

## An Integrative Approach to Pain



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Chair: US Pharmacopeia Dietary Supplements  
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Author of National Geographic's

*"Fortify Your Life", "Healthy At Home"  
and "Life Is Your Best Medicine"*

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## Pain



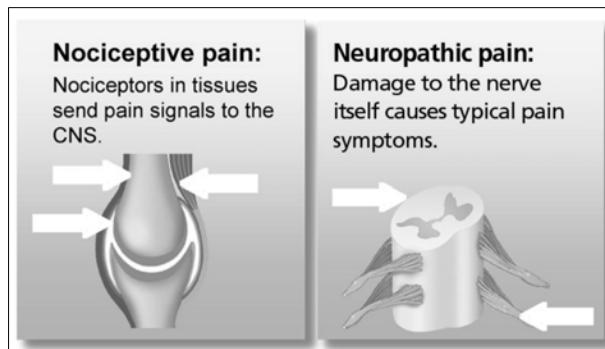
- Affects **>100 million Americans**, more than those with heart disease, cancer, and diabetes combined.
- **25.3 million adults suffer from daily chronic pain, while 23.4 million report severe pain.**
- Incidence of chronic low **back pain**, **neck pain**, and **arthritic pain** as high as 29%, 15.7%, and 28%, respectively, in adult population.

<http://iom.edu/Reports/2011/%20Relieving-Pain-in-America-A-Blueprint-for-Transforming-Prevention-Care-Education-Research/Report-Brief.aspx>

Nahin RL. Estimates of pain prevalence and severity in adults: United States, 2012. *J Pain* 2015 Aug;16(8):769-80.

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## Chronic Pain



- Complex, severe and debilitating condition, can lead to considerable reduction in function & quality of life.
- Chronic pain results from a number of identifiable causes; pain due to dysfunction of nerves, spinal cord or brain (neuropathic pain), or persistent pain caused by other non-malignant conditions, such as low-back pain or pain due to inflammation of various arthritic conditions.

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## Neuropathic Pain

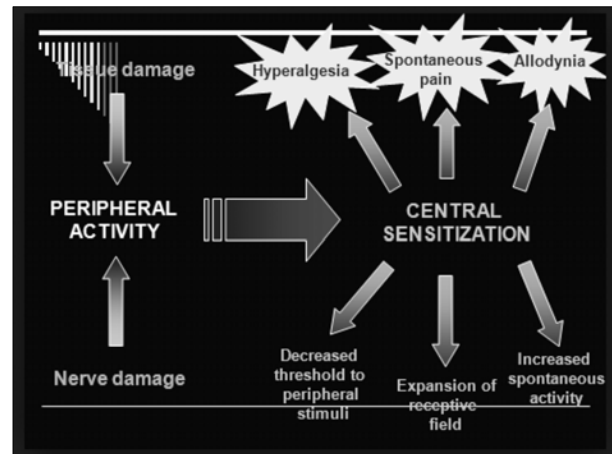
- The causes of neuropathic pain, defined as pain arising as a direct consequence of a lesion or disease of the somatosensory system (essentially all sensory experiences other than vision, hearing, taste and smell) are diverse.
- Trauma, poorly controlled diabetes, side effect from drugs, infections (e.g., HIV, shingles), and autoimmune conditions (e.g., multiple sclerosis) can all lead to neuropathic pain. Rates can be high in some populations.
- Primarily managed: antidepressants, anticonvulsants, opioids, and topical agents.
- Neuropathic pain can be particularly difficult to treat and is often accompanied by anxiety, depression, insomnia, and fibromyalgia.

DiBonaventura MD, et al. The prevalence of probable neuropathic pain in the US: results from a multimodal general-population health survey. *J Pain Res* 2017; 10: 2525–2538.

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## Central Sensitization

- Heightened sensitivity to pain and sensation of touch (also to other senses like light or sound).
- Because nervous system is in persistent state of heightened reactivity, simple touch can be registered in the brain as painful or uncomfortable even when it shouldn't.
- It increases feelings of anxiety, emotional distress, malaise, and poor concentration.



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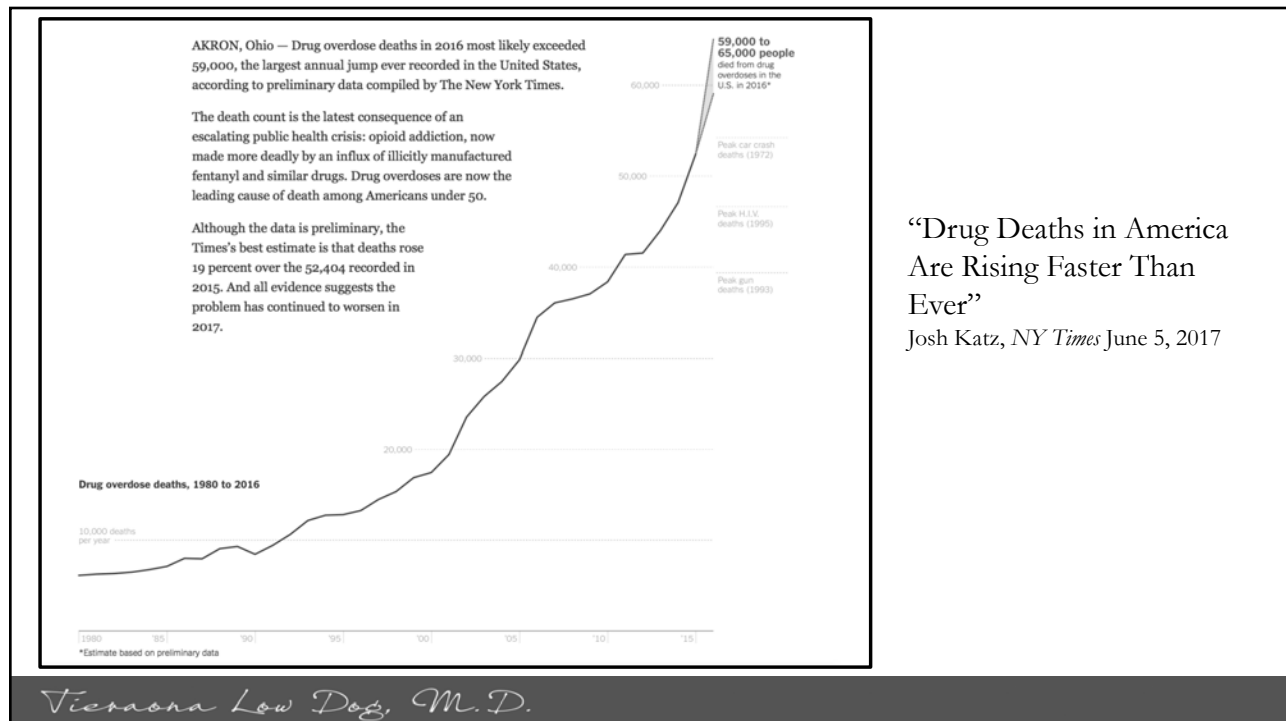
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## Opiates

- Opioid industry is now more than \$13 billion-a-year. Americans **comprise ~4% of the world's population, we use > 30% of all opioids**. US accounts for ~100% of hydrocodone (e.g., Vicodin), 81% for oxycodone (e.g., Percocet).
- **91 Americans die** every day from opioid overdose; 50% from prescription opiates.
- Clinicians ill-prepared to deal with complex problems associated with chronic pain and are crunched by time, creating an easy atmosphere for prescribing pain meds.
- Pharmaceutical companies pumped millions of dollars into telling health professionals and public that these medications were safe and effective for chronic pain, claims that are now being challenged in courtrooms across the US.

Haffajee RL, et al. Drug Companies' Liability for the Opioid Epidemic *N Engl J Med* 2017; 377:2301-2305

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## The Down Side to Long-Term Use

- Opioids incredibly effective for **short-term pain relief** but risks often outweigh the benefits for many people living with chronic pain.
- A well done review found for chronic non-cancer pain the absolute event rate for **any adverse event with opioids** in trials using a placebo as comparison was **78% with medium and long term use (average 6-16 weeks)**.
- These included **tolerance** (need more medication for same pain relief), **increased sensitivity to pain, physical dependence, lower sex drive, confusion, constipation, dry mouth, nausea and vomiting**, and an increased risk of **new onset depression** after 3 months of use.

Els C, et al. Adverse events associated with medium- and long-term use of opioids for chronic non-cancer pain: an overview of Cochrane Reviews. *Cochrane Database Syst Rev* 2017 Oct 30;10:CD012509.

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## Ibuprofen and Naproxen

- Large-scale Prospective Randomized Evaluation of Celecoxib Integrated Safety vs Ibuprofen or Naproxen (PRECISION) trial and individual patient data of nearly 500,000 patients concluded that “the evidence **would support avoidance of non-steroidal anti-inflammatory drugs (NSAID) use**, if possible, in patients with, or at high risk for, cardiovascular disease.
- If used, the **shortest-duration and lowest effective NSAID dose** should be chosen, given evidence that risk is duration- and dose-dependent.”
- The study also found that **ibuprofen** use was associated with a **significant increase in systolic blood pressure** and higher incidence of newly diagnosed hypertension.

Pepine CJ, et al. Cardiovascular safety of NSAIDs: Additional insights after PRECISION and point of view. *Clin Cardiol* 2017 Dec;40(12):1352-1356.

Ruschitzka F, et al. Differential blood pressure effects of ibuprofen, naproxen, and celecoxib in patients with arthritis: the PRECISION-ABPM (Prospective Randomized Evaluation of Celecoxib Integrated Safety Versus Ibuprofen or Naproxen Ambulatory Blood Pressure Measurement) Trial. *Eur Heart J* 2017 Nov 21;38(44):3282-3292.

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## Ibuprofen and Heart Disease

- An FDA warning about NSAID use in patients with cardiovascular disease (CVD) was released in 2005 and strengthened in July 2015, yet survey data shows that those with CVD *are more than twice as likely to use NSAIDs than those without CVD*.

Castelli G, et al. Rates of Nonsteroidal Anti-Inflammatory Drug Use in Patients with Established Cardiovascular Disease: A Retrospective, Cross-Sectional Study from NHANES 2009-2010. *Am J Cardiovasc Drugs* 2017 Jun;17(3):243-249.

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## Aspirin and GI Bleeding



Garcia Rodriguez LA, et al. Bleeding Risk with Long-Term Low-Dose Aspirin: A Systematic Review of Observational Studies. *PLoS One* 2016 Aug 4;11(8):e0160046.

- A systematic review found low dose aspirin associated with more than double the risk for upper GI bleeding and 80% increased risk for lower GI bleeding.
- With this increased risk from low-dose aspirin (81-85 mg per day), it is deeply concerning about the long-term use of higher dose aspirin (2000-3000 mg per day) used for pain.
- PPI can protect against bleed but come with own risks.

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## Acetaminophen (Paracetamol)

- Acetaminophen has superior safety profile to ibuprofen, naproxen, and aspirin; commonly recommended as a first line therapy for pain.
- Maximum “safe” dose is 4000 mg per day but is found in more than 600 OTC and prescription medications (e.g., Vicodin), dose can add up realizing it.

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## Adverse Effects

- 2017 report found acetaminophen responsible for nearly half of acute liver failure cases in US and is leading cause of liver transplantation.
- Study of 64,839 men and women (ages 50-76 years) followed for up to 8 years found almost two-fold increased risk of blood cancers associated with high use of acetaminophen ( $\geq 4$  days/week for  $\geq 4$  years).

Tittarelli R, et al. Hepatotoxicity of paracetamol and related fatalities. *Eur Rev Med Pharmacol Sci* 2017 Mar;21(1 Suppl):95-101.

Walter RB, et al. Long-term use of acetaminophen, aspirin, and other nonsteroidal anti-inflammatory drugs and risk of hematologic malignancies: results from the prospective Vitamins and Lifestyle (VITAL) study. *J Clin Oncol* 2011; 29(17):2424-31.

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## Blunts Empathy?

- Even more puzzling are results from Ohio State University research that found in healthy college students, acetaminophen reduces a user's ability to feel empathy for another's pain.
- This research must be confirmed by larger studies but it is hard not to find the researcher's statement somewhat chilling:
  - "Because empathy regulates prosocial and antisocial behavior, these drug-induced reductions in empathy raise concerns about the broader social side effects of acetaminophen, which is taken by almost a quarter of adults in the United States each week."

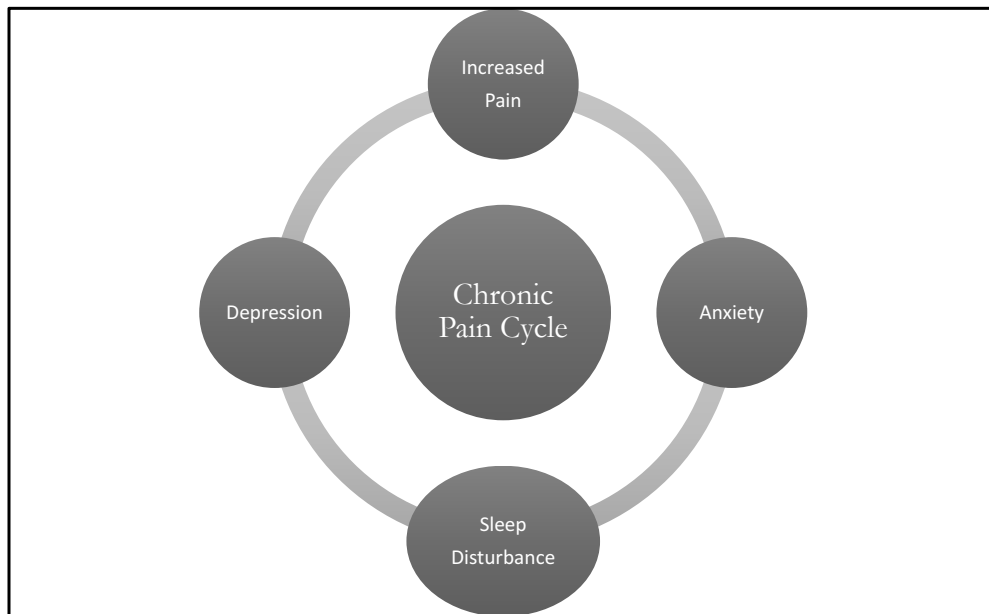
Mischkowski D, et al. From painkiller to empathy killer: acetaminophen (paracetamol) reduces empathy for pain. *Soc Cogn Affect Neurosci* 2016 Sep;11(9):1345-53.

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## The Need for Alternatives

- There is keen interest by researchers, clinicians and the public for additional/other options for managing chronic pain.
- Chronic pain is the leading indication for use of complementary and integrative medicine with 33% of adults and 12% of children in the US using it for this purpose.
- Although advances have been made in treatments for chronic pain, it remains inadequately controlled for many people.

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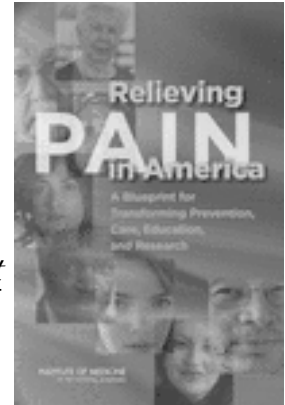


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## IOM Report

- *A cultural transformation is necessary to better prevent, assess, treat, and understand pain of all types.*
- *Healthcare providers should increasingly aim at tailoring pain care to each person's experience and self-management of pain should be promoted*



<http://iom.edu/Reports/2011/%20Relieving-Pain-in-America-A-Blueprint-for-Transforming-Prevention-Care-Education-Research/Report-Brief.aspx>

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## A Broader Approach

- A truly integrated approach would include treatments that address mind-body (e.g., meditation, yoga, tai-chi), nutrition (e.g., emphasis on plant based diet to reduce inflammation), manual medicine (e.g., massage, chiropractic), pain modulation (e.g., acupuncture, massage, botanicals, nutraceuticals), sleep and mood (e.g., cognitive behavioral therapy, guided imagery, botanicals, nutraceuticals).



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## Where Are They, Where Do They Want to Go



- An integrated approach will move beyond the pain and explore.....
  - Sleep and Rest
  - Work/Career
  - Diet and Food
  - Relationships
  - Mind-Body
  - Meaning and Purpose

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## The Role of Diet in Pain



- The role of diet has been recognized in numerous pain conditions but likely contributes to many pain disorders:
  - Irritable bowel syndrome
  - Inflammatory bowel disease
  - Migraine (food triggers, as well as fasting induced headaches)

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## Dietary Inflammatory Index (DII)

- Inflammation in the body is often driven by eating an anti- or pro-inflammatory dietary pattern. Inflammatory mediators can impact pain, mood, heart disease, insulin sensitivity, and DNA repair.
- The test can be downloaded as an app: Dietary Inflammatory Index (DII Screener).
- Patients can take the test and there is mechanism for them to submit the results to you.

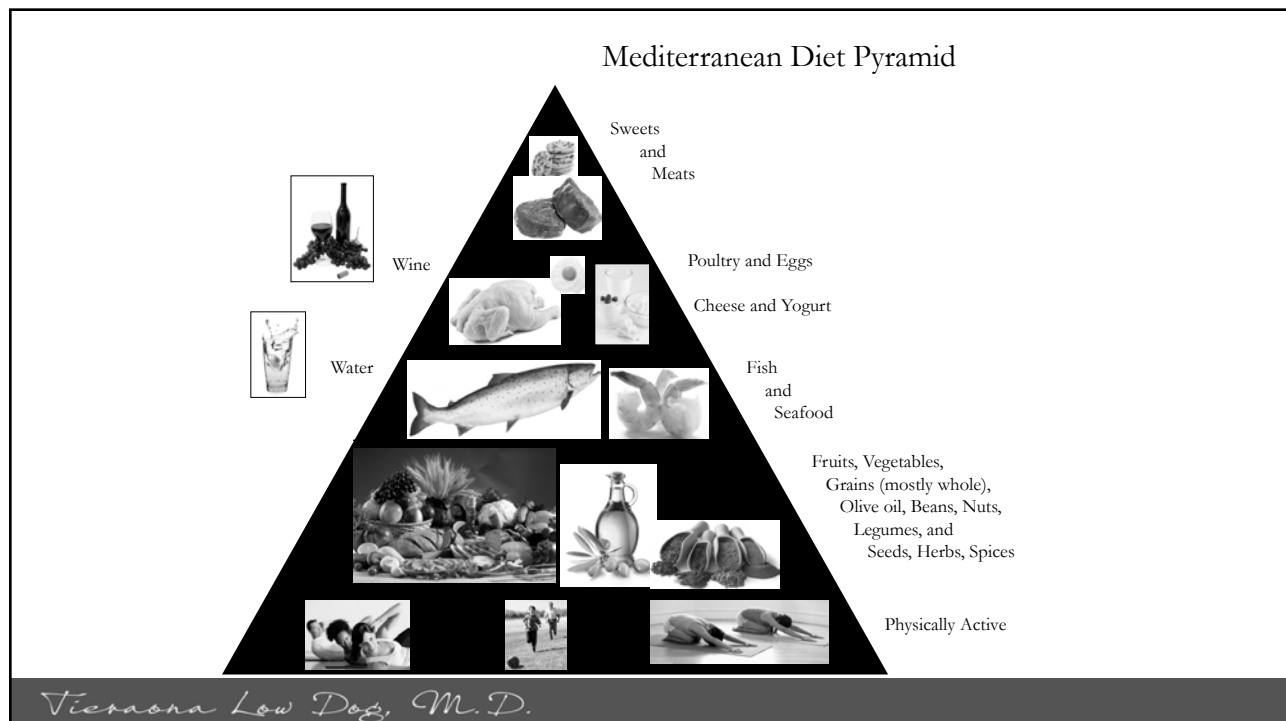
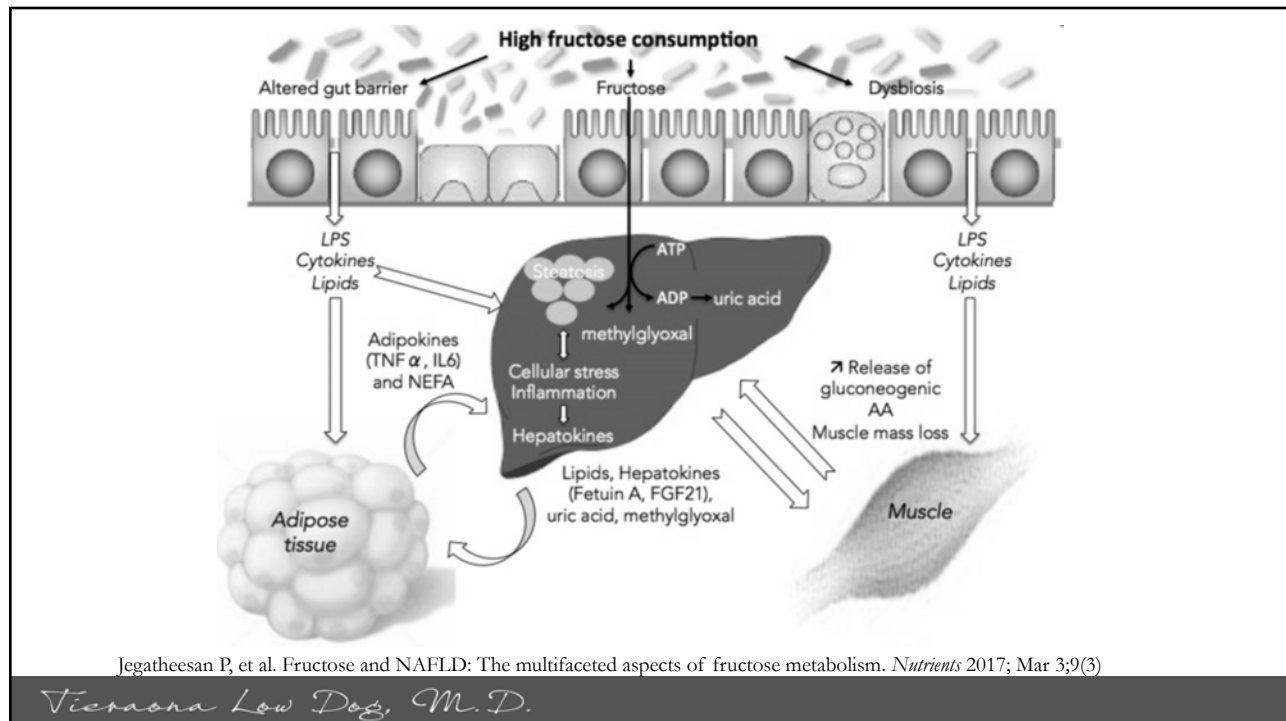
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## Inflammatory Food Ratings

200 or higher	Strongly anti-inflammatory
101 to 200	Moderately anti-inflammatory
0 to 100	Mildly anti-inflammatory
-1 to -100	Mildly inflammatory
-101 to 200	Moderately inflammatory
-201 or lower	Strongly inflammatory

FOOD	SERVING SIZE	SERVING SIZE (GRAMS)	IF RATING
AGAVE NECTAR	1 TBSP	21	-74
ALMOND BUTTER	¼ CUP	64	100
CHEESE, CHEDDAR	1 OUNCE	28.35	-20
CHICKEN BREAST, RSTD	3 OUNCES	85	-19
MILK, WHOLE	1 CUP	246	-46
OLIVE OIL	1 TBSP	14	74
ONIONS, COOKED	½ CUP	105	240
RICE, WHITE	1 CUP	158	-153
SPINACH	1 CUP	30	75
SALMON, SOHO BAKED	3 OUNCES	85	<b>450</b>
TURMERIC	½ TSP	1.5	338

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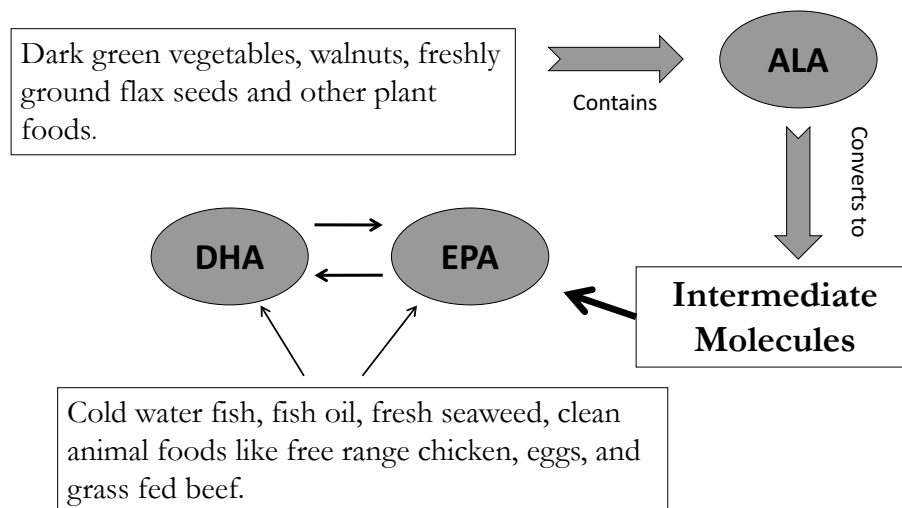
## Mediterranean Dietary Pattern

- 13 meta-analyses of observational studies and 16 meta-analyses of randomized controlled trials investigating the association between the adherence to the Mediterranean diet and 37 different health outcomes, for a total population of over than 12,800,000 subjects, were reviewed.
- Robust evidence ( $P\text{-value} < 0.001$ ) and large simple sizes showed that greater adherence to the Mediterranean diet was associated with *reduced risk* of **overall mortality, cardiovascular diseases, myocardial infarction, overall cancer incidence, diabetes, and neuro-degenerative diseases. Inflammatory mediators consistently reduced.**

Dinu M, et al. Mediterranean diet and multiple health outcomes: an umbrella review of meta-analyses of observational studies and randomized trials. *Eur J Clin Nutr* 2017; May 10. doi: 10.1038/ejcn.2017.58.

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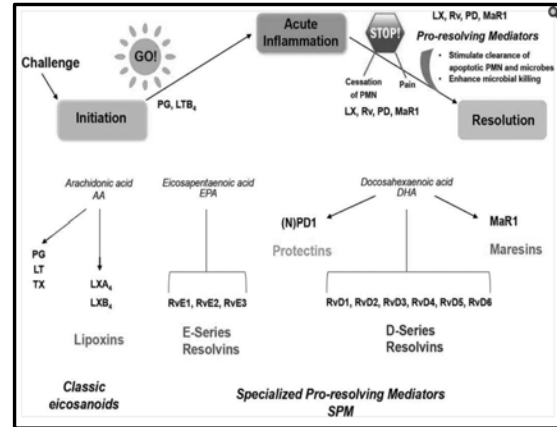
## Omega 3 Fatty Acids from Plants and Animals



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## Resolution Biology

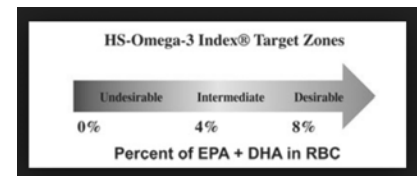
- Research shows that resolution of inflammation is an active, programmed response.
- Omega 3 fatty acids produce specialized **pro-resolving mediators** (SPM) – resolvins, protectins and maresins.
- Increasing omega 3 fatty acids in the diet can help with mood, pain and promote overall health.



Serhan CN, Chiang N. *Curr Opin Pharmacol* 2013; 13(4):632-40

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## Canadians and Omega 3



- Omega-3 Index indicates % of EPA+DHA in red blood cell fatty acids.
- Canadian government found the mean Omega-3 Index level of Canadians aged 20-79 was 4.5%. Fewer than 3% of adults had levels associated with low CHD risk; 43% had levels associated with high risk.
- What about chronic pain patients? Should we assess omega 3 fatty acid level to optimize their “anti-inflammatory” activity?

Langlois K, et al. *Health Rep* 2015; Nov 18;26(11):3-11

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## Choose Your Seafood Wisely



**The Seafood Watch App**

Available for iOS and Android

It's easier than ever to get the latest recommendations for seafood and sushi, learn more about the seafood you eat, and locate or share businesses that serve sustainable seafood.

Download on the App Store | GET IT ON Google play

View our App FAQs

**Features**

- Get free, up-to-date seafood recommendations
- Search for seafood quickly and easily by common market name
- Search for sushi by Japanese name as well as common market name
- Find restaurants and stores near you that serve ocean-friendly seafood
- Access in-depth conservation notes and reports

<https://www.seafoodwatch.org/seafood-recommendations/our-app>

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## Fish Oil: What Type is Best?

- Supplementation is an alternative to eating fish; however, not all supplements are equal.
- Randomized, crossover study of 35 healthy individuals compared four popular brands/types of omega 3 fatty acids:
  - Concentrated triglyceride (rTG)
  - Ethyl ester (EE)
  - Phospholipid krill oil (PL)
  - Triglyceride salmon oil (TG)

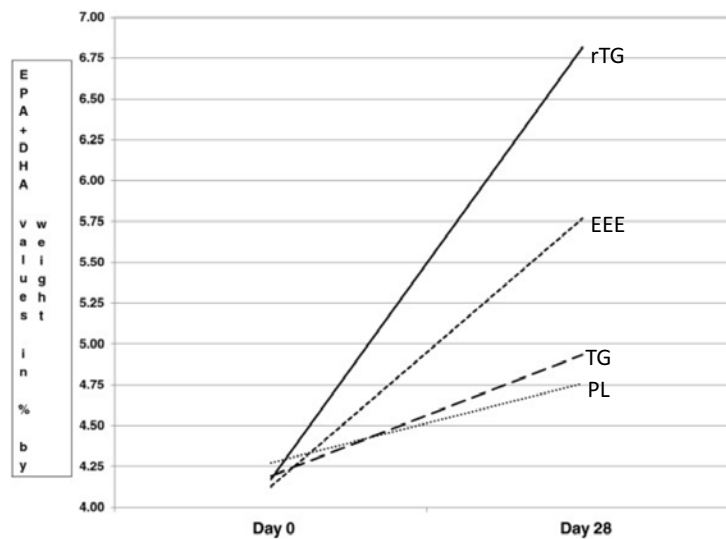
Laidlaw M, et al. *Lipids Health Dis* 2014; 13:99

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## Dosing According to Manufacturer's Recommendations

TRT	Product	EPA & DHA per capsule*	Tested values	Label use: caps/day	Daily dosage of EPA + DHA
rTG	Nordic Naturals ProOmega®	325 mg EPA	329.6 mg EPA	2	EPA: 650 mg
	Triglyceride	225 mg DHA	226.0 mg DHA		DHA: 450 mg
EE	Minami MorEPA®	756 mg EPA	774.2 mg EPA	1	EPA: 756 mg
	Platinum Ethyl Ester	228 mg DHA	233.7 mg DHA		DHA: 228 mg
PL	Source Naturals ArcticPure®	75 mg EPA	78.0 mg EPA	2	EPA: 150 mg
	Krill Oil Phospholipid	45 mg DHA	46.7 mg DHA		DHA: 90 mg
TG	New Chapter			2	
	Wholemega® Salmon	90 mg EPA	96.4 mg EPA		EPA: 180 mg
	Oil Triglyceride	110 mg DHA	109.5 mg DHA		DHA: 220 mg

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Mean levels of EPA + DHA for four supplement groups at Day 0 and Day 28.

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Hootman JM, et al. Updated Projected Prevalence of Self-Reported Doctor-Diagnosed Arthritis and Arthritis-Attributable Activity Limitation Among US Adults, 2015-2040. *Arthritis Rheumatol* 2016 Jul;68(7):1582-7.

## Musculoskeletal Pain

- Musculoskeletal conditions are the leading cause of long-term pain and disability around the globe.
- Aging, obesity and lack of regular physical activity are major risk factors for arthritis and back pain.
- In US, 52 million American adults have arthritis and by 2040, that number will reach 78.4 million, or roughly 26% of all adults.

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## Body Weight



- For every 12 pounds of weight gain, there is a 36% increased risk for developing OA.
- Lumbar spine and knee are two primary sites for pain in obese individuals.
- Reduction of body fat lowers mechanical and inflammatory stressors that contribute to OA.
- Weight loss has been strongly associated with a reduction in pain.

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## Anti-Inflammatory Herbs

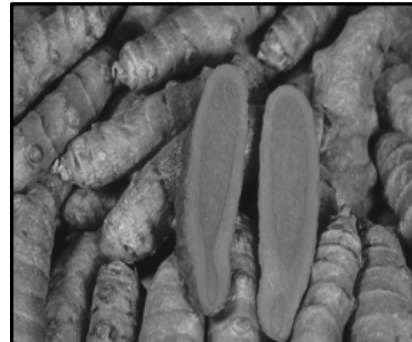
- There are many, but some to consider include:
  - Salix containing plants
  - Turmeric (*Curcuma longa* and other species)
  - Ginger (*Zingiber officinale*)
  - Boswellia (*Boswellia serrata*)
  - Chinese skullcap (*Scutellaria baicalensis*)
  - Devil's Claw (*Harpagophytum procumbens*)
  - Cat's Claw (*Uncaria tomentosa*)
  - Licorice (*Glycyrrhiza glabra*, *G. uralensis*)

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### Turmeric

(*Curcuma longa* and others)

- Rhizomes provide bright yellow-orange culinary spice and dye.
- Yellow pigments = curcuminoids, one example is curcumin.
- Long history of medicinal use for respiratory, skin, digestive and inflammatory conditions in India. Potent anti-inflammatory activity.
- More than 65 clinical trials have shed light on its *potential* role in CVD, diabetes, cancer, fatty liver, arthritis, neuro/psych disorders.



Kunnumakkara AB, et al. *Br J Pharmacol* 2016; Sep 17.  
doi: 10.1111/bph.13621.

Prasad S, et al. *Biotechnol Adv* 2014; 32(6): 1053-1064

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## Turmeric for Arthritis

- Turmeric has shown profound anti-inflammatory effects and studies show that turmeric reduces pain in people with rheumatoid arthritis and osteoarthritis.
- A systematic review concluded that randomized controlled trials of turmeric/curcumin provide scientific evidence that supports the efficacy of turmeric extract in the treatment of arthritis being equivalent to pain medications in five randomized studies.



Chin K-Y. *Drug Des Devel Ther* 2016; 10: 3029–3042

Peddada KV, et al. *Orth Surg* 2015; 7(3):222-31

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## Depression and Pain

- Multiple studies suggest a link between inflammation, depression and pain.
- Danish study (>73,000 adults) showed that those with the *highest levels of C-reactive protein (marker of inflammation)* were **twice as likely to have psychological distress and depression** than those with normal levels.



Wium-Anderson MK, et al. Elevated C-reactive protein levels, psychological distress, and depression in 73, 131 individuals. *JAMA Psychiatry* 2013; 70(2):176-184

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## Turmeric for Depression?

- A mini meta-analysis of 6 studies found curcumin reduced depression symptoms, particularly in middle-aged patients when given at higher doses for longer periods of time.
- Authors concluded, “there is supporting evidence that curcumin administration reduces depressive symptoms in patients with major depression.”
- Is this an impact on microbiome? Is it due to systemic reduction in inflammation?



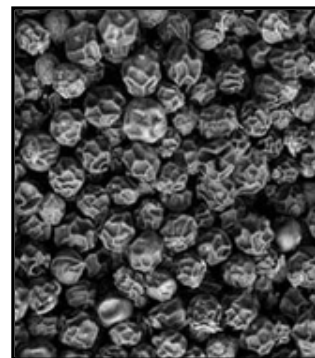
Al-Kawari D, et al. The Role of Curcumin Administration in Patients with Major Depressive Disorder: Mini Meta-Analysis of Clinical Trials. *Phytother. Res* 2016; 30(2):175-83

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*“Cancer Prevention in 21<sup>st</sup> Century”*

## Absorption and Safety Issues

- Turmeric/curcumin is not well absorbed into the bloodstream from the GI tract and what is absorbed is quickly metabolized and eliminated from the body.
- This means it is best to take turmeric/curcumin should be taken 2-3 times per day, rather than once per day, for best effects.
- Preparations that are bound to phosphatidylcholine, are nanoparticles, or include piperine, an alkaloid found in black pepper are the optimal forms for pain.
- Dose of 1200-1500 mg per day of extracts standardized to curcumin have been used in most of the trials.



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## Ginger (*Zingiber officinale*)

- Meta-analysis RCTs comparing ginger with placebo in OA patients aged >18 years found “Ginger was *modestly efficacious* and reasonably safe for treatment of osteoarthritis.”
- Studies show beneficial effect on lipids/glucose.
- 1-2 grams/d dried rhizome has not been associated with adverse effects.
- Doses higher than 4 grams per day can have a negative impact on blood clotting.



Wang J, et al. Beneficial effects of ginger *Zingiber officinale* Roscoe on obesity and metabolic syndrome: a review. *Annals of the New York Academy of Sciences* 2017; May 15. doi: 10.1111/nyas.

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- There are many ways to incorporate more turmeric into the daily diet as seen in my tips to the left.
- There are many recipes for golden milk – this is the one we use the most at my home.

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## *Cannabis sativa*

- Cannabis used to treat pain thousands of years.
- Major psychotropic component of cannabis is  $\Delta^9$ -tetrahydrocannabinol (THC), one of 120 naturally occurring phytocannabinoids.
- Cannabidiol (CBD) is another compound found in cannabis in large amounts.
- CBD does not produce euphoric effects but has antipsychotic, anxiolytic, anti-seizure, analgesic, and anti-inflammatory properties.

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## Cannabis and Pain

- Systematic review and meta-analysis of cannabinoids examined 28 randomized trials among 2454 patients with chronic pain indicated that, compared with placebo, cannabinoids were associated with greater a reduction in pain and greater average reduction in numerical pain ratings.
- Legal issues remain a significant challenge for making THC rich cannabis or non-euphoric CBD products available more widely to patients – it has also significantly limited the ability to conduct research in the US.

Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: a systematic review and meta-analysis. *JAMA*. 2015;313:2456–2473

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## Back Pain

- Lower back pain is highly disruptive, second leading cause of disability.
- It is acute if less than six weeks and chronic if persists > three months.
- Pain can be severe, making walking, standing and traveling long distances difficult, even though physical activity is effective for improving and preventing back pain.
- Back pain is frequently associated with anxiety, depression and irritability.
- Second major cause of short-term workplace absences; estimated 149 million days of work per year lost due to low back pain.

Freburger JK, et al. The Rising Prevalence of Chronic Low Back Pain. *Arch Intern Med*. 2009 Feb 9; 169(3): 251–258.

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## Clinical Practice Guidelines Back Pain

- American College of Physicians guideline is to provide treatment guidance based on the efficacy, comparative effectiveness, and safety of noninvasive pharmacologic and nonpharmacologic treatments for acute (<4 weeks), subacute (4 to 12 weeks), and chronic (>12 weeks) low back pain in primary care. Recommendations are on following slides.

Qaseem A, et al. Noninvasive Treatments for Acute, Subacute, and Chronic Low Back Pain: A Clinical Practice Guideline From the American College of Physicians. *Annals of Internal Medicine* 2017;166(7):514-530.

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## Acute or Subacute Low Back Pain: Guidance



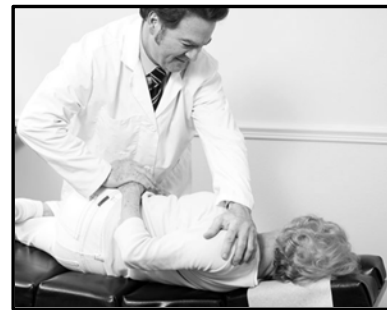
- Given that most patients with acute or subacute low back pain improve over time regardless of treatment, clinicians and patients should select non-pharmacologic treatment with *superficial heat* (moderate-quality evidence), *massage*, *acupuncture*, or *spinal manipulation* (low-quality evidence).
- If pharmacologic treatment is desired, clinicians and patients should select nonsteroidal anti-inflammatory drugs or skeletal muscle relaxants (moderate-quality evidence).

(Grade: strong recommendation)

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## Spinal Manipulation for *Acute* Back Pain

- 15 RCTS (more than 1,700 patients) found spinal manipulation resulted in an improvement in pain of about 10 points on a 100-point scale.
- 12 RCTS, some of which overlapped with above but not all, (~1,400 patients) found spinal manipulation resulted in improvements in function.



Paige NM, et al. Association of Spinal Manipulative Therapy With Clinical Benefit and Harm for Acute Low Back Pain: Systematic Review and Meta-analysis. *JAMA*. 2017;317(14):1451-1460.

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## Chronic Low Back Pain Guidance

- For patients with chronic low back pain, clinicians and patients should initially select non-pharmacologic treatment with *exercise, multidisciplinary rehabilitation, acupuncture, mindfulness-based stress reduction* (moderate-quality evidence), *tai chi, yoga, motor control exercise, progressive relaxation, electromyography biofeedback, low-level laser therapy, operant therapy, cognitive behavioral therapy, or spinal manipulation* (low-quality evidence).

(Grade: strong recommendation)



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5 randomized studies reported single-blinding and had a higher methodological quality; 7 studies were randomized but not blinded and had moderate quality; and 4 nonrandomized studies had low quality.

In 6 studies, yoga was used to treat patients with back pain; in 2 studies to treat rheumatoid arthritis; in 2 studies to treat patients with headache/migraine; and 6 studies enrolled individuals for other indications.

With respect to pain, random effect meta-analysis estimated the overall treatment effect at  $SMD = -.74$  (CI:  $-.97$ ;  $-.52$ ,  $P < .0001$ ) and  $SMD = -.79$  (CI:  $-1.02$ ;  $-.56$ ,  $P < .0001$ ) for pain related disability. There is evidence that yoga may be useful for several pain-associated disorders.

Bussing A, et al. Effects of yoga interventions on pain and pain associated disability: a meta-analysis. *J Pain* 2012; 13(1):1-9



*Vicraona Low Dog, M.D.*

## Headaches

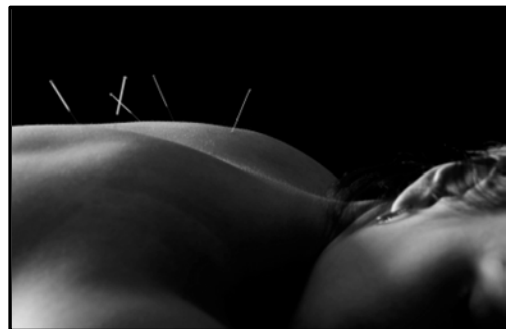
- Migraines and headaches are another significant source of pain, impacting approximately 13% of the US population.
- Burden of headache is highest in women ages 18-44, where the 3-month prevalence of migraine or severe headache is roughly 26%. Head pain is the third leading cause for emergency room visits.
- Surveys reveal 70% of those with migraines say their headaches have caused problems in their relationships, 59% have missed family and social events and 51% report that their migraines cut their work and school productivity in half.

Smitherman TA, et al. The prevalence, impact, and treatment of migraine and severe headaches in the United States: a review of statistics from national surveillance studies. *Headache* 2013 Mar;53(3):427-36.

*Victoria Low Dog, M.D.*

## Acupuncture for Migraine

- Cochrane review 22 trials (n=4985) concluded that the available evidence suggests adding acupuncture to symptomatic treatment of attacks reduces the frequency of headaches. The available trials also suggest that *acupuncture may be at least similarly effective as treatment with prophylactic drugs.*
- “Acupuncture can be considered a treatment option for patients willing to undergo this treatment.”



Linde K, et al. Acupuncture for the prevention of episodic migraine. *Cochrane Database Syst Rev* 2016; Jun 28; (6):CD001218

*Victoria Low Dog, M.D.*

## Magnesium for Migraines



Pringsheim T, et al. Canadian Headache Society guideline for migraine prophylaxis. *Can J Neurol Sci* 2012; 39(2Suppl) S1-S9

Chiu HY, et al. Effects of Intravenous and Oral Magnesium on Reducing Migraine: A Meta-analysis of Randomized Controlled Trials. *Pain Physician* 2016; 19(1):E97-112.

- Studies show that migraineurs have low brain Mg during migraine attacks and may have systemic Mg deficiency.
- Mg reduces recurrent pediatric migraine and tension headaches.
- Canadian Headache Society: strong recommendation for prophylaxis with 600 mg magnesium citrate.
- AAN/AHS gave level B recommendation (probably effective).
- Diarrhea most common side effect (mag glycinate and citrate less GI complaints than oxide). Caution in those with poor renal function.

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## Coenzyme Q10 for Migraines



Rajapakse T, et al. Nutraceuticals in migraine: a summary of existing guidelines for use. *Headache* 2016; Apr;56(4):808-16.

- The CHS guidelines gave CoQ10 a strong recommendation based on low quality evidence for the prophylaxis of migraine: 300 mg/d.
- The AAN/AHS gave a Level C recommendation, stating it is possibly effective and may be considered for migraine prevention.

*Vicraona Low Dog, M.D.*

## Riboflavin for Migraines



Rajapakse T, et al. Nutraceuticals in migraine: a summary of existing guidelines for use. *Headache* 2016; Apr;56(4):808-16.

- The CHS guidelines gave riboflavin a strong recommendation based on low quality evidence for benefit, and minimal side effects: *400 mg/d to eligible patients for migraine prophylaxis. (Question: smaller more frequent dosing?)*
- The AAN/AHS guidelines give riboflavin a Level B recommendation, stating it is probably effective and should be considered for migraine prevention.
- *Deficiency: increases light sensitivity*

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## Butterbur Extract for Migraines (*Petasites hybridus*)

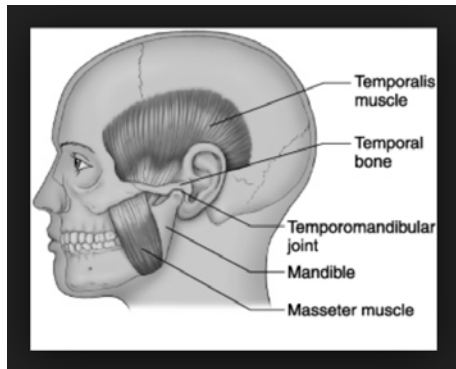
- Butterbur has a Level A recommendation for migraine prevention in adults from the American Academy of Neurology and American Headache Society.
- CHS give butterbur a strong recommendation for use based on moderate quality evidence for migraine prophylaxis at 75 mg twice daily.
- These recommendations may be revised (but have not) due to several cases of liver damage reported in the literature.
- Extracts must be PA free. All 10 products sold in Canada are licensed and tested free of PAs.



Rajapakse T, et al. Nutraceuticals in migraine: a summary of existing guidelines for use. *Headache* 2016; Apr;56(4):808-16.

*Vicraona Low Dog, M.D.*

## Temporomandibular Disorder



Okeson JP. *Management of temporomandibular disorders and occlusion*. 7 ed. Elsevier: Mosby; 2012.

- Temporomandibular disorders (TMD): term used to group conditions in the masticatory muscles and the temporomandibular joint (TMJ), impaired movement capacity of the mandible, and TMJ symptoms such as clicking, grating and locking of the jaw.
- Most common cause of chronic orofacial pain.

*Vicraona Low Dog, M.D.*

## TMD: Significant Cause of Pain



Manfredini D, et al. Research diagnostic criteria for temporomandibular disorders: a systematic review of axis I epidemiologic findings. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2011;112:453–462.

- Impacts 5-12% of the population. TMD is the second most common musculoskeletal condition (after chronic low back pain) resulting in pain and disability.
- 12 common TMD include arthralgia, myalgia, local myalgia, myofascial pain, myofascial pain with referral, four disc displacement disorders, degenerative joint disease, subluxation, and headache attributed to TMD.

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**Temporomandibular pain disorder screening instrument.**

1. In the last 30 days, on average, how long did any pain in your jaw or temple area on either side last?

- a. No pain
- b. From very brief to more than a week, but it does stop
- c. Continuous

2. In the last 30 days, have you had pain or stiffness in your jaw on awakening?

- a. No
- b. Yes

3. In the last 30 days, did the following activities change any pain (that is, make it better or make it worse) in your jaw or temple area on either side?

A. Chewing hard or tough food

- a. No
- b. Yes

B. Opening your mouth or moving your jaw forward or to the side

- a. No
- b. Yes

C. Jaw habits such as holding teeth together, clenching, grinding or chewing gum

- a. No
- b. Yes

D. Other jaw activities such as talking, kissing or yawning

- a. No
- b. Yes

Items 1 through 3A constitute the short version of the screening instrument, and items 1 through 3D constitute the long version. An a response receives 0 points, a b response 1 point and a c response 2 points.

## TMP Pain Screening Tool

- For clinical use, responses from the screener can be used as part of the diagnostic process for a pain-related TMD diagnosis.
- Sensitivity was 99.1% for both short (3 questions) and long questionnaire (6 questions): specificity was 95-98%.
- Radiographic imaging confirms TMD diagnosis.
- Patients are interested in treatment.

Gonzalez YM, et al. Development of a brief and effective temporomandibular disorder pain screening questionnaire. *J Am Dent Assoc.* 2011 Oct; 142(10): 1183-1191.

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## Care Option



- Ice or heat applications
- Soft foods when pain acute
- Self-care exercises
- Physical Therapy
- Splint
- Anti-inflammatory Diet
- Topical analgesics (e.g., capsaicin)
- Acupuncture

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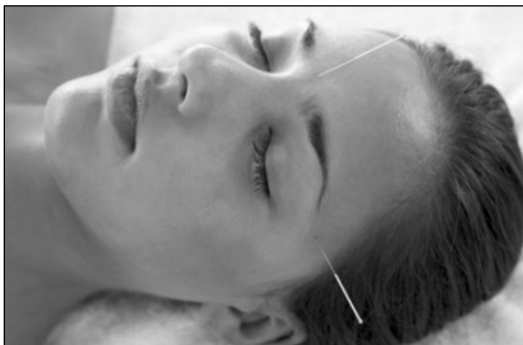
## Splint Versus Self Exercise

- 52 people with anterior disc displacement without reduction randomly assigned to **splint** or a joint mobilization **self-exercise** treatment group.
  - Warm-up, small mouth-opening and closing movements several times. Then, individual placed fingertips on edge of mandibular anterior teeth and slowly pulled the mandible down until pain occurred on the TMJ-affected side. 3 cycles of 30 seconds each were done 4 times per day.
  - Participants in the **splint group** wore a maxillary stabilization appliance while sleeping at night. Splint was adjusted to ensure occlusal contact of all mandibular teeth in centric relation and mandibular canine guidance in eccentric movement.
- All outcome variables significantly improved after 8 weeks of treatment in both groups (mouth opening range with and without pain, maximum daily pain intensity, limitation of daily functions. In particular, the mouth opening range increased more in the exercise group than in the splint group

Haketa T, et al. Randomized Clinical Trial of Treatment for TMJ Disc Displacement. *Journal of Dent Res* 2010; 89(11):1259-63

*Vicraona Low Dog, M.D.*

## Acupuncture and Dry Needling



- Small studies that used dry needling or acupuncture of the lateral pterygoid and posterior, periarticular connective tissue, masseter and temporalis muscles have shown improvements in pain and disability in patients with TMD.

Fernandes AC, et al. Acupuncture in Temporomandibular Disorder Myofascial Pain Treatment: A Systematic Review *J Oral Facial Pain Headache* 2017 Summer;31(3):225-232.

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## Mood, Sleep and Pain



- Depression and pain leading causes of global disability.
- Study of 273,952 individuals/47 countries found depression significantly associated with severe pain (odds ratio 3.93 (95% CI 3.54-4.37).
- It is well established that there is a high prevalence of concomitant pain and sleep disturbance and there is a bidirectional and reciprocal relationship.
- Pain can impair sleep but research also shows that insomnia and short sleep duration increases the risk for developing chronic pain.
- A study in healthy young women found after just two nights of fragmented sleep in an experimental setting, there was increased pain sensitivity in both superficial and deep tissues.

McWilliams LA, et al. A Network Analysis of Depressive Symptoms in Individuals Seeking Treatment for Chronic Pain. *Clin J Pain* 2017 Oct;33(10):899-904.  
Iacovides S, et al. Sleep Fragmentation Hypersensitizes Healthy Young Women to Deep and Superficial Experimental Pain. *J Pain* 2017 Jul;18(7):844-854.

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Table 1  
Self-report measures for assessment of insomnia

Domain	Scale	Time Frame	No. of Items	Comments
Postsleep evaluation	Wolff's Morning Questions <sup>15</sup>	Today	8	Yes/no questions detailing morning restedness, presence of bedpartner, etc.
Postsleep evaluation	Kryger's Subjective Measurements <sup>16</sup>	Today	9	Mixed format questions detailing sleep onset, sleep latency, etc.
Postsleep evaluation	Morning Sleep Questionnaire <sup>17</sup>	Today	4	Mixed format questions evaluating sleep goodness and other factors
Sleep quality	Pittsburgh Sleep Quality Index <sup>18</sup>	Past month	24	Mixed format questions and household-related questions that use an algorithm to score sleep disturbance
Sleep quality	Sleep Questionnaire <sup>19</sup>	Indefinite	59	Questions use Likert-type scale responses ranging from sleep depth to dream recall/vividness
Sleep quality	Sleep Disturbance Questionnaire <sup>20</sup>	Indefinite	12	Questions use Likert-type scale responses that assess mental anxiety and physical tension

Cheatle MD, et al. Assessing and Managing Sleep Disturbance in Patients with Chronic Pain. *Sleep Medicine Clinics*, 2016;11(4): 531-541

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## Cognitive Behavioral Therapy

- CBT has emerged as a recommended first-line therapy for insomnia. Scale can be an issue. Digital CBT has been shown to be effective for improving sleep, as well as mental health and well-being.
- CBT-I typically consists of:
  - Psychoeducation about sleep and insomnia
  - Stimulus control
  - Sleep restriction
  - Sleep hygiene
  - Relaxation training
  - Cognitive therapy
- Sleepio, CBT-I Coach (free)



Luik AI, et al. Digital cognitive behavioral therapy for insomnia: a state of the science review. *Curr Sleep Med Rep* 2017; 3(2): 48–56

*Vicraona Low Dog, M.D.*

## Melatonin

- Melatonin maintains sleep-wake cycle, acts as an antioxidant, **anti-inflammatory**, **pain reliever**, and **mood regulator**, making it ideal for many with chronic pain.
- A systematic review of **19 studies** found that melatonin significantly **decreases the pain intensity**, as evidenced by pain scores, regardless of the type of pain.
- Plays important role in gastrointestinal physiology: regulation of gastrointestinal motility, local anti-inflammatory reaction and moderation of visceral sensation. Studies show it **can improve symptoms and quality of life in people living with IBS**.

Cheatle MD, et al. Assessing and Managing Sleep Disturbance in Patients with Chronic Pain. *Sleep Medicine Clinics*, 2016;11(4): 531-541

Zhu C, et al. Exogenous melatonin in the treatment of pain: a systematic review and meta-analysis. *OncoTarget* 2017 Nov 21; 8(59): 100582–100592.

Esteban-Zubero E, et al. Melatonin's role as a co-adjuvant treatment in colonic diseases: A review. *Life Sci* 2017 Feb 1;170:72-81

*Vicraona Low Dog, M.D.*

## Melatonin Sleep and Safety

- Meta-analysis of **12 randomized, placebo-controlled trials** found convincing evidence that melatonin reduced sleep onset latency (the time it takes to fall asleep) in **primary insomnia** ( $p = 0.002$ ) and delayed sleep phase syndrome (when it takes 2 or more hours to fall asleep past conventional bedtime) ( $p < 0.0001$ ).
- Studies have **failed to show any serious adverse effects** with melatonin, even at extreme doses (100 mg) in adults. Taking melatonin doesn't suppress the endogenous production of melatonin and there is no rebound insomnia when it is discontinued. Dose generally 3 mg 2 hours before bed.

Auld F, et al. Evidence for the efficacy of melatonin in the treatment of primary adult sleep disorders. *Sleep Med Rev* 2017 Aug;34:10-22.

Andersen LP, et al. The Safety of Melatonin in Humans. *Clin Drug Investig* 2016 Mar;36(3):169-75.

*Vicraona Low Dog, M.D.*

## Current Recommendations

- Controlled-release melatonin and doxepin are recommended as first-line agents in older adults; the so-called z-drugs (zolpidem, eszopiclone, and zaleplon) should be reserved for use if the first-line agents are ineffective.
- Dose generally 3-5 mg melatonin.



Matheson E, et al. Insomnia: Pharmacologic Therapy. *Am Fam Physician* 2017; Jul 1;96(1):29-35.

*Vicraona Low Dog, M.D.*



## Nervines/Sedatives

- WHO lists for valerian: mild sedative, sleep promoting agent, milder alternative or substitute for stronger sedatives (e.g., benzodiazepines); and treatment of nervous excitation/sleep disturbances induced by anxiety.
- Germany's Commission E endorses hops for "discomfort due to restlessness or anxiety and sleep disturbances."
- Indigenous peoples of North and South American used passion flower as calmative, review found evidence for anxiolytic effects.
- Combination of valerian, hops, passionflower found equivalent to 10 mg zolpidem when taken nightly for two weeks in 91 patients with primary insomnia.

Blumenthal M, et al. *The Complete German Commission E Monographs*  
 WHO Monographs on Selected Medicinal Plants Vol. 1. Geneva: World Health Organization, 1999.  
 Maroo N, et al. *Indian J Pharmacol* 2013; 45(1):34-9  
 Sarris J, et al. *CNS Drugs* 2013; 27(4):301-19

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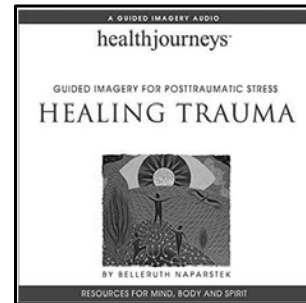
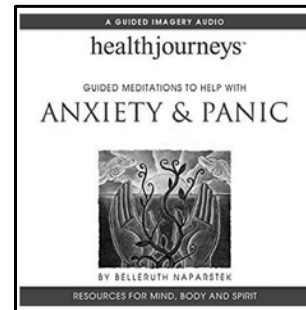
## Guided Imagery: *Imagine Yourself*.....

- An immersive, deeply relaxing intervention that uses calming words, soothing music and positive images to structure a healing experience.
- Like meditation, it focuses attention and calms the mind, working on those parts of the brain where the emotional self dwells.
- Imagery has been shown in clinical trials to reduce stress, anxiety, and depression; help with sleep; lower blood pressure, and help with posttraumatic stress.
- I have found guided imagery a fabulous tool for patients. Very helpful for those with anxiety, depression, pain, insomnia. And often an easier transition to meditation.

*Vicraona Low Dog, M.D.*

## Belleruth Naparstek

- Love, love, love her. Something for everyone.
- She has Guided Imagery Meditations for:
  - Anxiety and Panic
  - Anger and Forgiveness
  - Depression
  - Healing Trauma
  - Ease Grief
  - Relieving Stress
  - Undergoing Surgery
  - Chemotherapy and Radiation



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## Mindfulness Meditation

- Mindfulness meditation excellent as it can decrease pain intensity and stress levels.
- Long-time meditators have greater activation of areas responsible for sustaining attention, processing empathy, integrating emotion and cognition.
- Review of 47 trials found meditation improves:
  - Anxiety
  - Depression
  - Pain



Goyal M, et al. *JAMA Intern Med* 2014; 174(3):357-68

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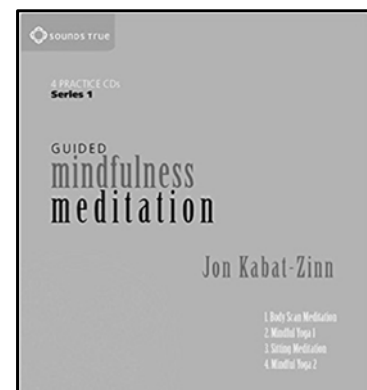
## Meditation Resources

- Obviously a local class is the very best option. But there are books, CDS and yes, there are apps.....
  - Insight Timer - ~4,000 guided meditations from more than 1,000 teachers (self-compassion, nature, stress, podcasts and more). More than 750 meditation music tracks. Free.
  - Headspace – very good for beginners with 10 minute meditations. Free.
  - The Mindfulness App – nice 5 days guided mediation program to get you started. Can be personalized and integrated into other health apps. Free.
  - Aura – multiple teachers, from 3-10 minute daily meditations. Customizable. #1 new app on Apple. \$29 for 6 months.

*Vicraona Low Dog, M.D.*

## *Guided Mindfulness Meditation: A Complete Guided Mindfulness Meditation Program* from Jon Kabat-Zinn

- Four-part home training course, this is simply one of the best ways to learn about mindfulness meditation. This might be a great choice for you if you feel anxious, are living with chronic pain, your stress is off the charts, or you just are interested in learning how to meditate without the spiritual overtones found in many other teachings. Pairs nicely with his book *Full Catastrophe Living*.
- This meditation program is one of the most researched in the world. You can purchase the audio CDs on Amazon for ~\$18.00



*Vicraona Low Dog, M.D.*

## Loneliness, Social Isolation & Your Health

- 148 studies on the effects of social isolation on health found it is:
  - As bad as smoking 15 cigarettes a day.
  - As dangerous as being an alcoholic.
  - As harmful as never exercising.
  - Twice as dangerous as obesity.

Cacioppo JT, et al. *Ann N Y Acad Sci* 2011; 1231:17-22

Holt-Lunstad J, et al. *PLoS Med* 2010; 7:e1000316



*Vicraona Low Dog, M.D.*

## Meaning and Purpose

- What truly gives a person a sense of *meaning and purpose* in life?
- How can someone discover her life purpose to focus on the essence of who she is? Her *be-ing*.
- How can one live from a “*deep place*” despite his or her pain?
- So important to explore..... it is often the key to *less suffering*.....

Listen.  
Are you  
breathing  
just a little  
and calling  
it a life?

~ Mary Oliver

*Vicraona Low Dog, M.D.*

One evening an old Cherokee told his grandson  
about a battle that goes on inside people

He said, "My son, the battle is between  
two "wolves" inside us all.

One is Evil.

It is anger, envy, jealousy, sorrow, regret, greed,  
arrogance, self-pity, guilt, resentment, inferiority, lies,  
false pride, superiority, and ego.

The other is Good.

It is joy, peace, love, hope, serenity,  
humility, kindness, benevolence, empathy,  
generosity, truth, compassion and faith."

The grandson thought about it for a minute  
and then asked his grandfather: "Which wolf wins?"

The old Cherokee simply replied,  
"The one you feed."



*Victoria Low Dog, M.D.*