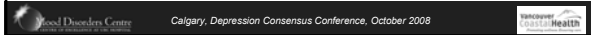


Complimentary and Alternative Medicine: Risks and Benefits

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Disclosure Statement 2007-2008

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Speaker/Advisory Boards

- AstraZeneca
- Biovail
- CANMAT
- Eli Lilly
- GlaxoSmithKline
- Janssen
- Litebook Company, Inc.
- Lundbeck
- Servier
- Wyeth

Stockholder

- None

Clinical Trials/Grants

- Advanced Neuromodulation Systems, Inc.
- AstraZeneca
- BrainCells, Inc.
- Canadian Institutes of Health Research
- CANMAT
- H. Lundbeck
- Litebook Company, Inc.
- Mathematics of Information and Advanced Technology Systems
- VGH-UBC Hospital Foundation

Outline

- Problems evaluating the evidence for efficacy
- Light therapy
- St. John's wort
- S-adenosyl methionine (SAM-e)
- Omega-3 fatty acids
- Other CAM treatments

Myths Associated with Complimentary and Alternative Medicine

- My Aunt Sally uses it, and it helps her.
- It must be effective, it's been used for thousands of years.
- It must be safe, it's a natural treatment.
- It must be safe, it's been used for thousands of years.
- It's better than putting chemicals into your system.
- Big pharma wants to shut down the use of non-drug treatments.
- There is no credible evidence for efficacy of CAM

Problems with Evaluating Evidence for Complimentary and Alternative Medicine

- Not patentable, so little business incentive to develop
- Plausible mechanisms of action?
- Few randomized controlled trials
- Challenging to design adequate placebo conditions
- Limited standardization of preparations or doses
- Trials usually limited by statistical variability
 - Heterogeneous diagnoses and entry criteria
 - Small sample sizes
 - Single centres
 - Short duration of treatment
- Side effects not systematically evaluated



CANMAT Depression Guidelines Revision, 2009



- Evidence-based update of 2001 CPA/CANMAT Guidelines
- Psychotherapy, pharmacotherapy, complimentary therapies, neurostimulation treatments
- Question-Answer format
- International commentary
- Published as a supplement in the Journal of Affective Disorders

www.canmat.org



CANMAT Depression Guidelines Revision, 2009

Chapter 5: Complimentary physical and nutraceutical treatments

Arun Ravindran, François L'Esperance, Marie-Josée Filteau, Raymond Lam

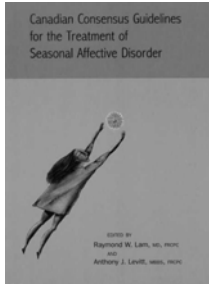
- Light therapy
- St. John's wort
- S-adenosyl methionine (SAM-e)
- Omega-3 fatty acids
- Exercise and yoga
- Tryptophan
- DHEA
- Acupuncture
- Other herbal remedies and nutraceuticals



Light Devices



Cost = \$150 to \$250

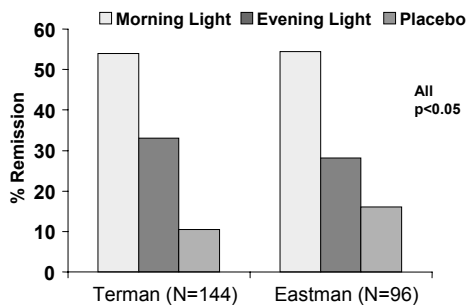


CCG-SAD, 1999 Protocol for Light Therapy

- Fluorescent light box
- 10,000 lux white light
- No ultraviolet
- 30 minutes daily
- Early morning exposure
- 2 to 4 weeks to gauge response

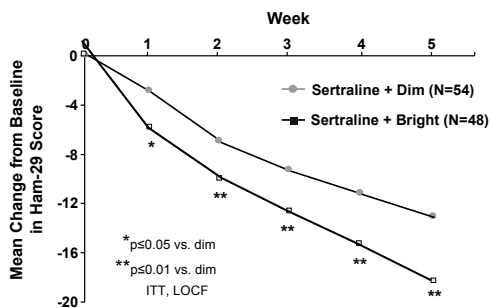
www.UBCsad.ca

Light Therapy is more effective than Placebo



Terman M, et al. Arch Gen Psychiatry 1998; 55:875-82.
Eastman C, et al. Arch Gen Psychiatry 1998; 55:883-89.

Adjunctive Bright Light in Non-Seasonal MDD



Martiny K. Acta Psychiatr Scand 2004.

Evidence for Efficacy of Light Therapy

Indication	Open Studies	RCTs	Meta-Analysis
SMDD	✓	✓	✓
MDD, monotherapy	✓	±	±
MDD, add-on to meds	✓	✓	
MDD in pregnancy	±	±	
Chronic MDD		±	
Bipolar depression	±		
Bulimia, PMDD	✓	±	

SMDD = seasonal major depressive disorder
MDD = non-seasonal major depression
PMDD = premenstrual depressive disorder

✓ = good support
± = small studies, or methodological limitations

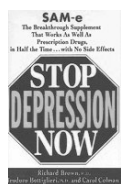
Complimentary and Alternative Medicine

- St. John's wort (hypericum)
 - Non-specific inhibitor of neurotransmitter reuptake?
 - Meta-analyses (N=37) and good quality RCTs available
 - Good evidence for efficacy in mild to moderate depression
 - No better than placebo in moderate to severe depression
 - Well tolerated with few side effects
 - May induce mania
 - Approved in Germany
 - Potential for drug interactions (induction of CYP 3A4 and CYP 1A2)



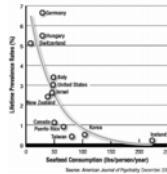
Complimentary and Alternative Medicine

- S-adenosyl methionine (SAM-e)
 - Methyl donor involved in synthesis of monoamines
 - Meta-analyses (N=28) and good quality RCTs available
 - Good evidence for efficacy in depression
 - Similar efficacy to antidepressants
 - Minor side effects (mostly GI and headache)
 - May induce mania



Complimentary and Alternative Medicine

- Omega-3 fatty acids
 - Found principally in fish and seafood
 - Eicosapentaenoic acid (EPA) is most studied
 - Inhibit signal transduction and alters membrane fluidity – neurotrophic effect?
 - Meta-analyses (N=10) and good quality RCTs available
 - Good evidence for efficacy in depression (and pregnancy)
 - Well tolerated with few side effects (fishy aftertaste, GI disturbance)
 - Publication bias, adequate blinding?





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- Light therapy
- St. John's wort
- S-adenosyl methionine (SAM-e)
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- Exercise and yoga
- Tryptophan
- DHEA
- Acupuncture
- Other herbal remedies and nutraceuticals

Complimentary and Alternative Medicine

- Many people are using CAM – must ask!
- Several CAM treatments have reasonable evidence for efficacy, including light therapy, St. John's wort, SAM-e and omega-3 fatty acids
- These may be used (in mild to moderate depression) alone or combined with antidepressants with the following caveats
 - Standardized dosing may not be available
 - Drug interactions still not well characterized
 - Significant side effects can still occur (e.g., mania)
- Better studies are still needed
