB approval process. Again, we shall see if this actually materializes.

I challenged Goldsmith during a lengthy discussion on Twitter, and he reassured me that his intentions are purely altruistic. He denies financial motivation and simply wants to prove to the world that his gift is real so that science might take the phenomenon seriously. He only wants to help reduce the pain and suffering of others. He has been treating patients for years and, according to Goldsmith, he only went public in order to help entice researchers to do the studies.

I am skeptical of his motivation. History has, time and time again, revealed that believers in highly implausible and unproven therapies don’t really care what the science says. Typically the studies end up having such poor methodology that a positive result is assured, and when proper studies fail to find a true effect, they are ignored. Regardless of the outcome, proponents can point to the fact that studies were even done in the first place as evidence of their pet remedy’s legitimacy.

It is abundantly clear that Goldsmith has already decided that he has the

ability to cure people through energy healing. He didn’t notice something odd and then look to science to determine if it was true. He noticed something was odd and then did it to people with real medical problems for years before agreeing to star in a television program highlighting it. In my opinion, the research angle is just marketing and I’m embarrassed for NYU.

Several weeks ago I summarized the evidence that demonstrates that when you delay cancer chemotherapy and substitute alternative medicine, you die sooner. Thank you to the tireless Edzard Ernst, who identified non-cancer evidence that demonstrates how choosing complementary and alternative medicine (CAM) instead of real medicine, can cause harm. In this case, the example is early inflammatory arthritis (EIA), and what was studied was the relationship between CAM use, and the delay to initiation of medical therapy. Time is of the essence with inflammatory arthritis, as there are medications that can reduce the risk of permanent joint damage. This new paper adds to the accumulated evidence to show that CAM, while it is commonly thought to be harmless, can indeed harm – not only from direct effects, but also from delaying the initiation of proper, effective medical treatment.

What is inflammatory arthritis?

Inflammatory arthritis is a term that describes inflammation of the joints (and other tissues). Inflammatory arthritis can include rheumatoid arthritis, and several other conditions. These are often autoimmune conditions, where your immune system treats its own tissues as foreign, and attacks it. Pain, swelling and tenderness are typical with inflammatory arthritis, and a diagnosis is usually based on a physical examination and laboratory tests. There are now many medications that can treat arthritis, ranging from the non-steroidal anti-inflammatory drugs (NSAIDs) such as naproxen and ibuprofen, to disease-modifying anti-rheumatic drugs which include biologic drugs that can be very effective and even put the disease into remission. While inflammation can be treated, joint destruction from arthritis can be permanent, so starting appropriate therapy, quickly, is important to reduce the risk of long-term damage. Today, aggressive treatment early in the course of the disease is considered to be the standard of care, so it is important for new cases to be recognized and referred for specialist assessment as quickly as possible. Barriers to early treatment include patient delays, but also system delays like wait times for referrals. Understanding why patients may not seek treatment is a question that led to this most recent study.

Studying CAM and inflammatory arthritis

Complementary and alternative medicine (CAM) is commonly used in different cultures, including Asian cultures, where traditional Chinese medicine may even be government-endorsed, despite the lack of evidence to show it is an effective system of medicine. When a group of researchers identified that many patients with a new diagnosis of arthritis had tried CAM prior to seeking medical treatment, they hypothesized that CAM may be delaying referral and medical therapy.

This paper is from Manjari Lahiri and colleagues and was published in the *International Journal of Rheumatic Diseases*. Entitled "Use of complementary and alternative medicines is associated with delay to initiation of disease-modifying anti-rheumatic drug therapy in early inflammatory arthritis", this was a prospective survey of patients with EIA. All patients seen at one of two hospitals in Singapore where they were invited to participate. Patients were included if they had a self-reported symptom of EIA, which was defined as inflammation of two or more joints, not caused by trauma. Patients were assessed at 3, 6, and 12 months, then annually for 3 years. All participants completed a nurse-administered questionnaire on demographic, health and lifestyle factors including CAM use. In this study, CAM was defined as the ingestion of tablets, herbs, powders or drinks purported to have medicinal properties. They could be prescribed (e.g., by a practitioner in traditional Chinese medicine) or purchase over the counter. Acupuncture, therapeutic massage and cupping, when used for the purpose of a therapeutic effect where included in the definition of CAM, while exercise (including yoga and tai chi), physiotherapy, and occupational therapy were not considered CAM. (This is among the more accurate delineations of CAM/non-CAM I've seen in a study.)

CAM users delay treatment

For this study, only the baseline (time=0) results were used. Overall, 180 patients were included. The median time from diagnosis to recruitment was 3 weeks. The median age was 51, and 71% of the participants were women.

When stratified by CAM use, Chinese patients more commonly used CAM, and oral tablets/powders and acupuncture were the most common forms of CAM. Full details are in Table 1:

Table 1 Baseline characteristics

Characteristic	Proportion (%) or median (IQR)			P-value
	Overall (n = 180)	CAM users (n = 71)	CAM non users (n = 105)	
Age at diagnosis, years, median (IQR)	51.1 (40.9–59.8)	53.9 (43.8–60.7)	47.3 (40.2–58.3)	0.05
Bottom tertile, 22.3–44.3 years	33.5	25.7	39.0	0.14
Middle tertile, 44.4–57.4 years	33.5	35.1	32.1	
Top tertile, 57.5–81.4 years	33.0	39.2	28.5	
Female	70.5	68.9	71.4	0.72
Race				
Chinese	58.3	82.4	40.9	< 0.001
Malay	18.3	5.4	27.5	
Indian	16.7	8.1	22.9	
Others	6.7	4.0	8.5	
Body mass index	24.3 (21.2–27.6)	24.0 (20.3–26.4)	24.9 (21.3–28.2)	0.25
Non-English speaking	30.2	50.0	16.4	< 0.001
Level of education				
None or primary	21.2	20.3	22.1	0.15
Secondary or vocational	46.1	51.0	40.1	
Diploma or degree	32.4	25.7	37.5	
Ever smokers	26.8	35.1	20.9	0.03
Diagnosis				
Rheumatoid arthritis	83.0	83.8	83.8	0.92
Psoriatic arthritis	12.8	13.5	12.4	
Undifferentiated arthritis	3.3	2.7	3.8	
Symptom duration, weeks‡	16.5 (9.2–26.6)	20.8 (13.1–30.1)	13.7 (8.7–21.8)	0.004
Disease duration, weeks§	3 (0–16.9)	3.2 (0–18)	4 (0–16)	0.25
Sero-positive¶	57.0	62.9	52.9	0.20
RF positive	50.3	55.5	46	0.12
ACPA positive	52.7	55.9	50.0	0.70
DAS28, median (IQR)	4.30 (2.84–5.71)	4.56 (3.15–5.78)	3.86 (2.47–5.58)	0.02
Low disease activity, DAS28 < 3.2	30.3	20.8	37.2	0.07
Moderate disease activity, DAS28 ≥ 3.2 to < 5.1	38.9	43.1	35.3	
High disease activity, DAS28 ≥ 5.1	30.9	35.1	27.4	
mHAQ, median (IQR)	0.37 (0–0.87)	0.37 (0.12–0.87)	0.37 (0–1)	0.92
mHAQ ≥ 1 (vs. < 1)	24.5	21.6	26.7	0.41

P-value for comparison between CAM users versus non-users using Chi-squared test or Mann–Whitney U-test. ‡From symptom onset to first rheumatologist review. §From time of diagnosis to recruitment to the Singapore Early Arthritis Cohort. ¶Either RF or ACPA positive. IDR, interquartile range; CAM, complementary and alternative medicines; ACPA, anti-citrullinated peptide antibody; DAS28, Disease Activity Score in 28 joints; mHAQ, modified Health Assessment Questionnaire; IQR, Interquartile range; RF, rheumatoid factor

Table 1: Baseline Characteristics

The CAM stratification also shows some additional differences between the groups. There are race, language, and smoking histories that are quite different. Note that the duration of symptoms (until rheumatologist review) was 13.7 weeks among non-users and 20.8 weeks among CAM users. That is, CAM users waited almost twice as long to see a specialist, compared to non-users. Not surprisingly, this meant a delay to the initiation of disease-modifying anti-rheumatic drugs (DMARDs). Figure 1 shows the overall difference between CAM users and non-users:

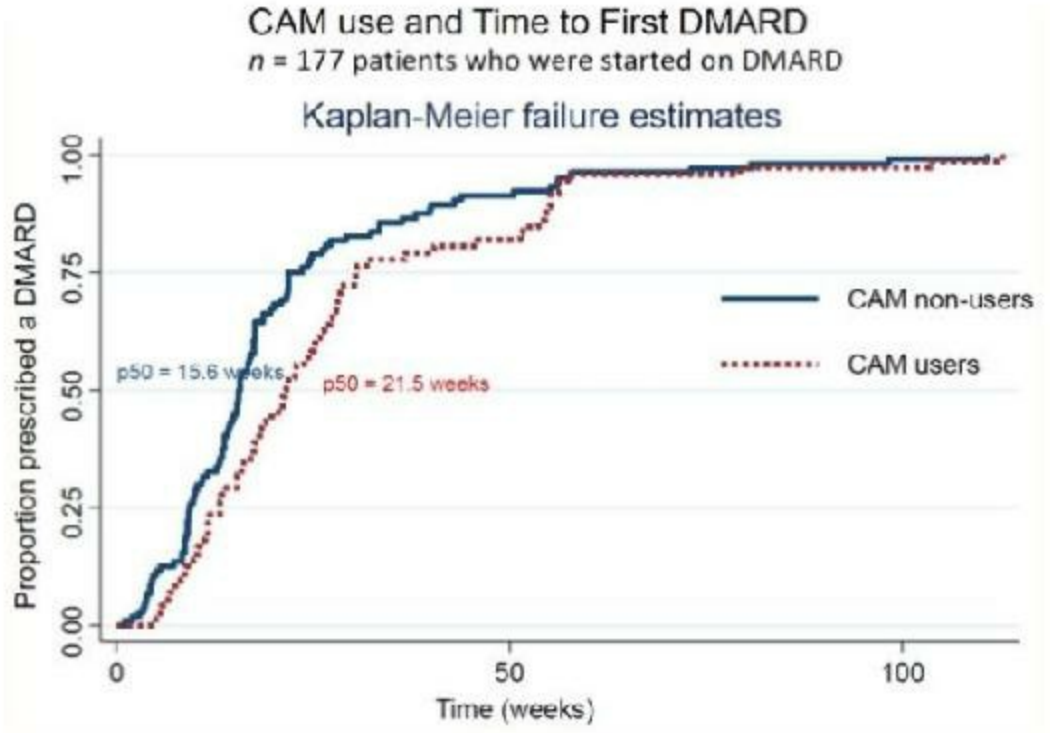


Figure 1 Kaplan–Meier plot of time to disease-modifying anti-rheumatic drugs (DMARDs) for complementary and alternative medicines (CAM) users versus non-users.

Only CAM use was significantly associated with the time to first DMARD initiation.

CAM use delays effective arthritis therapy

This small study illustrates what appears to be an unfortunate consequence of CAM use: It may be contributing to delays in seeking effective therapies, which may have additional negative consequences. While this study does not show direct harms from CAM use, the relationship between earlier therapy and positive disease outcomes is well established. The authors conclude that patient and public education programs to raise awareness about EIA, and the importance of early treatment, are essential. I would add that continuing to

raise awareness of the limitations of CAM, and the consequences of its use, need just as much awareness.

Placebo effects are largely misunderstood, even by professionals, and this leads to a lot of sloppy thinking about potential treatments. This problem has been exacerbated by the alternative medicine phenomenon.

Several decades ago, the proponents of so-called CAM promised that if only their preferred if unconventional treatments were properly tested medical science would discover how effective they are. “Effective” (or more precisely, “efficacy”) has a specific definition in medical science – it means that a treatment has been found to perform statistically significantly better than placebo in a blinded controlled trial. Several decades and thousands of studies later, the most popular CAM modalities (homeopathy, acupuncture, reiki, manipulation for medical indications, and more) have been shown to be no more effective than placebo. This means they don’t work.

Not to be deterred by reality, CAM proponents simply shifted the goal posts. Now many of them are saying that placebo effects are real, and therefore being as effective as placebo means that their treatments “work.” As part of this strategy they have promoted and amplified common myths about placebo effects. Let’s take a closer look at these myths and show why they are wrong.

Myth #1 – “The” placebo effect

The first and overriding myth about placebos is that there is one placebo effect (singular). This confusion is understandable, because scientists often refer to “the” placebo effect. However, they are referring to what is measured in the placebo arm of a clinical trial – that net effect (the difference between baseline or no treatment at all and a placebo treatment) is the placebo effect for that study.

There are multiple placebo effects contributing to that difference, however. Anything that might give the appearance of an improvement will contribute to the measured placebo effect. These placebo effects include: Regression to the mean – when symptoms flare, they are likely to return to baseline on their own. If you take any illness that fluctuates in severity, any treatment you take

when your symptoms are at their peak is likely by chance alone to be followed by a period of less intense symptoms.

Similar to this but distinct is the reality that many illnesses are self-limiting. If you have a cold, you will likely get better even if you do nothing – so anything you do will be followed by improvement. There is also bias in perceiving and reporting subjective symptoms. People want to feel better, they want to think that the treatment is working, and they may want to please the researcher or their physician. Further, researchers and doctors want their treatments to work.

There are also many possible non-specific effects just from the act of being treated. Hope can be a very positive emotion, and that alone may make people subjectively feel better. Subjects in a trial are also getting medical attention, and are likely paying more attention to their own health. They are likely to be more compliant with other treatments.

The treatment under study itself may have several components, some specific and some non-specific. Do people sometimes feel better after a session of reiki or acupuncture because they were laying down listening to music and smelling incense during the treatment? How much of a relaxation effect is at play? Does it matter if you actually stick the needles in alleged acupuncture points (the answer is no)?

Myth #2 – Placebo effects can cause healing

Because it is often believed that “the” placebo effect is one thing, that one thing is often believed to be a real mind-over-matter physical healing. There is no evidence to support this interpretation, however. In fact researchers looking for that real healing effect of placebos have only demonstrated that it doesn’t exist.

Part of the problem here is that the term “healing” is vague. It does not have a specific definition, but the implication is that biological repair is taking place. In practice researchers distinguish objective vs subjective markers of improvement. Subjective just means that the patient feels better in some way,

per their own report. They rate their own pain, for example. An objective outcome is something measurable, like blood pressure, survival, or tumor burden.

A systematic review of cancer research, for example, found that placebo interventions resulted in minor improvements in subjective symptoms, but no improvement in the cancer itself.

Placebo effects break down into several categories. One category is illusory – the misperception of improvement through regression to the mean or biased reporting. The second category is non-specific effects, such as emotional comfort from a practitioner, relaxation, or improved self-care or compliance. This third category is comprised of effects which can plausibly result from psychological interventions only. These relate mainly to stress, depression, anxiety, and the perception of pain and similar subjective symptoms. There is a mind-body connection – it's called the brain.

There is, however, no magical control of your brain over biological or physiological processes that are not networked with the brain through nerves or hormones.

Myth #3 – Animals and babies cannot have a placebo effect

This myth results from the false assumption that in order to have a placebo effect you need to believe that you are taking an active treatment. It is the belief that is causing the effect, and therefore it is a prerequisite. The logic then follows that animals and babies, who cannot know they are receiving a treatment, can therefore not have a placebo effect. Any improvement in this context, therefore, must be a physiological response to the treatment itself.

It should already be obvious, however, that these assumptions are incorrect. There are many sources of placebo effects that do not depend upon the subject knowing they are being treated, such as regression to the mean, the self-limiting nature of many ailments, and non-specific effects or benefits from simultaneous interventions.

Further, however, someone has to determine that the animal or baby has improved. That person is vulnerable to biased perception and reporting, and will also contribute to any measured effect.

This means that studies of treatments in animals or babies still need to be properly controlled, and whoever is assessing the outcome needs to be properly blinded to treatment allocation.

Myth #4 – Fanciful or alternative treatments yield better placebo effects

Desperate to salvage a role for their preferred but ineffective treatments, many alternative practitioners will argue that their real expertise is in maximizing placebo effects. OK, sure, the scientific evidence shows that my treatment is no better than placebo, but placebo effects are real, and I am very good at eliciting them. This is the “placebo medicine” gambit.

I have already debunked the first part of that claim. There is also no evidence for the second part, that alternative practitioners elicit more of a placebo effect. What the scientific evidence shows is that all interventions will produce some placebo effect, depending mainly on the outcome to be followed. The more subjective and amenable to variables such as mood, the larger the measured effect will be.

The existence of a placebo effect does not justify using inactive or pseudoscientific treatments. You can elicit the same effects from science-based interventions. Related to this is the notion of placebo effects without deception. This is certainly possible, if you include all the non-specific and statistical effects, but most patients would likely not be happy to be receiving a treatment that they were told was completely inert, just so it may bias their perception of their symptoms. All pseudoscientific treatments, even if they are justified through placebo effects, are given with a generous helping of deception, which violates patient autonomy.

The other variable that seems to be important, but requires further study, is the therapeutic relationship between practitioner and patient. Having a

positive relationship may enhance the measured placebo effect, but that may be just another measure of bias.

In any case, anything useful about placebo effects can be had with a positive therapeutic relationship, using science-based interventions, and following the ethical requirements of informed consent and patient autonomy.

Science Based Medicine

周一, 27 11月 2017

Science Based Medicine

[周一, 27 11月 2017]

- **Science Based Medicine**

Science Based Medicine

Exploring issues and controversies in the relationship between science and medicine

- **And the server migration continues apace…but where are the comments?** [周六, 25 11月 10:15]
  SBM is changing servers again. Unfortunately, that means that there are problems with the comments.
- **Happy Thanksgiving!** [周四, 23 11月 14:00]
  Happy Thanksgiving to our American readers, and to everyone else- have a great Thursday in November!
- **New Tools Against Antibiotic Resistance** [周三, 22 11月 20:24]
  Antibiotic resistance is a serious problem that may lead to a post-antibiotic era. However, there are potential solutions that deserve research priority.

And the server migration continues apace… but where are the comments? - Science-Based Medicine

As many of you noticed, there has been an issue with the comments that began last night. Here’s what happened. The Powers That Be decided to migrate the blog to a new server last night, and there were problems relinking Disqus to the new installation of WordPress. I am assured that the problem has been fixed, but also told that it could take 12 hours for all the old comments to redirect to our new location. So be patient, and the blog should be back to normal by tomorrow morning. There should be benefits to the new server as well, such as faster loading, less downtime, and the like. We’re sorry about the inconvenience today, but as one of our crew noted, for some reason migrations never seem to go as smoothly as we would like.

In any event, if after tomorrow there are still problems, let us know.

Happy Thanksgiving! - Science-Based Medicine

We celebrate Thanksgiving today in the U.S. and SBM is taking the day off. We are thankful for all of our readers and commenters and wish you a Happy Thanksgiving.

New Tools Against Antibiotic Resistance - Science-Based Medicine

Scientists are often placed in the role of Cassandra – because of their expertise and knowledge they may see potential serious problems on the horizon, but may also find it challenging to convince the general public. Sometimes they are working uphill against vested interests. Often scientists will warn against possible problems that they then work to prevent, and when successful it seems like their warnings were unwarranted. Or they may simply be calling for preparation for a possible event, like an epidemic, that still probably won't occur but you should be prepared ahead of time in case it does.

Also, as science communicators we don't want to overhype potential problems. It can be a delicate balance. With all that in mind, it is probably difficult to overstate the potential risk of antibiotic resistance. This is one of those looming issues that I genuinely worry about, but gets too little attention, if anything, in the media. It is also a manageable problem – there are things we can do to mitigate antibiotic resistance, if we take the issue seriously enough.

The World Health Organization summarizes the problem in stark terms:

> Antibiotic resistance is rising to dangerously high levels in all parts of the world. New resistance mechanisms are emerging and spreading globally, threatening our ability to treat common infectious diseases. A growing list of infections – such as pneumonia, tuberculosis, blood poisoning, gonorrhoea, and foodborne diseases – are becoming harder, and sometimes impossible, to treat as antibiotics become less effective.
>
> Where antibiotics can be bought for human or animal use without a prescription, the emergence and spread of resistance is made worse. Similarly, in countries without standard treatment guidelines, antibiotics are often over-prescribed by health workers and veterinarians and over-

> used by the public.
>
> Without urgent action, we are heading for a post-antibiotic era, in which common infections and minor injuries can once again kill.

I don't think they are overstating the problem.

The cause of antibiotic resistance is fairly easy to understand. Bacteria reproduce very quickly in large numbers. When someone takes an antibiotic, that provides a selective pressure towards resistance. If any individual bacterium has a gene which provides resistance to the mechanism of that antibiotic it will tend to survive the treatment and then reproduce a new generation of resistant bacteria.

Bacteria also have the ability to swap genes, so that are not just passed from parent to offspring, but horizontally to other bacteria in a process called conjugation. Bacteria may contain plasmids, which are loops of DNA. Those plasmids can be copied from one bacterium to another. A plasmid may contain one or even multiple genes that confer resistance – and so in one conjugation event a bacterium may receive resistance to multiple antibiotics.

The existence of bacterial plasmids with multiple resistant genes is a problem, because if they are exposed to one of the antibiotics to which they are resistant, that will favor the proliferation of the bacteria with plasmids that confer multiple resistance.

There is one potential bright spot in all this. Genes that confer antibiotic resistance often come at a price. They may make it more difficult for the bacteria to reproduce, or force them to expend more energy. That is why they don't have the feature in the first place. The selective pressure of antibiotics is necessary to favor the more costly feature. The hope is that in the absence of selective pressure from antibiotic, the resistant features will tend to fade away.

However, a new study suggests that this may not always be the case. Researchers looked at costly antibiotic resistance features in various strains of *E. coli*. They followed them for over a month and found that strains were able to maintain even costly antibiotic resistance in the absence of antibiotics if

they contained plasmids. The key is the conjugation rate – how frequently do bacteria exchange plasmids? The research found that, at least in these strains, the rate was high enough to maintain antibiotic resistance even in the absence of antibiotics.

This research suggests that limiting antibiotic use may not be enough to reverse existing antibiotic resistance. Of course, limiting use is essential to slowing the development and spread of resistance. This is the primary mechanism by which the medical community is trying to combat resistance, but even here we are not doing enough. Antibiotics are still massively overprescribed. Some countries allow for over-the-counter antibiotic use, and it is common for the public to take them for viral illnesses. Antibiotics are also heavily used in the farming industry.

Even if we achieved our goal to properly limit antibiotic use, and educated practitioners to optimally prescribe antibiotics, the current research suggests this may not be enough to reverse some types of resistance. However, the same research suggests there may be more active interventions that will.

There are potential drugs that can limit conjugation or induce bacteria to lose their plasmids. For example, a 2015 study identified features of synthetic fatty acids that were effective conjugation inhibitors. This would limit the horizontal spread of plasmids among bacteria, and therefore limit the spread of resistance.

Another approach is to prevent plasmid replication. Researchers are looking at ways to exploit the existing compatibility system in bacteria toward this end. Since bacteria are so promiscuous with their genes, they need mechanisms to know when plasmids are incompatible with their other DNA. You could essentially trick a bacterium into thinking its plasmid is incompatible, and therefore when the bacteria reproduces it will not replicate the plasmid. The plasmid will therefore be lost to the next generation. These treatments would not just limit the spread of resistance, but cause a population of bacteria to lose their resistance.

What all of this research suggests is that we should not only be researching novel antibiotic mechanisms, we should be investing in research into drugs that inhibit plasmid conjugation and induce plasmid loss. These treatments

can reduce the spread of resistance, and even potentially reverse resistance. Such treatments could be given alongside antibiotic regimens, or used in farming or similar contexts to limit the development of resistance.

My hope is that this type of research will eventually lead to a situation in which all those scientists and science-communicators who warned about the coming post-antibiotic era will look like Cassandras. Rather than getting the credit for identifying and then preventing a major problem, people will either forget them or falsely think the warnings were overhyped to begin with. But I will take that fate if it means avoiding a post-antibiotic era.
