

Integrative Medicine: *It's Not Alternative Anymore*



Tieraona Low Dog, M.D.

Chair: US Pharmacopeia
Dietary Supplements Admissions Joint
Standard Setting Sub-Committee

National Geographic's
Fortify Your Life
Healthy At Home
Life Is Your Best Medicine

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www.DrLowDog.com/Resources

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Blog Books Resources Events Study with Tieraona

Helpful Health Resources



Medicine Lodge Ranch

Dr. Low Dog has created a new **online classroom** called [Medicine Lodge Academy](#) to expand the reach of her natural medicine school located at her ranch in the heart of New Mexico's Santa Fe National Forest.

Through our **online courses**, **digital educational tools**, and **hands-on intensive classes** at our ranch, you will have access to the resources to make yourself & your family both healthier and more whole. [Learn more.](#)

Conference Handouts:

2022 Idaho State Dental Conference

Nutrition Prescription presentation - [handout](#)

Dietary Supplements presentation - [handout](#)

Life Is Your Best Medicine presentation - [handout](#)

Integrative Medicine presentation - [handout](#)

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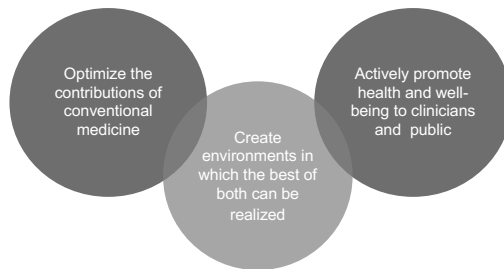
Healthcare in the United States

- America spends **more per person** on healthcare than any other country—and does not have the best health outcomes.
 - \$9237 annually per capita spending
 - 1 in 3 adults are considered obese
 - 117 million people have at least one chronic disease
 - Life-expectancy rate is declining (78.8 years, compared to an average of 82.2 years among comparable countries)
- National **health spending is projected to grow** at an average rate of 5.6% per year for the next decade.

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Fostering Health and Well-Being



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Imagine

Imagine a world, oriented toward healing rather than disease, where physicians believed in the natural healing capacity of human beings and emphasized prevention above treatment.

In such a world, doctors and patients would be partners working toward the same ends.

Andrew Weil, MD



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Integrative Medicine

*Integrative medicine and health reaffirms the importance of the relationship between practitioner and patient, focuses on the **whole person**, is informed by evidence, and makes use of **all appropriate therapeutic and lifestyle approaches, healthcare professionals and disciplines** to achieve **optimal health and healing**.*

Academic Consortium for Integrative Medicine & Health

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Nutrition Matters

Dietary factors are now single most important cause of death in the U.S.

- **Dietary factors**
- Tobacco smoking
- High blood pressure
- High BMI
- High plasma glucose
- Elevated cholesterol



JAMA 2018

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Nutritional Guidance

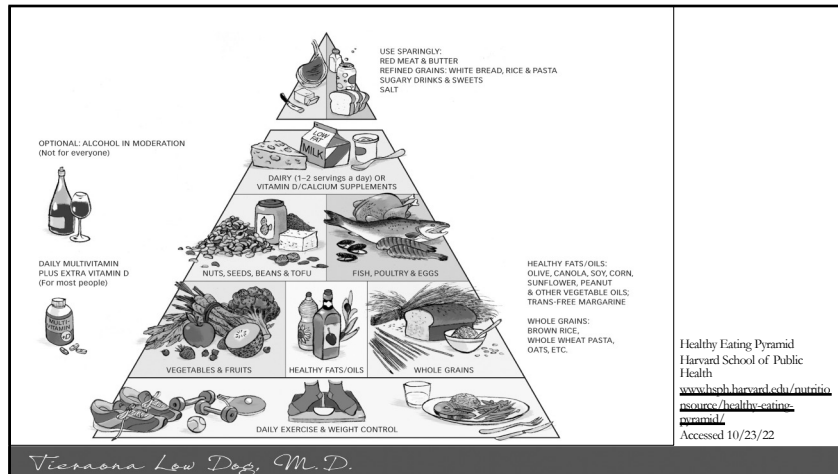


- Despite **overwhelming** evidence that **relatively small** dietary changes can significantly **improve health**, clinicians **seldom discuss nutrition** with patients.
- Nutrition-related health conditions, such as **cardiovascular disease, diabetes, obesity, HTN, and certain cancers**, are highly prevalent in the United States, yet only **12% of office visits include any counseling about diet.**

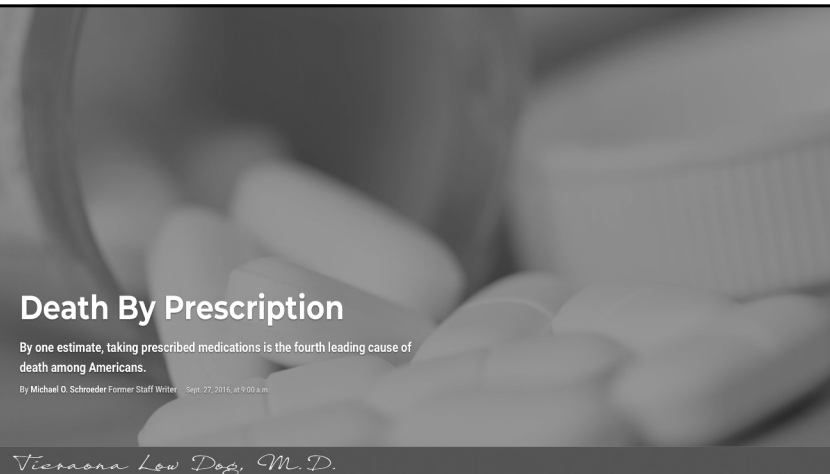
Kahan S, et al. Nutrition Counseling in Clinical Practice: How Clinicians Can Do Better. *JAMA*. 2017;318(12):1101-1102.

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Prescription Meds and Adverse Effects

- Prescription drugs offer many benefits: treating **serious infections**, **preventing stroke**, or **managing chronic conditions**.
- However, depending upon the source, adverse drug reactions result in **~1.5 - 2.7 million hospitalizations** each year.
- Reduce risk by **following directions** carefully, but **simply taking prescribed drugs** as directed can expose one to significant risk.
- **Ask questions** about medication you are prescribed. If your health changes, **medication may no longer be necessary** or the dose can be adjusted.

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The Epidemic of Pain



- **>100 million Americans**—more than heart disease, cancer, diabetes combined.
- 50 million adults have **chronic pain**.
- 20 million report **severe pain**.
- Incidence (adults):
 - chronic low back pain (29%)
 - arthritis pain (28%)
 - neck pain (15%)
 - migraine headache (13%)
 - TMD (11%)

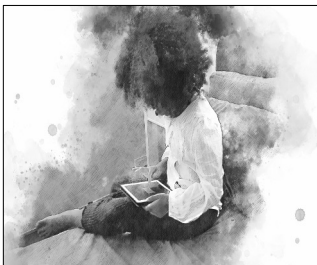
<https://www.cdc.gov/mmwr/volumes/67/wr/mm6736a2.htm>

Accessed March 1, 2022

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Pain in Children



- Prevalence of **chronic pain increases with age in children/teens** with female preponderance.
- **Headache, functional abdominal pain, back pain, musculoskeletal pain** common.
- Up to **38% of youth suffer from chronic pain**; large number of adolescents prescribed opioids for **headaches and sports injuries**.
- More than **one in four opioid overdoses** involve children/adolescents.

Liassi C, et al. Pediatric Chronic Pain: Biopsychosocial Assessment and Formulation *Pediatrics* November 2016; 138 (5) e20160331
[Crit Care Med 2020; doi:10.1097/01.ccm.0000618708.38414.ea](https://doi.org/10.1097/01.ccm.0000618708.38414.ea)

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Opiates

- Opioid industry more than \$13 billion-a-year. Americans **comprise ~4% of the world's population, use > 30% of all opioids**. US accounts for ~100% of hydrocodone (e.g., Vicodin), 81% for oxycodone (e.g., Percocet).
- In 2019, nearly **50,000 people** in the United States **died from opioid-involved overdoses**.
- Clinicians ill-prepared to deal with complex problems associated with chronic pain - **creates easy atmosphere for prescribing pain meds**.
- Pharmaceutical companies pumped millions of dollars into telling physicians and public that medications were **safe and effective for chronic pain**.
- Opioids effective for **short-term pain relief** but risks often outweigh benefits for many people living with **chronic pain**.

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

<https://nida.nih.gov/drug-topics/opioids/opioid-overdose-crisis>, Accessed April 25, 2022

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Ibuprofen & Naproxen

- Prospective Randomized Evaluation of Celecoxib Integrated Safety vs Ibuprofen or Naproxen (**PRECISION**) trial and patient data ~ 500,000 patients: evidence “**supports avoidance of NSAID use, if possible, in patients with, or at high risk for, cardiovascular disease.**”
- **FDA warning on NSAID use in those with CVD in 2005, strengthened in 2015**, but data show those with CVD **more than 2x as likely to use NSAIDs than those without CVD.**
- If used, **shortest-duration and lowest effective dose** should be chosen, evidence shows risk is both **duration and dose-dependent.”**
- **Ibuprofen associated with significant increase in systolic blood pressure** and higher incidence of **newly diagnosed hypertension.**

Pepine CJ, et al. *Clin Cardiol* 2017 Dec;40(12):1352-1356.
Ruschitzka F, et al. *Eur Heart J* 2017 Nov 21;38(44):3282-3292.

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Acetaminophen and Liver Toxicity



- **Superior safety** to ibuprofen, naproxen, and aspirin; commonly recommended **first line therapy**
- Over past 40 years, **acetaminophen (paracetamol) toxicity** accounts for **46% of all acute liver failure in the US and 40–70% of all cases in Great Britain and Europe.**
- 1975 *Lancet* editorial, “**Surely it is time to replace paracetamol with an effective analogue which cannot cause liver damage.**”

Tittarelli R, et al. Hepatotoxicity of paracetamol and related fatalities. *Eur Rev Med Pharmacol Sci* 2017 Mar;21(1 Suppl):95-101.
Lee WM. Acetaminophen toxicity: a history of serendipity and unintended consequences. *Clin Liver Dis* 2020; 16(Suppl 1): 34-44.

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Aspirin & GI Bleeding



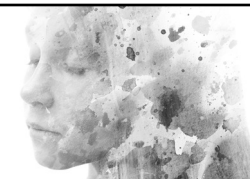
- Systematic review: low dose aspirin associated with **double the risk for upper GI bleeding and 80% increased risk for lower GI bleed.**
- With increased risk from low-dose aspirin (81–85 mg per day), deeply concerning about long-term use of **high dose aspirin (2–3 g/d)** for pain.
- **PPI can protect against bleed but comes with own risks.**

García Rodríguez 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.

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The Need for Alternatives



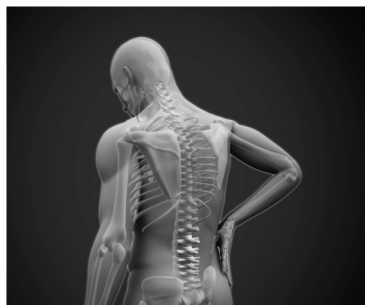
- Although advances have been made in treatments for chronic pain, it remains inadequately controlled for many people, including children.
- **Chronic pain is leading indication for complementary and integrative medicine: 33% of adults and 12% of children.**
- “**A cultural transformation is necessary 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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Other Options



Evidence supports the effectiveness of **exercise, psychological therapies, multidisciplinary rehabilitation, spinal manipulation, massage, and acupuncture** for **chronic low back pain**.

Chou R, et al. Nonpharmacologic Therapies for Low Back Pain: A Systematic Review for an American College of Physicians Clinical Practice Guideline. *Ann Intern Med* 2017 Apr 4;166(7):493-505.

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Spinal Manipulation for Acute Back Pain

- 15 RCTS: spinal manipulation improves pain by about 10 points on a 100-point scale.
- 12 RCTS: spinal manipulation resulted in improvements in function.
- Most reported adverse events were musculoskeletal related, transient in nature, and of mild to moderate severity.



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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Spinal Manipulation for Headaches

- Cervicogenic headaches are a common disorder.
- Systematic review found SMT provides superior short-term effects for pain intensity, frequency and disability.
- Spinal and cervical manipulation are included in numerous practice guidelines for chronic neck pain and headache.



Fernandez M, et al. *Eur J Pain* 2020 Oct;24(9):1687-1702.

Practice Guidelines *JOSPT* 2017; 47(7): 444-A83

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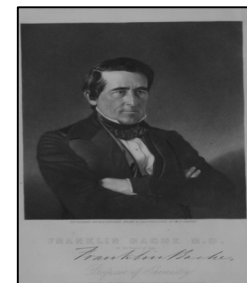
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Acupuncture in the United States

- Dr. Franklin Baché, great grandson Benjamin Franklin and founder University of PA/first medical school in US, noted **acupuncture highly effective for pain-management**. **1825**: translated **French medical text** on acupuncture into English.
- *Elements of Operative Surgery* (1829) contained section describing acupuncture techniques.
- 1836: Dr. William Markley Lee recommended acupuncture for pain relief in the *Southern Medical Journal* and the *Boston Medical and Surgical Journal* published article on **acupuncture for pain management**.
- With opiates and syringes, it fell into relative obscurity.



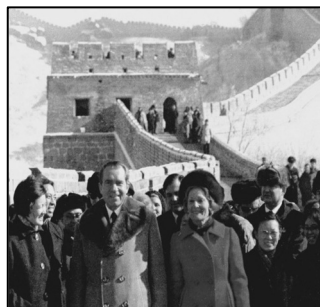
Lu DP, et al. An Historical Review and Perspective on the Impact of Acupuncture on U.S. Medicine and Society. *Med Augustin* 2013 Oct; 28(5): 311-316.

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Nixon, China, and Acupuncture

- In **1972**, James Reston, *New York Times* reporter **fell ill with appendicitis** while covering President Nixon's trip to China.
- Surgeons in Beijing successfully used **acupuncture as anesthesia** during the reporter's surgery and then to **control post-operative pain**. He was *awake* whole time.
- Acupuncture part of **comprehensive system of medicine** that uses a very **different diagnostic criteria** than that used in western medicine.



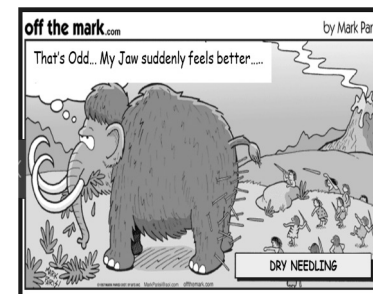
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Acupuncture for Chronic Pain

Meta-analysis: data from 20,827 patients in 39 clinical trials found: acupuncture is **effective** for treatment of **chronic musculoskeletal pain, headache, and osteoarthritis pain**, and that treatment effects **persist over time**.

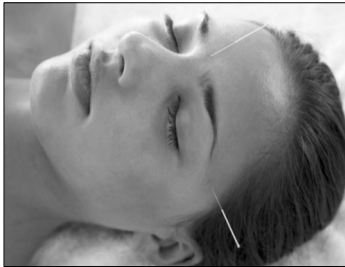
Vickers AJ, et al. Acupuncture for Chronic Pain: Update of an Individual Patient Data Meta-Analysis. *J Pain* 2018 May;19(5):455-474.



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Acupuncture & TMD



Small studies show **dry needling or acupuncture of lateral pterygoid and posterior, periarticular connective tissue, masseter, and temporalis muscles improves pain and disability in those 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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Acupuncture & Women's Health

- Data show acupuncture is beneficial for **labor pain, back pain in pregnancy, and dysmenorrhea.**
- Unclear if it is effective for **chemotherapy-induced nausea and vomiting, and menopausal hot flashes**, though it may improve **menopause related sleep disturbances.**



Bishop KC, et al. Acupuncture in Obstetrics and Gynecology. *Obstet Gynecol Surv* 2019 Apr;74(4):241-251.

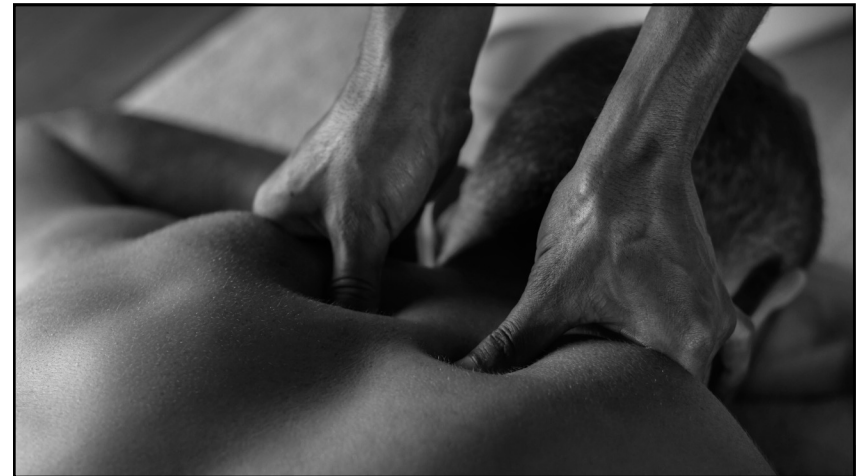
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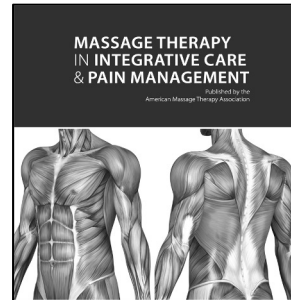
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Massage Therapy

- **Manual manipulation of soft tissue** intended to promote **health and well-being**.
- Key component of **pain management, overall health, and wellness**.
- Incorporating into broader pain management plan can help both **chronic and acute pain**.
- Licensed massage therapists integrated into teams at Dana-Farber Cancer Institute, Memorial Sloan-Kettering Cancer Center, Mayo Clinic, Duke Health System, M.D. Anderson Cancer Center and many others.



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Evidence Based Massage Recommendations

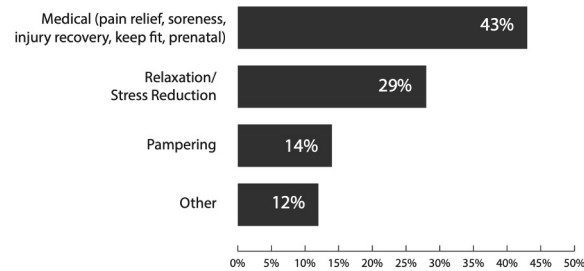
CHRONIC PAIN MANAGEMENT (pages 9–11)	BEHAVIORAL HEALTH TREATMENT (pages 12–13)	CARE FOR REHABILITATION/ PHYSICAL TRAINING (pages 13–16)	ACUTE MEDICAL TREATMENT (pages 16–20)
Back pain	Anxiety and stress	Performance training/ injury treatment	Cancer management
Neck and shoulder pain	Depression	Ergonomics and job-related injuries	Post-operative pain
Headache	PTSD	Cardiac rehab	Lifestyle diseases
Carpal tunnel syndrome	Substance use disorder recovery	Joint replacement surgery	Maternity and newborn care
Osteoarthritis		Scar management	
Fibromyalgia			
Hospice			

https://www.amtamassage.org/globalassets/documents/publications-and-research/mt_in_integrative_care_and_pain_management.pdf, Accessed October 23, 2022

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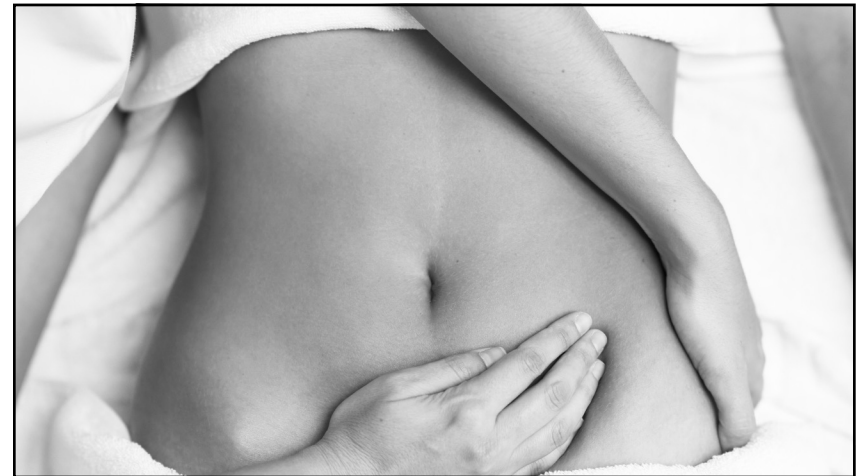
Figure 1: Top Reasons for Getting a Massage in 2017



https://www.amtamassage.org/globalassets/documents/publications-and-research/mt_in_integrative_care_and_pain_management.pdf, Accessed October 23, 2022

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Examples of Different Massage Types

- **Swedish:** most common. Uses effleurage (long flowing strokes), petrissage (rolling, kneading), friction (deep, circular strokes), tapotement (tapping with cupped hand, hand edge). Relaxing.
- **Deep tissue:** slow deep strokes apply pressure to specific problem areas.
- **Sports:** variety of techniques promote flexibility, prevent injuries and/or promote recovery. Used before, during, after training.
- **Shiatsu:** uses rhythmic pressure on acupressure points.
- **Thai:** put into variety of positions to mobilize joints, compress muscles.
- **Pregnancy:** relieve swelling, stress, muscle and joint pain.

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Yoga: Union of the Mind and Body

- **Originated in northern India 5,000 years ago.**
- Incorporates **breathing exercises, different postures, stretches, and meditation** to help one gain **greater acceptance, compassion, and centering.**
- **Many different types of yoga.**



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Some Types of Yoga

- **Hatha:** umbrella term for all **physical postures** of yoga. **Good for beginners, slower paced, focused on postures and breathing.**
- **Iyengar:** focuses on **alignment**, poses held for long time while teacher carefully adjusts poses. Good for those with **injuries.**
- **Vinyasa:** considered **most athletic style, faster paced.**
- **Ashtanga:** **physically demanding** sequence of poses. **Advanced** students.
- **Bikram/Hot yoga:** 26 basic postures (each performed twice) in a room **set to 105 degrees F and 40% humidity.**
- **Prenatal:** adapted for pregnancy with **pelvic floor and breath work**, slow, uses props for support. Highly recommend.

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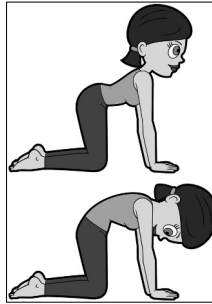


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Yoga Has Many Health Benefits

- Scientific evidence supports yoga for **stress management, mental health, mindfulness, healthy eating, weight loss and quality sleep.**
- Can improve **strength, balance and flexibility**, making it useful for all age, particularly **elders**
- American College of Physicians recommends as **first-line treatment for chronic low back pain.**

<https://www.hopkinsmedicine.org/health/wellness-and-prevention/9-benefits-of-yoga>



Cat Cow Pose

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Downward Facing Dog Pose

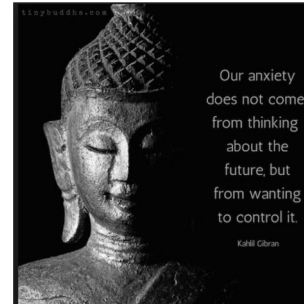


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Meditation



Our anxiety does not come from thinking about the future, but from wanting to control it.

Kahlil Gibran

- Meditation is a mind-body practice with a long history of use for increasing **calmness and physical relaxation**, improving **psychological balance, coping with illness**, and enhancing overall health and well-being.
- It's about learning to **observe thoughts and feelings without judging them.**

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Meditation for Health

- Excellent for **reducing stress perception** and **pain intensity**, while **elevating mood**.
- Long-time meditators have greater activation of areas responsible for **sustaining attention**, **processing empathy**, **integrating emotion** and **cognition**.
- Review of **47 trials** found that meditation improves:
 - **Anxiety**
 - **Depression**
 - **Pain**



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

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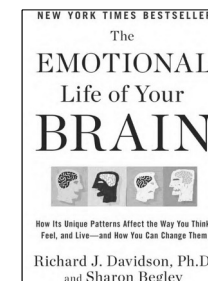
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National Institutes of Health: The Evidence

- Mind-body therapies shown to relieve **anxiety, stress, fatigue; improve mood** and **sleep disturbances**, improve the **quality of life** of **cancer patients**.
- **Meditation may reduce blood pressure.**
- **Meditation-based programs may be helpful in reducing common menopausal symptoms.**

www.nccih.nih.gov/health/tips/things-to-know-about-meditation-for-health

Accessed October 23, 2022



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Resources for Stress Reduction

- **Calm** - Great app for guided meditation, bedtime stories, breathing exercises. (free to \$60 annual subscription)
- **Insight Timer** - ~4,000 guided meditations >1,000 teachers (self-compassion, nature, stress, podcasts). Music tracks (free to \$5/mo.)
- **Headspace** - Meditation, videos, meditations music. (free basic course, \$12.99 mo., \$95/year)
- **10% Happier** - Performance enhancement. Busy people, stressed lives. (free one-week intro, then \$100 per year)
- **Buddhify** - For more advanced meditator. Can sort by location, activity and/or emotion. (small monthly fee, premium is \$30/yr.)

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Turmeric Rhizome (*Curcuma longa*)

- **Significantly more effective than placebo for pain relief/functional improvement.**
- No significant differences between curcumin and placebo in **safety outcomes**.
- **Curcuminoids** similar efficacy to **NSAIDs**; **significantly less likely** to cause gastrointestinal adverse events.
- Curcumin formulations could be “valuable addition to knee OA treatment regimens by relieving symptoms while reducing safety risks.”



Bannuru RR, et al. Efficacy of curcumin and Boswellia for knee osteoarthritic: Systematic review and meta-analysis. *Semin Arthritis Rheum* 2018 Mar 10; pii: S0049-0172(18)30002-7

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Ginger Rhizome (*Zingiber officinale*)



- Use dates back >5,000 years, cultivated India and China for spice, medicine. Important trade to Romans 2,000 years ago.
- 14th century value 1 pound = 1 sheep.
- Henry 8th passionate about ginger
- Queen Elizabeth credited 1st gingerbread man.
- Used fresh, dried, pickled, preserved, crystallized, candied, and ground.
- Actives increase with age —9 months for greater spice, 5 months milder flavor.
- Contains many bioactive components, including gingerols, pungent active.

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Nausea & Vomiting of Pregnancy

- Nausea and vomiting affects up to 85% of women during pregnancy.
- Studies done in *more severe* hyperemesis gravidarum.
- Meta-analyses: **ginger more effective than placebo** for hyperemesis gravidarum.
- Ginger **did not pose a risk for side-effects or adverse events** during pregnancy at doses of **250 mg dried ginger 4 times per day** (or 500 mg twice daily). *Do not exceed 1,500 mg per day.*



McParlin C et al. *J-AM* 4 2016; 316(13):1392-1401
O'Donnell A, et al. *Health Technol Assess* 2016; 20(74):1-268

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ACOG PRACTICE BULLETIN
Clinical Management Guidelines for Obstetrician–Gynecologists

NUMBER 189, JANUARY 2018 (Replaces Practice Bulletin 153, September 2015)
Committee on Obstetric Practice—This Practice Bulletin was developed by the American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics in collaboration with Susan M. Ramis, MD.

First Line Therapy:
Nonpharmacologic Options
Convert prenatal to folic acid supplement only
→ **Ginger capsules 250 mg four times daily**
Consider P6 acupressure with wrist bands

↓ persistent symptoms

Pharmacologic Options
Vitamin B6 (pyridoxine) 10-25 mg orally (either taken alone or in combination with doxylamine 12.5 mg orally), 3–4 times per day. Adjust schedule and dose according to severity of patient's symptoms.
OR
Vitamin B6 (pyridoxine) 10 mg/doxylamine 10 mg combination product, two tablets orally at bedtime initially up to four tablets per day (one tablet in morning, one tablet in midafternoon and 2 tablets at bedtime).

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Peppermint Leaf (Mentha × piperita)

- High in menthol
- Anti-inflammatory, analgesic, antimicrobial, antiseptic, astringent, carminative, fungicidal effects, nervine stimulant, decongestant, antispasmodic
- Effective painful menstruation and IBS
- Relieves itching: herpes, ringworm, scabies, poison oak, and ivy
- Decongestant: nasal congestion, cough




<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4606594/>

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Peppermint Essential Oil

- **Meta-analysis:** soluble fiber, peppermint oil, antispasmodic drugs, and gut-brain neuromodulators for IBS.
- **Peppermint EO ranked first for efficacy when global symptoms** were outcome measure, and **tricyclic antidepressants** ranked first when **abdominal pain** used as the outcome measure.
- Dose 0.2 ml in **enteric coated caps** taken 2-3 times daily.



Black CJ, et al. *Lancet Gastroenterol Hepatol*. 2019 Dec 16. pii: S2468-1253(19)30324-3.

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Peppermint: Headache



- **Topical treatment with peppermint essential oil** shown significantly more effective than placebo in controlled studies.
- **Efficacy comparable to aspirin or acetaminophen.** Peppermint oil in ethanol licensed for treatment of tension-type headache in adults and children above 6 years in Germany.

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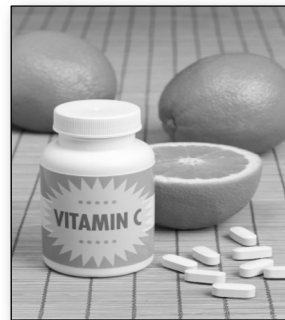
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Vitamin C

- Deficiency leads to **impaired immunity and greater risk of infection.**¹
- Maintains *epithelial barrier* function, increases alveolar fluid clearance, and attenuates pro-inflammatory response.
- **Only 1 in 10** Americans get recommended daily intake for **fruits and vegetables.**²
- **~15.7 million** Americans have serious vitamin C deficiency; **~60 million** have marginal status.
- **Infection** depletes levels due to increased inflammation and metabolism.



1. Vorithon P, et al. *Eur J Clin Pharmacol* 2019; 75(3):303-311.
2. https://www.cdc.gov/nutrition/odnrcs/66/ser/nut66d5d.htm?ci=nm66d5d_w
Accessed November 24, 2020
3. https://www.cdc.gov/nutritionreport/pdf/Nutrition_Book_complete508_final.pdf

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Prevalence of Vitamin C Deficiency and Low Vitamin C Concentration in US Population

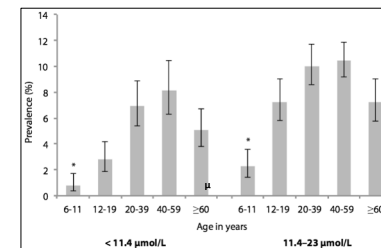


Figure H.1.f. Prevalence estimates of vitamin C deficiency (serum concentrations less than 11.4 μmol/L) and low vitamin C concentrations (11.4-23 μmol/L) in the U.S. population aged 6 years and older by age group, National Health & Nutrition Examination Survey, 2003-2006.

Error bars represent 95% of confidence intervals. *Prevalence in children is significantly lower than prevalence in persons 20 years and older ($p < 0.05$).

Scurvy induced when dietary vitamin C intake < 10 mg/d and/or plasma vitamin C levels **below 11 μmol/L**

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MAIN FUNCTIONS	GOOD SOURCES				
<ul style="list-style-type: none"> • Antioxidant defense • Enhances immune function • Needed to make collagen, carnitine, and the neurotransmitters serotonin and norepinephrine 	<table border="1"> <thead> <tr> <th>Fruit</th> <th>Vegetables</th> </tr> </thead> <tbody> <tr> <td> <ul style="list-style-type: none"> • Kiwifruit, 1 medium-sized, 90 mg • Strawberries (whole), 1 cup, 85 mg </td> <td> <ul style="list-style-type: none"> • broccoli + kale + tomatoes • Sweet Red Pepper, ½ cup chopped, 95 mg </td> </tr> </tbody> </table>	Fruit	Vegetables	<ul style="list-style-type: none"> • Kiwifruit, 1 medium-sized, 90 mg • Strawberries (whole), 1 cup, 85 mg 	<ul style="list-style-type: none"> • broccoli + kale + tomatoes • Sweet Red Pepper, ½ cup chopped, 95 mg
Fruit	Vegetables				
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<p>DAILY RECOMMENDATION</p> <p>400 mg</p> <p>All Adults</p>	<p>SPECIAL NOTES</p> <ul style="list-style-type: none"> • Heat destroys vitamin C. Try to eat fresh foods and cook by steaming, microwaving, or stir-frying. • Vitamin C in food is identical to vitamin C in supplements. • The Daily Recommendation listed is specific to the LPI based on extensive review of the scientific evidence. The Institute of Medicine's Recommended Dietary Allowance (RDA) is 90 mg/day for men and 75 mg/day for women. 				

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Vitamin D & Respiratory Infection



Martineau AR, et al. Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data. *BMJ* 2017; 356: i6583.

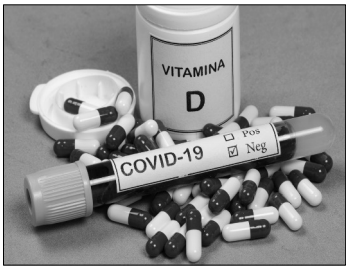
- Acute respiratory infection kills **~2.65 million people/year**.
- Vitamin D releases antimicrobial peptides in the lungs, helps to mount immune response.
- **25 eligible randomized controlled trials (n=10,933, aged 0–95 years).**
- Supplementation **reduced risk of acute respiratory infection** among all participants (NNT=33) and **those who were vitamin D deficient experienced the most benefit (NNT=4).**

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Vitamin D & COVID

- 212 cases COVID-19: **vitamin D deficient patients had 19.6-fold higher risk of critical outcome** compared to those with sufficient levels ($p < 0.001$).¹
- Retrospective study: **780 confirmed cases SARS-CoV-2 infection** found those vitamin D deficient **~13 times more likely to die**.²
- Israeli data: **26% of COVID patients died** if vitamin D deficient soon before hospitalization, compared to **3% who had normal levels of vitamin D**.
- Hospitalized patients **who were vitamin D deficient 14 times more likely to end up in severe or critical condition than others**.³



1. Alipio, M. Vitamin D Supplementation Could Possibly Improve Clinical Outcomes of Patients Infected with Coronavirus-2019 (COVID-2019). *SREVEvidence J*. 2020; doi:10.2139/ssrn.3571484;
2. Raharison P, et al. Patterns of COVID-19 Mortality and Vitamin D: An Indonesian Study. *SREVEvidence J*. 2020; doi: 10.2139/ssrn.358561
3. <https://www.timesofisrael.com/1-in-4-hospitalized-covid-patients-who-lack-vitamin-d-die-israeli-study/>

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Vitamin D Deficiency

- **Serum 25(OH)D level** is used to determine vitamin D status. According to the American Endocrine Society:
 - Preferable level **40–60 ng/mL** (100–150 nmol/L)
 - **Sufficiency is 30 ng/mL** (75 nmol/L) and above
 - **Insufficiency** defined as **20–29 ng/mL**
 - **Deficiency** defined as **<20 ng/mL** (<50 nmol/L)
 - **Severe deficiency** **<12 ng/mL** (<30 nmol/L)
- **66.8 million Americans** 1 year and older levels between **12–20 ng/ml**
- **23 million Americans** 1 year and older: levels **less than 12 ng/ml**
 - Most at risk were **women and non-Hispanic blacks**
- **2000–4000 IU per day** appears necessary to maintain sufficient levels

CDC: 2nd National Report on Biochemical Indicators of Diet and Nutrition in the U.S., Population: all rights reserved.
Holick MF, et al. *J Clin Endocrinol Metab* 2011; 94(7):1911-30

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Thailand Approves Asian Herb Andrographis to Treat COVID-19


<http://herbalgram.org/resources/herbalgram/volumes/volume-18/volume-18-issue-1-january-2021/thailand-approves-asian-herb-andrographis-to-treat-covid-19/thailand-approves-asian-herb-andrographis-to-treat-covid-19/>

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Acute Respiratory Tract Infections

- **2017 systematic review** (33 RCT, N = 7,175): **andrographis improved cough, sore throat and overall symptoms** compared to placebo and other herbal treatments.
- **Meta-analysis (12 studies):** compared to **usual care** (analgesics, antibiotics, anti-inflammatories, antivirals, corticosteroids) indicated **statistically significant reduction in sore throat and sick leave with andrographis**.
- **AE ~10%, most common nonserious GI.**




Hu XY, et al. *PLoS One*. 2017;12(8): doi: 10.1371/journal.pone.0181780
Worakunpharich W, et al. *Pharmacopidemiol Drug Saf*. 2021;30(6):727-739.

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Elder Flower/Berry (*Sambucus nigra*)



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Table 3. Human clinical studies on the effects of various *Sambucus nigra* treatments against influenza

Study	Treatment	dosage	n	Results	p
Zakay-Rones et al., 1995	Sambucol®	4 tsp (all adults) once daily for 2 days 4 tsp (adults) or 2 tsp (children) once daily for 2 days	25 27	Absence of side-effects in healthy adults Recovery from fever in 4 days instead of 6 or more days Symptomatic improvement in 2 days instead of 5 or more days Complete recovery in 2-3 days instead of 5 or more days	<0.01 <0.001 <0.001 <0.001
Konlee, 1998 Zakay-Rones et al., 2004	Sambucol® Sambucol®	15 mL four times daily for 5 days	60	Lessened duration of illness All individual symptoms relieved in 2-4 days instead of 7-8 days Global assessment showed pronounced improvement after 3 days instead of 7 days Less use of rescue medication than control Absence of side-effects in patients	<0.001 <0.001 <0.001 <0.001
Kong, 2009	Elderberry extract lozenge from HerbalScience Singapore Pte. Ltd.	4 lozenges daily for 2 days	64	24 h: significant improvement in all symptoms except coughing and mucus discharge 48 h: significant improvement in all symptoms 48 h: complete eradication of all symptoms in 28% of treatment group and 0% of control group	<0.0001 <0.0001 <0.0001
Tiralongo et al., 2016	Rubini capsules	2 capsules/day priming (9 days), then 3 capsules/day (6 days)	29 312	Absence of side effects in patients Lessened symptom severity Lessened illness duration No significant difference in use of rescue medications Less occurrence of illness in treatment group (not significant)	0.05 0.02 0.9 0.2

All studies were randomized, double-blinded, and placebo-controlled, with acceptable patient compliance.
Copyright © 2017 John Wiley & Sons, Ltd. *Phytother. Res.* 31: 533-554 (2017)

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Echinacea and Elderberry

- 473 patients with flu symptoms less than 48 hours randomized to **240 mg echinacea herb/root extract + elderberry fruit** (Vogel Bioforce) or **tamiflu**.
- **No difference between recovery rates**, antibiotic use, intermediate doctor visits, use of over-the-counter medications for symptoms, “ability to return to normal daily activities,” or physician- and patient-reported efficacy of the treatments.
- Safety positive.

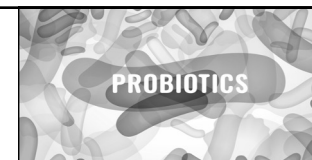


Raus K, et al. *Curr Ther Res.* 2015 Dec; 77: 66–72.

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Probiotics



- **Live microorganisms** administered in adequate amounts confer *health benefit to the host*.
- Regulate/modulate immune functions, **reduce risk intestinal infection**.
- Improve **intestinal barrier functions**, **reduce endotoxemia**.
- Induce hypo-responsiveness to **food antigens**.
- Improve **glucose control** and **reduce inflammatory cytokines**.
- Inhibit tumorigenesis and **may inhibit cancer progression**.

Gianotti L, et al. *World J Gastroenterol.* 2010;16:167–175

Szalinska M, et al. *Nutrients* 2018, 10(6), 773; <https://doi.org/10.3390/nu10060773>

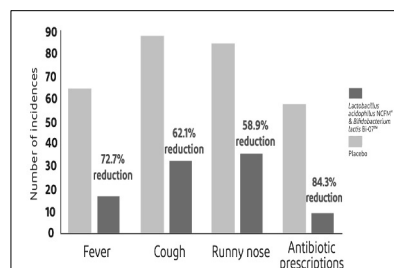
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Prevention Cold and Flu-Like Symptoms

- **DBPCT 326 children** (3–5 years age) randomized to placebo (N = 104), *L. acidophilus* NCFM (N = 110), or *L. acidophilus* NCFM + *Bifidobacterium lactis* Bi-07 (N = 112). Children treated 2 x daily for 6 months.
- Both products superior to placebo but greater benefit seen for combination.

Leyer GJ, et al. Probiotic effects on cold and influenza-like symptom incidence and duration in children. *Pediatrics* 2009 Aug;124(2):e172-9.



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Probiotics & Respiratory Infection



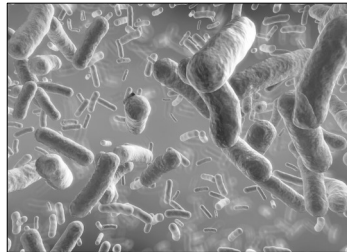
- **Meta-analysis 23 trials** (6269 children newborn—18 years) found probiotics reduced number of children having respiratory infections with fewer days absent from school.
- **Based on available data and taking into account the safety profile of the RCTs**, “probiotic consumption appears to be a feasible way to decrease the incidence of RTIs in children.”¹

1. Wang Y, et al. *Medicine* 2016 Aug;95(31):e4509

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Vaccine Adjuvant



Lei WT, et al. Effect of Probiotics and Prebiotics on Immune Response to Influenza Vaccination in Adults: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. *Nutrients*. 2017 Oct 27;9(11).

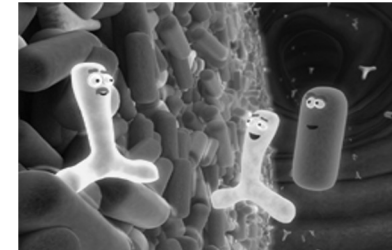
- 20 studies found “supplementation of influenza vaccines with **probiotics or prebiotics before vaccination** increased the immunogenicity to specific influenza viral strains, including the H1N1, H3N2, and B strains.”
- **Longer duration of pre-supplementation, the greater the response.** The older the adult, the more protection offered.
- Strains most active were *L. casei*, *L. paracasei*, and *B. longum*.

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Acute Infectious Diarrhea

- High quality evidence support use in **acute infectious diarrhea (e.g., traveling, kids in daycare, etc.)**
 - Start first sign of diarrhea + 2 weeks beyond; start 2 days before travel + trip duration.
- Meta-analysis **17 RCTs** (2,102 children): significant **reduction in duration** of diarrhea *S. boulardii* (20 fewer hours).²
- Meta-analysis **8 RCTs** (1,229 children): *L. reuteri* reduced duration of diarrhea (25 fewer hours), increased cure rate on days 1 and 2.³



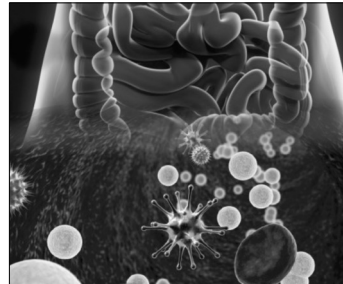
1. <https://www.aafp.org/afp/2017/0801/p170.html>. Accessed December 22, 2020
2. Feizizadeh S, et al. Efficacy and safety of *Saccharomyces boulardii* for acute diarrhea. *Pediatrics*. 2014;134(1):e176-e191.
3. Urbanska M, et al. Systematic review with meta-analysis: *Lactobacillus reuteri* DSM 17938 for diarrhoeal diseases in children. *Aliment Pharmacol Ther*. 2016;43(10):1025-1034.

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Proton Pump Inhibitors: GI Infection

- **PPIs disrupt microbiota.**
- Meta-analysis 23 studies (n=300,000): **65% increased risk *C. difficile* associated diarrhea.** (CDC lists *C. diff* “urgent threat”).¹
- PPI users **5 times risk of developing GI infections** compared to non-users.²
- Significant association **between acid-suppressive therapies and risk of *C. difficile* and pneumonia in children.**³



1. Janarthanan S, et al. *Am J Gastroenterol* 2012;107:1001-10
2. Hafiz RA, et al. *Ann Pharmacother*. 2018 Jul;52(7):613-622.
3. De Bruyne P, et al. *Arch Dis Child* 2018; 103(1):78-82

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PPI + Probiotics in Children



- 128 children with GERD randomized to **12 weeks PPI** (esomeprazole 1 mg/kg/d; max 40 mg) **plus probiotics** (*Lactobacillus reuteri* DM 17938) or identical placebo. Control: 120 healthy age-matched children.
- After 12 weeks, **dysbiosis occurred in 56.2% of group receiving placebo versus 6.2% of those taking probiotics (p<0.001).**
- **Probiotics + PPI significantly decreased prevalence of SIBO** among children with GERD compared to PPI and placebo ($P < 0.001$).

Belei O, et al. *J Neurogastroenterol Motil*. 2018 Jan 30;24(1):51-57.

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PPIs and the Immune System

- PPIs are risk factor for rotavirus, influenza, norovirus, and Middle East respiratory syndrome coronavirus infections; increased risk of acute gastroenteritis during periods of highest circulation of enteric viruses.¹
- Review by Cedars-Sinai (53,130 people): once daily dosing conferred **215% increased risk positive COVID test**, twice daily dosing **367% increased risk**.
- Study in Korea found 79% **greater risk of severe COVID** if taking PPI.³

1. Charpiat B, et al. Proton Pump Inhibitors are Risk Factors for Viral Infections: Even for COVID-19? *Clin Drug Investig* 2020 Oct;40(10):897-899.
 2. Almaro CV, et al. Increased Risk of COVID-19 Among Users of Proton Pump Inhibitors. *Am J Gastroenterol* 2020 Oct;115(10):1707-1715.
 3. Lee SW, et al. Severe clinical outcomes of COVID-19 associated with proton pump inhibitors: a nationwide cohort study with propensity score matching. *Gut* 2021 Jan;70(1):76-84.

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Outcome	Reference	No. of studies/ participants	Evidence of benefit?	Prevention and treatment of Crohn's disease and ulcerative colitis	Reference	No. of studies/ participants	Evidence of benefit?	Prevention and treatment of Crohn's disease and ulcerative colitis
Clostridium difficile associated diarrhoea in adults and children	Goldenberg et al (2017) ¹¹	39/9955	Yes	Yes	Saez-Lana et al (2015) ¹⁰³	14/821	Yes	Yes
Necrotising enterocolitis	Al Falah et al (2014) ¹¹² Rees et al (2017) ¹¹³	17/5338	Yes	Yes	Ananathan et al (2016) ¹¹⁴	9/275	Yes	Yes
Antibiotic associated diarrhoea in children	Goldenberg et al (2015) ¹¹⁴	26/3898	Yes	Yes	Akbari et al (2016) ¹¹⁵	13/805	Yes	Yes
Probiotics for preventing acute upper respiratory tract infections	Hao et al (2015) ¹¹⁵	12/3720	Yes	Yes	Zhang et al (2016) ¹¹⁶	7/425	Yes	Yes
Urinary tract infections	Schwenger et al (2015) ¹¹⁴	9/735	No	No	Athalye-Jape et al (2016) ¹¹⁶	6/1778	Yes	Yes
Prevention of asthma and wheeze in infants	Azad et al (2013) ¹¹⁷	6/1364	No	No	Masidi et al (2017) ¹¹⁷	19/935	Yes	Yes
Prevention of eczema in infants and children	Mansfield et al (2014)	16/2797	Yes	Yes	Hendijani et al (2017) ¹¹⁸	11/641	Yes	Yes
Prevention of invasive fungal infections in preterm neonates	Agrawal et al (2015) ¹¹⁸	19/4912	Unclear	Unclear	Wu et al (2017) ¹¹⁹	15/976	Yes	Yes
Prevention of nosocomial infections	Marzbanes et al (2015) ¹²⁰	30/2972	Yes	Yes	Wallace and Miley (2017) ¹²⁰	6/1080	Yes	Yes
Treatment of rotavirus diarrhoea in infants and children	Ahmadi et al (2015) ¹²¹	14/1149	Yes	Yes	Xie et al (2016) ¹²¹	10/1656	Yes	Yes

From: Valdes AM, et al. Role of gut microbiota in nutrition and health. *BMJ* 2018;361:2179

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Resource: www.usprobioticguide.com



Clinical Guide to Probiotic Products Available in USA

Indications, Dosage Forms and Clinical Evidence to Date - 2019 Edition

AEProBio

INDICATIONS FOR PEDIATRIC HEALTH

Show ▾ ▾ entries

	Brand Name	Probiotic Strain	Dosage Form	CFU/Dose	No. of Doses/Day	Indications (Level of Evidence)
	Bio-Kult Infant ¹	L. casei PDR 31™ L. rhamnosus GG™ L. acidophilus PDR 30™ B. infantis PDR 31™ B. lactis PDR 32™	Sachet	100billion	1-1 sachet	CEAD - Childhood exsiccant Atopic dermatitis (I) Colic - Colic (I) HPI - Helicobacter pylori - Adjunct to standard eradication therapy (I)
(I)	BioGaia Profectib Baby Drops with Vitamin D ¹	L. reuteri DSM 17928	Drops	100M5/drops	5 drops	AAD - Antibiotic associated diarrhea - Prevention (I) C - Constipation (I) CEAD - Childhood exsiccant Atopic dermatitis (I) CDI - Clostridium difficile disease - community acquired (I) Colic - Colic (I) BSFAP - Irritable bowel syndrome/functional abdominal pain (I) Regurg GI Mot - Reduces regurgitation/ Improves gastrointestinal motility (I)
(I)	BioGaia Profectib ¹	L. reuteri DSM 17928	Chewable Tablets	100M5/drops	1 tab. 5 drops	AAD - Antibiotic associated diarrhea - Prevention (I) C - Constipation (I) CEAD - Childhood exsiccant Atopic dermatitis (I) CDI - Clostridium difficile disease - community acquired (I) Colic - Colic (I) BSFAP - Irritable bowel syndrome/functional abdominal pain (I) Regurg GI Mot - Reduces regurgitation/ Improves gastrointestinal motility (I)
(I)	GoodBacteria Baby's Soothe Powder Infant Formula ²	L. reuteri DSM 17928	Powder	100gram	Refrigerated feeding if alternative to breast milk is required	AAD - Antibiotic associated diarrhea - Prevention (I) Colic - Colic (I) BSFAP - Irritable bowel syndrome/functional abdominal pain (I) Regurg GI Mot - Reduces regurgitation/ Improves gastrointestinal motility (I)
(I)	GoodBacteria Baby's Soothe Pediatric ³	L. reuteri DSM 17928	Drops	100M5 drops	5 drops	AAD - Antibiotic associated diarrhea - Prevention (I) C - Constipation (I) CEAD - Childhood exsiccant Atopic dermatitis (I) CDI - Clostridium difficile disease - community acquired (I) Colic - Colic (I) BSFAP - Irritable bowel syndrome/functional abdominal pain (I) Regurg GI Mot - Reduces regurgitation/ Improves gastrointestinal motility (I)

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Patient: Doctor, I don't feel well and I'm not sure why.



Doctor: I want you to meditate for 20 minutes, twice a day, exercise for at least 30 minutes a day, avoid processed foods, eat plenty of organic fruit and veg, spend more time in nature and less indoors, stop worrying about things you can't control and ditch your T.V. Come back in 3 weeks.

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