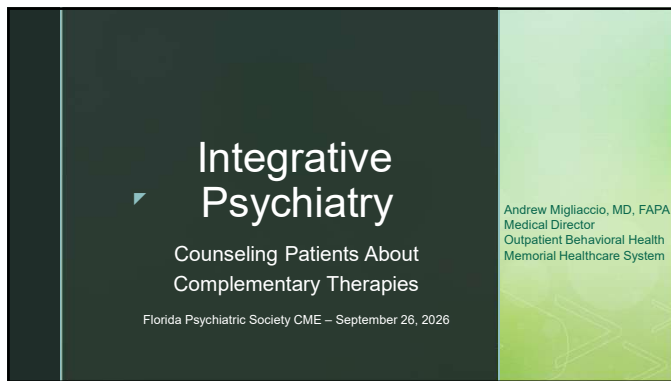




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2



3



Why This Matters

- ◉ CAM use common and rising: ~1/4 of people with psychiatric disorders
- ◉ Historical surveys – CAM use ~1/3 patients with panic disorder > 50% with severe depression, as well as “anxiety attacks”
- ◉ Most patients do not spontaneously disclose CAM use
- ◉ Ask specifically about vitamins, supplements, herbs, teas, and alternative practices
- ◉ Patients ask us about these therapies daily
- ◉ Deserve informed, non-judgmental guidance; Safety and counseling are important

4

Guiding Principles



- ◉ Evidence-informed and safety-driven
- ◉ Complement, do not replace: standard pharmacotherapy and/or psychotherapy usually remain first-line for MDD and other common disorders
- ◉ Shared decision-making and patient-centered care throughout
- ◉ Emphasize high quality, trusted products

5

The Integrative Psychiatry Framework

- Medication
- Psychotherapy
- + Lifestyle medicine
- + Complementary therapies
- + Recovery-oriented care

6

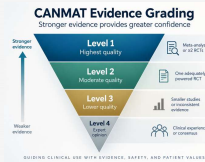
How We Will Review Interventions



7

Strength of the Evidence

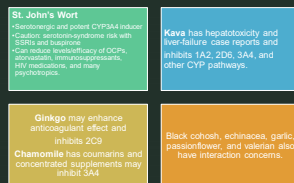
- CANMAT MDD guidelines dedicate a section to CAM and grade evidence from Level 1 through Level 4
- Level 1 includes meta-analysis with narrow confidence intervals or at least two adequately powered RCTs
- Level 4 represents expert opinion, case reports, or lower-quality evidence
- Line-of-treatment recommendations also weigh risk-benefit, tolerability, and safety; this framing will be used throughout



8

Safety and CYP450

Herbal products are pharmacologically active and frequently affect cytochrome P450 enzymes



9

Clinical Roadmap

Boosters	Busters	Bolsters
Case 1 Augmenting partial-response in depression	Case 2 Reducing residual anxiety and stress amid medical complexity and polypharmacy	Case 3 Supporting resilience, prevention, or treating mild illness in a patient preferring a "natural" approach

10

Case 1: Booster



Your patient has persistent depressive symptoms with multiple medication trials, only partial response, and pharma fatigue/reluctance

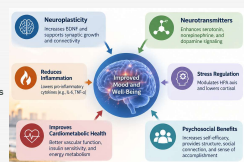
Clinical frame: the patient is not asking to abandon standard treatment, is already in therapy, and wants additional tools

Candidate complementary augmentation strategies: exercise, L-methylfolate, SAMe, and EPA-predominant omega-3

11

Exercise: Science

- Strong and robust evidence: 2024 network meta-analysis included 218 RCTs and >14k participants
- Walking/jogging, yoga, and strength training reduced depression compared with active controls; effects proportional to intensity
- Multiple recent meta-analyses show moderate effect sizes (SMD -0.6 vs active controls to -0.9 vs no treatment); comparable to psychotherapy and antidepressants
- Effects shrink in low-risk-of-bias studies, but clinical signal remains meaningful and consistent
- CANMAT: exercise is first-line, Level 1, for mild-to-moderate MDD and second-line adjunct for moderate-to-severe MDD [1-4]



12

Exercise: Safety + Script

- **Safety:** very favorable; strength training and yoga among best-tolerated modalities
 - Screen for cardiac or MSK contraindications and consider baseline fitness, fall risk, and risk of injury
- **Script:** aim for about 3 hours/week of moderate-intensity activity as a general physical-health target
 - CANMAT dose: 30-40 minutes, 3-4 times/week
 - APA/RCT minimum: at least 30 minutes, at least 3 times/week
 - Allow about 9 weeks for a full trial; benefit is often seen with 13-36 sessions
 - Implementation: meet patients where they are, consider a trainer, exercise with others, make it enjoyable, and use motivational interviewing [1]



13

L-methylfolate: Science

- Bioavailable folate that crosses the blood-brain barrier and supports monoamine synthesis
- Two sequential-parallel RCTs: only one found 15 mg/day superior to placebo as SSRI augmentation in SSRI-resistant MDD
- Estimated NNT is ~6 in augmentation trials
- Meta-analyses of adjunctive folate/L-methylfolate show modest improvements in response and remission
- Greater benefit seen with obesity and/or elevated inflammatory markers
- CANMAT: adjunctive L-methylfolate as second-line, Level 2, for mild-to-moderate MDD [5-9]



14

L-methylfolate: Safety + Script

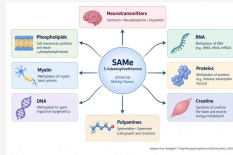
- **Safety:** well tolerated, adverse-event rates similar to placebo in RCTs
 - A 12-month open-label study supported durable tolerability; no significant CYP interactions are known
- **Script:** 15 mg/day is the studied augmentation dose; 7.5 mg/day was ineffective
- Consider as an early augmentation option in partial responders, especially with high BMI or inflammatory phenotype
- Clinical positioning: adjunctive strategy, not a replacement for optimized antidepressant treatment [5,10]



15

SAMe: Science

- Methyl donor central to monoamine synthesis; evidence is genuinely mixed
- A 2024 meta-analysis of 23 trials found SAMe monotherapy superior to placebo (SMD -0.58), and comparable to antidepressants
 - Did not find advantage as an adjunct to antidepressants but likely depends on methodology; better when pooling non-responders
- The 2016 Cochrane review rated evidence low or very-low certainty and did not find monotherapy superior to placebo overall
- Mixed results in escitalopram/placebo-controlled RCT; parent study saw no differences while single-site subsample reported higher remission with SAMe
- CANMAT downgraded adjunctive SAMe to third-line, Level 2, due to mixed recent RCTs [11-14]



16

SAMe: Safety + Script

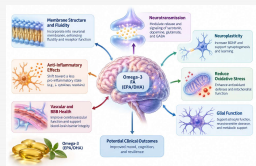
- **Safety:** generally well tolerated; trials found fewer adverse effects than imipramine
- Caution in bipolar disorder because mania/hypomania has been reported
- Do not combine with 5-HTP; reasonable safety data exist alongside antidepressants, and SAMe may help tachyphylaxis
- **Script:** start 400 mg once daily in the morning on an empty stomach
- After 1 week, increase to 400 mg BID; then titrate by 400 mg every 1-2 weeks
- Maximum dose: 1,600 mg/day



17

Omega-3 / EPA: Science

- Best supported as an EPA-predominant adjunct rather than a stand-alone antidepressant
- Meta-analyses show a small but significant benefit that depends on formulation
 - Efficacy is associated with EPA ≥60% of total EPA + DHA
 - Pure-DHA products and very-high-dose EPA have not shown similar benefit
- The 2021 Cochrane review found only a small, low-certainty effect, SMD approximately -0.4
- Benefit appears greatest as adjunct and in inflammatory or comorbid presentations; CANMAT downgraded omega-3 to third-line, Level 3 [15-18]



18

Omega-3 / EPA: Safety + Script

- **Safety:** minor GI upset and fishy aftertaste are common practical barriers
- Theoretical bleeding risk at high doses should be considered in patients on anticoagulants or with high bleeding risk
- **Script:** choose a high-EPA product, roughly EPA:DHA 3:2
- Dose: ~1,000-2,000 mg/day total omega-3, with at least 1 g/day EPA
- Refrigerate to reduce rancidity and counsel patients to choose a reputable product
- Clinical positioning: most attractive as adjunctive care, especially when inflammation or cardiometabolic comorbidity is present



19

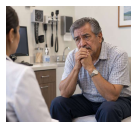
Boosters: Key Practice Points



- When to augment: partial response with residual symptoms and reluctance to change/add prescription
- Exercise has robust evidence, is reasonable for nearly everyone able and has broad psychiatric and cardiometabolic benefits
- L-methylfolate has the highest quality evidence of the "boosters"; especially appealing in inflammatory or high-BMI phenotypes
- SAME and omega-3 require more nuance because evidence is slightly weaker and mixed
- Frame these as adjuncts to, not replacements for, optimized standard treatment
- Document that CAM is complementary and that supplements are not FDA-regulated

20

Case 2: Busters



Your patient is medically complex with polypharmacy concerns, has poorly managed stress and residual anxiety symptoms despite multiple trials/agents

Goal: reduce anxiety and physiologic stress while minimizing added drug burden and risk of interactions

Candidate options: mind-body practices, L-theanine, lavender/Silexan, magnesium, and ashwagandha

21

Mind-Body Practices: Science

- Mindfulness-based interventions, including MBSR and MBCT, produce significant short-term reductions in anxiety
- TAME RCT (276 adults w/ anxiety disorders) studied 8-week MBSR or escitalopram
 - MBSR was noninferior to escitalopram on CGI-S
- Yoga improves anxiety symptoms across small trials
 - Proposed mechanisms include increased thalamic GABA, serotonin, dopamine, and oxytocin
- Additional yoga & mind-body pathways: reduced HPA-axis/autonomic dysregulation, normalized HRV, lower cortisol, BDNF-related cognitive benefit, and mindfulness-mediated stress reduction [19-21]



22

Mind-Body: Safety + Script

- **Safety:** very favorable; in TAME, adverse events occurred in about 15% with MBSR versus about 70% with escitalopram
 - There were no MBSR dropouts due to adverse events
- Yoga carries a physical-injury risk, so match the modality to baseline fitness and mobility
- **Script:** an 8-week structured MBSR or MBCT course is the studied "dose," with in-person delivery having the strongest evidence
- For yoga, Hatha is beginner-friendly; studied styles include Kundalini, Iyengar, and Sudarshan Kriya
 - Emphasize breathwork and meditation components, not just physical poses [21]



23

L-theanine: Science

- Amino acid in green tea, approximately 20-40 mg per cup
- Small lab-based RCTs show reduced stress response and lower self-reported anxiety
 - Physiologic signals include decreased heart rate and blood pressure, improved HRV, and increased EEG alpha activity
- 2026 Meta-analysis indicates improved attention, modest reduction in stress, possible anti-depressant effect warrants replication
- Clinical translation: "relaxed but alert" rather than sedated
- Evidence base remains small and should be presented as promising but limited [47]



24

L-theanine: Safety + Script

- **Safety:** well-tolerated with low interaction potential, making it attractive in polypharmacy
- **Script:** Dose 200 mg BID-TID, up to 400 mg TID PRN or as tolerated
- Best fit: mild residual anxiety, heightened stress response, ADHD anxiety evening activation
- Because it is low risk, it can be reasonable when the patient wants an option with minimal medication burden
- Counseling frame: may help physiologic stress reactivity, but evidence remains small



25

Lavender / Silexan: Science

- Silexan is a standardized oral lavender oil and one of the better-supported anxiolytic botanicals
- Meta-analysis of 5 RCTs (n=1,213): 80 mg/day superior to placebo for HAM-A
- Responder rate ratio was 1.34 compared with placebo
- Pooled and comparative data show efficacy comparable to lorazepam 0.5mg and paroxetine 20mg in subsyndromal anxiety and GAD
- 160 mg/day is effective in GAD, with 80 mg/day at the lower end of the therapeutic range
- Note: CANMAT lists lavender as third-line for mild MDD [22-25]



26

Silexan: Safety + Script

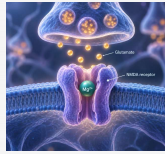
- **Safety:** notably clean; adverse events are largely eructation and mild transient GI symptoms
- No significant drug interactions, sedation, dependence, sexual dysfunction, weight gain, or withdrawal signal
- This profile makes Silexan particularly appealing in medically complex, polypharmacy patients
- **Script:** Silexan 80 mg once daily; may increase to 160 mg/day for GAD
- Allow about 2 weeks for onset and 6-10 weeks for full effect
- Counsel patients that the studied product is standardized oral lavender oil, not aromatherapy lavender [23,25]



27

Magnesium: Science

- Cofactor in more than 300 reactions; modulates NMDA receptors and HPA-axis activity
- Data isolated to anxiety disorders is limited; Magnesium plus B6 improved "stress" and anxiety in adults with low magnesemia
- Observational data show an inverse dose-dependent association between magnesium intake and depression
- Open-label crossover RCT (n=126), found about 248 mg/day elemental magnesium improved PHQ-9 and GAD-7 within 2 weeks
- Meta-analysis of RCTs shows benefit on depression scores
- Strongest rationale is when intake or levels are low [26-29]



28

Magnesium: Safety + Script

- **Safety:** generally well tolerated; dose-related diarrhea is the main adverse effect
- Renal impairment requires caution or renal dosing because of hypermagnesemia risk
- Chelated forms, such as glycinate and threonate, are generally better tolerated than oxide (laxative)
- **Script:** about 200-350 mg/day elemental magnesium
- Glycinate or citrate are practical options
- Clinical frame: reasonable low-cost, low-interaction adjunct, especially when intake appears low or chronic stress



29

Ashwagandha: Science

- Ayurvedic adaptogen; withanolides have GABA-mimetic properties
- Meta-analysis of 12 RCTs (n=1,002): significant reductions in anxiety (SMD -1.55) and stress (SMD -1.75)
 - RCTs report reduced perceived stress and cortisol
- Benefits seem to follow a dose-response signal suggesting greater anxiety benefit at higher doses
- Important limitation: high heterogeneity and low certainty [30-33]



30

Ashwagandha: Safety + Script

- **Safety:** generally well tolerated, most often GI upset or drowsiness
- Rare hepatotoxicity is an emerging concern; counsel patients and avoid in liver disease
- Theoretical additive effects with sedatives; may raise thyroid levels
- Use caution in hyperthyroidism, pregnancy, and with immunosuppressants
- **Script:** standardized root extract 300 mg BID (~600 mg/day) for 6-8 weeks
- Use a product standardized to withanolides with third-party testing



31

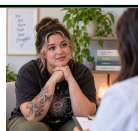
Busters: Key Practice Points



- Prioritize options that reduce medication and interaction burden
- Mind-body practices, L-theanine, Sillexan, and magnesium are attractive when interactions matter
- Yoga, Sillexan, and magnesium help both depression- & anxiety-related stress
- Screen renal function and hypermagnesemia risk before magnesium when clinically indicated
- Screen liver or thyroid disease before ashwagandha; avoid in pregnancy or immunosuppressants
- Individualize recommendations to medical complexity and patient preference

32

Case 3: Bolsters



Your patient with no PPHx presents with mild depression, adjustment-related anxiety/stress, and preference for a non-pharmaceutical approach

Clinical frame: build resilience, prevent progression, and reinforce healthy habits – goals for *all* of our patients

Candidate strategies: nutrition/dietary pattern, vitamin D, vitamin B12, and St. John's Wort

Previously covered: omega-3, exercise, Sillexan, magnesium

33

Nutrition: Science

- The strongest nutritional-psychiatry signal is for whole dietary patterns rather than individual nutrients
- SMILES RCT: modified-Mediterranean diet in moderate-to-severe MDD produced greater MADRS improvement than social support
 - Remission was 32% versus 8%, with NNT ~4
- AMMEND replicated large depressive-symptom improvement in young men
- HELFIMED showed Mediterranean diet plus fish oil improved mood and quality of life
- Mediterranean pattern benefits mood and lowers depression risk, likely via anti-inflammatory and **gut-microbiome** effects [34-38]



34

Nutrition: Safety + Script

- **Safety:** no pharmacologic risk and meaningful general cardiometabolic benefit
- Refer to a dietitian for a structured intervention where feasible
- **Script:** emphasize vegetables, fruit, whole grains, legumes, nuts, olive oil, and fish
- Reduce ultra-processed foods, refined sugar, and pro-inflammatory foods
- Frame nutrition as an evidence-based adjunct, not a substitute for treatment



35

Vitamin D: Science

- Evidence is mixed and nuanced
- Meta-analyses suggest supplementation modestly reduces depressive symptoms, especially in symptomatic and deficient patients
- Short-term dosing appears more favorable when deficiency is present
- The large VITAL RCT found vitamin D3 did not prevent depression or improve mood in generally replete middle-aged or older adults
- VA/DoD guideline does not support vitamin D monotherapy for depression, particularly without documented deficiency
- Best framed as correcting deficiency, not as a stand-alone antidepressant [39-43]



36

Vitamin D: Safety + Script

- **Safety:** safe at replacement doses; hypercalcemia or toxicity can occur with very high chronic dosing
- **Script:** check a 25-OH vitamin D level and replete if low
- Common maintenance dosing: 1,000-2,000 IU/day
- Common repletion option: 50,000 IU weekly until levels normalize
- Do not position vitamin D as monotherapy for MDD



37

Vitamin B12

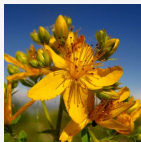
- **Science:** deficiency can cause or worsen depressive and cognitive symptoms; correction is standard care
- Supplementation in non-deficient patients has limited independent antidepressant evidence
- Clinical value lies in identifying and treating true deficiency
- **Safety:** vitamin B12 is very safe and water-soluble
- **Script:** screen B12 in depression with fatigue, cognitive complaints, poor diet, older age, metformin/PPI use, or vegan diet
- Replete deficiency (insufficiency) according to standard protocols



38

St. John's Wort: Science

- For mild-to-moderate depression, St. John's Wort is superior to placebo and comparable to standard antidepressants
- Cochrane and ACP network meta-analyses support equivalence to antidepressants in mild-to-moderate illness
- It generally has fewer side effects than standard antidepressants
- CANMAT lists it first-line, Level 1, monotherapy for mild-to-moderate MDD
 - CANMAT lists it second-line adjunct for moderate illness (rare in combination)
- Evidence in severe depression is weaker, and results are more favorable in German-speaking-country trials [44-46]



39

St. John's Wort: Safety

- The counseling centerpiece: it is both serotonergic and a potent CYP3A4 inducer
- Serotonin-syndrome risk increases with SSRIs, SNRIs, & buspirone
- CYP3A4 induction can lower oral contraceptive levels and increase unplanned pregnancy risk
- It can lower immunosuppressant levels and create transplant-rejection risk
- It also interacts with HIV medications, statins, warfarin, and many psychotropics
- Avoid in pregnancy/breastfeeding: photosensitivity occurs at higher doses; do a careful medication reconciliation before recommending



40

St. John's Wort: Script

- Studied extracts are standardized to hypericin 0.1-0.3% or hyperforin 1-6%
- Typical dose: 300 mg TID, about 900 mg/day total
- Studied range is approximately 500-1,800 mg/day
- Only recommend as monotherapy in an otherwise unmedicated or minimally medicated patient after screening for interacting drugs
- Do not recommend as an add-on to an SSRI
- This may be a reasonable option only when patient preference, illness severity, and interaction review align



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Bolsters: Key Practice Points



- Build resilience and prevent progression through diet, exercise, sleep, and targeted supplements
- Personalize recommendations to the patient's goals, medical context, and willingness to make lifestyle changes
- Nutrition and exercise are foundational; vitamin D and B12 are strongest when correcting deficiency
- Reserve St. John's Wort for carefully selected, minimally medicated patients

42

Choosing Quality Supplements

- Supplements are not FDA-approved or regulated like prescription medications
- Products may be mislabeled or contaminated, including heavy metals in botanicals
- Counsel patients to choose third-party testing and certifications such as USP, NSF, or GMP
- Avoid proprietary blends that obscure ingredient amounts
- Review interactions before starting and document supplement use and counseling in the chart

43

Counseling Pearls: The 6 A's

- Ask about all CAM use, including vitamins, herbs, teas, supplements, and alternative practices
- Acknowledge patient values non-judgmentally
- Assess evidence, safety, interactions, comorbidities, and product quality
- Advise with an evidence-informed recommendation
- Agree on a shared plan that complements standard care
- Arrange follow-up to reassess response and tolerability

44

Clinician & Patient Resources

- NIH Office of Dietary Supplements: botanical supplement fact sheets and HerbList app
- NIH NCCIH: depression and complementary health approaches
- Memorial Sloan Kettering "About Herbs": clinical summaries and interactions
- ConsumerLab.com and Examine.com: quality and evidence summaries
- Flockhart CYP450 Drug Interaction Table

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Session Takeaways

Use	Ask	Counsel	Complement	Empower
Use Science-Safety-Script for every intervention	Ask every patient about CAM use	Counsel confidently and non-judgmentally	Complement – never replace – evidence-based care	Empower patients through shared decision-making and product-quality guidance

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Thank you!
▀ Questions & Discussion

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