

32 depression-relevant abstracts

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(Allaire, Couture et al. 2016; Bron, Bijlenga et al. 2016; Cozza, Fisher et al. 2016; de Vries, de Jonge et al. 2016; Hallahan, Ryan et al. 2016; Hansen, Sønderkov et al. 2016; Hopfinger, Berking et al. 2016; Janssen, Lowry et al. 2016; Kendler 2016; Kisely, Sawyer et al. 2016; Kohler, Gasse et al. 2016; Koukouna, Bossini et al. 2016; Kvam, Kleppe et al. 2016; Li, He et al. 2016; Meier, Mattheisen et al. 2016; Melo, Daher et al. 2016; Moor and de Graaf 2016; Pemberton and Fuller Tyszkiewicz 2016; Rector, Adabag et al. 2016; Salagre, Fernandes et al. 2016; Sarris, Murphy et al. 2016; Schroder, Berger et al. 2016; Schuch, Vancampfort et al. 2016; Shear, Reynolds et al. 2016; Spiers, Qassem et al. 2016; Stickley and Koyanagi 2016; Stubbs, Vancampfort et al. 2016; Tseng, Chen et al. 2016; van den Berg, Marijnissen et al. 2016; Waller, Kaprio et al. 2016; Weissman, Berry et al. 2016)

Allaire, J., P. Couture, et al. (2016). **"A randomized, crossover, head-to-head comparison of eicosapentaenoic acid and docosahexaenoic acid supplementation to reduce inflammation markers in men and women: The comparing epa to dha (compared) study."** *The American Journal of Clinical Nutrition* 104(2): 280-287.

<http://ajcn.nutrition.org/content/104/2/280.abstract>

(Available in free full text) Background: To date, most studies on the anti-inflammatory effects of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) in humans have used a mixture of the 2 fatty acids in various forms and proportions. Objectives: We compared the effects of EPA supplementation with those of DHA supplementation (re-esterified triacylglycerol; 90% pure) on inflammation markers (primary outcome) and blood lipids (secondary outcome) in men and women at risk of cardiovascular disease. Design: In a double-blind, randomized, crossover, controlled study, healthy men (n = 48) and women (n = 106) with abdominal obesity and low-grade systemic inflammation consumed 3 g/d of the following supplements for periods of 10 wk: 1) EPA (2.7 g/d), 2) DHA (2.7 g/d), and 3) corn oil as a control with each supplementation separated by a 9-wk washout period. Primary analyses assessed the difference in cardiometabolic outcomes between EPA and DHA. Results: Supplementation with DHA compared with supplementation with EPA led to a greater reduction in interleukin-18 (IL-18) ($-7.0\% \pm 2.8\%$ compared with $-0.5\% \pm 3.0\%$, respectively; $P = 0.01$) and a greater increase in adiponectin ($3.1\% \pm 1.6\%$ compared with $-1.2\% \pm 1.7\%$, respectively; $P < 0.001$). Between DHA and EPA, changes in CRP ($-7.9\% \pm 5.0\%$ compared with $-1.8\% \pm 6.5\%$, respectively; $P = 0.25$), IL-6 ($-12.0\% \pm 7.0\%$ compared with $-13.4\% \pm 7.0\%$, respectively; $P = 0.86$), and tumor necrosis factor- α ($-14.8\% \pm 5.1\%$ compared with $-7.6\% \pm 10.2\%$, respectively; $P = 0.63$) were NS. DHA compared with EPA led to more pronounced reductions in triglycerides ($-13.3\% \pm 2.3\%$ compared with $-11.9\% \pm 2.2\%$, respectively; $P = 0.005$) and the cholesterol:HDL-cholesterol ratio ($-2.5\% \pm 1.3\%$ compared with $0.3\% \pm 1.1\%$, respectively; $P = 0.006$) and greater increases in HDL cholesterol ($7.6\% \pm 1.4\%$ compared with $-0.7\% \pm 1.1\%$, respectively; $P < 0.0001$) and LDL cholesterol ($6.9\% \pm 1.8\%$ compared with $2.2\% \pm 1.6\%$, respectively; $P = 0.04$). The increase in LDL-cholesterol concentrations for DHA compared with EPA was significant in men but not in women (P -treatment \times sex interaction = 0.046). Conclusions: DHA is more effective than EPA in modulating specific markers of inflammation as well as blood lipids. Additional studies are needed to determine the effect of a long-term DHA supplementation per se on cardiovascular disease risk.

Bron, T. I., D. Bijlenga, et al. (2016). **"Prevalence of ADHD symptoms across clinical stages of major depressive disorder."** *Journal of Affective Disorders* 197: 29-35. <http://www.sciencedirect.com/science/article/pii/S016503271530608X>

Background Depression and ADHD often co-occur in clinical samples. Depression severity may be linked to ADHD symptomatology. We therefore assessed ADHD symptoms across clinical stages of major depressive disorder (MDD). Methods We used 4-year follow-up data of the Netherlands Study of Depression and Anxiety (September 2008 until April 2011), including healthy controls, groups with remitted and current MDD (N=2053; age range 21-69 years; 66.8% females). Probable ADHD was defined as having current ADHD symptoms on the Conners Adult ADHD Rating Scale and a positive score on childhood or early-adolescent ADHD indicators. We examined ADHD symptom rates across (i) those with and without lifetime MDD, (ii) clinical characteristics of MDD including severity, course and outcomes, (iii) clinical stages of MDD. Results (i) The prevalence of ADHD symptoms was 0.4% in healthy controls, 5.7% in remitted MDD and 22.1% in current MDD (OR=4.5; 95% CI 3.1-6.5). (ii) ADHD symptom rates and odds were significantly increased among those with more severe depression (29.4%; OR=6.8; 95% CI 2.9-16.1), chronic depression (21.8%; OR=3.8; 95% CI 2.5-5.7), earlier age of onset of depressive symptoms (9.9%; OR=1.5; 95% CI 1.0-2.3), and comorbid anxiety disorders (29.0%; OR=3.4; 95% CI 2.0-5.7). (iii) ADHD symptom rates increased across clinical stages of MDD, up to 22.5% in chronic MDD. Limitations We used self-reports on ADHD symptoms. Also, clinical staging models have not yet been validated for mental disorders. Conclusions ADHD symptoms are very common among MDD patients, especially among those in recurrent and chronic stages of MDD. Considering ADHD may be an important step forward in improving the treatment of depression.

Cozza, S. J., J. E. Fisher, et al. (2016). **"Performance of DSM-5 persistent complex bereavement disorder criteria in a community sample of bereaved military family members."** *American Journal of Psychiatry* 173(9): 919-929. <http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2016.15111442>

Objective: The purpose of this article was to examine the accuracy of DSM-5 proposed criteria for persistent complex bereavement disorder in identifying putative cases of clinically impairing grief and in excluding nonclinical cases. Performance of criteria sets for prolonged grief disorder and complicated grief were similarly assessed. Method: Participants were family members of U.S. military service members who died of any cause since September 11, 2001 (N=1,732). Putative clinical and nonclinical samples were derived from this community sample using cutoff scores from the Inventory of Complicated Grief and the Work and Social Adjustment Scale. Items from a self-report grief measure (Complicated Grief Questionnaire) were matched to DSM-5 persistent complex bereavement disorder, prolonged grief disorder, and complicated grief criteria. Endorsed items were used to identify cases. Results: Criteria sets varied in their ability to identify clinical cases. DSM-5 persistent complex bereavement disorder criteria identified 53%, prolonged grief disorder criteria identified 59%, and complicated grief criteria identified more than 90% of putative clinical cases. All criteria sets accurately excluded virtually all nonclinical grief cases and accurately excluded depression in the absence of clinical grief. Conclusions: The DSM-5 persistent complex bereavement disorder criteria accurately exclude nonclinical, normative grief, but also exclude nearly half of clinical cases, whereas complicated grief criteria exclude nonclinical cases while identifying more than 90% of clinical cases. The authors conclude that significant modification is needed to improve case identification by DSM-5 persistent complex bereavement disorder diagnostic criteria. Complicated grief criteria are superior in accurately identifying clinically impairing grief.

de Vries, Y. A., P. de Jonge, et al. (2016). **"Influence of baseline severity on antidepressant efficacy for anxiety disorders: Meta-analysis and meta-regression."** *The British Journal of Psychiatry* 208(6): 515-521. <http://bjp.rcpsych.org/content/208/6/515>

Background Antidepressants are established first-line treatments for anxiety disorders, but it is not clear whether they are equally effective across the severity range. **Aims** To examine the influence of baseline severity of anxiety on antidepressant efficacy for generalised anxiety disorder (GAD), social anxiety disorder (SAD), obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD) and panic disorder. **Method** Fifty-six trials of second-generation antidepressants for the short-term treatment of an anxiety disorder were included. Baseline and change scores were extracted for placebo and treatment groups in each trial. Mixed effects meta-regression was used to investigate the effects of treatment group, baseline severity and their interaction. **Results** Increased baseline severity did not predict greater improvement in drug groups compared with placebo groups. Standardised regression coefficients of the interaction term between baseline severity and treatment group were 0.04 (95% CI -0.13 to 0.20, $P = 0.65$) for GAD, -0.06 (95% CI -0.20 to 0.09, $P = 0.43$) for SAD, 0.04 (95% CI -0.07 to 0.16, $P = 0.46$) for OCD, 0.16 (95% CI -0.22 to 0.53, $P = 0.37$) for PTSD and 0.002 (95% CI -0.10 to 0.10, $P = 0.96$) for panic disorder. For OCD, baseline severity did predict improvement in both placebo and drug groups equally ($\beta = 0.11$, 95% CI 0.05 to 0.17, $P = 0.001$). **Conclusions** No relationship between baseline severity and drug-placebo difference was found for anxiety disorders. These results suggest that if the efficacy of antidepressants is considered clinically relevant, they may be prescribed to patients with anxiety regardless of symptom severity.

Hallahan, B., T. Ryan, et al. (2016). **"Efficacy of omega-3 highly unsaturated fatty acids in the treatment of depression."** *The British Journal of Psychiatry* 209(3): 192-201

Background Trials evaluating efficacy of omega-3 highly unsaturated fatty acids (HUFAs) in major depressive disorder report discrepant findings. **Aims** To establish the reasons underlying inconsistent findings among randomised controlled trials (RCTs) of omega-3 HUFAs for depression and to assess implications for further trials. **Method** A systematic bibliographic search of double-blind RCTs was conducted between January 1980 and July 2014 and an exploratory hypothesis-testing meta-analysis performed in 35 RCTs including 6665 participants receiving omega-3 HUFAs and 4373 participants receiving placebo. **Results** Among participants with diagnosed depression, eicosapentaenoic acid (EPA)-predominant formulations (>50% EPA) demonstrated clinical benefits compared with placebo (Hedge's $G = 0.61$, $P < 0.001$) whereas docosahexaenoic acid (DHA)-predominant formulations (>50% DHA) did not. EPA failed to prevent depressive symptoms among populations not diagnosed for depression. **Conclusions** Further RCTs should be conducted on study populations with diagnosed or clinically significant depression of adequate duration using EPA-predominant omega-3 HUFA formulations.

Hansen, B. T., K. M. Sønderskov, et al. (2016). **"Daylight savings time transitions and the incidence rate of unipolar depressive episodes."** *Epidemiology* Publish Ahead of Print.

http://journals.lww.com/epidem/Fulltext/publishahead/Daylight_savings_time_transitions_and_the.98946.aspx

BACKGROUND: Daylight savings time transitions affect approximately 1.6 billion people worldwide. Prior studies have documented associations between daylight savings time transitions and adverse health outcomes, but it remains unknown whether they also cause an increase in the incidence rate of depressive episodes. This seems likely because daylight savings time transitions affect circadian rhythms, which are implicated in the etiology of depressive disorder. Therefore, we investigated the effects of daylight savings time transitions on the incidence rate of unipolar depressive episodes. **METHODS:** Using time series intervention analysis of nationwide data from the Danish Psychiatric Central Research Register from 1995 to 2012 we compared the observed trend in the incidence rate of hospital contacts for unipolar depressive episodes after the transitions to and from summer time to the predicted trend in the incidence rate. **RESULTS:** The analyses were based on 185,419 hospital contacts for unipolar depression and showed that the transition from summer time to standard time were associated with an 11% increase (95% CI: 7%, 15%) in the incidence rate of unipolar depressive episodes that dissipated over approximately 10 weeks. The transition from standard time to summer time was not associated with a parallel change in the incidence rate of unipolar depressive episodes. **CONCLUSION:** This study shows that the transition from summer time to standard time was associated with an increase in the incidence rate of unipolar depressive episodes. Distress associated with the sudden advancement of sunset, marking the coming of a long period of short days, may explain this finding.

Hopfinger, L., M. Berking, et al. (2016). **"Emotion regulation mediates the effect of childhood trauma on depression."** *Journal of Affective Disorders* 198: 189-197. <http://www.sciencedirect.com/science/article/pii/S0165032715312544>

Background Childhood trauma increases the risks of both depression and dysfunctional emotion regulation, which is a factor that has been strongly linked to depression. Because of these demonstrated relationships, it can be hypothesized that dysfunctional emotion regulation is a mediator of the association between childhood trauma and depression. **Methods** To test this hypothesis, we assessed the indirect effect of emotion regulation (Emotion Regulation Skills Questionnaire) on the relationship between childhood trauma (Childhood Trauma Questionnaire) and depression severity (24-item Hamilton Rating Scale for Depression) as well as depression lifetime persistency (i.e., lifetime percentage spent in major depressive episodes; assessed via SCID and Life Chart Interviews) in 269 patients with major depressive disorder (MDD). **Results** Bootstrapping-enhanced mediation analyses indicated that deficits in general emotion regulation mediated the association of childhood trauma to both depression severity and depression lifetime persistency. Further exploratory analyses indicated that specific emotion regulation skills (such as the ability to mindfully observe, accept, and tolerate undesired emotions or the willingness to voluntarily confront situations that prompt negative emotions in order to attain personally relevant goals) significantly mediated the association between childhood trauma and depression severity. Willingness to confront was a mediator for both depression outcomes (depression severity and lifetime persistency). **Limitations** The employed mediation analyses are cross-sectional in nature, which limits any firm conclusions regarding causality. **Conclusions** The findings support the assumption that a sophisticated emotion regulation may help prevent the onset or unfavorable course of depression in individuals who have experienced childhood trauma.

Janssen, C. W., C. A. Lowry, et al. (2016). **"Whole-body hyperthermia for the treatment of major depressive disorder: A randomized clinical trial."** *JAMA Psychiatry* 73(8): 789-795. <http://dx.doi.org/10.1001/jamapsychiatry.2016.1031>

Importance Limitations of current antidepressants highlight the need to identify novel treatments for major depressive disorder. A prior open trial found that a single session of whole-body hyperthermia (WBH) reduced depressive symptoms; however, the lack of a placebo control raises the possibility that the observed antidepressant effects resulted not from hyperthermia per se, but from nonspecific aspects of the intervention. **Objective** To test whether WBH has specific antidepressant effects when compared with a sham condition and to evaluate the persistence of the antidepressant effects of a single treatment. **Design, Setting, and Participants** A 6-week, randomized, double-blind study conducted between February 2013 and May 2015 at a university-based medical center comparing WBH with a sham condition. All research staff conducting screening and outcome procedures were blinded to randomization status. Of 338 individuals screened, 34 were randomized, 30 received a study intervention, and 29 provided at least 1 postintervention assessment and were included in a modified intent-to-

treat efficacy analysis. Participants were medically healthy, aged 18 to 65 years, met criteria for major depressive disorder, were free of psychotropic medication use, and had a baseline 17-item Hamilton Depression Rating Scale score of 16 or greater. Interventions A single session of active WBH vs a sham condition matched for length of WBH that mimicked all aspects of WBH except intense heat. Main Outcomes and Measures Between-group differences in postintervention Hamilton Depression Rating Scale scores. Results The mean (SD) age was 36.7 (15.2) years in the WBH group and 41.47 (12.54) years in the sham group. Immediately following the intervention, 10 participants (71.4%) randomized to sham treatment believed they had received WBH compared with 15 (93.8%) randomized to WBH. When compared with the sham group, the active WBH group showed significantly reduced Hamilton Depression Rating Scale scores across the 6-week postintervention study period (WBH vs sham; week 1: -6.53 , 95% CI, -9.90 to -3.16 , $P < .001$; week 2: -6.35 , 95% CI, -9.95 to -2.74 , $P = .001$; week 4: -4.50 , 95% CI, -8.17 to -0.84 , $P = .02$; and week 6: -4.27 , 95% CI, -7.94 to -0.61 , $P = .02$). These outcomes remained significant after evaluating potential moderating effects of between-group differences in baseline expectancy scores. Adverse events in both groups were generally mild. Conclusions and Relevance Whole-body hyperthermia holds promise as a safe, rapid-acting, antidepressant modality with a prolonged therapeutic benefit.

Kendler, K. S. (2016). **"The phenomenology of major depression and the representativeness and nature of DSM criteria."** *American Journal of Psychiatry* 173(8): 771-780.

<http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2016.15121509>

How should DSM criteria relate to the disorders they are designed to assess? To address this question empirically, the author examines how well DSM-5 symptomatic criteria for major depression capture the descriptions of clinical depression in the post-Kraepelin Western psychiatric tradition as described in textbooks published between 1900 and 1960. Eighteen symptoms and signs of depression were described, 10 of which are covered by the DSM criteria for major depression or melancholia. For two symptoms (mood and cognitive content), DSM criteria are considerably narrower than those described in the textbooks. Five symptoms and signs (changes in volition/motivation, slowing of speech, anxiety, other physical symptoms, and depersonalization/derealization) are not present in the DSM criteria. Compared with the DSM criteria, these authors gave greater emphasis to cognitive, physical, and psychomotor changes, and less to neurovegetative symptoms. These results suggest that important features of major depression are not captured by DSM criteria. This is unproblematic as long as DSM criteria are understood to index rather than constitute psychiatric disorders. However, since DSM-III, our field has moved toward a reification of DSM that implicitly assumes that psychiatric disorders are actually just the DSM criteria. That is, we have taken an index of something for the thing itself. For example, good diagnostic criteria should be succinct and require minimal inference, but some critical clinical phenomena are subtle, difficult to assess, and experienced in widely varying ways. This conceptual error has contributed to the impoverishment of psychopathology and has affected our research, clinical work, and teaching in some undesirable ways.

Kisely, S., E. Sawyer, et al. (2016). **"The oral health of people with anxiety and depressive disorders – a systematic review and meta-analysis."** *Journal of Affective Disorders* 200: 119-132.

<http://www.sciencedirect.com/science/article/pii/S0165032716302555>

Abstract Background Many psychological disorders are associated with comorbid physical illness. There are less data on dental disease in common psychological disorders such as depression and anxiety in spite of risk factors in this population of diet, lifestyle or antidepressant-induced dry mouth. Methods We undertook a systematic search for studies of the oral health of people with common psychological disorders including depression, anxiety and dental phobia. We searched MEDLINE, PsycInfo, EMBASE and article bibliographies. Results were compared with the general population. Outcomes included partial or total tooth-loss, periodontal disease, and dental decay measured through standardized measures such as the mean number of decayed, missing and filled teeth (DMFT) or surfaces (DMFS). Results There were 19 papers on depression and/or anxiety, and seven on dental phobia/anxiety (total $n=26$). These covered 334,503 subjects. All the psychiatric diagnoses were associated with increased dental decay on both DMFT and DMFS scores, as well as greater tooth loss ($OR=1.22$; 95%CI=1.14–1.30). There was no association with periodontal disease, except for panic disorder. Limitations Cross-sectional design of included studies, heterogeneity in some results, insufficient studies to test for publication bias. Conclusion The increased focus on the physical health of psychiatric patients should encompass oral health including closer collaboration between dental and medical practitioners. Possible interventions include oral health assessment using standard checklists that can be completed by non-dental personnel, help with oral hygiene, management of iatrogenic dry mouth, and early dental referral. Mental health clinicians should also be aware of the oral consequences of inappropriate diet and psychotropic medication.

Kohler, O., C. Gasse, et al. (2016). **"The effect of concomitant treatment with ssris and statins: A population-based study."** *Am J Psychiatry* 173(8): 807-815. <http://ajp.psychiatryonline.org/doi/full/10.1176/appi.ajp.2016.15040463>

OBJECTIVE: Both preclinical studies and clinical trials have indicated that the combination of a selective serotonin reuptake inhibitor (SSRI) and a statin may have superior antidepressant effects compared with SSRI treatment alone. The authors sought to assess whether this beneficial effect can be generalized to a more heterogeneous population of SSRI users. METHOD: In a nationwide cohort study that included all incident SSRI users in Denmark between 1997 and 2012, the authors compared people who had periods of concomitant use of SSRIs and statins with people who had periods of SSRI treatment alone. Outcomes included the rates of psychiatric hospital contacts (any cause), psychiatric hospital contacts due to depression, suicidal behavior, and all-cause mortality. Using Cox regression and competing risk analysis, the authors calculated crude and adjusted hazard ratios for these outcomes. RESULTS: The authors identified 872,216 incident SSRI users, of whom 113,108 (13.0%) used a statin concomitantly. Compared with SSRI treatment alone, the combined use of an SSRI and a statin was associated with a significantly lower risk for both psychiatric hospital contacts (adjusted hazard ratio=0.75 (95% CI=0.69, 0.82) and psychiatric hospital contacts due to depression (adjusted hazard ratio=0.64, 95% CI=0.55, 0.75). Compared with SSRI treatment alone, the concomitant use of SSRIs and statins was not associated with significant increases in all-cause mortality (adjusted hazard ratio=1.04, 95% CI=0.96, 1.12) or suicidal behavior (adjusted hazard ratio=0.85, 95% CI=0.61, 1.18). CONCLUSIONS: In a large naturalistic cohort, concomitant treatment with SSRIs and statins resulted in robust advantages compared with SSRIs alone.

Koukouna, D., L. Bossini, et al. (2016). **Light therapy as a treatment for sexual dysfunction; focus on testosterone levels.** 29th European College of Neuropsychopharmacology (ECNP) Congress Vienna.

Seasonality has shown to have a significant influence on sexual function and the pineal gland plays a key role in the neuroendocrine control of sexual activity. The retinohypothalamic tract carries information on the cycles light/dark to the suprachiasmatic nucleus of the hypothalamus that projects to the pineal gland and inhibits the production of melatonin [1]. When these impulses stop (at night, when light no longer stimulates the hypothalamus), pineal inhibition ceases and melatonin is released. Melatonin increases the secretion of prolactin, which contributes to sexual dysfunction. We aimed at demonstrating that inhibition of the pineal gland activity through a light treatment may favorably affect sexual function reducing plasma levels of melatonin. We recruited a sample of 38 male subjects among outpatients referred to the Urology Department of the

University of Siena on the basis of a diagnosis of primary hypoactive sexual desire disorder (HSDD) and sexual arousal disorder (SAD). Participants were randomly assigned to active light treatment (ALT) or placebo light treatment (L-PBO) and assessed before and after 2 weeks of treatment ALT/L-PBO via the Structured Clinical Interview for DSM-IV sexual disorders (SCID-d) and self-administered rating scale of the level of sexual satisfaction (1 to 10); testosterone levels were also assessed at baseline and after two weeks of treatment through blood samples. The ALT consisted of daily exposure to a white fluorescent light box (Super-Lite 3S), fitted with an ultraviolet filter and rated at 10,000 lx at a distance of 1 meter from screen to cornea for 30 min as soon as possible after awakening, between 7.00 a.m. and 8.00 a.m. The L-PBO was an identical light box fitted with a neutral density gel filter to reduce light exposure to 100 lx. The Mann-Whitney test for nonparametric data has been applied to analyze the differences between the ALT and L-PBO group at the time of recruitment and after 2 weeks of therapy. At baseline the two groups were clinically comparable; results after 2 weeks of therapy showed a significant improvement in sexual satisfaction in the group treated with ALT approximately 3 times higher than the group that received the placebo ($p < 0.05$), while no significant improvement was observed in the group L-PBO. Testosterone levels (range 2.7–10.9 ng/ml) at baseline were 2.1 ± 1.3 ng/ml in ALT and 2.3 ± 0.6 ng/ml in L-PBO group; after two weeks they raised at 3.6 ± 1.1 ng/ml in ALT group ($p < 0.05$) while no significant difference emerged in L-PBO group. Our results suggest that the level of sexual satisfaction at baseline was roughly comparable in the two groups, with no statistically significant differences. After 2 weeks of treatment the group that received ALT showed a significant improvement in sexual function with respect to baseline level, about 3 times higher than the group that received L-PBO. This difference could also be attributed to increased levels of testosterone in subjects treated with active light therapy. [Medscape comment: Study investigator Andrea Fagiolini, MD, chairman, Division of Psychiatry, University of Siena School of Medicine, Italy, told Medscape Medical News that "Although it cannot be said at this time that light therapy will replace Viagra, we did see a very strong effect." The investigators plan to repeat the study with larger numbers of patients. "The good thing is that it's basically safe. Unless people have some eye problems, it's really unlikely that this gives problems, whereas any medication has much more problems in terms of side effects and dangerous interactions with other medications," he said. "Even if I would recommend not to use it until we have results from larger trials, if somebody wants to use it, it's not going to give too many problems, because it is a treatment that is already used for another disorder, and we know it's pretty safe," Dr Fagiolini added ... After 2 weeks of therapy, individuals who received active light treatment had experienced significant improvements in sexual satisfaction compared with those receiving placebo light treatment ($P < .05$) ... "The increased levels of testosterone explain the greater reported sexual satisfaction. In the Northern hemisphere, the body's testosterone production naturally declines from November through April and then rises steadily through the spring and summer, with a peak in October," said Dr Fagiolini. "You see the effect of this in reproductive rates, with the month of June showing the highest rate of conception. The use of the light box really mimics what nature does. We believe that there may be several explanations to explain the underlying mechanism. For instance, light therapy inhibits the pineal gland in the center of the brain, and this may allow the production of more testosterone, and there are probably other hormonal effects." Cautionary Note: Commenting on the findings, Eduard Vieta, MD, PhD, chair of the Department of Psychiatry and Psychology at the University of Barcelona Hospital Clinic, Spain, who is treasurer of the ECNP, commented that "light therapy has been used successfully in the past to treat some forms of depression, and this study suggests now that it may also work to treat low sexual desire in men. The mechanism of action appears to be related to the increase of testosterone levels," he said. However, Dr Vieta sounded a note of caution over its use at this stage for the treatment of low sexual desire. "Before this kind of treatment, which is likely to be better tolerated than pharmacological therapy, gets ready for routine use, there are many steps to be implemented, including replication of the results in a larger, independent study and verifying whether the results are long-lasting and not just short-term," he said.]

Kvam, S., C. L. Kleppe, et al. (2016). **"Exercise as a treatment for depression: A meta-analysis."** *Journal of Affective Disorders* 202: 67-86. <http://www.sciencedirect.com/science/article/pii/S0165032715314221>

Abstract Background This meta-analysis of randomized controlled trials (RCTs) examines the efficacy of physical exercise as treatment for unipolar depression, both as an independent intervention and as an adjunct intervention to antidepressant medication. **Methods** We searched PsycINFO, EMBASE, MEDLINE, CENTRAL, and Sports Discus for articles published until November 2014. Effect sizes were computed with random effects models. The main outcome was reduction in depressive symptoms or remission. **Results** A total of 23 RCTs and 977 participants were included. Physical exercise had a moderate to large significant effect on depression compared to control conditions ($g = -0.68$), but the effect was small and not significant at follow-up ($g = -0.22$). Exercise compared to no intervention yielded a large and significant effect size ($g = -1.24$), and exercise had a moderate and significant effect compared to usual care ($g = -0.48$). The effects of exercise when compared to psychological treatments or antidepressant medication were small and not significant ($g = -0.22$ and $g = -0.08$, respectively). Exercise as an adjunct to antidepressant medication yielded a moderate effect ($g = -0.50$) that trended toward significance. **Limitations** Use of the arms with the largest clinical effect instead of largest dose may have overestimated the effect of exercise. **Conclusions** Physical exercise is an effective intervention for depression. It also could be a viable adjunct treatment in combination with antidepressants.

Li, F.-D., F. He, et al. (2016). **"Tea consumption is inversely associated with depressive symptoms in the elderly: A cross-sectional study in eastern china."** *Journal of Affective Disorders* 199: 157-162. <http://www.sciencedirect.com/science/article/pii/S0165032716300039>

Abstract Background Epidemiological studies suggest that higher tea consumption was associated with lower risk of depressive symptoms, but this has not been found consistently. Moreover, the effect of different types of tea on depressive symptoms needs to be further explored. This study aimed to examine the association between tea consumption and depressive symptoms in Chinese elderly. **Methods** We analyzed the baseline data from Zhejiang Major Public Health Surveillance Program including 9371 participants. Depressive symptoms was assessed through the application of Patient Health Questionnaire-9 scale (PHQ-9). Logistic regression models, controlled for an extensive range of potential confounders, were generated to evaluate the association between tea consumption and risk of depressive symptoms. **Results** The black tea drinkers had a significantly decreased risk of depressive symptoms ($p < 0.01$), whereas no association was found in green tea drinkers. Compared with non-drinkers, the adjusted ORs (95% CIs) were 0.48 (0.23, 0.99) and 0.35 (0.17, 0.72) for participants consuming < 3 cups and ≥ 3 cups of black tea per day, respectively (P for trend: < 0.01). A linear association between concentration of black tea and depressive symptoms was also confirmed in our study. **Limitations** Cross-sectional data could not make a causation conclusion, and the observed association in our study could not be ascribed to any specific component in tea. **Conclusions** Our results indicated that higher black tea consumption was associated with a lower prevalence of depressive symptoms in the elderly.

Meier, S. M., M. Mattheisen, et al. (2016). **"Increased mortality among people with anxiety disorders: Total population study."** *The British Journal of Psychiatry* 209(3): 216-221 <http://bjp.rcpsych.org/content/early/2016/06/27/bjp.bp.115.171975>
Background Anxiety disorders and depression are the most common mental disorders worldwide and have a striking impact on global disease burden. Although depression has consistently been found to increase mortality; the role of anxiety

disorders in predicting mortality risk is unclear. Aims To assess mortality risk in people with anxiety disorders. Method We used nationwide Danish register data to conduct a prospective cohort study with over 30 million person-years of follow-up. Results In total, 1066 (2.1%) people with anxiety disorders died during an average follow-up of 9.7 years. The risk of death by natural and unnatural causes was significantly higher among individuals with anxiety disorders (natural mortality rate ratio (MRR) = 1.39, 95% CI 1.28–1.51; unnatural MRR = 2.46, 95% CI 2.20–2.73) compared with the general population. Of those who died from unnatural causes, 16.5% had comorbid diagnoses of depression (MRR = 11.72, 95% CI 10.11–13.51). Conclusions Anxiety disorders significantly increased mortality risk. Comorbidity of anxiety disorders and depression played an important part in the increased mortality.

Melo, M. C. A., E. D. F. Daher, et al. (2016). **"Exercise in bipolar patients: A systematic review."** *Journal of Affective Disorders* 198: 32-38. <http://www.sciencedirect.com/science/article/pii/S0165032715314063>

Abstract Background Sedentary lifestyle is frequent in psychiatric disorders, however the directions of this association and benefits of physical activity are unclear. This is a systematic review about exercise in patients with bipolar disorder. Methods We performed a systematic literature search of studies published in English (1995 Jan to 2016 Jan) in PubMed, and Cochrane Library combining the medical terms 'physical activity' or 'sedentary' or 'physical exercise' with 'bipolar disorder' or 'mania' or 'bipolar depression'. Results Thirty-one studies were selected and included 15,587 patients with bipolar disorder. Sedentary lifestyle varied from 40% to 64.9%. Physical activity was associated with less depressive symptoms, better quality of life and increased functioning. Some evidence indicates a relationship between vigorous exercises and mania. Three prospective cohorts were reported; and no prospective randomized controlled trial was identified. Three studies focused on biomarkers in bipolar patients; and one reported the relationship between exercise and sleep in this group. Two assessed physical exercise in adolescents. Limitations (1) Differences between studies preventing a unified analysis; (2) most studies were cross-sectional; (3) motivation for exercising is a selection bias in most studies; (4) no intervention study assessing only physical exercise; (5) lack of studies comparing exercise across mood states. Conclusion Generally, exercise was associated with improved health measures including depressive symptoms, functioning and quality of life. Evidence was insufficient to establish a cause-effect relationship between mood and physical exercise. Future research including randomized trials is needed to clarify the role of physical activity in bipolar patients.

Moor, N. and P. M. de Graaf (2016). **"Temporary and long-term consequences of bereavement on happiness."** *Journal of Happiness Studies* 17(3): 913-936. <http://dx.doi.org/10.1007/s10902-015-9624-x>

(Available in free full text) In this article, we examine the temporary and long-term consequences of the death of a parent or child on happiness. According to set-point theory external conditions are expected to only have a short-term or limited influence on happiness. This directly contradicts the basic assumption of affective theories on happiness, which states that major life-events have a lasting influence on well-being. Moreover, we test whether the association between bereavement and happiness is equally strong across the life course. To test our hypotheses we make use of the fourth wave of the European Values Study. Our research findings demonstrate that people who lost their father, mother or child are more likely to feel unhappy than people without this experience. Ten years after the death of a parent or child we still find a significant difference in happiness between people who have and have not experienced this loss. The assumption of set-point theory, that major life events only have a temporary impact on SWB, is not supported by our data. Moreover, the association between bereavement and SWB strongly differs across the life-course. We might even conclude that the age at which the loss occurred is more decisive for the strength of the association between bereavement and SWB than the duration of the loss.

Pemberton, R. and M. D. Fuller Tyszkiewicz (2016). **"Factors contributing to depressive mood states in everyday life: A systematic review."** *Journal of Affective Disorders* 200: 103-110. <http://www.sciencedirect.com/science/article/pii/S0165032715305784>

Background Although accumulated evidence suggests that fluctuations in depressed mood are common among individuals with depression, and may be associated with onset, duration, and severity of illness, a systematic appraisal of putative predictors of depressed mood is lacking. Methods A systematic search for relevant studies in the literature was conducted using PsycInfo and PubMed databases via EbscoHost in February 2016. The search was limited to articles using the experience sampling method, an approach suitable for capturing in situ fluctuations in mood states. Results Forty-two studies met inclusion criteria for the review, from which three key risk factors (poor sleep, stress, and significant life events) and two protective factors (physical activity and quality of social interactions) were identified. The majority of papers supported concurrent and lagged associations between these putative protective/risk factors and depressed mood. Limitations Despite support for each of the proposed protective/risk factors, few studies evaluated multiple factors in the same study. Moreover, the time course for the effects of these predictors on depressed mood remains largely unknown. Conclusions The present review identified several putative risk and protective factors for depressed mood. A review of the literature suggests that poor sleep, negative social interactions, and stressful negative events may temporally precede spikes in depressed mood. In contrast, exercise and positive social interactions have been shown to predict subsequent declines in depressed mood. However, the lack of multivariate models in which the unique contributions of various predictors could be evaluated means that the current state of knowledge prevents firm conclusions about which factors are most predictive of depressed mood. More complex modeling of these effects is necessary in order to provide insights useful for clinical treatment in daily life of the depressed mood component of depressive disorders.

Rector, T. S., S. Adabag, et al. (2016). **"Outcomes of citalopram dosage risk mitigation in a veteran population."** *American Journal of Psychiatry* 173(9): 896-902. <http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2016.15111444>

Objective: A public safety communication issued by the Food and Drug Administration declared that citalopram dosages exceeding 40 mg/day were no longer considered safe because of a newly recognized risk of dosage-dependent QT interval prolongation. The authors compared the incidence of hospitalizations and mortality when higher dosages of citalopram were or were not reduced to ≤ 40 mg/day. Method: National electronic medical records compiled by the Veterans Health Administration were used to conduct a retrospective study of a population filling citalopram prescriptions for more than 40 mg/day when the safety communication was first issued in August 2011. Hospitalizations and mortality after dosages of citalopram were or were not reduced to ≤ 40 mg/day were compared using multivariable Cox regression. Results: The at-risk cohort of 35,848 veterans (mean age, 58 years [SD=11]; 92% male) had citalopram prescriptions for 64 mg/day (SD=8.3), on average. Within 180 days after the safety communication was issued, 60% had filled prescriptions for ≤ 40 mg/day. All-cause hospitalizations or deaths were found to significantly increase after dosage reductions (adjusted hazard ratio=4.5, 95% CI=4.1–5.0), as were hospitalizations for depression or all-cause death (adjusted hazard ratio=2.2, 95% CI=1.8–2.6). Mortality did not decline (adjusted hazard ratio=1.0, 95% CI=0.8–1.3), and neither did hospitalizations for arrhythmias or all-cause deaths (adjusted hazard ratio=1.3, 95% CI=1.0–1.7). Conclusions: Reduction of prescribed citalopram dosages to a new safety limit was associated with a higher rate of hospitalization in a large patient population who had been treated with substantially higher

dosages. Stipulating a safety limit for citalopram dosages before the benefits and risks of doing so were firmly established appears to have had unintended clinical consequences.

Salagre, E., B. S. Fernandes, et al. (2016). **"Statins for the treatment of depression: A meta-analysis of randomized, double-blind, placebo-controlled trials."** *Journal of Affective Disorders* 200: 235-242. <http://www.sciencedirect.com/science/article/pii/S016503271630009X>

Abstract Background In epidemiological studies, statins appear to benefit mood, and there are now some randomized controlled trials examining the efficacy of statins. However, the role of statins in depression remains uncertain. Thus the aim of this paper was to assess the effect of statins on depressive symptoms by performing a meta-analysis of all double-blind, randomized, placebo controlled clinical trials (RCT) conducted in subjects with depression. **Methods** A systematic search was executed using PubMed and ClinicalTrials.gov in November 30th, 2015 for all double-blind, RCT of statins versus placebo in persons with depressive symptoms. Sixty-seven potential articles were identified through search of electronic databases, of those three met inclusion criteria and were included in the meta-analysis. The outcome measure was change in Hamilton Depression Rating Scale (HDRS) scores associated with statin use. A meta-analysis was conducted and standardized mean differences (SMDs) with 95% confidence intervals (CIs) were calculated. GRADE was used to assess study quality. **Results** The three articles included provided data on 165 participants with moderate to severe depression. Of these, 82 were randomized to statins as an adjuvant therapy to antidepressant treatment (i.e., citalopram or fluoxetine) and 83 to the placebo arm. All studies were double-blind RCTs, with a follow-up of 6–12 weeks. The statin agents evaluated were lovastatin, atorvastatin, and simvastatin. When compared to placebo, statins, as add-on to treatment as usual, largely improved depressive symptoms as assessed by the HDRS (SMD = -0.73, 95% IC -1.04 to -0.42, p < 0.001, 3 between-group comparisons, n = 165). No serious adverse effects were reported. **Conclusions** Our results suggest that adjunctive treatment with statins could be useful for the treatment of depressive symptoms. Additional double-blind, randomised, placebo-controlled trials are necessary to settle the matter.

Sarris, J., J. Murphy, et al. (2016). **"Adjunctive nutraceuticals for depression: A systematic review and meta-analyses."** *American Journal of Psychiatry* 173(6): 575-587. <http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2016.15091228>

Objective: There is burgeoning interest in augmentation strategies for improving inadequate response to antidepressants. The adjunctive use of standardized pharmaceutical-grade nutrients, known as nutraceuticals, has the potential to modulate several neurochemical pathways implicated in depression. While many studies have been conducted in this area, to date no specialized systematic review (or meta-analysis) has been conducted. **Method:** A systematic search of PubMed, CINAHL, Cochrane Library, and Web of Science was conducted up to December 2015 for clinical trials using adjunctive nutrients for depression. Where sufficient data were available, a random-effects model analyzed the standard mean difference between treatment and placebo in the change from baseline to endpoint, combining the effect size data. Funnel plot and heterogeneity analyses were also performed. **Results:** Primarily positive results were found for replicated studies testing S-adenosylmethionine (SAMe), methylfolate, omega-3 (primarily EPA or ethyl-EPA), and vitamin D, with positive isolated studies for creatine, folic acid, and an amino acid combination. Mixed results were found for zinc, folic acid, vitamin C, and tryptophan, with nonsignificant results for inositol. No major adverse effects were noted in the studies (aside from minor digestive disturbance). A meta-analysis of adjunctive omega-3 versus placebo revealed a significant and moderate to strong effect in favor of omega-3. Conversely, a meta-analysis of folic acid revealed a nonsignificant difference from placebo. Marked study heterogeneity was found in a Higgins test for both omega-3 and folic acid studies; funnel plots also revealed asymmetry (reflecting potential study bias). **Conclusions:** Current evidence supports adjunctive use of SAMe, methylfolate, omega-3, and vitamin D with antidepressants to reduce depressive symptoms.

Schroder, J., T. Berger, et al. (2016). **"Internet interventions for depression: New developments."** *Dialogues Clin Neurosci* 18(2): 203-212. <http://www.ncbi.nlm.nih.gov/pubmed/27489460>

A wide range of Internet interventions, mostly grounded in methods of cognitive behavioral therapy, have been developed and tested for several mental disorders. The evidence to date shows that these interventions are effective in reducing symptoms of depression. Metaanalyses report small-to-medium effect sizes when Internet interventions are delivered as stand-alone self-help interventions (d = 0.25-0.36), and medium-to-large effect sizes when delivered as therapist-guided interventions (d = 0.58-0.78), both compared with usual care. Only a minority of people suffering from depression receive adequate treatment, and Internet interventions might help bridge the large treatment gap. This review summarizes the current body of evidence and highlights pros and cons of Internet interventions. It also outlines how they could be implemented in mental health care systems and points out unresolved questions, as well as future directions, in this research field.

Schuch, F. B., D. Vancampfort, et al. (2016). **"Exercise as a treatment for depression: A meta-analysis adjusting for publication bias."** *Journal of Psychiatric Research* 77: 42-51. <http://www.sciencedirect.com/science/article/pii/S0022395616300383>

The effects of exercise on depression have been a source of contentious debate. Meta-analyses have demonstrated a range of effect sizes. Both inclusion criteria and heterogeneity may influence the effect sizes reported. The extent and influence of publication bias is also unknown. Randomized controlled trials (RCTs) were identified from a recent Cochrane review and searches of major electronic databases from 01/2013 to 08/2015. We included RCTs of exercise interventions in people with depression (including those with a diagnosis of major depressive disorder (MDD) or ratings on depressive symptoms), comparing exercise versus control conditions. A random effects meta-analysis calculating the standardized mean difference (SMD, 95% confidence interval; CI), meta-regressions, trim and fill and fail-safe n analyses were conducted. Twenty-five RCTs were included comparing exercise versus control comparison groups, including 9 examining participants with MDD. Overall, exercise had a large and significant effect on depression (SMD adjusted for publication bias = 1.11 (95% CI 0.79–1.43)) with a fail-safe number of 1057. Most adjusted analyses suggested publication bias led to an underestimated SMD. Larger effects were found for interventions in MDD, utilising aerobic exercise, at moderate and vigorous intensities, in a supervised and unsupervised format. In MDD, larger effects were found for moderate intensity, aerobic exercise, and interventions supervised by exercise professionals. Exercise has a large and significant antidepressant effect in people with depression (including MDD). Previous meta-analyses may have underestimated the benefits of exercise due to publication bias. Our data strongly support the claim that exercise is an evidence-based treatment for depression.

Shear, M., C. F. Reynolds, et al. (2016). **"Optimizing treatment of complicated grief: A randomized clinical trial."** *JAMA Psychiatry* 73(7): 685-694. <http://dx.doi.org/10.1001/jamapsychiatry.2016.0892>

Importance To our knowledge, this is the first placebo-controlled randomized clinical trial to evaluate the efficacy of antidepressant pharmacotherapy, with and without complicated grief psychotherapy, in the treatment of complicated grief. **Objective** To confirm the efficacy of a targeted complicated grief treatment (CGT), determine whether citalopram (CIT)

enhances CGT outcome, and examine CIT efficacy without CGT. Design, Setting, and Participants Included in the study were 395 bereaved adults who met criteria for CG recruited from March 2010 to September 2014 from academic medical centers in Boston, Massachusetts; New York, New York; Pittsburgh, Pennsylvania; and San Diego, California. Co-occurring substance abuse, psychosis, mania, and cognitive impairment were exclusionary. Study participants were randomized using site-specific permuted blocks stratified by major depression into groups prescribed CIT (n = 101), placebo (PLA; n = 99), CGT with CIT (n = 99), and CGT with PLA (n = 96). Independent evaluators conducted monthly assessments for 20 weeks. Response rates were compared under the intention-to-treat principle, including all randomized participants in a logistic regression with inverse probability weighting. Interventions All participants received protocolized pharmacotherapy optimized by flexible dosing, psychoeducation, grief monitoring, and encouragement to engage in activities. Half were also randomized to receive manualized CGT in 16 concurrent weekly sessions. Main Outcomes and Measures Complicated grief-anchored Clinical Global Impression scale measurements every 4 weeks. Response was measured as a rating of "much improved" or "very much improved." Results Of the 395 study participants, 308 (78.0%) were female and 325 (82.3%) were white. Participants' response to CGT with PLA vs PLA (82.5% vs 54.8%; relative risk [RR], 1.51; 95% CI, 1.16-1.95; P = .002; number needed to treat [NNT], 3.6) suggested the efficacy of CGT, and the addition of CIT did not significantly improve CGT outcome (CGT with CIT vs CGT with PLA: 83.7% vs 82.5%; RR, 1.01; 95% CI, 0.88-1.17; P = .84; NNT, 84). However, depressive symptoms decreased significantly more when CIT was added to treatment (CGT with CIT vs CGT with PLA: model-based adjusted mean [standard error] difference, -2.06 [1.00]; 95% CI, -4.02 to -0.11; P = .04). By contrast, adding CGT improved CIT outcome (CIT vs CGT with CIT: 69.3% vs 83.7%; RR, 1.21; 95% CI, 1.00-1.46; P = .05; NNT, 6.9). Last, participant response to CIT was not significantly different from PLA at week 12 (45.9% vs 37.9%; RR, 1.21; 95% CI, 0.82-1.81; P = .35; NNT, 12.4) or at week 20 (69.3% vs 54.8%; RR, 1.26; 95% CI, 0.95-1.68; P = .11; NNT, 6.9). Rates of suicidal ideation diminished to a substantially greater extent among participants receiving CGT than among those who did not. Conclusions and Relevance Complicated grief treatment is the treatment of choice for CG, and the addition of CIT optimizes the treatment of co-occurring depressive symptoms.

Spiers, N., T. Qassem, et al. (2016). **"Prevalence and treatment of common mental disorders in the English national population, 1993-2007."** *The British Journal of Psychiatry* 209(2): 150-156.
<http://bjp.rcpsych.org/content/early/2016/05/31/bjp.bp.115.174979>

Background The National Psychiatric Morbidity Surveys include English cross-sectional household samples surveyed in 1993, 2000 and 2007. Aims To evaluate frequency of common mental disorders (CMDs), service contact and treatment. Method Common mental disorders were identified with the Clinical Interview Schedule - Revised (CIS-R). Service contact and treatment were established in structured interviews. Results There were 8615, 6126 and 5385 participants aged 16-64. Prevalence of CMDs was consistent (1993: 14.3%; 2000: 16.0%; 2007: 16.0%), as was past-year primary care physician contact for psychological problems (1993: 11.3%; 2000: 12.0%; 2007: 11.7%). Antidepressant receipt in people with CMDs more than doubled between 1993 (5.7%) and 2000 (14.5%), with little further increase by 2007 (15.9%). Psychological treatments increased in successive surveys. Many with CMDs received no treatment. Conclusions Reduction in prevalence did not follow increased treatment uptake, and may require universal public health measures together with individual pharmacological, psychological and computer-based interventions.

Stickley, A. and A. Koyanagi (2016). **"Loneliness, common mental disorders and suicidal behavior: Findings from a general population survey."** *Journal of Affective Disorders* 197: 81-87.
<http://www.sciencedirect.com/science/article/pii/S0165032715310442>

Abstract Background Loneliness has been linked to an increased risk of engaging in suicidal behavior. To date, however, there has been comparatively little research on this in the general adult population, or on the role of common mental disorders (CMDs) in this association. The current study examined these associations using nationally representative data from England. Methods Data came from the Adult Psychiatric Morbidity Survey 2007. Information was obtained from 7403 household residents aged ≥ 16 years on perceived loneliness and lifetime and past 12-month suicide ideation and attempts. The Clinical Interview Schedule Revised (CIS-R) was used to assess six forms of CMD. Logistic regression analysis was used to examine these associations. Results Loneliness was associated with suicidal behavior. Although adjusting for CMDs attenuated associations, higher levels of loneliness were still significantly associated with suicidal ideation and suicide attempts with odds ratios (OR) for those in the most severe loneliness category ranging from 3.45 (lifetime suicide attempt) to 17.37 (past 12-month suicide attempt). Further analyses showed that ORs for suicidal behavior were similar for individuals who were lonely without CMDs, and for those respondents with CMDs who were not lonely. Lonely individuals with CMDs had especially elevated odds for suicidal ideation. Limitations This study used cross-sectional data and a single-item measure to obtain information on loneliness. Conclusion Loneliness is associated with suicidal behavior in the general adult population. This highlights the importance of efforts to reduce loneliness in order to mitigate its harmful effects on health and well-being.

Stubbs, B., D. Vancampfort, et al. (2016). **"The prevalence and predictors of obstructive sleep apnea in major depressive disorder, bipolar disorder and schizophrenia: A systematic review and meta-analysis."** *Journal of Affective Disorders* 197: 259-267. <http://www.sciencedirect.com/science/article/pii/S0165032715311939>

Background Obstructive sleep apnea (OSA) is a health hazard since it is associated with neurocognitive dysfunction and cardio-metabolic diseases. The prevalence of OSA among people with serious mental illness (SMI) is unclear. Method We searched major electronic databases from inception till 06/2015. Articles were included that reported the prevalence of OSA determined by polysomnography (PSG) or an apnea-hypopnea index (AHI) $> \text{ or } = 5$ events/hr, in people with major depressive disorder (MDD), bipolar disorder (BD) or schizophrenia. A random effects meta-analysis calculating the pooled prevalence of OSA and meta-regression of potential moderators were performed. Results Twelve articles were included representing 570,121 participants with SMI (mean age=38.3 years (SD=7.5)), 45.8% male (range=32-80.4) and mean body mass index (BMI) 25.9 (SD=3.7). The prevalence of OSA in SMI in clinical studies was 25.7% (95% CI 13.9 to 42.4%, n=1,535). Higher frequencies of OSA were seen in MDD (36.3%, 19.4-57.4%, n=525) than in BD (24.5%, 95% CI 10.6-47.1, n=681) and schizophrenia (15.4%, 95% CI 5.3-37.1%, n=329). The prevalence of OSA in 568,586 people with SMI from population cohort studies was 10.7% (95% CI 2.4-37.0%) and 19.8% (95% CI 2.5-70.0%) in 358,853 people with MDD. Increasing age ($\beta=0.063$, 95% CI 0.0005-0.126, p=0.04, N=10) and BMI predicted increased prevalence of OSA ($\beta=0.1642$, 95% CI 0.004-0.3701, p=0.04, N=9). Conclusion People with SMI (particularly MDD) have a high prevalence of OSA. Screening for and interventions to manage OSA in SMI including those focused on reducing BMI are warranted.

Tseng, P.-T., Y.-W. Chen, et al. (2016). **"Light therapy in the treatment of patients with bipolar depression: A meta-analytic study."** *European Neuropsychopharmacology* 26(6): 1037-1047.
<http://www.sciencedirect.com/science/article/pii/S0924977X16000754>

Light therapy (LT) has been widely used in the treatment of seasonal affective disorder. Recently some evidence indicated that LT may play a role in bipolar depression, either as monotherapy or in combination with total sleep deprivation

(TSD). However, the studies examining the treatment effect of LT in bipolar depression resulted in inconsistent findings. To clarify the role of LT in the disorder, we conducted a meta-analysis to compare the efficacy of LT in the treatment of bipolar depression. The results of individual studies were synthesized by a random effects model. Nine studies including 489 patients with bipolar depression were included in this current meta-analysis. We found that disease severity was significantly decreased after LT, in both with and without TSD, and with concomitant medication ($p < 0.001$). Augmentation treatment with LT significantly decreased disease severity compared to treatment without LT ($p = 0.024$). Our results highlight the significant efficacy of LT, either as monotherapy or in combination with TSD, in the treatment of bipolar depression. However, the detailed mechanism of LT still remains elusive. Further well-designed controlled trials are required to investigate the optimal intensity and frequency of LT in the treatment of bipolar depression.

van den Berg, K. S., R. M. Marijnissen, et al. (2016). **"Vitamin d deficiency, depression course and mortality: Longitudinal results from the netherlands study on depression in older persons (NESDO)."** *Journal of Psychosomatic Research* 83: 50-56. <http://www.sciencedirect.com/science/article/pii/S0022399916300393>

Abstract Objective To study the effect of vitamin D levels on depression course and remission status after two years, as well as attrition and mortality, in an older cohort. **Methods** This study was part of the Netherlands Study on Depression in Older persons (NESDO), a prospective cohort study. 367 depressed older persons (≥ 60 years) were included. Baseline vitamin D status, reasons for loss to follow up, clinical depression diagnosis at two-year follow up, and six-monthly symptom scores were obtained. Data were analyzed by logistic regression and random coefficient models and adjusted for confounders of vitamin D status. **Results** Vitamin D had no effect on the course of depression or remission, except for a trend towards lower remission rates in the severely deficient subgroup (25-(OH) vitamin D ≤ 25 nmol/l). Patients who died during follow up had significantly lower 25-(OH) vitamin D and 1,25-(OH) $_2$ vitamin D levels than patients with continued participation. **Conclusions** For the total sample we found no effect of vitamin D levels on the course of depression or remission rates. However, we did find an effect of lower vitamin D levels on mortality. This strengthens the interpretation of vitamin D deficiency being a marker for poor somatic health status. The trend towards lower remission rates in the severely deficient subgroup raises the question whether this group could benefit from supplementation. Randomized controlled trials are necessary to study this.

Waller, K., J. Kaprio, et al. (2016). **"Persistent leisure-time physical activity in adulthood and use of antidepressants: A follow-up study among twins."** *Journal of Affective Disorders* 200: 172-177. <http://www.sciencedirect.com/science/article/pii/S0165032716302051>

Abstract Background To study whether persistent leisure-time physical activity (PA) during adulthood predicts use of antidepressants later in life. **Methods** The Finnish Twin Cohort comprises same-sex twin pairs born before 1958, of whom 11 325 individuals answered PA questions in 1975, 1981 and 1990 at a mean age of 44 years (range 33–60). PA volume over 15-years was used as the predictor of subsequent use of antidepressants. Antidepressant use (measured as number of purchases) for 1995–2004 were collected from the Finnish Social Insurance Institution (KELA) prescription register. Conditional logistic regression was conducted to calculate odds ratios (OR) with 95% confidence intervals (CI) for the use of antidepressants in pairs discordant for PA (642, including 164 monozygotic (MZ) pairs). **Results** Altogether 229 persons had used at least one prescribed antidepressant during the study period. Active co-twins had a lower risk (unadjusted OR 0.80, 95%CI 0.67–0.95) for using any amount of antidepressants than their inactive co-twins; trends being similar for DZ (0.80, 0.67–0.97) and MZ pairs (0.78, 0.51–1.17). The lowest odds ratio (0.51, 0.26–0.98) was seen among MZ pairs after adjusting for BMI, smoking and binge drinking. The point estimates were similar but non-significant for long-term antidepressant use (4+ purchases equivalent to 12 months use). **Limitations** Self-reported physical activity and low number of discordant MZ pairs. **Discussion** Use of antidepressants was less common among physically active co-twins even when shared childhood experiences and genetic background were controlled for. Physical activity in midlife may therefore be important in preventing mild depression later in life.

Weissman, M. M., O. O. Berry, et al. (2016). **"A 30-year study of 3 generations at high risk and low risk for depression."** *JAMA Psychiatry* 73(9): 970-977. <http://dx.doi.org/10.1001/jamapsychiatry.2016.1586>

Importance The increased risk of major depression in the offspring of depressed parents is well known. Whether the risk is transmitted beyond 2 generations is less well known. To our knowledge, no published study with direct interviews of family members and the generations in the age of risk for depression has evaluated beyond 2 generations. This information is important for detecting individuals at highest risk who may benefit from early intervention. **Objective** To examine the familial aggregation of psychiatric disorder and functioning in grandchildren by their biological parents' and grandparents' depression status. **Design, Setting, and Participants** Longitudinal retrospective cohort family study of 251 grandchildren (generation 3 [mean age, 18 years]) interviewed a mean of 2.0 times and their biological parents (generation 2) interviewed a mean of 4.6 times and grandparents (generation 1) interviewed up to 30 years. The study dates were January 1982 (wave 1) to June 2015 (wave 6). **Main Outcomes and Measures** Cumulative rates of psychiatric disorders and functioning collected for all generations by clinically trained interviewers and best-estimate diagnosis made blind to diagnoses in members of previous generations. **Results** There were 91 families (G1) in the original sample, of whom 77 were eligible for inclusion (had a grandchild older than 5 years), and 80.5% (62 of 77) participated in the study. When first examining only 2 generations, the biological children (generation 3) of depressed compared with nondepressed parents (generation 2) had 2-fold increased risk for major depressive disorder (MDD) (hazard ratio [HR], 2.02; 95% CI, 1.08-3.79; $P = .03$), any disruptive disorder (HR, 1.70; 95% CI, 1.05-2.75; $P = .03$), substance dependence (HR, 2.96; 95% CI, 1.24-7.08; $P = .01$), any suicidal ideation or gesture (HR, 2.44; 95% CI, 1.28-4.66; $P = .007$), and poor functioning ($F = 38.25$, $P < .001$). When 3 generations were examined stratified by parental and grandparental depression status, association of a parent's MDD on the grandchild's MDD but not other disorders varied with the grandparent's depression status: grandchildren with both a depressed parent and grandparent ($n = 38$) were at highest risk for MDD. Among grandchildren without a depressed grandparent, those with ($n = 14$) vs without ($n = 74$) a depressed parent had overall poorer functioning ($F = 6.31$, $P = .01$) but not higher rates of any of the disorders. Potential confounding variables did not have a meaningful effect on the association between grandchild outcomes and parental or grandparental depression. **Conclusions and Relevance** In this study, biological offspring with 2 previous generations affected with major depression were at highest risk for major depression, suggesting the potential value of determining family history of depression in children and adolescents beyond 2 generations. Early intervention in offspring of 2 generations affected with moderate to severely impairing MDD seems warranted. The specificity of the transmission of depression across 3 generations may make this group a homogeneous sample for biological marker studies.