20 depression-relevant abstracts may '18 newsletter

Kendler, K. S., H. Ohlsson, et al. (2018). ***"Sources of parent-offspring resemblance for major depression in a national swedish extended adoption study."*** JAMA Psychiatry 75(2): 194-200. http://dx.doi.org/10.1001/jamapsychiatry.2017.3828

Importance Twin studies have assessed sibling resemblance for major depression (MD) but cannot address sources of resemblance across generations.Objective To clarify the relative importance of genetic and rearing effects on the parent-offspring resemblance for MD.Design This Swedish population register–based study examined parents and children from the following 5 family types: intact (2 041 816 offspring), adoptive (14 104 offspring), not-lived-with (NLW) father (116 601 offspring), stepfather (67 826 offspring), and triparental (29 205 offspring). The 5 family types permitted quantification of parent-offspring resemblance for genes plus rearing, genes-only, and rearing-only associations. Treated MD was assessed from national primary care, specialist care, and inpatient registries. Data were collected from January 1, 1960, through December 31, 2016.Exposure Diagnosis of MD vs no diagnosis in parents.Main Outcomes and Measures Registration for MD.Results The study population included 2 269 552 offspring (51.5% male and 48.5% female; median age, 42; range, 26-56 years). The weighted tetrachoric correlations for MD across family types and across mothers and fathers were r = 0.17 (95% CI, 0.16-0.17) for genes plus rearing, r = 0.08 (95% CI, 0.06-0.09) for genes-only, and r = 0.08 (95% CI, 0.07-0.09) for rearing-only parent-child associations. Only the genes plus rearing association differed significantly between mothers (weighted tetrachoric correlation, r = 0.18; 95% CI, 0.18-0.18) and fathers (weighted tetrachoric correlation, r = 0.15; 95% CI, 0.15-0.16). In triparental families, the parent-offspring correlations for MD were estimated at r = 0.19 (95% CI, 0.17-0.22) for mothers in the genes plus rearing association, r = 0.10 (95% CI, 0.07-0.13) for NLW fathers in the genes-only association, and r = 0.08 (95% CI, 0.05-0.11) for stepfathers in the rearing-only association. In adoptive families, the effect of affected biological and affected adoptive parents on adoptee risk for MD was additive. In intact families, parental MD diagnosed by specialists in hospital or outpatient settings and primary care physicians affected equally the risk for MD in offspring.Conclusions and Relevance The parent-offspring resemblance for treated MD arises from genetic factors and rearing experiences to an approximately equal extent. Both forms of cross-generational transmission act additively on the risk for MD in the offspring.

Li, Z., W. Wang, et al. (2018). ***"Association of total zinc, iron, copper and selenium intakes with depression in the us adults."*** Journal of Affective Disorders 228: 68-74. http://www.sciencedirect.com/science/article/pii/S016503271731128X

Background The aim of present study was to examine the associations of total zinc, iron, copper and selenium intakes from diet and supplements with depression. Methods Cross-sectional study used data from the National Health and Nutrition Examination Survey (NHANES) 2009–2014 in the present study. Logistic regression models and restricted cubic spline models were applied to examine the associations of total zinc, iron, copper and selenium intakes with depression. Results A total of 14834 adults aged 18 years or older (7399 men and 7435 women) were included in the present study. Total zinc, iron, copper and selenium intakes were inversely associated with depression in unadjusted model and age- and gender-adjusted model. The multivariate adjusted odds ratios (ORs) with 95% confidence intervals (CIs) of depression were 0.68 (0.49–0.94) and 0.46 (0.32–0.67) for the highest versus lowest quartile of copper and selenium intakes, respectively. The inverse associations of depression were statistically significant for the quartile 3 versus lowest quartile of total zinc (OR: 0.70; 95% CI: 0.49–0.99) and iron intake (OR: 0.66 95% CI: 0.50–0.87). Compared to those below the RDA (Recommended Dietary Allowance), participants who met the RDA for zinc (OR: 0.74; 95% CI: 0.56–0.99), copper (OR: 0.68; 95% CI: 0.56–0.82) and selenium (OR: 0.52; 95% CI: 0.39, 0.71) had significantly lower odds of depression. Limitations This was a cross-sectional study, limiting causal inferences. Assessment of depression was based on a self- report scale. Conclusion Total zinc, iron, copper and selenium intakes may be inversely associated with depression.

Lyall, L. M., C. A. Wyse, et al. (2018). ***"Seasonality of depressive symptoms in women but not in men: A cross-sectional study in the uk biobank cohort."*** Journal of Affective Disorders 229: 296-305. http://www.sciencedirect.com/science/article/pii/S0165032717318566

Background We examined whether seasonal variations in depressive symptoms occurred independently of demographic and lifestyle factors, and were related to change in day length and/or outdoor temperature. Methods In a cross-sectional analysis of >150,000 participants of the UK Biobank cohort, we used the cosinor method to assess evidence of seasonality of a total depressive symptoms score and of low mood, anhedonia, tenseness and tiredness scores in women and men. Associations of depressive symptoms with day length and mean outdoor temperature were then examined. Results Seasonality of total depressive symptom scores, anhedonia and tiredness scores was observed in women but not men, with peaks in winter. In women, increased day length was associated with reduced reporting of low mood and anhedonia, but with increased reporting of tiredness, independent of demographic and lifestyle factors. Associations with day length were not independent of the average outdoor temperature preceding assessment. Limitations This was a cross-sectional investigation – longitudinal studies of within-subject seasonal variation in mood are necessary. Outcome measures relied on self-report and measured only a subset of depressive symptoms. Conclusion This large, population-based study provides evidence of seasonal variation in depressive symptoms in women. Shorter days were associated with increased feelings of low mood and anhedonia in women. Clinicians should be aware of these population-level sex differences in seasonal mood variations in order to aid recognition and treatment of depression and subclinical depressive symptoms.

Michael E. Thase, Jesse H. Wright, et al. (2018). ***"Improving the efficiency of psychotherapy for depression: Computer-assisted versus standard cbt."*** American Journal of Psychiatry 175(3): 242-250. https://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2017.17010089

Objective:The authors evaluated the efficacy and durability of a therapist-supported method for computer-assisted cognitive-behavioral therapy (CCBT) in comparison to standard cognitive-behavioral therapy (CBT).Method:A total of 154 medication-free patients with major depressive disorder seeking treatment at two university clinics were randomly assigned to either 16 weeks of standard CBT (up to 20 sessions of 50 minutes each) or CCBT using the "Good Days Ahead" program. The amount of therapist time in CCBT was planned to be about one-third that in CBT. Outcomes were assessed by independent raters and self-report at baseline, at weeks 8 and 16, and at posttreatment months 3 and 6. The primary test of efficacy was noninferiority on the Hamilton Depression Rating Scale at week 16.Results:Approximately 80% of the participants completed the 16-week protocol (79% in the CBT group and 82% in the CCBT group). CCBT met a priori criteria for noninferiority to conventional CBT at week 16. The groups did not differ significantly on any measure of psychopathology. Remission rates were similar for the two groups (intent-to-treat rates, 41.6% for the CBT group and 42.9% for the CCBT group). Both groups maintained improvements throughout the follow-up.Conclusions:The study findings indicate that a method of CCBT that blends Internet-delivered skill-building modules with about 5 hours of therapeutic contact was noninferior to a conventional course of

CBT that provided over 8 additional hours of therapist contact. Future studies should focus on dissemination and optimizing therapist support methods to maximize the public health significance of CCBT.

Ng, Q. X., C. Peters, et al. (2018). ***"A meta-analysis of the use of probiotics to alleviate depressive symptoms."*** Journal of Affective Disorders 228: 13-19. http://www.sciencedirect.com/science/article/pii/S016503271731488X

Introduction Some preclinical and clinical studies have demonstrated the positive impact of probiotic supplementation on depressive symptoms. This paper aims to provide an updated meta-analysis on the topic. Methods Using the keywords [probiotics OR gut OR microflora OR microbiome OR bacteria OR yeast OR yoghurt OR lactobacillus OR bifidobacterium] AND [mood OR depression OR MDD OR suicide], a preliminary search on the PubMed, Ovid, Clinical Trials Register of the Cochrane Collaboration Depression, Anxiety and Neurosis Group (CCDANTR) and Cochrane Field for Complementary Medicine database yielded 917 papers published in English between 1-Jan-1960 and 1-June-2017. Results 10 clinical trials with a total of 1349 patients were reviewed, comparing the use of probiotics to placebo controls. There was no significant difference in mood between the treatment and placebo group post-intervention as the standardized mean difference (SMD) was −0.128 (95% CI −0.261 to 0.00463, P=0.059). A separate subgroup analysis of studies conducted in healthy versus depressed individuals found significant improvements in the moods of individuals with mild to moderate depressive symptoms (SMD −0.684, 95% CI −1.296 to −0.0712, P=0.029) and non-significant effects in healthy individuals (SMD −0.0999, 95% CI −0.235 to 0.0348, P=0.146). Limitations Inter-study discrepancies with respect to probiotic dosing, bacterial strains and strain combinations limit the comparability of current clinical trials. Furthermore, majority of existing RCTs were conducted in healthy individuals, making it difficult to extrapolate the results to depressed individuals. Conclusion Probiotic supplementation has an overall insignificant effect on mood. Future studies should be conducted on more patients with clinically diagnosed depression.

Nöbbelin, L., M. Bogren, et al. (2018). ***"Risk factors for recurrence in depression in the lundby population, 1947–1997."*** Journal of Affective Disorders 228: 125-131. http://www.sciencedirect.com/science/article/pii/S0165032717311990

Background Depression is a common disorder in both men and women, and the recurrence rate is high. The aim of this study was to identify risk factors for recurrence in depression in the Lundby Study. Methods The Lundby Study is a community-based longitudinal study with focus on mental health. The study started in 1947 and three follow-ups have been carried out since, the last one in 1997. The population consists of 3563 subjects. Data from 508 subjects afflicted by depression was gathered. Premorbid factors (gender, socioeconomic status, marital status, personality and heredity) and factors related to the first depressive episode (age, degree of impairment and melancholic depression) were investigated regarding their influence on the risk for recurrence in depression. Multiple logistic regression was used in the calculations. Results Risk factors associated with recurrent depression were melancholic depression at first onset (OR 3.52 [95% CI 1.62–7.66, $p < 0.001$]), young age as compared to old age at first onset (OR 0.51 [95% CI 0.28–0.92, $p = 0.03$]) and a premorbid nervous/tense personality (OR 1.77 [95% CI 1.22–2.56, $p < 0.01$]). Demographic factors, including gender, had no effect on the odds of recurrence. Limitations The Lundby Study spans over 50 years, making the results vulnerable to changes in diagnostic regimes and recall bias. Conclusion Melancholia at onset, regardless of severity of symptoms, had the greatest impact on the risk of recurrence in depression in the Lundby Study. Information about risk factors for recurrence in depression are useful in offering effective preventive measures in the form of psychotropic drugs and psychotherapy, and deciding the length of follow-up.

Parikh, S. V. and S. H. Kennedy (2018). ***"More data, more answers: Picking the optimal antidepressant."*** The Lancet. http://dx.doi.org/10.1016/S0140-6736(18)30421-5

(Available in free full text) In an era of increasingly large datasets for health and emphasis on so-called big data analyses, key clinical questions remain unpretentiously simple. For example, do some antidepressants work better than others for depression? And are some more tolerable than others, at least as measured in dropout rates? A quick PubMed search of antidepressant meta-analyses yields more than 2000 hits, but the complexity of understanding which antidepressants are better or more tolerable than others is made particularly daunting by the fact that more than 40 antidepressants are available. Andrea Cipriani and colleagues1 provided a novel answer to these questions originally in a paper published in The Lancet in 2009, introducing the new method of network meta-analysis to psychiatry and showing that four of the 12 then newer antidepressants were more efficacious than the rest. In that landmark study, the authors examined 117 trials with nearly 26 000 participants. 9 years later in The Lancet, Cipriani and colleagues2 report their work applying a similar method to address the same question; this time they evaluated 21 antidepressants and placebo in 522 double-blind trials with 116 477 participants. Chief among the findings are detailed new results on efficacy (8-week outcomes) and acceptability (8-week dropout rates due to all causes). The study found that all antidepressants were more efficacious than placebo, with odds ratios (ORs) ranging from 2·13 (95% credible interval [CrI] 1·89–2·41) for amitriptyline to 1·37 (1·16–1·63) for reboxetine. Additionally, the study found reduced differences between antidepressants compared with the 2009 study, with ORs (usually with broad CrIs) from 1·15 to 1·55 for efficacy and from 0·64 to 0·83 for acceptability (tolerability). More specifically, head-to-head efficacy comparisons of antidepressants disclosed seven agents (agomelatine, amitriptyline, escitalopram, mirtazapine, paroxetine, venlafaxine, and vortioxetine) as distinctly more effective and four agents (fluoxetine, fluvoxamine, reboxetine, and trazodone) to be somewhat less effective than the other antidepressants … A key question—raised in 2009—remains, what is the implication of superiority of outcomes at 8 weeks for long-term effects, particularly functional outcomes?9 Although network meta-analysis is exemplary as a technique to combine aggregate data, such aggregation does not allow for analysis at the individual patient level and so cannot provide finer detail on who might preferentially respond or who might be more vulnerable to side-effects … An additional important facet missed by network meta-analysis involves the heterogeneity of response within major depressive disorder, identified by other statistical approaches. Using growth mixture modelling, distinct trajectories of responders (76%) and non-responders (24%) to duloxetine were identified.10 Although clinical phenotyping on the basis of traditional specifiers of melancholia, atypical symptoms, and anxiety have not been helpful in predicting treatment response,11 the integration of clinical and biological markers shows more promise. One recent study12 integrated clinical and neuroimaging markers to identify four distinct neurophysiological biotypes in more than 1000 patients with major depressive disorder on the basis of resting-state functional connectivity. These biotypes were linked to clinical dimensions of anhedonia and anxiety, and predicted response to repetitive transcranial magnetic stimulation. Ultimately, the field requires different research strategies to identify response at the level of the individual patient, not just network meta-analysis with larger sample sizes. Nevertheless, Cipriani and colleagues have made a major contribution. This study of antidepressant outcomes identified significant differences between antidepressants that are relevant to health-care economists and policy makers, clinicians, and patients. In everyday clinical practice, medications with the highest net efficacy and acceptability ratings merit discussion with patients for use as the first treatment. The demonstration of the extent of antidepressant superiority over placebo reassures patients and health-care professionals of the efficacy of treatment despite high placebo response rates.

Patten, S. B., J. V. A. Williams, et al. (2018). ***"Major depression and secondhand smoke exposure."*** Journal of Affective Disorders 225: 260-264. http://www.sciencedirect.com/science/article/pii/S0165032717300551

(Available in free full text) Background Epidemiological studies have consistently linked smoking to poor mental health. Among non-smokers, some studies have also reported associations between secondhand smoke exposure and psychological symptoms. However, an association between secondhand smoke exposure and depressive disorders has not been well established. Methods This analysis used cross-sectional data from a series of 10 population surveys conducted in Canada between 2003 and 2013. The surveys targeted the Canadian household population, included a brief structured interview for past year major depressive episode (MDE) and included items assessing secondhand smoke exposure. We used two-stage individual-level random-effects meta-regression to synthesize results from these surveys. Results Over the study interval, about 20% of non-smokers reported substantial exposure to secondhand smoke. In this group, the pooled annual prevalence of MDE was 6.1% (95% CI 5.3–6.9) compared to 4.0% (95% CI 3.7–4.3) in non-smokers without secondhand smoke exposure. The crude odds ratio was 1.5 (95% CI 1.4–1.7). With adjustment for a set of potential confounding variables the odds ratio was unchanged, 1.4 (95% CI 1.2 – 1.6). Conclusions These results provide additional support for public health measures aimed at reducing secondhand smoke exposure. A causal connection between secondhand smoke exposure and MDEs cannot be confirmed due to the cross-sectional nature of the data. Longitudinal studies are needed to establish temporal sequencing.

Rosenblat, J. D. and R. S. McIntyre (2018). ***"Efficacy and tolerability of minocycline for depression: A systematic review and meta-analysis of clinical trials."*** Journal of Affective Disorders 227: 219-225. http://www.sciencedirect.com/science/article/pii/S0165032717319985

Background Minocycline has been identified as a potential novel treatment for depression. The objective of the current review is to determine the overall antidepressant efficacy and tolerability of minocycline. Methods Completed and ongoing clinical trials of minocycline for depression (both bipolar and unipolar) published prior to September 12, 2017 were identified through searching relevant databases. Using a random-effects model, data from randomized controlled trials (RCTs) were pooled to determine the antidepressant effect size of minocycline compared to placebo. Relative risk of all-cause discontinuation was determined to assess overall tolerability. Results Eighteen clinical studies (including published and unpublished RCTs, open label studies, ongoing clinical trials and a case report) were identified for inclusion in the qualitative synthesis. Only three RCTs (n = 158) met inclusion criteria for quantitative synthesis. The overall antidepressant effect size of minocycline compared to placebo was − 0.78 [95% confidence interval − 0.4 to − 1.33 (P = 0.005)], indicative of a large and statistically significant antidepressant effect. Heterogeneity of the pooled sample was moderate (I2 = 62%). There was no statistically significant difference in reported adverse effects or all-cause discontinuation in the minocycline group compared to placebo (p = 0.16). Limitations The small number of published RCTs, small sample sizes, heterogeneity of included studies, and potential publication bias were significant limitations. Conclusions Overall, a large antidepressant effect was observed for minocycline compared to placebo with good tolerability. The current analysis provides a proof-of-concept for the antidepressant effects of minocycline and provides impetus for future larger RCTs as well as identification of subgroups more likely to benefit from this intervention.

Rucklidge, J. J., et al. (2018). "Vitamin-mineral treatment improves aggression and emotional regulation in children with ADHD: a fully blinded, randomized, placebo-controlled trial." Journal of Child Psychology and Psychiatry **59**(3): 232-246. http://dx.doi.org/10.1111/jcpp.12817

Background: Evaluation of broad-spectrum micronutrient (vitamins and minerals) treatment for childhood ADHD has been limited to open-label studies that highlight beneficial effects across many aspects of psychological functioning. Method: This is the first fully blinded randomized controlled trial of medication-free children (n = 93) with ADHD (7–12 years) assigned to either micronutrients (n = 47) or placebo (n = 46) in a 1:1 ratio, for 10 weeks. All children received standardized ADHD assessments. Data were collected from clinicians, parents, participants and teachers across a range of measures assessing ADHD symptoms, general functioning and impairment, mood, aggression and emotional regulation. Results: Intent-to-treat analyses showed significant between-group differences favouring micronutrient treatment on the Clinical Global Impression-Improvement (ES = 0.46), with 47% of those on micronutrients identified as 'much' to 'very much' improved versus 28% on placebo. No group differences were identified on clinician, parent and teacher ratings of overall ADHD symptoms (ES ranged 0.03–0.17). However, according to clinicians, 32% of those on micronutrients versus 9% of those on placebo showed a clinically meaningful improvement on inattentive (OR = 4.9; 95% CI: 1.5–16.3), but no group differences on improvement in hyperactive-impulsive symptoms (OR = 1.0; 95% CI: 0.4–2.5). Based on clinician, parent and teacher report, those on micronutrients showed greater improvements in emotional regulation, aggression and general functioning compared to placebo (ES ranged 0.35–0.66). There were two dropouts per group, no group differences in adverse events and no serious adverse events identified. Blinding was successful with guessing no better than chance. Conclusions: Micronutrients improved overall function, reduced impairment and improved inattention, emotional regulation and aggression, but not hyperactive/impulsive symptoms, in this sample of children with ADHD. Although direct benefit for core ADHD symptoms was modest, with mixed findings across raters, the low rate of adverse effects and the benefits reported across multiple areas of functioning indicate micronutrients may be a favourable option for some children, particularly those with both ADHD and emotional dysregulation.

Schleider, J. and J. Weisz (2018). ***"A single-session growth mindset intervention for adolescent anxiety and depression: 9-month outcomes of a randomized trial."*** Journal of Child Psychology and Psychiatry 59(2): 160-170. http://dx.doi.org/10.1111/jcpp.12811

Background: Single-session interventions (SSIs) show promise in the prevention and treatment of youth psychopathology, carrying potential to improve the scalability and accessibility of youth psychological services. However, existing SSIs have conferred greater benefits for youths with anxiety, compared to depression or comorbid problems, and their effects have generally waned over time – particularly for follow-ups exceeding 3 months. Method: To help address these discrepancies, we tested whether a novel SSI teaching growth mindset of personality (the belief that personality is malleable) could reduce depression and anxiety and strengthen perceived control in high-risk adolescents (N = 96, ages 12–15). At baseline, youths were randomized to receive a 30-min, computer-guided growth mindset intervention or a supportive-therapy control. Youths and parents reported youth anxiety and depressive symptoms, and youths reported their levels of perceived control, at baseline and across a 9-month follow-up period. Results: Compared to the control program, the mindset intervention led to significantly greater improvements in parent-reported youth depression (d = .60) and anxiety (d = .28), youth-reported youth depression (d = .32), and youth-reported perceived behavioral control (d = .29) by 9-month follow-up. Intervention effects were nonsignificant for youth-reported anxiety, although 9-month effect sizes reached the small-to-medium range (d = .33). Intervention group youths also experienced more rapid improvements in parent-reported depression, youth-reported depression, and perceived behavioral control across the follow-up period, compared to control group youths. Conclusions: Findings suggest a promising, scalable SSI for reducing internalizing distress in high-risk adolescents.

Shafiee, M., S. Arekhi, et al. (2018). ***"Saffron in the treatment of depression, anxiety and other mental disorders: Current evidence and potential mechanisms of action."*** Journal of Affective Disorders 227: 330-337. http://www.sciencedirect.com/science/article/pii/S0165032717315884

Background Depression and anxiety are two common mental health problems with high economic and social costs. Currently, a number of treatments are available for patients with depression and anxiety disorders such as psychotherapy, electroconvulsive therapy and antidepressant drugs. Due to safety concerns, adverse effects, limited efficacy and low tolerability associated with many antidepressant and anti-anxiety medications, identification of novel agents with less toxicity and more favorable outcome is warranted. Methods The current article provides a non-systematic review of the available in vitro, in vivo and clinical evidence on the efficacy, safety and mechanisms of action of saffron and its active ingredients in the treatment of anxiety, depression and other mental disorders. Results Several interesting data have been reported about the antidepressant and anti-anxiety properties of saffron, the dried stigmas of Crocus sativus L., in several preclinical and clinical studies. In particular, a number of clinical trials demonstrated that saffron and its active constituents possess antidepressant properties similar to those of current antidepressant medications such as fluoxetine, imipramine and citalopram, but with fewer reported side effects. Conclusion Saffron may exert antidepressant effects and represents an efficacious and safe treatment.

Sit, D. K. Y., J. McGowan, et al. (2018). ***"Adjunctive bright light therapy for bipolar depression: A randomized double-blind placebo-controlled trial."*** American Journal of Psychiatry 175(2): 131-139. https://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2017.16101200

Objective: Patients with bipolar disorder have recurrent major depression, residual mood symptoms, and limited treatment options. Building on promising pilot data, the authors conducted a 6-week randomized double-blind placebo-controlled trial to investigate the efficacy of adjunctive bright light therapy at midday for bipolar depression. The aims were to determine remission rate, depression symptom level, and rate of mood polarity switch, as well as to explore sleep quality.Method:The study enrolled depressed adults with bipolar I or II disorder who were receiving stable dosages of antimanic medication (excluding patients with hypomania or mania, mixed symptoms, or rapid cycling). Patients were randomly assigned to treatment with either 7,000-lux bright white light or 50-lux dim red placebo light (N=23 for each group). Symptoms were assessed weekly with the Structured Interview Guide for the Hamilton Depression Scale With Atypical Depression Supplement (SIGH-ADS), the Mania Rating Scale, and the Pittsburgh Sleep Quality Index. Remission was defined as having a SIGH-ADS score of 8 or less.Results: At baseline, both groups had moderate depression and no hypomanic or manic symptoms. Compared with the placebo light group, the group treated with bright white light experienced a significantly higher remission rate (68.2% compared with 22.2%; adjusted odds ratio=12.6) at weeks 4–6 and significantly lower depression scores (9.2 [SD=6.6] compared with 14.9 [SD=9.2]; adjusted β=−5.91) at the endpoint visit. No mood polarity switches were observed. Sleep quality improved in both groups and did not differ significantly between them. Conclusions:The data from this study provide robust evidence that supports the efficacy of midday bright light therapy for bipolar depression.

Stubbs, B., D. Vancampfort, et al. (2018). ***"Relationship between sedentary behavior and depression: A mediation analysis of influential factors across the lifespan among 42,469 people in low- and middle-income countries."*** Journal of Affective Disorders 229: 231-238. http://www.sciencedirect.com/science/article/pii/S0165032717321699

Background Sedentary behavior (SB) is associated with diabetes, cardiovascular disease and low mood. There is a paucity of multi-national research investigating SB and depression, particularly among low- and middle-income countries. This study investigated the association between SB and depression, and factors which influence this. Methods Cross-sectional data were analyzed from the World Health Organization's Study on Global Ageing and Adult Health. Depression was based on the Composite International Diagnostic Interview. The association between depression and SB (self-report) was estimated by multivariable linear and logistic regression analyses. Mediation analysis was used to identify influential factors. Results A total of 42,469 individuals (50.1% female, mean 43.8 years) were included. People with depression spent 25.6 (95%CI8.5–42.7) more daily minutes in SB than non-depressed participants. This discrepancy was most notable in adults aged ≥ 65y (35.6min more in those with depression). Overall, adjusting for socio-demographics and country, depression was associated with a 1.94 (95%CI1.31–2.85) times higher odds for high SB (i.e., ≥ 8h/day). The largest proportion of the SB-depression relationship was explained by mobility limitations (49.9%), followed by impairments in sleep/energy (43.4%), pain/discomfort (31.1%), anxiety (30.0%), disability (25.6%), cognition (16.1%), and problems with vision (11.0%). Other health behaviors (physical activity, alcohol consumption, smoking), body mass index, and social cohesion did not influence the SB-depression relationship. Conclusion People with depression are at increased risk of engaging in high levels of SB. This first multi-national study offers potentially valuable insight for a number of hypotheses which may influence this relationship, although testing with longitudinal studies is needed.

Sun, X., B. Zheng, et al. (2018). ***"Sleep behavior and depression: Findings from the china kadoorie biobank of 0.5 million chinese adults."*** Journal of Affective Disorders 229: 120-124. http://www.sciencedirect.com/science/article/pii/S0165032717321717

(Available in free full text) Background Mixed results have shown the association between sleep behavior and depression, but evidence relating the joint effect of sleep duration and sleep disturbances is limited, especially in Chinese population. Methods A total of 512,891 adults aged 30–79 years from China Kadoorie Biobank (CKB) were included. Depression was defined by Composite International Diagnostic Inventory-short form (CIDI-SF). Sleep duration and sleep disturbances, including difficulty initiating and maintaining sleep (DIMS), early morning awakening (EMA), daytime dysfunction (DDF) and any sleep disturbances (ASD), were obtained by a self-reported questionnaire. Logistic regression was applied to examine the association between sleep behavior and depression. Results About 23.1% of participants reported short sleep duration (≤ 6h), and 5.1% reported long sleep duration (> 9h). Compared with normal sleep duration (7–9h), both groups were associated greater likelihood of having depression (short sleep: OR = 2.32, 95%CI: 2.14–2.51; long sleep: OR = 1.56, 96%CI: 1.34–1.81). Participants reported sleep disturbances were significantly associated with depression (odds ratios ranged from 3.31 to 4.17). Moreover, the associations tended to be stronger for those who reported both abnormal sleep duration and sleep disturbances (p for interactions < 0.05), especially for those who slept long. Limitations The cross-sectional nature of the study design limits the interpretation of the results. Conclusions Abnormal sleep duration and sleep disturbances were associated with depression. The associations were stronger for abnormal sleep duration accompanied with sleep disturbances, especially for a long duration. More attention should be paid on these persons in clinical practice.

Suzuki, M., S. Dallaspezia, et al. (2018). ***"Does early response predict subsequent remission in bipolar depression treated with repeated sleep deprivation combined with light therapy and lithium?"*** Journal of Affective Disorders 229: 371-376. http://www.sciencedirect.com/science/article/pii/S0165032717321262

Background The combination of three cycles of sleep deprivation (SD), light therapy (LT), and lithium has recently been proposed as a possible first-line treatment for bipolar depression. However, it is unclear whether early improvement predicts final response/remission in bipolar depression treated with this regimen. Method We studied 220 consecutively admitted inpatients with a major depressive episode in the course of bipolar disorder. The relation between response to first SD and response/remission at the end of the treatment (day 6) was analyzed using logistic regression analysis. Severity of depression was rated using the Hamilton Depression Rating Scale (HDRS). Clinical response was defined as a ≥50% reduction in HDRS

scores, and remission was defined as an HDRS score of ≤7. Results Among the 217 completers, 67.7% showed response and 54.4% reached remission at the end of the treatment. Multiple logistic regression analysis revealed that response after first recovery sleep (day 2) predicted final response and remission at the end of the treatment with high odds ratios (10.9 for response and 8.2 for remission); however, response immediately after the first SD (day 1) did not predict final response or remission. Limitations Whether our results can be generalized to unipolar depression remains uncertain. Conclusion Clinical status after first recovery sleep is a strong predictor of successful final outcome in patients with bipolar depression treated with the combination of repeated SD, LT, and lithium. Recovery sleep may play a role in inducing the antidepressant effect associated with the success of treatment.

van Diermen, L., S. van den Ameele, et al. (2018). ***"Prediction of electroconvulsive therapy response and remission in major depression: Meta-analysis."*** The British Journal of Psychiatry 212(2): 71-80. https://www.cambridge.org/core/article/prediction-of-electroconvulsive-therapy-response-and-remission-in-major-depression-metaanalysis/259FD7600E652E9D272481FC6D87F4F9

Background Electroconvulsive therapy (ECT) is considered to be the most effective treatment in severe major depression. The identification of reliable predictors of ECT response could contribute to a more targeted patient selection and consequently increased ECT response rates. Aims To investigate the predictive value of age, depression severity, psychotic and melancholic features for ECT response and remission in major depression. Method A meta-analysis was conducted according to the PRISMA statement. A literature search identified recent studies that reported on at least one of the potential predictors. Results Of the 2193 articles screened, 34 have been included for meta-analysis. Presence of psychotic features is a predictor of ECT remission (odds ratio (OR) = 1.47, P = 0.001) and response (OR = 1.69, P < 0.001), as is older age (standardised mean difference (SMD) = 0.26 for remission and 0.35 for response (P < 0.001)). The severity of depression predicts response (SMD = 0.19, P = 0.001), but not remission. Data on melancholic symptoms were inconclusive. Conclusions ECT is particularly effective in patients with depression with psychotic features and in elderly people with depression. More research on both biological and clinical predictors is needed to further evaluate the position of ECT in treatment protocols for major depression.

Wagner, G., M.-T. Schultes, et al. (2018). ***"Efficacy and safety of levomilnacipran, vilazodone and vortioxetine compared with other second-generation antidepressants for major depressive disorder in adults: A systematic review and network meta-analysis."*** Journal of Affective Disorders 228: 1-12. http://www.sciencedirect.com/science/article/pii/S0165032717315379

Background Second-generation antidepressants dominate the medical management of major depressive disorder (MDD). Levomilnacipran, vilazodone and vortioxetine are the latest therapeutic options approved for the treatment of MDD. This systematic review aims to compare the benefits and harms of vilazodone, levomilnacipran, and vortioxetine with one another and other second-generation antidepressants. Methods We searched electronic databases up to September 2017 and reviewed reference lists and pharmaceutical dossiers to detect published and unpublished studies. Two reviewers independently screened abstracts and full text articles, and rated the risk of bias of included studies. Randomized controlled trials (RCTs) and controlled observational studies including adult outpatients with MDD were eligible for inclusion. We conducted network meta-analyses on response to treatment using frequentist multivariate meta-analyses models. Placebo- and active-controlled trials were eligible for network meta-analyses. Results Twenty-four studies met our inclusion criteria. Direct comparisons were limited to vilazodone versus citalopram, and vortioxetine versus duloxetine, paroxetine, or venlafaxine XR (extended release). Results of head-to-head trials and network meta-analyses, overall, indicated similar efficacy among levomilnacipran, vilazodone, or vortioxetine and other second-generation antidepressants. Although rates of overall adverse events and discontinuation due to adverse events were similar, RCTs reported several differences in specific adverse events. For most outcomes the strength of evidence was low. Limitations Limitations are the focus of literature searches on studies published in English, possible reporting biases, and general methodological limitations of network meta-analyses. Conclusions Overall, the available evidence does not indicate greater benefits or fewer harms of levomilnacipran, vilazodone, and vortioxetine compared with other second-generation antidepressants.

Zhou, T.-h., W.-m. Dang, et al. (2018). ***"Clinical efficacy, onset time and safety of bright light therapy in acute bipolar depression as an adjunctive therapy: A randomized controlled trial."*** Journal of Affective Disorders 227: 90-96. http://www.sciencedirect.com/science/article/pii/S0165032717301465

Background Bright light therapy (BLT) is an effective treatment for seasonal affective disorder and non- seasonal depression. The efficacy of BLT in treating patients with bipolar disorder is still unknown. Aims The aim of this study is to examine the efficacy, onset time and clinical safety of BLT in treating patients with acute bipolar depression as an adjunctive therapy (trial registration at ClinicalTrials.gov: NCT02009371). Methods This was a multi-center, single blind, randomized clinical trial. Seventy-four participants were randomized in one of two treatment conditions: BLT and control (dim red light therapy, dRLT). Sixty-three participants completed the study (33 BLT, 30 dRLT). Light therapy lasted for two weeks, one hour every morning. All participants were required to complete several scales assessments at baseline, and at the end of weeks 1 and 2. The primary outcome measures were the clinical efficacy of BLT which was assessed by the reduction rate of HAMD-17 scores, and the onset time of BLT which was assessed by the reduction rate of QIDS-SR16 scores. The secondary outcome measures were rates of switch into hypomania or mania and adverse events. Results 1) Clinical efficacy: BLT showed a greater ameliorative effect on bipolar depression than the control, with response rates of 78.19% vs. 43.33% respectively ($p < 0.01$). 2) Onset day: Median onset day was 4.33 days in BLT group. 3) BLT-emergent hypomania: No participants experienced symptoms of hypomania. 4) Side effects: No serious adverse events were reported. Conclusion BLT can be considered as an effective and safe adjunctive treatment for patients with acute bipolar depression.

Zisook, S., M. K. Shear, et al. (2018). ***"Treatment of complicated grief in survivors of suicide loss: A heal report."*** J Clin Psychiatry 79(2). http://www.psychiatrist.com/JCP/article/Pages/2018/v79n02/17m11592.aspx?sclick=1

Objective: Suffering associated with complicated grief (CG) is profound. Because suicide loss survivors are susceptible to developing CG, identifying effective treatments for suicide loss survivors with CG is a high priority. This report provides data on the acceptability and effectiveness of antidepressant medication and complicated grief therapy (CGT), a CG-targeted psychotherapy, for suicide loss survivors with CG identified by an Inventory of Complicated Grief score ≥ 30. Methods: This is a secondary analysis of data collected from March 2010 to September 2014 for a 4-site, double-blind, placebo-controlled randomized trial comparing the effectiveness of antidepressant medication alone or in combination with CGT for participants with CG (score ≥ 30 on the Inventory of Complicated Grief) who were bereaved by suicide (SB; n = 58), accident/homicide (A/H; n = 74), or natural causes (NC; n = 263). Using mode of death as a grouping factor, we evaluated acceptability of treatments by comparing 12-week medication and 16-session CGT completion; we evaluated effectiveness by comparing response at week 20, defined by a score of 1 or 2 on the Complicated Grief Clinical Global Impressions-Improvement scale (CG-CGI-I), and additional secondary response measures. Results: Among participants receiving medication alone, SB medication completion rates (36%) were lower than rates for A/H (54%) and NC (68%; $\chi 2 = 11.76$, $P < .01$). SB medication completion

rates were much higher for SB individuals receiving CGT (82%; $\chi 2 = 12.45$, $P < .001$) than for SB individuals receiving medication alone. CGT completion rates were similar in the 3 groups (SB = 74%, A/H = 64%, NC = 77%; $\chi 2 = 2.48$, $P = .29$). For SB participants receiving CGT, CG-CGI-I response rates were substantial (64%), but lower compared to the other groups (A/H = 93%, NC = 84%; $\chi 2 = 8.00$, $P < .05$). However, on all other outcomes, changes from baseline for SB participants were comparable to those for A/H and NC participants, including number and severity of grief symptoms, suicidal ideation, and grief-related impairment, avoidance, and maladaptive beliefs. Conclusions: These results raise concern about the acceptability of medication alone as a treatment for complicated grief in treatment-seeking suicide-bereaved adults. In contrast, CGT is an acceptable and promising treatment for suicide-bereaved individuals with complicated grief.