Section 5. Complementary and Alternative Medicine Treatments.

Supplemental Online eTables

Supplemental eTable 5.1. Evidence for light therapy.

Authors	Year	Type	n	Effect Size	Key Findings
Perera et al.	2016	Meta-analysis	20	SMD = −0.41, 95% CI: −0.64, −0.18	Superior to placebo/control as monotherapy or augmentation in non-seasonal mild to severe MDD
Bauer et al.	2013	Systematic review	NR	Not reported	Supports 2009 recommendations for seasonal MDD
Dirmaier et al.	2012	Systematic review	NR	Not reported	Supports 2009 recommendations
Güleç	2011	Systematic review	NR	Not reported	Supports 2009 recommendations; effective for seasonal and non-seasonal depression
Mårtensson et al	2015	Meta-analysis	10 trials, n=714	SMD = −0.54, 95% CI: 0.95, 0.13	Generally effective for moderate seasonal MDD, but evidence not unequivocal
Pail et al.	2011	Systematic review	NR	Not reported	Supports 2009 recommendations for mild to severe MDD
Lam et al.	2015	RCT	122	1. d = 0.80; 95% CI: 0.28 to 1.31; p = 0.006 2. d = 1.11; 95% CI: 0.54 to 1.64; p < 0.001	1. Monotherapy superior to placebo for non-seasonal moderate MDD 2. Augmentation superior to placebo for non-seasonal MDD
Martiny et al.	2012	RCT	75	OR = 2.8; 95% CI: 1.1–7.3, p = 0.04	Augmentation with chronotherapeutic techniques (LT, SD, wake therapy) superior to augmentation with exercise for mild to severe non-seasonal MDD
Martiny et al.	2015	RCT (follow-up)	75	OR = 2.6, CL: 1.3–5.6, p = 0.01	Superiority of chronotherapeutic techniques as augmentation maintained after 20 weeks of treatment for mild to severe non-seasonal MDD
Rohan et al.	2015a	RCT	177	χ2 = 0.003 and 1.06, p = 0.96 and 0.30	Similar efficacy to CBT (as monotherapy or augmentation) for moderate seasonal MDD
Rohan et al.	2015b	RCT (naturalistic follow-up)	177	Fewer recurrences for CBT (27.3%) than light therapy (45.6%)	CBT superior in relapse prevention at two-year follow-up for moderate seasonal MDD

Supplemental eTable 5.2. Evidence for sleep deprivation.

Authors	Year	Type	n	Effect Size	Key Findings
Ravindran and da Silva	2013	Systematic review	16	Not reported	Supports use of SD as augmentation to antidepressants in mild to severe MDD
Kundermann et al.	2009	RCT	18	Not significant	No significant clinical effect as augmentation to psychotherapy to moderate to severe MDD
Martiny et al.	2012	RCT	75	OR = 2.8; 95% CI: 1.1–7.3, $p = 0.04$	Augmentation to antidepressants with chronotherapeutic techniques (SD, LT, wake therapy) superior to augmentation with exercise for non-seasonal mild to severe MDD

Supplemental eTable 5.3. Evidence for exercise.

Authors	Year	Type	n	Effect Size	Key Findings
Cooney et al.	2013	Meta-analysis	39 trials, n=2,326	1. SMD = −0.62, 95% CI: −0.81 to −0.42; n=35 2. SMD = −0.03, 95% CI: −0.32 to 0.26, n=7 3. SMD = −0.11, 95% CI: −0.34 to 0.12, n=4 4. SMD = −0.33, 95% CI: −0.63 to −0.03; n=8	In mild to severe MDD, 1. Superior to no-treatment control conditions 2. Comparable to psychotherapy 3. Comparable to pharmacotherapy 4. Small effect for long-term benefits
Josefsson et al.	2014	Meta-analysis	13 trials, n=720	Hedges' g = –0.77, 95% CI: –1.14 to –0.41, $p < 0.001$	Superior to no-treatment control conditions and comparable to psychotherapy or pharmacotherapy for mild to moderate unipolar depression
Krogh et al.	2011	Meta-analysis	1. 13 trials, n=687 2. 5 trials, n=328	1. SMD = −0.40, 95% CI: −0.66 to −0.14 2. SMD = −0.01, 95% CI: −0.28 to 0.26	For mild to moderate MDD, 1. Effective as augmentation in short-term 2. No beneficial effect for interventions longer than 10 weeks

Rosenbaum et al.	2014	Meta-analysis	20 trials, n=1,298	SMD = 0.80, 95% CI: 0.47 to 1.13, $p < 0.001$	Superior to TAU, wait-list, or placebo conditions for moderate to severe depressive symptoms
Silveira et al.	2013	Meta-analysis	10 trials, n=758	SMD = 0.61, 95% CI: –0.88 to –0.33, $p < 0.001$	Superior to control conditions for mild to moderate MDD
Danielsson et al.	2013	Systematic review	14	SMD = −0.06, 95% CI: −0.36 to 0.23	Comparable to pharmacotherapy for mild to severe MDD
Nyström et al.	2015	Systematic review	12	Not reported	Effective as monotherapy for mild to severe MDD
Stanton and Reaburn	2013	Systematic review	5 trials, n=?	Mean frequency = 3.8 sessions/wk; mean duration = 9.3 wks (4-12)	Examined program variables only
Carneiro et al.	2015	RCT	26	1.04, 95% CI: −26.48 to −1.45, $p = 0.031$	Exercise as augmentation superior to TAU for women with mild to moderate MDD or dysthymia

Supplemental eTable 5.4. Evidence for Yoga.

Authors	Year	Type	n	Effect Size	Key Findings
Cramer et al.	2013	Meta-analysis	12 trials, n=619	SMD = −0.69, 95% CI: −0.99, −0.39; $p < 0.001$	Effective as augmentation, compared to TAU for mild to severe MDD

Supplemental eTable 5.5. Evidence for acupuncture.

Authors	Year	Type	n	Effect Size	Key Findings
Chan et al.	2015	Meta-analysis	13 trials, n=1,046	SMD = −2.52, 95% CI: 4.12 to 0.92, $p < 0.01$	More effective in augmentation than medication alone for moderate to severe MDD
Smith et al.	2010	Systematic review	30	Inconsistent findings	No consistent beneficial effect compared with waitlist or sham controls for mild to severe MDD
Zhang et al.	2010	Meta-analysis	20 trials, n=1,998	WMD = 0.31, 95% CI: −0.94–1.56, p = 0.63; n=16	Acupuncture monotherapy as effective as medication alone, but not superior to sham for mild to severe MDD Insufficient evidence for augmentation in mild to severe MDD
Wu et al.	2012	Systematic review	21	Not reported	Beneficial as monotherapy and more effective in augmentation than medication alone, for mild to severe depression

MacPherson et al.	2013	RCT	755	1. $p = 0.41$, 95% CI: −1.77 to 0.25 2. $d = -0.39$, 95% CI: −0.58 to −0.19 3. Reduction in mean depression scores = −1.55, 95% CI: −2.41 to −0.70	For moderate to severe MDD, 1. Similar efficacy to counseling 2. Superior as augmentation to medication alone 3. Monotherapy and augmentation benefits sustained long-term
Quah-Smith et al.	2013	RCT	47	$p < 0.001$	Monotherapy superior to placebo for moderate to severe MDD, but only on objective measures of depression

Supplemental eTable 5.6. Evidence for St. John's wort.

Authors	Year	Type	n	Effect Size	Key Findings
Carpenter	2011	Systematic review	17 trials, n=3,938	*M* ES = 0.64	Superior to placebo for mild to moderate MDD
Rahimi et al.	2009	Systematic review	13	WMD = 0.32, 95% CI: −1.28–0.64, $p = 0.52$	Comparable to antidepressants for mild to severe MDD
Mannel et al.	2010	RCT	200	1. $d = 0.33$ 2. $p = 0.02$; $d = 0.61$	For mild to moderate MDD, 1. Monotherapy superior to placebo 2. Particularly effective for moderate atypical depression
Sarris et al.	2012	RCT	124	$p = 0.61$	No difference between SJW, sertraline, and placebo for mild MDD or subthreshold depression

Supplemental eTable 5.7. Evidence for Omega-3 Fatty Acids.

Authors	Year	Type	n	Effect Size	Key Findings
Appleton et al.	2015	Meta-analysis	25 trials, n=1,438	SMD = −0.32, 95% CI: −0.12, −0.52	Small-to-modest effect as adjunctive compared to placebo for severe MDD
Bloch and Hannestad	2012	Meta-analysis	13 trials, n=731	SMD = 0.11, 95% CI: −0.04, 0.26	No significant effect for monotherapy or augmentation in mild to moderate MDD
Grosso et al.	2014	Meta-analysis	11 trials, n=418	SD = 0.47, 95% CI: 0.29, 0.66	Superior to placebo as monotherapy or augmentation for mild to severe *MDD*
Sublette et al.	2011	Meta-analysis	15 trials, n=916	SMD for EPA ≥ 60% = 0.558, 95% CI: 0.277, 0.838, $p = 0.001$	EPA-dominant formulations superior to DHA-based formulations (as monotherapy or augmentation) for mild to severe MDD
Rocha Araujo et al.	2010	Systematic review	19	Not reported	Mixed evidence for benefit in mild to severe MDD
Sarris et al.	2009	Systematic review	NR	Not reported	Superior to placebo as augmentation for mild to severe MDD

Sarris et al.	2010	Systematic review	4	Not reported	Superior to placebo as augmentation for moderate to severe MDD

Supplemental eTable 5.8. Evidence for SAM-e.

Authors	Year	Type	n	Effect Size	Key Findings
Carpenter	2011	Systematic review	9	Mean effect size = 1.0 (range 0.33-1.60)	Monotherapy superior to placebo for mild to moderate MDD
De Berardis et al.	2015	Systematic review	48	Not reported	Monotherapy superior to antidepressants for mild MDD Effective as augmentation in moderate to severe MDD
Sarris et al.	2010	Systematic review	NR	Not reported	Effective as augmentation in mild to severe MDD
Sarris et al.	2009	Narrative review	NR	Not reported	Effective as augmentation in moderate to severe MDD
Sarris et al.	2015	RCT (post-hoc analysis)	189	$p = 0.034$; $d = 0.95$	More effective than placebo in males, but not in females, for moderate to severe MDD

Supplemental eTable 5.9. Evidence for Tryptophan.

Authors	Year	Type	n	Effect Size	Key Findings
Sarris et al.	2010	Systematic review	9	Not reported	Mixed evidence for augmentation in mild to severe MDD
Sarris et al.	2009	Narrative review	9	Not reported	Insufficient evidence for monotherapy in mild to severe MDD
Jangid et al.	2013	RCT	70	Not reported	Similar efficacy to fluoxetine in moderate to severe MDD

Supplemental eTable 5.10. Evidence for Other Natural Health Products.

Authors	Year	Type	n	Effect Size	Key Findings
Folate preparations					
Almeida et al.	2015	Meta-analysis	11 trials, n=2,204	1 long-term study: odds ratio (OR) = 0.33, 95% CI: 0.12, 0.94	Long-term use may reduce risk of relapse No effect for short-term augmentation in moderate MDD
Sarris et al.	2010	Systematic review	2	Not reported	Effective as augmentation in moderate MDD
Fava and Mischoulon	2009	Narrative review	10	Not reported	Support for monotherapy or augmentation in moderate to severe MDD
Papakostas et al.	2012	Narrative review	11	Not reported	Support for augmentation with several folate forms, particularly L-methylfolate, in moderate to severe MDD

Ginsberg et al.	2011	Retrospective analysis	242	$p = 0.01$	L-methylfolate augmentation superior to antidepressant monotherapy in moderate MDD
Inositol					
Mukai et al.	2014	Meta-analysis	9 trials, n=242	Not significant	No benefit as monotherapy or augmentation in moderate to severe MDD and premenstrual dysphoric disorder
Iovieno et al.	2011	Systematic review	6	Not reported	No benefit as monotherapy or augmentation in moderate to severe MDD
Sarris et al.	2010	Systematic review	3	Not reported	Mixed evidence for monotherapy of augmentation in moderate to severe MDD
Sarris et al.	2009	Narrative review	4	Not reported	No benefit as monotherapy or augmentation in moderate to severe MDD
Acetyl-L-carnitine					
Wang et al.	2014	Narrative review	8	Not reported	Monotherapy superior to placebo and comparable to fluoxetine and amisulpride for mild to severe MDD and dysthymia
Crocus sativus					
Hausenblas et al.	2013	Meta-analysis	5 trials, n=177	1. *M* ES = −0.15, 95% CI: −0.52-0.22, $p = 0.42$; n=2 2. *M* ES = 1.62, 95% CI: 1.10-2.14, $p < 0.001$; n=3	For mild to moderate MDD, 1. Effective as monotherapy 2. Similar efficacy to antidepressants
Dwyer	2011	Systematic review	6	Not reported	Effective as monotherapy for mild to moderate MDD
Hausenblas et al.	2015	Systematic review	6	Not reported	Effective as monotherapy for mild to moderate MDD
Lopresti and Drummond	2014	Systematic review	6	Not reported	Effective as monotherapy for mild to moderate MDD
Talaei et al.	2015	RCT	40	$p < 0.0001$	Superior as augmentation to SSRIs vs. SSRIs alone for mild to moderate MDD
Lavandula					
Nikfarjam et al.	2013	RCT	80	$p < 0.01$	Lavandula combined with citalopram more effective than citalopram alone for moderate to severe MDD
Rhodiola rosea					
Mao et al.	2015	RCT	57	1. $p = 0.79$ 2. OR = 1.39 (0.38-5.04)	For mild to moderate MDD, 1. No difference between R. rosea, sertraline, and placebo 2. R. rosea superior to placebo in global improvement