

Integrative Medicine

Evidence-based summaries and critical reviews on
the latest developments in integrative therapies [ALERT]

CARDIOVASCULAR DISEASE

SPECIAL FEATURE

Fried Foods: Friend or Foe?

By *Luke Fortney, MD*

UnityPoint-Meriter McKee Clinic, Madison, WI

Dr. Fortney reports no financial relationships relevant to this field of study.

SYNOPSIS: Frequent consumption of food fried (four or more times a week) in reused oils significantly increases obesity and type 2 diabetes, hypertension, and hyperlipidemia, and is associated with increased risk of cardiovascular disease. What remains unknown, however, is the ideal duration, temperature, and method for safe frying, as well as how often oil can be reasonably reused.

SOURCE: Gadiraju TV, et al. Fried food consumption and cardiovascular health: A review of current evidence. *Nutrients* 2015;7: 8424-7430.

What we eat, and perhaps more importantly what we *don't* eat, has long been a key question in nutrition research in terms of health promotion and disease prevention. However, in the modern era, patients and clinicians alike often find that dietary guidelines are often incomplete, outdated, or confusing. The standard American diet has long been the standard for how *not* to eat, and is an example where fad diets and misinformation can lead us astray. For example, the “low-fat” craze of the 1980s and '90s ushered in years of unhealthy, scattered, and confused eating patterns that only lead to worsening health and obesity in the United States.¹ One of the main reasons for this was the substitution

of sugar in place of fat (fructose in particular) in many processed foods, as well as widespread use of the now maligned trans-fats.

Evidence pointing toward this concerning health decline comes from temporal comparisons of U.S. adults between 1988-1994 and 2001-2006, which found significant increases in body mass index (BMI) and alcohol consumption, while exercise and fruit/vegetable intake decreased. Overall, general adherence to a healthy lifestyle decreased by nearly half (15% to 8% of all U.S. adults between these time periods).¹ This is particularly concerning given that the larger European Prospective Investigation

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Summary Points

- Not all fried oil is equal. Like the phenomenon of the “French Paradox” there appears to be a protective “Spanish Paradox” with fried foods, particularly when compared with frying techniques in the United States.
- Eating fried food in general should occur infrequently, ≤ 3 times per week.
- When choosing oils for frying, refined olive oil (not extra-virgin) is the sensible choice (see resources for culinary recommendations).
- Fried foods are calorie-dense and contribute significantly to weight gain and obesity, which then increase diabetes, hypertension, and hyperlipidemia, which in turn are the most important factors leading to cardiovascular disease such as heart attack and stroke.
- Avoid reusing oil for prolonged frying, which increases the production of harmful phytosterol oxidation products and polycyclic aromatic hydrocarbons.
- Although specific data and guidelines are lacking, it is sensible to use lower temperatures for shorter periods of time when frying.

Into Cancer and Nutrition study (EPIC) found that the incidence of type 2 diabetes mellitus (T2DM), cardiovascular disease (CVD), and cancer could be significantly reduced by simply not smoking, maintaining a reasonable weight (BMI $< 30 \text{ kg/m}^2$), getting at least 3.5 hours of exercise per week, and eating a reasonably healthy diet.²

From the nutrition aspect of this health decline, much more has been learned about the beneficial qualities of healthy fats such as olive oil. As the old medical adage states: *Nutrition is just as much about the quality of calories as it is about the quantity.* When it comes to fats, it is becoming clearer that both the type of fat and how it is used in food preparation are very important, particularly with high-heat frying.

Dietary intake of fats used for grilling, pan-frying, and deep-frying is one of the major ways to be exposed to polycyclic aromatic hydrocarbons (PAHs) through use of high cooking temperatures. PAHs are important because they contribute to lifetime cancer and CVD risk.³ In addition, frying foods in oil also results in formation of phytosterol oxidation products (POPs), which are similarly cumulatively deleterious to health over time. What's interesting and relatively new information is the observation that pan-frying and longer frying times (e.g., 30 vs 60 minutes vs 120 vs 240 or more

minutes) generates more POPs.⁴ The longer oils and fats are exposed to the higher cooking temperatures used in frying, the more POPs and other deleterious compounds are generated.⁴

■ COMMENTARY

While it may seem obvious that fried food consumption is deleterious to health, its actual effects on cardiovascular and cancer-related deaths are still subjects of debate. What has remained surprisingly unknown is to what extent frying contributes to and causes disease in human beings. A recent study approached this question by reviewing the evidence, and found that there is an association between fried food consumption and CVD, particularly with hypertension, hyperlipidemia, diabetes, and obesity.⁵ However, most of the data come from questionnaires as the main tool to capture fried food intake and are limited to case-control and cohort studies. Interestingly, the review by Gadiraju et al identified only a small number of studies that, to date, have reported an actual association between frequency of fried food intake and risk of CVD (such as coronary artery disease and heart failure). What's surprising is the lack of follow-up studies to confirm these associations.

Based on this and other reviews, there are significant gaps in the current medical literature that include a lack of information on the type of oils used for

Resources for Culinary Recommendations

- Culinary guidelines for frying oils: <http://www.serious-eats.com/2014/05/cooking-fats-101-whats-a-smoke-point-and-why-does-it-matter.html>
- Updated general dietary guidelines: <http://health.gov/dietaryguidelines/>

frying, temperature and duration of frying, how often oils were reused, whether food was fried at home or in a restaurant, actual frying procedures, and the influence of other lifestyle factors. From a research standpoint, there is an overall lack of understanding about other contributing dietary patterns with frying, in terms of risk stratification for what foods might be more harmful when fried.⁵

In terms of scientific certainty and understanding, the best that can be stated to date about the health effects from fried food is that frequent consumption is significantly associated with incidence of T2DM (see article on page 35), but only moderately with developing CVD. However, most of this association appears to be mediated directly by increasing obesity, which then drives incidence of diabetes, hypertension, and hyperlipidemia.⁶

Recently, two large, long-term, prospective trials involving two cohorts of U.S. men and women concluded that there is enough evidence to suggest a higher risk of developing at least one chronic disease of lifestyle when fried foods are consumed four or more times a week, but much more high-quality research is needed to clarify the actual, specific, adverse impact on health as well as mechanisms of action.⁶

HEALTHY OILS FOR FRYING? THE MEDITERRANEAN EFFECT AND THE 'SPANISH PARADOX'

There is emerging evidence to suggest that the quality and type of oils used for frying may be important, as well as specific cooking techniques. The Spanish cohort of the EPIC study helped address these questions by prospectively evaluating the associations between fried food consumption and CVD among 40,757 adults from 1992 to 2004.⁷ Ultimately, in Spain, where olive oil and sunflower oil are predominantly used for frying, the consumption of fried foods was *not* associated with coronary heart disease or with all-cause mortality.

The authors of this large study cited the potential mitigating effects of sunflower and olive oils compared to others. For example, olive oil is less prone to oxidation at standard frying temperatures than other fats. Similar results were found in a non-fatal

myocardial infarction study based in Costa Rica, where palm and soy oil are commonly used for frying (both are liquid at room temperature).⁸

On the other hand, frying solid fats, such as lard and butter (compared to the liquid nature of plant-based olive and sunflower oil at room temperature), is also known to increase levels of harmful trans-fats and POPs through the high-heat cooking process. In addition, the frying in particular (compared to boiling) in some foods, such as eggs, has been found to increase the production of angiotensin-converting enzyme inhibitory peptides (which help lower blood pressure) as well as reduce paraoxonase activity (an enzyme that inhibits oxidation of LDL “bad” cholesterol). What’s more, and not surprisingly, reused oil has been shown to impair arterial endothelial function more than previously unused oil.⁹ However, the frying process is complex, and still not yet completely understood in terms of health consequences, with many laboratory studies showing that fried foods affect the body in many ways, which are particularly difficult to anticipate.

The authors of the Spanish cohort of the EPIC study also pointed out that most fried foods in the Spanish-Mediterranean diet are prepared at home with fresh ingredients and oils compared to reused oils common to many fast food and other restaurants in the United States. Consumption of fried processed snacks, which are also high in salt and sugar, is relatively low in Spain compared to the United States, where consumption of fast food is often a proxy for slower, home-cooked food. That being said, these and other variables were controlled and accounted for in this and other high-quality studies.

ADVERSE RISK OF FRIED FOOD: THE ‘STANDARD AMERICAN DIET’ STRIKES AGAIN

To emphasize this point, in the Nurses’ Health Study (NHS) in the United States, a prospective cohort of 121,700 female nurses, as well as 51,529 men from the Health Professionals Follow-Up Study (HPFS) were followed over many years. Cahill et al found that fried food consumption was significantly associated with the risk of incident T2DM and coronary artery disease, as mentioned above.⁶ These associations remain significant after controlling for demographic, diet, and other lifestyle factors such as smoking. This was the first study, interestingly, to actually examine and report these adverse health associations with frequency of fried food consumption. These two prospective U.S. studies also did not find any correlation with types of foods being used and consumed with frying (e.g., red meat and potatoes). Furthermore, similar to the Spanish study, fried foods consumed away from home (i.e., at a restaurant and fast food) were more strongly associated with diabetes and heart disease.

The authors attributed these disparities to the advanced, deleterious deterioration (increased polymerization, oxidation, and hydrogenation in the formation of unhealthy trans-fat, as well as increased degradation of healthy polyunsaturated fat) of reused fats from the frying process as well as larger portion sizes in the United States compared to Spain and other places in the world. Not surprisingly, both the HPFS and NHS studies pointed to increases over time in BMI, hypertension, T2DM, and hyperlipidemia with increased frequency of fried foods. ■

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BONE HEALTH

ABSTRACT & COMMENTARY

Chiropractic for Ankle Sprains?

By David Kiefer, MD, Editor

SYNOPSIS: Ankle joint chiropractic manipulation as adjunctive therapy to typical rehabilitation improves symptoms of chronic ankle instability from repeated sprains.

SOURCE: Lubbe D, et al. Manipulative therapy and rehabilitation for recurrent ankle sprain with functional instability: A short-term, assessor-blind, parallel-group randomized trial. *J Manipulative Physiol Ther* 2015;38:22-34. doi: 10.1016/j.jmpt.2014.10.001.

Ankle sprains, usually related to an inversion mechanism, are a common injury. The authors of this study found that 40% of such injuries progress to chronic instability and/or pain, a major justification for the search for techniques to strengthen and improve functionality in the ankle in the long term.

Damage to the anterior talofibular ligament, if not all three of the lateral collateral ligaments, as well as loss of dorsiflexion, and, as the authors detailed, “loss of the posterior glide of the talus” and proprioception, all contribute to instability with activity that may or may not be detectable during a physical examination. Traditional treatments include proprioceptive exercises and muscle strength training, both of which have documentation in the medical literature for their utility. The authors wanted to expand on this research by studying joint manipulation as an adjunctive therapy to standard rehabilitation techniques.

The study included patients with “recurrent ankle sprain with functional instability,” a modification of the original inclusion criterion of “chronic ankle instability (CAI)”¹; the researchers found it difficult to

meet the strict definition of CAI, so they broadened their search for participants. Participants had to have had a history of inversion ankle injuries (but none within the last 6 weeks) and mortise joint tenderness and/or pain. Thirty-nine patients met these eligibility criteria, and were then screened for inclusion in the study (see Table 1); five patients did not meet the criteria for inclusion and one declined to participate,

Summary Points

- This is a randomized, parallel group (no placebo), 5-week clinical trial in 33 patients with chronic ankle joint instability.
- Ankle manipulation administered by chiropractors relieved pain to a greater degree than rehabilitation alone.
- There was no statistically significant improvement in ankle function as per a standardized test.

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> • Tenderness or pain at the site of injury (the presence of swelling or bruising wasn't necessary) • A history of recurrent sprains • Minimal (or no) varus laxity or anterior drawer sign 	<ul style="list-style-type: none"> • Full range of motion with no pain • Significant varus laxity or anterior drawer sign • Acute (within 6 weeks) injury • Balance disorders, neurological disease, connective tissue disorders, peripheral vascular disease

Table 2: Visual Analog Scale (VAS) and Foot and Ankle Disability Index (FADI) Results

	FADI Baseline	FADI 5 weeks	VAS Baseline	VAS 5 weeks
Rehabilitation only	75.9	91.3 ($P = 0.003$ vs baseline)	40.0	22.1 ($P = 0.0016$ vs baseline)
Manipulation and rehabilitation	80.4	98.9 ($P = 0.001$ vs baseline)	47.3	6.2 ($P < 0.0001$ vs baseline)
		$P = 0.26$ between groups		$P = 0.0059$ between groups
Note: An improvement in ankle symptoms and function occurred with a lower VAS and/or a higher FADI. Also, there was no "manipulation only" group.				

leaving 33 patients for randomization. Randomization was to either standard care (18 people), or standard care plus manipulation (15 people) for 5 weeks. Standard care rehabilitation was done daily and included balance board and coordination training exercises, and strength training, the specifics of which were detailed in the article (in case the reader would like to duplicate in clinical practice).

An instructor reviewed the protocol with the participant at the beginning of the study, and then the study participant completed daily exercise at home, with printed instructions to reference if necessary. The manipulation group completed the same rehabilitation protocol as described above while also receiving six manipulation treatments over the course of the 5 weeks from an "experienced chiropractic clinician." The manipulation type was high-velocity-low-amplitude thrust-type and involved the mortise, subtalar, and/or tarsal joints. (See Figure 1.) There was some variability of the joint manipulated in each participant depending on the findings of the chiropractor with respect to joint restrictions. The researchers decided to have different practitioners examine the research participants for the presence of joint restrictions than the clinicians who administered the treatments. Separate providers, essentially a "blind assessor" and a treating clinician, were deemed necessary to avoid examination bias.

The primary outcome was pain as determined by the Visual Analog Scale (VAS; 0-100 mm) and the Foot and Ankle Disability Index (FADI; 26 items, 4 for pain, and 22 for activity-related items; 104

total points, 0-4 points per item). A higher score on the FADI indicates better ankle function, whereas a higher VAS score indicates more pain. A secondary outcome was joint motion palpation as determined by the "experienced chiropractic clinician." Data were analyzed using an intention-to-treat analysis.

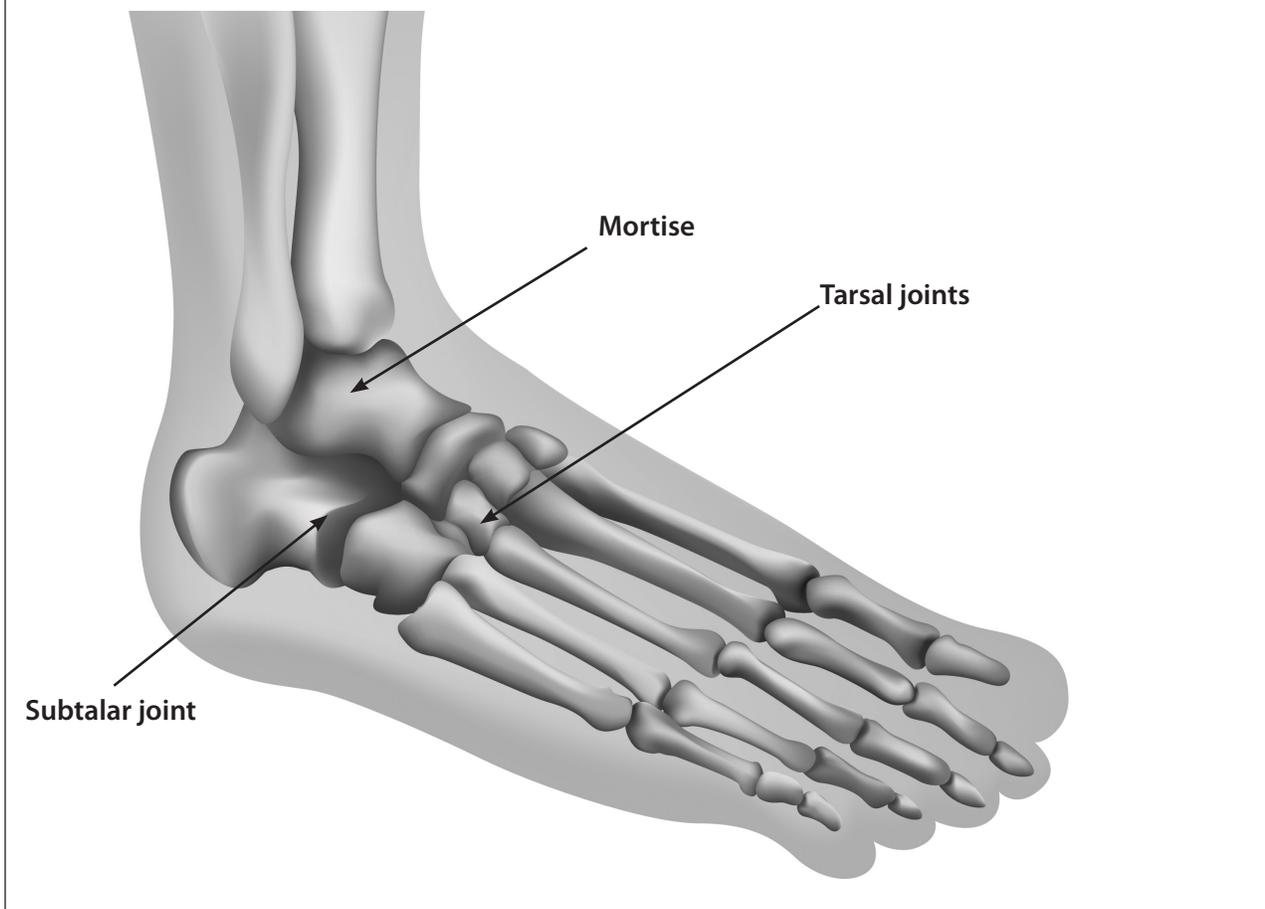
For the 33 participants, the average age was 26, the average number of days with symptoms ranged from 136-484 (average 270), and participants had an average of five prior ankle sprains. During the study, participants completed an average of 30 rehabilitation sessions (out of 35 possible). The results of the VAS and FADI testing are shown in Table 2. Only the VAS showed statistically significant differences between the manipulation-rehabilitation and rehabilitation groups after the 5-week study period. Of note, the FADI and the VAS improved from baseline in both groups. No adverse events were reported, and there were no complications of the treatment, such as persistent severe pain, stiffness, or disability.

■ COMMENTARY

Perhaps, manipulation isn't just for the back anymore. Practitioners of manipulation (physical therapists, osteopathic physicians, and chiropractors) have long known of the utility of the technique for a variety of locales beyond the spine. This study lends some credence to its usefulness for pathology in a distal joint, in this case, the ankle.

In this trial, the VAS for pain showed improvements in the manipulation group compared to the rehabilitation group, whereas the FADI, weaving in some functional

Figure 1: Ankle Joints



assessments, did not differ significantly between the two groups. It is tempting to ascribe these findings simply to a “provider effect,” the well-known benefits that come with a hands-on aspect of a clinical encounter. This study could be explained completely in this way. Furthermore, the lack of a placebo group complicates our attempt to definitively comment on either of the therapies (rehabilitation or manipulation) studied here. Perhaps, soft tissue massage would have accomplished the same outcomes if touch were the important intervention. All told, what seems to be lacking in making an argument that there is more going on here than simply clinician touch is a convincing mechanism of action; although there are known restrictions in joint motion after an injury or other pathological disease states, why would removing those restrictions necessarily improve functionality? It makes one wonder how that might be studied and clarified.

Predictably, given the known benefits to a dedicated rehabilitation program, all groups showed improvements in both the FADI and VAS when the 5-week assessments were compared to baseline. This reaffirms that ankle rehabilitation works, and all

patients with one-time or repeated injuries or lingering symptomatology should be encouraged to stick with a prescribed course of treatment.

Do these results translate easily into clinical practice? Chronic ankle instability is not uncommon, so presumably such patients will appear on our schedules at some point. “Real life” will have the diagnosing and treating clinician as the same person, so having different providers involved in this study seems to complicate the treatment, even possibly creating miscommunication and improper treatment, an issue the researchers acknowledged as well. However, these results might be enhanced, and the clinical utility bolstered, with the same clinician diagnosing and treating, as would happen in daily clinical practice — grounds for another study.

Is there any reason not to offer manipulation to a rehabilitation program? The researchers commented on the lack of adverse effects, although the methodology didn’t outline a specific approach to collecting that information. It might be safe. There is a cost issue such that the researchers offer a suggestion: Try 1 month of rehabilitation exercises and then

add manipulation if the participant doesn't achieve satisfactory results, with an earlier start if pain is the primary symptom or to address "joint restriction," especially in athletes. It is unclear why our athletic patients should have manipulative therapies sooner

than others. Perhaps, once again, the way to weave in this treatment approach is a negotiation between patient and provider using the art of medicine to color the sparse facts that have arisen from this, and other, clinical trials. ■

WOMEN'S HEALTH

ABSTRACT & COMMENTARY

That's Not a Hot Flash, It's Kidney Yin Deficiency: Try Acupuncture?

By David Kiefer, MD, Editor

SYNOPSIS: Both real and sham acupuncture provide benefits for women suffering from menopausal hot flashes, including for months after the treatment ends.

SOURCE: Ee C, et al. Acupuncture for menopausal hot flashes: A randomized trial. *Ann Intern Med* 2016;164:146-154. doi:10.7326/M15-1380.

Menopausal vasomotor symptoms, including hot flashes and night sweats, are often imperfectly treated by conventional and integrative therapies, and the data for acupuncture are mixed, rife with methodological flaws and small sample sizes. The authors of this trial pointed to only one prior acupuncture study with a sham, or nonfunctional, acupuncture arm. Hence, their justification to expand the literature on this topic.

This is a randomized, blinded (except for acupuncturists), parallel, sham-controlled trial. Women were included if they were postmenopausal or in late menopausal transition (> 12 months without menstruation, or elevated follicle stimulating hormone plus vasomotor symptoms plus > 2 months amenorrheic, respectively). Also, the trial included women with a hot flash score of at least 14 (*see Figure 1*), or who had kidney yin deficiency. Kidney yin deficiency, per the authors, is common in women who are postmenopausal and have symptoms; this diagnosis was determined by experienced acupuncturists via history, and tongue and pulse examination. There were extensive exclusion criteria, the most likely of which to affect a typical clinical practice were any acupuncture within the prior 2 years, medical reasons for amenorrhea, uncontrolled thyroid disease, hormone replacement therapy or vaginal estrogen therapy, or vasomotor treatment in the prior 3 months.

The acupuncture treatment was a standardized protocol, based on Chinese acupuncture to treat kidney yin deficiency as extrapolated from effective treatments described in a reputable textbook, medical literature, and clinical trials, and from three experts'

Summary Points

- Menopausal vasomotor symptoms respond to 8 weeks of either real or sham acupuncture treatments.
- Benefits are seen in number and severity of hot flashes, quality of life, and anxiety/depression, and these benefits persist even for 6 months after the acupuncture treatments end.
- Real acupuncture causes a greater number of mild side effects, such as pain and bruising, than does sham acupuncture.

commentaries. Treatments were for 20 minutes, and were administered twice weekly for 2 weeks, then weekly for 6 weeks (a total of 8 weeks). Sham acupuncture used a device that replicated the visual and physical sensation of receiving acupuncture without any needle insertion. The researchers cited literature that differentiates the clinical effect of sham vs true acupuncture and supports this methodology. There was no placebo group.

The primary outcome was the number and severity of hot flashes at the end of 8 weeks. Study participants recorded numbers of mild, moderate, severe, and very severe hot flashes. A hot flash score was calculated as delineated in Figure 1. Table 1 displays the information collected at different time points of the study, and included the above-mentioned hot flash diary, as well as the Menopause-Specific Quality

Figure 1: Calculation of Hot Flash Score

Hot Flash Score = (number of mild hot flashes x 1) + (number of moderate hot flashes x 2) + (number of severe hot flashes x 3) + (number of very severe hot flashes x 4)

Table 1: Data Collected During and After the Acupuncture Study

	Time				
	Baseline	4 weeks	8 weeks (end of trial)	3 months after trial	6 months after trial
Demographics					
Hot flash diary	Hot flash diary	Hot flash diary	Hot flash diary	Hot flash diary	Hot flash diary
MSQLQ	MSQLQ	MSQLQ	MSQLQ	MSQLQ	MSQLQ
HADS	HADS	HADS	HADS	HADS	HADS
			Inquiry about other hot flash treatments	Inquiry about other hot flash treatments	

MSQLQ = Menopause-Specific Quality of Life Questionnaire; HADS = Hospital Anxiety and Depression Scale

of Life Questionnaire (MSQLQ) and the Hospital Anxiety and Depression Scale (HADS).

The researchers screened 2140 women and, after exclusions and participation declinations, an acupuncturist examined 347 patients, 338 of whom had kidney yin deficiency, and 327 were then randomly assigned (163 to acupuncture, 164 to sham acupuncture). At the end of treatment, 16% of women in the acupuncture group and 13% in the sham acupuncture group were lost to follow-up. A total of 279 women had data included from the end of the trial, though some of these data were incomplete; for example, 46 women did not complete all acupuncture (real or sham) treatments. Researchers provided detailed information about dropouts and missing data. Women who were lost to follow-up or dropped out underwent an intention-to-treat analysis.

The mean age of the study participants was 55 years, and baseline characteristic analyses were similar between treatment and sham groups, except for the fact that women in the sham acupuncture group had more prior experience with acupuncture (78% vs 64%). Overall, both the sham and true acupuncture groups showed improvements in hot flash score, frequency, and severity, and in the MSQLQ and HADS from baseline to 4 and 8 weeks. These results approximated a 40% improvement, and were sustained to 3 and 6 months post-trial. There were no statistically significant differences in any of the time points group-by-group.

No serious adverse events were reported in the trial, although the acupuncture group had more mild-moderate events (21 vs 5), such as pain or bleeding/

bruising, that the researchers ascribed as being “intrinsic” to acupuncture and not of concern.

■ COMMENTARY

This is not the first randomized, controlled trial exploring the use of acupuncture for menopausal hot flashes, nor is it the only integrative therapeutic studied for this condition. Given the less-than-convincing efficacy (and safety) of conventional treatments, many of our patients with hot flashes continue to suffer, necessitating a search for viable options. We have reviewed other trials for acupuncture and hot flashes,¹ and surely will do so again until the research refines itself. The methodology of this trial is impressive, and had the possibility of providing definitive proof of the utility of acupuncture for this condition. Except for the fact that, in this case, acupuncture didn’t work.

Where did it all go wrong? Acupuncture should have shown efficacy in this trial. It has a plausible mechanism, and the researchers cited research showing that acupuncture might affect monoamines, which are relevant to the development of hot flashes. In addition, this trial was well-organized, adequately powered, and grounded in traditional Chinese medicine diagnosis and treatment. The large numbers of dropouts and participants lost to follow-up are certainly implicated in the interpretation of the final results, although the researchers analyzed the data in many different ways to factor in these effects, failing to find clinically relevant information in missing vs non-missing data.

Another factor possibly accounting for a lack of acupuncture effect is that sham does not equal placebo; the device, considered “...the best available sham acupuncture method at the time of study design...,”

still provides a needle prick sensation with only “minor” physiological effects. This phenomenon catapults us into the philosophical stratosphere of the meaning behind placebos and whether it is possible to have a non-functioning placebo to which other treatments are compared, or even whether it matters; in clinic, we want the placebo (the *positive* placebo) to be involved in healing. In the case of hot flashes, researchers have an uphill battle due to a disproportionately high placebo effect that is difficult to outperform with any particular treatment. Maybe there is an effect with acupuncture, but we just can’t see it.

Perhaps, clinicians should just fall in line with Cochrane²; acupuncture works for hot flashes when compared to no treatment at all, but not when

compared to sham acupuncture. So, please do *something* for your patients with hot flashes, rather than nothing at all (as we all know, avoid “Sorry, there’s nothing I can do for you.”). At least we know, from this study and others, that we can provide relief to our patients with menopausal hot flashes, until a better comparative treatment (adequate sham) is being worked out by researchers to tell us whether that relief comes from “true” acupuncture or something close to it. ■

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SHORT REPORT

Chinese Herbal Medicine for Esophageal Cancer

By *Concepta Merry, MB, BCh, BAO, BA*

Associate Professor, Global Health, School of Medicine, Trinity College Dublin; Integrative Medicine Fellow, University of Arizona, Tucson

Dr. Merry reports no financial relationships relevant to this field of study.

SYNOPSIS: Although Chinese herbal medicine probably does not slow disease progression or improve survival in esophageal cancer patients, it may improve quality of life and reduce adverse effects of radiotherapy and chemotherapy.

SOURCE: Chen X, et al. Chinese medicinal herbs for oesophageal cancer. *Cochrane Database Syst Rev* 2016 Jan 22; CD004520.

Esophageal cancer ranks as the seventh leading cause of cancer deaths globally.¹ Triggers for the disease are largely lifestyle-related and include nutrition,² cigarette smoking,² alcohol consumption,³ or drinking hot beverages.⁴ Traditional Chinese herbal medicine is sometimes used for advanced esophageal cancer. There are 3813 published studies examining the use of Chinese herbal medicine in esophageal cancer.⁵ Two possible reasons for the high level of interest in Chinese herbal medicine for esophageal cancer are: 1) Esophageal cancer is relatively common in northern China,¹ and 2) A limited number of effective allopathic treatment options for advanced esophageal cancer are available.

Several papers have suggested possible benefits of Chinese herbal medicines in esophageal cancer. For example, herbs such as mugwort (*Artemisia annua*, qinghaosu)⁶ and *Hedyotis diffusa* (*Oldenlandia diffusa*, spreading hedyotis)⁷ may play a role in inhibiting tumor growth.

Chen et al reviewed the efficacy and tolerability of Chinese herbal medicine when added to chemotherapy

Summary Point

- This Cochrane review found that Chinese herbal medicines for esophageal cancer may help improve quality of life and stave off the side effects of chemotherapy and radiation, but not benefit cancer overall.

or radiotherapy for patients with esophageal cancer.⁵ They assessed 3813 published studies and even phoned authors to get more detail. Only 9 of the 3813 studies were deemed methodologically sound and of high enough quality to be included in the final Cochrane review. Overall, the authors found no evidence that Chinese herbal medicine is an effective adjunctive treatment for esophageal cancer. However, they concluded that Chinese herbal medicine probably is beneficial in terms of quality of life and increased tolerance of the side effects caused by radiotherapy or chemotherapy.

The Chinese herbal medicines studied were tailored to the root cause of the illness for each individual patient, which meant using a wide variety of treatments. Most Chinese herbal medicines prescribed consisted of a variety of different herbs and not a single herb. This variability would mean that a large number of patients would have to be studied to draw any reliable conclusions using the randomized, controlled trial model. The reviewers also commented that the Chinese physicians appeared to “misunderstand” the importance of random allocation in the research process. Finally, no placebo was used in any of the control groups.

Larger, more rigorously designed studies are needed to detect clinically important effects and minimize the risk of bias. Perhaps another conclusion could be that the randomized, controlled trial is not the ideal way to evaluate some types of treatments, especially

those stemming from whole medical systems or individualized treatments. ■

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SHORT REPORT

Perils of High-dose Vitamin D Supplementation

By *William C. Haas III, MD, MBA*

Integrative Medicine Fellow, Department of Family and Community Medicine, University of Arizona, Tucson

Dr. Haas reports no financial relationships relevant to this field of study.

SOURCE: Bischoff-Ferrari H, et al. Monthly high-dose vitamin D treatment for the prevention of functional decline. *JAMA Intern Med* 2016; doi:10.1001.

The Endocrine Society recommends that adults ≥ 70 years of age should supplement with 800 IU of vitamin D daily.¹ Unfortunately, raising blood levels of 25-hydroxy vitamin D above the level of insufficiency (> 30 ng/mL) often requires at least 1500-2000 IU daily.² Recent trials also indicate that supplementing with 800 IU daily neither improves physical function nor reduces the risk of injurious falls.^{3,4}

In an attempt to determine whether high-dose vitamin D would lower the risk of functional decline and/or falls, Bischoff-Ferrari et al conducted a 12-month clinical trial involving different levels of vitamin D supplementation. Two-hundred patients > 70 years of age were randomized into three different groups: Group 1 received 24,000 IU of vitamin D3 once per month (equivalent to 800 IU/day), group 2 received 60,000 IU of vitamin D3 once per month (equivalent to 2000 IU/day), and group 3 received 24,000 IU of vitamin D3 + 300 mcg of calcifediol (liver metabolite of vitamin D). The latter two groups represented the high-dose treatment groups. The primary outcome was improvement of lower extremity function, while

Summary Point

- High-dose vitamin D supplementation (~ 2000 IU daily) increased the risk of falls in elderly patients > 70 years of age without improving physical functioning.

the secondary outcome was the number of monthly falls. Lower extremity function was assessed using the Short Physical Performance Battery (SPPB), consisting of timed walking speed, successive chair stands, and a balance test.

When compared to the low-dose group, the two high-dose groups did not experience improvements in lower extremity physical performance. In fact, physical performance failed to improve despite the fact that 80% of the high-dose participants achieved 25-hydroxy vitamin D levels of ≥ 30 ng/mL. Of note, approximately 50% of the low-dose group achieved

25-hydroxy vitamin D levels of ≥ 30 ng/mL and also failed to improve physical performance. With regard to secondary outcomes, the high-dose groups experienced a significantly increased overall risk of falls ($P = 0.048$) compared to the low-dose group (60,000 IU = 66.9%; 95% confidence interval [CI], 54.4%-77.5%; 24,000 IU + 300 mcg calcifediol = 66.1%; 95% CI, 53.5%-76.8%; 24,000 IU = 47.9%; 95% CI, 35.8-60.3). In terms of actual falls during the 12-month follow-up period, the 60,000 IU group experienced an average of 1.47 falls compared to an average of 1.24 and 0.94 for the 24,000 IU + 300 mcg calcifediol and 24,000 IU groups, respectively ($P = 0.09$).

The present study confirms that much remains to be learned regarding vitamin D supplementation. Additional studies are required to make definitive

claims regarding vitamin D supplementation and physical performance/fall risk. Suggestions for follow-up studies include supplementing with the same protocol on a daily basis mirroring typical consumption patterns as well as supplementing at a slighter higher dose (5000 IU/day) mirroring common prescribing patterns. ■

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SHORT REPORT

Potatoes Increase Risk of Type 2 Diabetes Mellitus

By William C. Haas III, MD, MBA

Integrative Medicine Fellow, Department of Family and Community Medicine, University of Arizona, Tucson

Dr. Haas reports no financial relationships relevant to this field of study.

SOURCE: Muraki I, et al. Potato consumption and risk of type 2 diabetes: Results from three prospective cohort studies. *Diabetes Care* 2015; pii: dc150547.

Few would question the recommendation to increase daily vegetable intake. Yet, an important question arises — are all vegetables created equal?

A group of researchers recently evaluated the effect of potato consumption on the risk of developing type 2 diabetes mellitus (T2DM). Potatoes were selected because of high consumption patterns in the United States in addition to their ability to rapidly raise blood sugar levels based on their high glycemic index. Researchers retrospectively evaluated potato consumption from three major prospective cohort studies: the Nurses' Health Study (NHS), NHS-II, and the Health Professionals Follow-up Study (HPFS). In addition to overall consumption levels, the form of consumption was evaluated, i.e. baked, boiled, mashed, or fried.

Higher total potato consumption was significantly associated with an elevated risk for developing T2DM. Compared to consuming < 1 serving/week, the pooled hazard ratio (HR) was 1.07 (95% confidence interval [CI], 0.97-1.18) for 2-4 servings/week and 1.33 (95%

Summary Point

- Potato consumption, particularly in the form of French fries, is strongly correlated with the development of type 2 diabetes.

CI, 1.17-1.52) for ≥ 7 servings/week. With regard to the form consumed, French fries were associated with a higher HR compared to baked/boiled/mashed forms; 1.19 (95% CI, 1.13-1.25) and 1.04 (95% CI, 1.01 to -1.08), respectively. Interestingly, the HR for T2DM dropped to 0.88 (95% CI, 0.84-0.91) when replacing three total servings/week of potatoes with the same amount of whole grains.

When providing nutritional counseling to your patients, keep in mind that all vegetables may not be created equal. If the thought of replacing potatoes with kale or collard greens is off-putting, consider swapping out French fries for baked or boiled potatoes at the very least. ■

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CME INSTRUCTIONS

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CME QUESTIONS

1. Which of the following statements is true regarding the adverse health effects of frying?
 - a. Prolonged frying in reused fats and oils generates increased POPs and other deleterious substances.
 - b. Previously unused sunflower and olive oils are preferred for frying compared to solid fats, such as lard and butter.
 - c. Eating fried foods more than four times a week contributes to increased obesity, diabetes, hypertension, hyperlipidemia, and cardiovascular disease.
 - d. All of the above.
2. Which of the following statements is true regarding the clinical trial involving manipulation for chronic ankle instability?
 - a. Rehabilitation exercises provided no benefit in ankle pain or function after 5 weeks.
 - b. Manipulation plus rehabilitation improved ankle function more than the rehabilitation-only group.
 - c. The placebo group also showed improvement in ankle pain after 5 weeks.
 - d. There were no reported adverse effects or complications from the manipulation treatment.
3. Which of the following statements is true regarding the benefits of real acupuncture?
 - a. Real acupuncture causes less adverse effects than sham acupuncture.
 - b. At 6 months, the benefits from real or sham acupuncture disappear.
 - c. Real and sham acupuncture had similar positive effects at all time points.
 - d. The placebo group outperformed the sham but not the real acupuncture group.
4. A recent review of traditional Chinese medicine for esophageal cancer found that it:
 - a. increases short-term survival.
 - b. is standardized.
 - c. uses just one herb per patient.
 - d. may make it easier to tolerate chemotherapy or radiotherapy.

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