

What is the Evidence Behind Dietary Supplements?

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Disclosure

I have no actual or potential conflict of interest in relation to this presentation.

Goals and Objectives

1. Understand the medical evidence for benefits of selected dietary supplements for specific conditions.
2. Understand limitations or conflicting evidence of selected dietary supplements for specific conditions.
3. Review side effects and potential medication interactions of selected dietary supplements.

Scenario 1

- 16-year-old male cross-country runner
- Wants to build muscle and increase speed
- Cross training using weights and bicycle
- No past medical history
- Asks about creatine supplementation



Creatine Benefits in Men



Shown to be effective at improving training and performance of short-duration (6-30 seconds), high-intensity exercise

Meta-analysis of seven trials of young men, creatine supplementation plus resistance training increased maximal lifting weight for bench press and squat

Increases rate of phosphocreatine resynthesis during recovery from short, high-intensity exercises

Creatine Benefits in Older Men



Demonstrated benefits of creatine plus resistance training

- Creatine plus resistance training leads to greater improvements in total body mass, fat-free mass, and strength compared with resistance training alone
- Relevant for mitigating sarcopenia and dynapenia which are associated with increased risk of falls, frailty, and loss of independence

Emerging evidence of favorable effects on bone health

Potential cognitive benefits on memory and attention (more study needed)

Creatine Benefits in Women

Lower endogenous creatine stores

- May make them more responsive to supplementation, especially during periods of hormonal supplementation

In younger women, modest improvement in anaerobic performance and recovery



Creatine Benefits in Older Women

In older women, gains in upper and lower body strength are most pronounced with longer-term supplementation (>24 weeks)

- May help counteract age-related sarcopenia

Emerging evidence of positive effect on mood and cognitive function



Creatine Lack of Benefit

No good evidence of improvement in performance of other types of muscular effort

Inconsistent results in performance in endurance sports



Creatine Side Effects

Weight gain from water retention, reduced joint mobility, muscle cramping

- Water retention may improve thermoregulation in hot, humid conditions

No evidence of adverse effects on kidney function in patients with normal baseline renal function

Long-term effects unknown, so American College of Sports Medicine recommends it only be used by physically mature, well-developed athletes

Creatine Dosing

Loading 20 g/day in 4 divided doses for 5-7 days

Maintenance 3-5 g/day



Scenario 2

- 68-year-old woman with DJD knees limiting her ability to play pickleball
- Tylenol not effective
- Valvular a-fib on warfarin so cannot take NSAIDs
- Asks about glucosamine and chondroitin



Glucosamine Benefits

Glucosamine is required for the synthesis of glycosaminoglycans, proteoglycans, and hyaluronic acid.

Glucosamine sulfate is modestly beneficial for improving pain and function in knee osteoarthritis when taken by mouth for at least 4 weeks.

Glucosamine hydrochloride only seems to be beneficial when used in combination with chondroitin.

Most commonly taken in single or divided doses of 1500 mg daily.

Glucosamine Benefits

Glucosamine sulfate reduces pain similarly to ibuprofen 400 mg TID

- 2 weeks for NSAIDs
- 4-8 weeks for glucosamine

Glucosamine sulfate 1500 mg daily for 6 months might be more effective for reducing symptoms than acetaminophen 1 gram TID in patients with moderate knee osteoarthritis



Glucosamine Limitations

One meta-analysis: some improvement in pain intensity but does not reduce pain when moving or improve function compared with placebo

Glucosamine may not work for severe, long-standing arthritis

Unclear if glucosamine can slow disease progression or improve symptoms in other forms of osteoarthritis

Great variability across products

- Actual content labeled varies from 0% to 115%

Glucosamine Side Effects and Interactions

Bloating, nausea, diarrhea, constipation

Glucosamine increases the effects of warfarin, so the two shouldn't be taken together

- Weak level of evidence but high severity
- 20+ case reports to World Health Organization



Chondroitin Benefits

Chondroitin sulfate seems to modestly reduce osteoarthritis pain and improves function

Meta-analyses of RCTs in patients with knee osteoarthritis

- 800-2000 mg daily for at least 3 months
- Reduces pain and disability compared with placebo
- Improvement seems to persist for up to 3 months after cessation

Sub-group analysis showed that 16 patients need to take chondroitin for 6 months for 1 patient to experience at least 20% reduction in pain

Chondroitin Benefits

Seems to have disease-modifying benefits

Chondroitin 800 mg daily for ≥ 2 years modestly reduces joint degeneration and narrowing in knee and hip compared with placebo



Chondroitin Side Effects

Abdominal pain, bloating, constipation, diarrhea, heartburn, nausea

Typically 800-1200 mg daily; up to 2000 mg daily safely.



Glucosamine plus Chondroitin Benefits

Large, prospective observational study:

- Glucosamine hydrochloride plus chondroitin sulfate associated with reductions in pain, stiffness, and need for other analgesics
- Most pronounced at 16-24 weeks

Mixed benefit of glucosamine for arthritis of the spine, hip, or hand

Glucosamine plus Chondroitin Limitations

Limited head-to-head comparisons of sulfate and hydrochloride

Does not seem to PREVENT osteoarthritis



Scenario 3

- Same patient messages you and asks about turmeric for her knees
- Wants to be able to jump like her friend



Turmeric

Several meta-analyses show that turmeric extracts compared with placebo:

- Reduce knee pain and stiffness
- Improve physical function
- Reduce need for rescue medication

Reduced effect with increasing age or BMI

Low- to moderate-quality studies;
heterogeneous; variety of products



Turmeric vs NSAIDs

Mixed evidence whether turmeric is as effective or more effective than NSAIDs

Meta-analysis comparing 6 interventions in adults with knee DJD suggests that curcumin monotherapy or curcumin with NSAIDs improves scores related to pain, function, and stiffness.



Topical Turmeric

One clinical study demonstrated reduction in pain due to knee DJD by 11/100 points compared with placebo



Turmeric in Combination

Turmeric with glucosamine, chondroitin, Boswellia serrata, ashwagandha, and zinc can improve pain and functionality in patients with osteoarthritis



Turmeric Side Effects

Generally well tolerated

Constipation, dyspepsia, GERD, nausea, vomiting



Turmeric Dosing

Generally 500-1500 mg of curcumin per day for arthritis



Scenario 4

- 75-year-old woman
- Competitive runner on a local track team
- Known DJD in the left knee which causes pain and stiffness
- Hypertension controlled with amlodipine
- Will a Boswellia supplement help me?



Boswellia serrata Benefits

Tree native to India and Africa

Source of frankincense

Available as herbal formulation or extract

Improvement in pain, stiffness, and functionality with herbal formulation (15-600 mg daily) for 1-8 weeks compared with placebo

Reduced pain and stiffness and improved function with extract (100-1000 mg daily) for 1-8 weeks compared with placebo



Boswellia Side Effects and Limitations

Abdominal pain, diarrhea, headache, heartburn, itching, nausea

May inhibit cytochrome P450 enzymes (in vitro so theoretic risk)



Boswellia Dosing

Arthritis Foundation suggests 300-400 mg three times daily of a product that contains 60% boswellic acids



Scenario 5

- 75-year-old man
- Active runner who competes in 10Ks
- History of anxiety and insomnia which he manages with regular exercise
- History of hypertension managed with lisinopril
- Should I consider Ashwaghandha?



Ashwagandha Benefits

Evergreen shrub found in India, Middle East, and parts of Africa



Anxiety

- Meta-analysis of small RCTs showed ashwagandha 600-12,000 mg daily for 6-10 weeks moderately improves anxiety scores compared with placebo (study limited by heterogeneity)
- Several other small clinical studies showed reduced anxiety symptoms
- Study of young adults at 225-400 mg daily for 30 days did not improve anxiety, stress, or depression scores

Ashwagandha Benefits

Three clinical trials showed modest improvement in anxiety symptoms in patients with GAD (60 mg to 4 g daily)

Modest improvement in sleep in patients with insomnia or non-restorative sleep (125-600 mg daily)

Seems to help reduce stress and may reduce stress-related weight gain

Ashwagandha Side Effects

Diarrhea, GI upset, nausea and vomiting

- Rare with typical doses



May interact with diabetes medications and increase risk of hypoglycemia.

May interact with antihypertensives and increase risk of **hypotension**.

May increase sedative effects of benzodiazepines and CNS depressants.

Ashwagandha Dosing

Generally 500 mg daily for anxiety or insomnia. Not more than 1000 mg daily.



Scenario 6

- 48-year-old female triathlete
- No medical issues except overuse injuries
- Lots of exposure to sun, chlorine, salt water, and wind
- Concerned about appearance of her skin, especially face
- Does oral collagen work?



Collagen Benefits for Aging Skin

Oral collagen peptides seem to improve skin hydration and elasticity in older adults

- Meta-analyses with wide dosing range 372 mg to 12 grams daily for 4-12 weeks

Unclear if collagen peptides reduce skin wrinkles to a cosmetically significant degree



Collagen Benefits for Dry Skin

Oral collagen peptides seem to improve skin hydration and elasticity in adults with dry skin

- Improve skin roughness
- Decrease peeling
- Increase stratum corneum and epidermis water content



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