36 depression-relevant abstracts march '17 newsletter

(Beecher, Eggett et al. 2016; Brander, Rydell et al. 2016; Bromberger, Kravitz et al. 2016; Chojnacka, Antosik-Wójcińska et al. 2016; Cui and Zheng 2016; Dash, O'Neil et al. 2016; Griffiths, Johnson et al. 2016; Grosso, Micek et al. 2016; Grosso, Micek et al. 2016; Hearing, Chang et al. 2016; Huang, Hsieh et al. 2016; Kappelmann, Lewis et al. 2016; Kruger 2016; Latvala, Kuja-Halkola et al. 2016; Malhi and Byrow 2016; McGirr, Vöhringer et al. 2016; McNamara 2016; Mojtabai, Olfson et al. 2016; Murray, Quattrone et al. 2016; Ravindran, Balneaves et al. 2016; Redmore, Kipping et al. 2016; Riecher-Rössler 2016; Rueger, Malecki et al. 2016; Salk, Petersen et al. 2016; Shackman, Tromp et al. 2016; Sweeney and MacBeth 2016; Tham, Jonsson et al. 2016; Alda, McKinnon et al. 2017; Jacka, O'Neil et al. 2017; Lisa A. Pan, Petra Martin et al. 2017; Lopresti and Drummond 2017; Neufeld, Dunn et al. 2017; Ploubidis, Sullivan et al. 2017; Priebe, Ramjaun et al. 2017; Rice, Eyre et al. 2017; Schaakxs, Comijs et al. 2017)

Alda, M., M. McKinnon, et al. (2017). ***"Methylene blue treatment for residual symptoms of bipolar disorder: Randomised crossover study."*** The British Journal of Psychiatry 210(1): 54-60. http://bjp.rcpsych.org/content/210/1/54

Background Residual symptoms and cognitive impairment are among important sources of disability in patients with bipolar disorder. Methylene blue could improve such symptoms because of its potential neuroprotective effects. Aims We conducted a double-blind crossover study of a low dose (15 mg, 'placebo') and an active dose (195 mg) of methylene blue in patients with bipolar disorder treated with lamotrigine. Method Thirty-seven participants were enrolled in a 6-month trial (trial registration: NCT00214877). The outcome measures included severity of depression, mania and anxiety, and cognitive functioning. Results The active dose of methylene blue significantly improved symptoms of depression both on the Montgomery–Åsberg Depression Rating Scale and Hamilton Rating Scale for Depression (P = 0.02 and 0.05 in last-observation-carried-forward analysis). It also reduced the symptoms of anxiety measured by the Hamilton Rating Scale for Anxiety (P = 0.02). The symptoms of mania remained low and stable throughout the study. The effects of methylene blue on cognitive symptoms were not significant. The medication was well tolerated with transient and mild side-effects. Conclusions Methylene blue used as an adjunctive medication improved residual symptoms of depression and anxiety in patients with bipolar disorder.

Beecher, M. E., D. Eggett, et al. (2016). ***"Sunshine on my shoulders: Weather, pollution, and emotional distress."*** Journal of Affective Disorders 205: 234-238. //www.sciencedirect.com/science/article/pii/S0165032716306553

Background Researchers have examined the relationship between mental health and weather/pollution with mixed results. The current study aimed to examine a range of weather and atmospheric phenomena and their association with time-bound mental health data. Methods Nineteen different weather/pollution variables were examined in connection with an archive of self-reported mental health data for university students participating in mental health treatment (n=16,452) using the Outcome Questionnaire 45.2 (OQ-45). Statistical approach involved randomly selecting 500 subjects from the sample 1000 different times and testing each variable of interest using mixed models analyses. Results Seasonal changes in sun time were found to best account for relationships between weather variables and variability in mental health distress. Increased mental health distress was found during periods of reduced sun time hours. A separate analysis examining subjects' endorsement of a suicidality item, though not statistically significant, demonstrated a similar pattern. Initial results showed a relationship between pollution and changes in mental health distress; however, this was mediated by sun time. Limitations This study examined a relatively homogenous, predominantly European American, and religious sample of college counseling clients from an area that is subject to inversions and is at a high altitude and a latitude where sun time vacillates significantly more than locations closer to the equator. Conclusions Seasonal increases in sun time were associated with decreased mental health distress. This suggests the need for institutions and public health entities to plan for intervention and prevention resources and strategies during periods of reduced sun time.

Brander, G., M. Rydell, et al. (2016). ***"Association of perinatal risk factors with obsessive-compulsive disorder: A population-based birth cohort, sibling control study."*** JAMA Psychiatry 73(11): 1135-1144. http://dx.doi.org/10.1001/jamapsychiatry.2016.2095

(Available in free full text) Importance Perinatal complications may increase the risk of obsessive-compulsive disorder (OCD). Previous reports were based on small, retrospective, specialist clinic–based studies that were unable to rigorously control for unmeasured environmental and genetic confounding.Objective To prospectively investigate a wide range of potential perinatal risk factors for OCD, controlling for unmeasured factors shared between siblings in the analyses. Design, Setting, and Participants This population-based birth cohort study included all 2 421 284 children from singleton births in Sweden from January 1, 1973, to December 31, 1996, who were followed up through December 31, 2013. From the 1 403 651 families in the cohort, differentially exposed siblings from the 743 885 families with siblings were evaluated; of these, 11 592 families included clusters of full siblings that were discordant for OCD. Analysis of the data was conducted from January, 26, 2015, to September, 5, 2016. Exposures Perinatal data were collected from the Swedish Medical Birth Register and included maternal smoking during pregnancy, labor presentation, obstetric delivery, gestational age (for preterm birth), birth weight, birth weight in relation to gestational age, 5-minute Apgar score, and head circumference. Main Outcomes and Measures Previously validated OCD codes (International Statistical Classification of Diseases and Health Related Problems, Tenth Revision, code F42) in the Swedish National Patient Register. Results Of 2 421 284 individuals included in the cohort, 17 305 persons were diagnosed with OCD. Of these, 7111 were men (41.1%). The mean (SD) age of individuals at first diagnosis of OCD was 23.4 (6.5) years. An increased risk for OCD remained after controlling for shared familial confounders and measured covariates (including sex, year of birth, maternal and paternal age at birth, and parity), for smoking 10 or more cigarettes per day during pregnancy (hazard ratio [HR], 1.27; 95% CI, 1.02-1.58), breech presentation (HR, 1.35; 95% CI, 1.06-1.71), delivery by cesarean section (HR, 1.17; 95% CI, 1.01-1.34), preterm birth (HR, 1.24; 95% CI, 1.07-1.43), birth weight 1501 to 2500 g (HR, 1.30; 95% CI, 1.05-1.62) and 2501 to 3500 g (HR, 1.08; 95% CI, 1.01-1.16), being large for gestational age (HR, 1.23; 95% CI, 1.05-1.45), and Apgar distress scores at 5 minutes (HR, 1.50; 95% CI, 1.07-2.09). Gestational age and birth weight followed inverse dose-response associations, whereby an increasingly higher risk for OCD was noted in children with a shorter gestational age and lower birth weight. We also observed a dose-response association between the number of perinatal events and increased OCD risk, with HRs ranging from 1.11 (95% CI, 1.07-1.15) for 1 event to 1.51 (95% CI, 1.18-1.94) for 5 or more events. Conclusions and Relevance A range of perinatal risk factors is associated with a higher risk for OCD independent of shared familial confounders, suggesting that perinatal risk factors may be in the causal pathway to OCD.

Bromberger, J. T., H. M. Kravitz, et al. (2016). ***"Patterns of depressive disorders across 13 years and their determinants among midlife women: Swan mental health study."*** Journal of Affective Disorders 206: 31-40. //www.sciencedirect.com/science/article/pii/S016503271630252X

Background Little is known about the course of depression in midlife women. This study aims to identify factors that distinguish risk factors for persistent or recurrent depression from those of a milder course across 13-years of follow-up. Methods 297 Black and White premenopausal women aged 42–52 were enrolled at the Study of Women's Health Across the Nation Pittsburgh site. Psychiatric interviews obtained information on lifetime psychiatric diagnoses at baseline and occurrences of depression annually. We identified four depression patterns: 91(31%) had Persistent/recurrent major depressive disorder (MDD), 27(9%) Single Episode MDD, 35(12%) Minor Depression (minD) only, 144(48%) No Depression. We compared baseline risk factors for the Persistent/recurrent MDD group with each of the other three. Results A lifetime history of major or minor depression (p-values =.001–.08) and 2+ very upsetting life events in the previous year (p-values=.003–.04) were more likely to be reported by women in the Persistent/recurrent group than in the other three. The Persistent/recurrent group was more likely to report a family history of depression (p=.03) than the MinD group, and to report current sleep problems (p=.002) at baseline than the Single Episode MDD group. Limitations Small numbers of women with minD or a Single Episode MDD. Childhood maltreatment and family depression history were retrospectively reported. Conclusions A Persistent/recurrent depression course is common during midlife. In addition to personal and family histories of depression, providers of midlife health care should recognize that current sleep problems and recent very upsetting events are strong risk factors for a pernicious depression course.

Chojnacka, M., A. Z. Antosik-Wójcińska, et al. (2016). ***"A sham-controlled randomized trial of adjunctive light therapy for non-seasonal depression."*** Journal of Affective Disorders 203: 1-8. http://www.sciencedirect.com/science/article/pii/S0165032715309101

Background The aim of the study was to examine the efficacy and safety of morning bright light therapy (BLT) in the treatment of patients with a current major depressive episode (MDE) in bipolar and unipolar disorder without a seasonal pattern. It was a randomized, sham-controlled trial. Methods Adults, ages 18–70 years were randomized to treatment either with BLT or a sham negative ion generator (as a placebo control). The subjects were required to be on a stable and therapeutic dose of psychotropic medication for at least 4 weeks prior to enrollment and their treatment had to be insufficiently effective. Their clinical state was monitored at the baseline and at the end of treatment. The Hamilton Depression Rating Scale-21 items (HDRS-21), Montgomery-Asberg Depression Rating Scale (MADRS), Beck Depression Inventory (BDI-II), Clinical Global Impression-Severity (CGI-S) and Patient Global Impression (PGI) were used. The results were analyzed with an intention-to-treat (ITT) analysis. Results Ninety-five patients were enrolled (50 diagnosed with bipolar disorder and 45 with unipolar depression). Fifty-two patients were randomized to treatment with BLT and forty-three were in the placebo group (ITT population). Eighty-three subjects completed the study. There were 12 dropouts (5 in the light group and 7 in the placebo group). After 14 days of treatment, a significant improvement was found in all groups ($p<0.001$). The subjects treated with BLT did not significantly differ in terms of improvement in HDRS-21 scores at the endpoint when compared to patients treated with placebo ($p=0.2$). However, further analysis demonstrated significantly higher response (50% v. 27.9%, $p=0.02$) and remission rates (28.8% v. 11.6%, $p=0.04$) among patients treated with morning BLT when compared to placebo group. It should be noted that in the population of drug-resistant patients, BLT was more efficacious than placebo. There were no statistically significant differences between unipolar and bipolar disorders ($p=0.4$). Conclusion Although overall improvement in HDRS-21 scores were not superior in the BLT group, both response and remission rates were significantly higher among patients treated with BLT relative to those receiving the sham intervention. BLT was also more efficacious than placebo in the population of patients with drug-resistant depression. Further studies to define the subpopulation of patients with non-seasonal depression who may benefit the most from BLT are needed.

Cui, Y.-h. and Y. Zheng (2016). ***"A meta-analysis on the efficacy and safety of St John's wort extract in depression therapy in comparison with selective serotonin reuptake inhibitors in adults."*** Neuropsychiatric Disease and Treatment 12: 1715-1723

(Available in free full text) Objective: The aim of the study was to investigate the efficacy and safety of St John's wort extract and selective serotonin reuptake inhibitors (SSRIs) in the treatment of depression. Methods: Databases were searched for studies comparing efficacy and/or safety of St John's wort extract with SSRIs in depression from 1966 to April 2015. Stata software was used for statistical analysis. Results: Twenty-seven studies met the study entry criteria. A total of 3,126 patients with depression were included. St John's wort extract did not differ from SSRIs in clinical response, remission, and mean reduction in Hamilton Rating Scale for Depression score. St John's wort extract had a significantly lower rate of adverse events compared to SSRIs (summary relative risk: 0.77; 95% confidence interval: 0.70, 0.84, P=0.00) and had fewer withdrawals due to adverse events. St John's wort extract had superior safety in the management of patients with depression. Conclusion: Both St John's wort extract and SSRIs are effective in treating mild-to-moderate depression. St John's wort extract is safer than SSRIs.

Dash, S. R., A. O'Neil, et al. (2016). ***"Diet and common mental disorders: The imperative to translate evidence into action."*** Frontiers in Public Health 4: 81. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4850164/

(Available in free full text) The globalization of the food industry has lead to substantial dietary changes across developed and developing economies, comprising a shift toward the consumption of higher energy, less nutritious foods at the expense of traditional, more healthful, dietary patterns. These dietary changes have led to clear public health challenges as the burden of obesity and other diet-related non-communicable disorders (NCDs) continue to rise. In 2015, the Global Burden of Disease study identified unhealthy diet as the leading cause of early mortality worldwide. At the same time, mental and substance use disorders are recognized as the leading contributors to global disability. Of these, the common mental disorders (CMDs) – depression and anxiety – contribute the greatest proportion of disability, accounting for 40.5 and 14.6% of disease burden respectively. Only recently has it been recognized that unhealthy diet and CMDs are related: unhealthy diet is a significant risk factor not only for NCDs, such as cardiovascular diseases, some cancers, and diabetes, but also for CMDs. Dietary interventions may, thus, provide a far-reaching and low risk public health opportunity for the prevention and treatment of CMDs.

Griffiths, R. R., M. W. Johnson, et al. (2016). ***"Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial."*** Journal of Psychopharmacology 30(12): 1181-1197. http://journals.sagepub.com/doi/abs/10.1177/0269881116675513

(Available in free full text) Cancer patients often develop chronic, clinically significant symptoms of depression and anxiety. Previous studies suggest that psilocybin may decrease depression and anxiety in cancer patients. The effects of psilocybin were studied in 51 cancer patients with life-threatening diagnoses and symptoms of depression and/or anxiety. This randomized, double-blind, cross-over trial investigated the effects of a very low (placebo-like) dose (1 or 3 mg/70 kg) vs. a high

dose (22 or 30 mg/70 kg) of psilocybin administered in counterbalanced sequence with 5 weeks between sessions and a 6-month follow-up. Instructions to participants and staff minimized expectancy effects. Participants, staff, and community observers rated participant moods, attitudes, and behaviors throughout the study. High-dose psilocybin produced large decreases in clinician- and self-rated measures of depressed mood and anxiety, along with increases in quality of life, life meaning, and optimism, and decreases in death anxiety. At 6-month follow-up, these changes were sustained, with about 80% of participants continuing to show clinically significant decreases in depressed mood and anxiety. Participants attributed improvements in attitudes about life/self, mood, relationships, and spirituality to the high-dose experience, with >80% endorsing moderately or greater increased well-being/life satisfaction. Community observer ratings showed corresponding changes. Mystical-type psilocybin experience on session day mediated the effect of psilocybin dose on therapeutic outcomes.

Grosso, G., A. Micek, et al. (2016). ***"Coffee, tea, caffeine and risk of depression: A systematic review and dose–response meta-analysis of observational studies."*** Molecular Nutrition & Food Research 60(1): 223-234. http://dx.doi.org/10.1002/mnfr.201500620

Scope: The aim of the study was to systematically review and analyze results from observational studies on coffee, caffeine, and tea consumption and association or risk of depression. Methods and results: Embase and PubMed databases were searched from inception to June 2015 for observational studies reporting the odds ratios or relative risks (RRs) and 95% confidence intervals (CI) of depression by coffee/tea/caffeine consumption. Random effects models, subgroup analyses, and dose–response analyses were performed. Twelve studies with 23 datasets were included in the meta-analysis, accounting for a total of 346 913 individuals and 8146 cases of depression. Compared to individuals with lower coffee consumption, those with higher intakes had pooled RR of depression of 0.76 (95% CI: 0.64, 0.91). Dose–response effect suggests a nonlinear J-shaped relation between coffee consumption and risk of depression with a peak of protective effect for 400 mL/day. A borderline nonsignificant association between tea consumption and risk of depression was found (RR 0.70, 95% CI: 0.48, 1.01), while significant results were found only for analysis of prospective studies regarding caffeine consumption (RR = 0.84, 95% CI: 0.75, 0.93). Conclusion: This study suggests a protective effect of coffee and, partially, of tea and caffeine on risk of depression.

Grosso, G., A. Micek, et al. (2016). ***"Dietary n-3 PUFA, fish consumption and depression: A systematic review and meta-analysis of observational studies."*** Journal of Affective Disorders 205: 269-281. //www.sciencedirect.com/science/article/pii/S0165032716307546

Background Fish consumption and n-3 polyunsaturated fatty acids (PUFA) have been hypothesized to exert preventive effects toward depressive disorders, but findings are contrasting. We aimed to systematically review and perform meta-analysis of results from observational studies exploring the association between fish, n-3 PUFA dietary intake, and depression. Methods A search on the main bibliographic source of the observational studies up to August 2015 was performed. Random-effects models of the highest versus the lowest (reference) category of exposure and dose-response meta-analysis were performed. Results A total of 31 studies including 255,076 individuals and over 20,000 cases of depression, were examined. Analysis of 21 datasets investigating relation between fish consumption and depression resulted in significant reduced risk (RR=0.78, 95% CI: 0.69, 0.89), with a linear dose-response despite with moderate heterogeneity. Pooled risk estimates of depression for extreme categories of both total n-3 PUFA and fish-derived n-3 PUFA [eicosapentaenoic acid (EPA)+docosahexaenoic acid (DHA)] resulted in decreased risk for the highest compared with the lowest intake (RR=0.78, 95% CI: 0.67, 0.92 and RR=0.82, 95% CI: 0.73, 0.92, respectively) and dose-response analysis revealed a J-shaped association with a peak decreased risk for 1.8 g/d intake of n-3 PUFA (RR=0.30, 95% CI: 0.09, 0.98). Limitation Design of the studies included and confounding due to lack adjustment for certain variables may exist. Conclusions The present analysis supports the hypothesis that dietary n-3 PUFA intake are associated with lower risk of depression.

Hearing, C. M., W. C. Chang, et al. (2016). ***"Physical exercise for treatment of mood disorders: A critical review."*** Curr Behav Neurosci Rep 3: 350-359. http://paperity.org/p/78253682/physical-exercise-for-treatment-of-mood-disorders-a-critical-review

(Available in free full text) The purpose of this review is to critically assess the evidence for exercise as an adjunct intervention for major depressive disorder and bipolar disorder, chronic conditions characterized by frequent comorbid conditions as well as interepisodic symptoms with poor quality of life and impaired functioning. Individuals with these mood disorders are at higher risk of cardiovascular disease and premature death in part because of increased rates of obesity, inactivity, and diabetes mellitus compared to the general population. Exercise may not only mitigate the increased risk of cardiovascular disease, but could also potentially improve the long term outcomes of mood disorders. Recent findings We conducted a literature review on the impact of exercise on mood disorders and associated comorbid conditions as well as possible biological mechanisms. We found that exercise impacts both the physical health parameters of mood disorders as well as mental health outcomes. Exercise also positively impacts conditions frequently comorbid with mood disorders (i.e. anxiety, pain, and insomnia). There are multiple candidate biomarkers for exercise, with brain-derived neurotrophic factor and oxidative stress as two main promising components of exercise's anti-depressant effect. Summary Exercise appears to be a promising adjunct treatment for mood disorders. We conclude with recommendations for future research of exercise as an adjunct intervention for mood disorders.

Huang, R.-Y., K.-P. Hsieh, et al. (2016). ***"Use of lithium and cancer risk in patients with bipolar disorder: Population-based cohort study."*** The British Journal of Psychiatry 209(5): 393-399

Background Lithium inhibits glycogen synthase kinase-3, which is an enzyme involved in the pathogenesis of cancer. Aims To investigate the association between lithium and cancer risk in patients with bipolar disorder. Method A retrospective cohort study was designed using the National Health Insurance Research Database (NHIRD) in Taiwan. Patients using lithium comprised the index drug group and patients using anticonvulsants only comprised the control group. Time-dependent Cox regression was used to evaluate the hazard ratios (HRs) for risk of cancer. Results Compared with anticonvulsant-only exposure, lithium exposure was associated with significantly lower cancer risk (HR = 0.735, 95% CI 0.554–0.974). The hazard ratios for the first, second and third tertiles of the cumulative defined daily dose were 0.762 (95% CI 0.516–1.125), 0.919 (95% CI 0.640–1.318) and 0.552 (95% CI 0.367–0.831), respectively. Conclusions Lithium is associated with reduced overall cancer risk in patients with bipolar disorder. A dose–response relationship for cancer risk reduction was observed.

Jacka, F. N., A. O'Neil, et al. (2017). ***"A randomised controlled trial of dietary improvement for adults with major depression (the 'SMILES' trial)."*** BMC Medicine 15(1): 23. http://dx.doi.org/10.1186/s12916-017-0791-y

(Available in free full text) Background The possible therapeutic impact of dietary changes on existing mental illness is largely unknown. Using a randomised controlled trial design, we aimed to investigate the efficacy of a dietary improvement program for the treatment of major depressive episodes. Methods 'SMILES' was a 12-week, parallel-group, single blind, randomised controlled trial of an adjunctive dietary intervention in the treatment of moderate to severe depression. The intervention consisted of seven individual nutritional consulting sessions delivered by a clinical dietician. The control condition

comprised a social support protocol to the same visit schedule and length. Depression symptomatology was the primary endpoint, assessed using the Montgomery–Åsberg Depression Rating Scale (MADRS) at 12 weeks. Secondary outcomes included remission and change of symptoms, mood and anxiety. Analyses utilised a likelihood-based mixed-effects model repeated measures (MMRM) approach. The robustness of estimates was investigated through sensitivity analyses. Results We assessed 166 individuals for eligibility, of whom 67 were enrolled (diet intervention, n = 33; control, n = 34). Of these, 55 were utilising some form of therapy: 21 were using psychotherapy and pharmacotherapy combined; 9 were using exclusively psychotherapy; and 25 were using only pharmacotherapy. There were 31 in the diet support group and 25 in the social support control group who had complete data at 12 weeks. The dietary support group demonstrated significantly greater improvement between baseline and 12 weeks on the MADRS than the social support control group, $t(60.7) = 4.38$, $p < 0.001$, Cohen's $d = -1.16$. Remission, defined as a MADRS score <10, was achieved for 32.3% (n = 10) and 8.0% (n = 2) of the intervention and control groups, respectively ($\chi 2$ (1) = 4.84, p = 0.028); number needed to treat (NNT) based on remission scores was 4.1 (95% CI of NNT 2.3–27.8). A sensitivity analysis, testing departures from the missing at random (MAR) assumption for dropouts, indicated that the impact of the intervention was robust to violations of MAR assumptions. Conclusions These results indicate that dietary improvement may provide an efficacious and accessible treatment strategy for the management of this highly prevalent mental disorder, the benefits of which could extend to the management of common co-morbidities.

Kappelmann, N., G. Lewis, et al. (2016). ***"Antidepressant activity of anti-cytokine treatment: A systematic review and meta-analysis of clinical trials of chronic inflammatory conditions."*** Mol Psychiatry. http://dx.doi.org/10.1038/mp.2016.167

(Available in free full text) Inflammatory cytokines are commonly elevated in acute depression and are associated with resistance to monoaminergic treatment. To examine the potential role of cytokines in the pathogenesis and treatment of depression, we carried out a systematic review and meta-analysis of antidepressant activity of anti-cytokine treatment using clinical trials of chronic inflammatory conditions where depressive symptoms were measured as a secondary outcome. Systematic search of the PubMed, EMBASE, PsycINFO and Cochrane databases, search of reference lists and conference abstracts, followed by study selection process yielded 20 clinical trials. Random effect meta-analysis of seven randomised controlled trials (RCTs) involving 2370 participants showed a significant antidepressant effect of anti-cytokine treatment compared with placebo (standardised mean difference (SMD)=0.40, 95% confidence interval (CI), 0.22-0.59). Anti-tumour necrosis factor drugs were most commonly studied (five RCTs); SMD=0.33 (95% CI; 0.06-0.60). Separate meta-analyses of two RCTs of adjunctive treatment with anti-cytokine therapy and eight non-randomised and/or non-placebo studies yielded similar small-to-medium effect estimates favouring anti-cytokine therapy; SMD=0.19 (95% CI, 0.00-0.37) and 0.51 (95% CI, 0.34-0.67), respectively. Adalimumab, etanercept, infliximab and tocilizumab all showed statistically significant improvements in depressive symptoms. Meta-regression exploring predictors of response found that the antidepressant effect was associated with baseline symptom severity (P=0.018) but not with improvement in primary physical illness, sex, age or study duration. The findings indicate a potentially causal role for cytokines in depression and that cytokine modulators may be novel drugs for depression in chronically inflamed subjects. The field now requires RCTs of cytokine modulators using depression as the primary outcome in subjects with high inflammation who are free of other physical illnesses. [Note: "About a third of patients who are resistant to antidepressants show evidence of inflammation," adds Dr Khandaker. "So, anti-inflammatory treatments could be relevant for a large number of people who suffer from depression.]

Kruger, M. e. (2016). ***"Novel concepts and controversies surrounding omega-3 polyunsaturated fatty acid."*** Journal of Nutrition & Intermediary Metabolism 5: 1-116. http://www.sciencedirect.com/science/journal/23523859/5/supp/C

This freely downloadable edition of the journal contains a whole series of articles on omega-3 fatty acids.

Latvala, A., R. Kuja-Halkola, et al. (2016). ***"Association of resting heart rate and blood pressure in late adolescence with subsequent mental disorders: A longitudinal population study of more than 1 million men in sweden."*** JAMA Psychiatry 73(12): 1268-1275. http://dx.doi.org/10.1001/jamapsychiatry.2016.2717

(Available in free full text) Importance Differences in cardiovascular autonomic activity between individuals with psychiatric disorders and healthy controls have been observed, but whether cardiovascular autonomic abnormalities are associated with subsequent psychiatric disorders is unknown. Objective To investigate whether differences in cardiac autonomic function as indexed by resting heart rate and blood pressure are associated with psychiatric disorders during the lifetime of men in Sweden. Design, Setting, and Participants We conducted a longitudinal register-based study of Swedish men whose resting heart rate (n = 1 039 443) and blood pressure (n = 1 555 979) were measured at military conscription at a mean (SD) age of 18.3 (0.6) years during the period from 1969 to 2010, with register-based follow-up data available until the end of 2013. Analyses were performed from November 18, 2015, to June 9, 2016.Main Outcomes and Measures Dates of inpatient/outpatient diagnoses of anxiety disorders, obsessive-compulsive disorder, posttraumatic stress disorder, depressive disorders, bipolar disorder, schizophrenia, and substance use disorders and convictions for violent crimes, between 1973 and 2013, were obtained from nationwide registers. Adjustments were made for height, weight, body mass index, cardiorespiratory fitness, cognitive ability, and socioeconomic covariates.Results After adjustment for covariates, Cox regression models with up to 45 years of follow-up data showed that men (mean [SD] age of 18.3 [0.6] years at conscription) with resting heart rates above 82 beats per minute had a 69% (95% CI, 46%-94%) increased risk for obsessive-compulsive disorder, a 21% (95% CI, 11%-33%) increased risk for schizophrenia, and an 18% (95% CI, 13%-22%) increased risk for anxiety disorders compared with men with resting heart rates below 62 beats per minute. Similar associations were observed with systolic/diastolic blood pressure. In contrast, lower resting heart rate and lower systolic blood pressure were associated with substance use disorders and violent criminality. Conclusions and Relevance Our results suggest that for men, differences in heart rate and blood pressure in late adolescence are associated with lifetime major psychiatric disorders, with higher levels associated with obsessive-compulsive disorder, schizophrenia, and anxiety disorders and lower levels associated with substance use disorders and violent behavior. Differences in autonomic nervous system functioning may predate or represent an early marker of psychiatric disorders.

Lisa A. Pan, Petra Martin, et al. (2017). ***"Neurometabolic disorders: Potentially treatable abnormalities in patients with treatment-refractory depression and suicidal behavior."*** American Journal of Psychiatry 174(1): 42-50. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2016.15111500

Objective:Treatment-refractory depression is a devastating condition with significant morbidity, mortality, and societal cost. At least 15% of cases of major depressive disorder remain refractory to treatment. The authors previously identified a young adult with treatment-refractory depression and multiple suicide attempts with an associated severe deficiency of CSF tetrahydrobiopterin, a critical cofactor for monoamine neurotransmitter synthesis. Treatment with sapropterin, a tetrahydrobiopterin analogue, led to dramatic and long-lasting remission of depression. This sentinel case led the authors to hypothesize that the incidence of metabolic abnormalities contributing to treatment-refractory depression is

underrecognized.Method:The authors conducted a case-control, targeted, metabolomic evaluation of 33 adolescent and young adult patients with well-characterized histories of treatment-refractory depression (at least three maximum-dose, adequate-duration medication treatments), and 16 healthy comparison subjects. Plasma, urine, and CSF metabolic profiling were performed by coupled gas chromatography/mass spectrometry and high-performance liquid chromatography electrospray ionization tandem mass spectrometry.Results:CSF metabolite abnormalities were identified in 21 of the 33 participants with treatment-refractory depression. Cerebral folate deficiency (N=12) was most common, with normal serum folate levels and low CSF 5-methyltetrahydrofolate (5-MTHF) levels. All patients with cerebral folate deficiency, including one with low CSF levels of 5-MTHF and tetrahydrobiopterin intermediates, showed improvement in depression symptom inventories after treatment with folinic acid; the patient with low tetrahydrobiopterin also received sapropterin. None of the healthy comparison subjects had a metabolite abnormality.Conclusions:Examination of metabolic disorders in treatment-refractory depression identified an unexpectedly large proportion of patients with potentially treatable abnormalities. The etiology of these abnormalities remains to be determined.

Lopresti, A. L. and P. D. Drummond (2017). ***"Efficacy of curcumin, and a saffron/curcumin combination for the treatment of major depression: A randomised, double-blind, placebo-controlled study."*** Journal of Affective Disorders 207: 188-196. http://dx.doi.org/10.1016/j.jad.2016.09.047

Background Several studies have supported the antidepressant effects of curcumin (from the spice turmeric) and saffron for people with major depressive disorder. However, these studies have been hampered by poor designs, small sample sizes, short treatment duration, and similar intervention dosages. Furthermore, the antidepressant effects of combined curcumin and saffron administration are unknown. Methods In a randomised, double-blind, placebo-controlled study, 123 individuals with major depressive disorder were allocated to one of four treatment conditions, comprising placebo, low-dose curcumin extract (250 mg b.i.d.), high-dose curcumin extract (500 mg b.i.d.), or combined low-dose curcumin extract plus saffron (15 mg b.i.d.) for 12 weeks. The outcome measures were the Inventory of Depressive Symptomatology self-rated version (IDS-SR30) and Spielberger State-Trait Anxiety Inventory (STAI). Results The active drug treatments (combined) were associated with significantly greater improvements in depressive symptoms compared to placebo (p=.031), and superior improvements in STAI-state (p<.001) and STAI-trait scores (p=.001). Active drug treatments also had greater efficacy in people with atypical depression compared to the remainder of patients (response rates of 65% versus 35% respectively, p=.012). No differences were found between the differing doses of curcumin or the curcumin/saffron combination. Limitations Investigations with larger sample sizes are required to examine the efficacy of differing doses of curcumin and saffron/curcumin combination. Its effects in people with atypical depression also require examination in larger scale studies. Conclusions Active drug treatments comprising differing doses of curcumin and combined curcumin/saffron were effective in reducing depressive and anxiolytic symptoms in people with major depressive disorder.

Malhi, G. S. and Y. Byrow (2016). ***"Exercising control over bipolar disorder."*** Evidence Based Mental Health 19(4): 103-105. http://ebmh.bmj.com/content/19/4/103.short

(Available in free full text) Following extensive research exercise has emerged as an effective treatment for major depressive disorder, and it is now a recognised therapy alongside other interventions. In contrast, there is a paucity of research examining the therapeutic effects of exercise for those with bipolar disorder. Given that dysfunctional reward processing is central to bipolar disorder, research suggests that exercise can perhaps be framed as a reward-related event that may have the potential to precipitate a manic episode. The behavioural activation system (BAS) is a neurobehavioural system that is associated with responding to reward and provides an appropriate framework to theoretically examine and better understand the effects of exercise treatment on bipolar disorder. This article discusses recent research findings and provides an overview of the extant literature related to the neurobiological underpinnings of BAS and exercise as they relate to bipolar disorder. This is important clinically because depending on mood state in bipolar disorder, we postulate that exercise could be either beneficial or deleterious with positive or negative effects on the illness. Clearly, this complicates the evaluation of exercise as a potential treatment in terms of identifying its optimal characteristics in this population.

McGirr, A., P. A. Vöhringer, et al. (2016). ***"Safety and efficacy of adjunctive second-generation antidepressant therapy with a mood stabiliser or an atypical antipsychotic in acute bipolar depression: A systematic review and meta-analysis of randomised placebo-controlled trials."*** The Lancet Psychiatry 3(12): 1138-1146. //www.sciencedirect.com/science/article/pii/S2215036616302644

Summary Background Although mania and hypomania define bipolar disorder, depressive episodes are more common and impairing, with few proven treatments. Adjunctive therapy with second-generation antidepressants is widely used to treat acute bipolar depression, but their efficacy and safety remain controversial. Methods In this systematic review and meta-analysis, we searched MEDLINE, Embase, the Cochrane Central Register of Controlled Trials, and ClinicalTrials.gov from inception to Jan 31, 2016, for randomised, double-blind, placebo-controlled trials of second-generation antidepressants adjunctive to a mood stabiliser or an antipsychotic in patients with acute bipolar depression. We extracted data from published reports. The primary outcome was change in clinician-rated depressive symptom score; secondary outcomes were clinical response, clinical remission, treatment-emergent mania or hypomania, and tolerability (using dropout rates as a proxy). We used pooled random-effects models, subgroup comparisons, and meta-regression for analyses. We made subgroup comparisons on the basis of mood stabiliser or antipsychotic treatment and did meta-regression examining trial duration. This study is registered with PROSPERO, number CRD#42015016024. Findings We identified six trials representing 1383 patients with bipolar depression. Second-generation antidepressants were associated with a small but significant improvement in clinician-rated depressive symptom score (standardised mean differences 0·165 [95% CI 0·051–0·278], p=0·004). However, clinical response and remission rates did not differ significantly between patients receiving adjunctive antidepressants and those receiving placebo (1·158 [0·840–1·597], p=0·371 for clinical response; 1·220 [0·874–1·703], p=0·243 for remission). Acute treatment was not associated with an increased risk of treatment-emergent mania or hypomania (0·926 [0·576–1·491], p=0·753), but 52 week extension periods were associated with an increase in risk (1·774 [1·018–3·091], p=0·043). Interpretation Adjunctive second-generation antidepressants are associated with reduced symptoms of acute bipolar depression, but the magnitude of benefit is small because they do not increase clinical response or remission rates. However, these medications should be used only in the short term because prolonged use is associated with an increased risk of treatment-emergent mania or hypomania. Funding None.

McNamara, R. K. (2016). ***"Role of omega-3 fatty acids in the etiology, treatment, and prevention of depression: Current status and future directions."*** Journal of Nutrition & Intermediary Metabolism 5: 96-106. http://www.sciencedirect.com/science/article/pii/S2352385915300153

(Available in free full text) Over the past three decades a body of translational evidence has implicated dietary deficiency in long-chain omega-3 (LCn-3) fatty acids, including eicosapenaenoic acid (EPA) and docosahexaenoic acid (DHA), in the pathophysiology and etiology of major depressive disorder (MDD). Cross-national and cross-sectional data suggest that

greater habitual intake of preformed EPA + DHA is associated with reduced risk for developing depressive symptoms and syndromal MDD. Erythrocyte EPA and DHA composition is highly correlated with habitual fish or fish oil intake, and case-control studies have consistently observed lower erythrocyte EPA and/or DHA levels in patients with MDD. Low erythrocyte EPA + DHA composition may also be associated with increased risk for suicide and cardiovascular disease, two primary causes of excess premature mortality in MDD. While controversial, dietary EPA + DHA supplementation may have antidepressant properties and may augment the therapeutic efficacy of antidepressant medications. Neuroimaging and rodent neurodevelopmental studies further suggest that low LCn-3 fatty acid intake or biostatus can recapitulate central pathophysiological features associated with MDD. Prospective findings suggest that low LCn-3 fatty acid biostatus increases risk for depressive symptoms in part by augmenting pro-inflammatory responsivity. When taken collectively, these translational findings provide a strong empirical foundation in support of dietary LCn-3 fatty acid deficiency as a modifiable risk factor for MDD. This review provides an overview of this translational evidence and then discusses future directions including strategies to translate this evidence into routine clinical screening and treatment algorithms.

Mojtabai, R., M. Olfson, et al. (2016). ***"National trends in the prevalence and treatment of depression in adolescents and young adults."*** Pediatrics

(Available in free full text) OBJECTIVES: This study examined national trends in 12-month prevalence of major depressive episodes (MDEs) in adolescents and young adults overall and in different sociodemographic groups, as well as trends in depression treatment between 2005 and 2014. METHODS: Data were drawn from the National Surveys on Drug Use and Health for 2005 to 2014, which are annual cross-sectional surveys of the US general population. Participants included 172 495 adolescents aged 12 to 17 and 178 755 adults aged 18 to 25. Time trends in 12-month prevalence of MDEs were examined overall and in different subgroups, as were time trends in the use of treatment services. RESULTS: The 12-month prevalence of MDEs increased from 8.7% in 2005 to 11.3% in 2014 in adolescents and from 8.8% to 9.6% in young adults (both $P < .001$). The increase was larger and statistically significant only in the age range of 12 to 20 years. The trends remained significant after adjustment for substance use disorders and sociodemographic factors. Mental health care contacts overall did not change over time; however, the use of specialty mental health providers increased in adolescents and young adults, and the use of prescription medications and inpatient hospitalizations increased in adolescents. CONCLUSIONS: The prevalence of depression in adolescents and young adults has increased in recent years. In the context of little change in mental health treatments, trends in prevalence translate into a growing number of young people with untreated depression. The findings call for renewed efforts to expand service capacity to best meet the mental health care needs of this age group.

Murray, R. M., D. Quattrone, et al. (2016). ***"Should psychiatrists be more cautious about the long-term prophylactic use of antipsychotics?"*** The British Journal of Psychiatry 209(5): 361-365

Patients who recover from an acute episode of psychosis are frequently prescribed prophylactic antipsychotics for many years, especially if they are diagnosed as having schizophrenia. However, there is a dearth of evidence concerning the long-term effectiveness of this practice, and growing concern over the cumulative effects of antipsychotics on physical health and brain structure. Although controversy remains concerning some of the data, the wise psychiatrist should regularly review the benefit to each patient of continuing prophylactic antipsychotics against the risk of side-effects and loss of effectiveness through the development of supersensitivity of the dopamine D2 receptor. Psychiatrists should work with their patients to slowly reduce the antipsychotic to the lowest dose that prevents the return of distressing symptoms. Up to 40% of those whose psychosis remits after a first episode should be able to achieve a good outcome in the long term either with no antipsychotic medication or with a very low dose.

Neufeld, S. A. S., V. J. Dunn, et al. (2017). ***"Reduction in adolescent depression after contact with mental health services: A longitudinal cohort study in the UK."*** The Lancet Psychiatry 4(2): 120-127. http://dx.doi.org/10.1016/S2215-0366(17)30002-0

(Available in free full text) Background Evidence regarding the association between service contact and subsequent mental health in adolescents is scarce, and previous findings are mixed. We aimed to longitudinally assess the extent to which depressive symptoms in adolescents change after contact with mental health services. Methods As part of a longitudinal cohort study, between April 28, 2005, and March 17, 2010, we recruited 1238 14-year-old adolescents and their primary caregivers from 18 secondary schools in Cambridgeshire, UK. Participants underwent follow-up assessment at months 18 and 36. Trained researchers assessed the adolescents for current mental disorder using the Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime version (K-SADS-PL). Caregivers and adolescents reported contact with mental health services in the year before baseline. Adolescents self-reported depressive symptoms (Mood and Feelings Questionnaire [MFQ]) at each timepoint. We assessed change in MFQ sum scores from baseline contact with mental health services using multilevel mixed-effects regression adjusted for sociodemographic, environmental, individual, and mental health confounders, with multiple imputation of missing data. We used propensity score weighting to balance confounders between treatment (users of mental health services) and control (non-users of mental health services) groups. We implemented an MFQ clinical cutoff following the results of receiver operating characteristic analysis. Findings 14-year-old adolescents who had contact with mental health services in the past year had a greater decrease in depressive symptoms than those without contact (adjusted coefficient −1·68, 95% CI −3·22 to −0·14; p=0·033). By age 17 years, the odds of reporting clinical depression were more than seven times higher in individuals without contact than in service users who had been similarly depressed at baseline (adjusted odds ratio 7·38, 1·73–31·50; p=0·0069). Interpretation Our findings show that contact with mental health services at age 14 years by adolescents with a mental disorder reduced the likelihood of depression by age 17 years. This finding supports the improvement of access to adolescent mental health services.

Ploubidis, G. B., A. Sullivan, et al. (2017). ***"Psychological distress in mid-life: Evidence from the 1958 and 1970 British birth cohorts."*** Psychological Medicine 47(2): 291-303. https://www.cambridge.org/core/article/div-class-title-psychological-distress-in-mid-life-evidence-from-the-1958-and-1970-british-birth-cohorts-div/43F04DCFE2E3771DED949BB02068F02D

Background This paper addresses the levels of psychological distress experienced at age 42 years by men and women born in 1958 and 1970. Comparing these cohorts born 12 years apart, we ask whether psychological distress has increased, and, if so, whether this increase can be explained by differences in their childhood conditions. Method Data were utilized from two well-known population-based birth cohorts, the National Child Development Study and the 1970 British Cohort Study. Latent variable models and causal mediation methods were employed.ResultsAfter establishing the measurement equivalence of psychological distress in the two cohorts we found that men and women born in 1970 reported higher levels of psychological distress compared with those born in 1958. These differences were more pronounced in men (b = 0.314, 95% confidence interval 0.252–0.375), with the magnitude of the effect being twice as strong compared with women (b = 0.147, 95% confidence interval 0.076–0.218). The effect of all hypothesized early-life mediators in explaining these differences was modest. Conclusions Our findings have implications for public health policy, indicating a higher average level of psychological distress among a cohort born in 1970 compared with a generation born 12 years earlier. Due to increases in life expectancy, more

recently born cohorts are expected to live longer, which implies – if such differences persist – that they are likely to spend more years with mental health-related morbidity compared with earlier-born cohorts.

Priebe, S., G. Ramjaun, et al. (2017). ***"Do patients prefer optimistic or cautious psychiatrists? An experimental study with new and long-term patients."*** BMC Psychiatry 17(1): 26. http://dx.doi.org/10.1186/s12888-016-1182-1

(Available in free full text) Background Patients seeking treatment may be assumed to prefer a psychiatrist who suggests a new treatment with confidence and optimism. Yet, this might not apply uniformly to all patients. In this study, we tested the hypothesis that new patients prefer psychiatrists who present treatments optimistically, whilst patients with longer-term experience of mental health care may rather prefer more cautious psychiatrists. Methods In an experimental study, we produced video-clips of four psychiatrists, each suggesting a pharmacological and a psychological treatment once with optimism and once with caution. 100 'new' patients with less than 3 months experience of mental health care and 100 'long-term' patients with more than one year of experience were shown a random selection of one video-clip from each psychiatrist, always including an optimistic and a cautious suggestion of each treatment. Patients rated their preferences for psychiatrists on Likert type scales. Differences in subgroups with different age (18–40 vs. 41–65 years), gender, school leaving age (≤16 vs. >16 years), and diagnosis (ICD 10 F2 vs. others) were explored. Results New patients preferred more optimistic treatment suggestions, whilst there was no preference among long-term patients. The interaction effect between preference for treatment presentations and experience of patients was significant (interaction p-value = 0.003). Findings in subgroups were similar. Conclusion In line with the hypothesis, psychiatrists should suggest treatments with optimism to patients with little experience of mental health care. However, this rule does not apply to longer-term patients, who may have experienced treatment failures in the past.

Ravindran, A. V., L. G. Balneaves, et al. (2016). ***"Canadian network for mood and anxiety treatments (canmat) 2016 clinical guidelines for the management of adults with major depressive disorder: Section 5. Complementary and alternative medicine treatments."*** The Canadian Journal of Psychiatry 61(9): 576-587. http://cpa.sagepub.com/content/61/9/576.abstract

(Available in free full text) Background: The Canadian Network for Mood and Anxiety Treatments (CANMAT) conducted a revision of the 2009 guidelines by updating the evidence and recommendations. The scope of the 2016 guidelines remains the management of major depressive disorder (MDD) in adults, with a target audience of psychiatrists and other mental health professionals. Methods: Using the question-answer format, we conducted a systematic literature search focusing on systematic reviews and meta-analyses. Evidence was graded using CANMAT-defined criteria for level of evidence. Recommendations for lines of treatment were based on the quality of evidence and clinical expert consensus. "Complementary and Alternative Medicine Treatments" is the fifth of six sections of the 2016 guidelines. Results: Evidence-informed responses were developed for 12 questions for 2 broad categories of complementary and alternative medicine (CAM) interventions: 1) physical and meditative treatments (light therapy, sleep deprivation, exercise, yoga, and acupuncture) and 2) natural health products (St. John's wort, omega-3 fatty acids; S-adenosyl-L-methionine [SAM-e], dehydroepiandrosterone, folate, Crocus sativus, and others). Recommendations were based on available data on efficacy, tolerability, and safety. Conclusions: For MDD of mild to moderate severity, exercise, light therapy, St. John's wort, omega-3 fatty acids, SAM-e, and yoga are recommended as first- or second-line treatments. Adjunctive exercise and adjunctive St. John's wort are second-line recommendations for moderate to severe MDD. Other physical treatments and natural health products have less evidence but may be considered as third-line treatments. CAM treatments are generally well tolerated. Caveats include methodological limitations of studies and paucity of data on long-term outcomes and drug interactions.

Redmore, J., R. Kipping, et al. (2016). ***"Analysis of trends in adolescent suicides and accidental deaths in england and wales, 1972–2011."*** The British Journal of Psychiatry 209(4): 327-333

(Available in free full text) Background Previous analyses of adolescent suicides in England and Wales have focused on short time periods. Aims To investigate trends in suicide and accidental deaths in adolescents between 1972 and 2011.MethodTime trend analysis of rates of suicides and deaths from accidental poisoning and hanging in 10- to 19-year-olds by age, gender and deprivation. Rate ratios were estimated for 1982–1991, 1992–2001 and 2002–2011 with 1972–1981 as comparator. Results Suicide rates have remained stable in 10- to 14-year-olds, with strong evidence for a reduction in accidental deaths. In males aged 15–19, suicide rates peaked in 2001 before declining. Suicide by hanging is the most common method of suicide. Rates were higher in males and in 15- to 19-year-olds living in more deprived areas. Conclusions Suicide rates in adolescents are at their lowest since the early 1970s with no clear evidence that changes in coroners' practices underlie this trend.

Rice, F., O. Eyre, et al. (2017). ***"Adolescent depression and the treatment gap."*** The Lancet Psychiatry 4(2): 86-87. http://dx.doi.org/10.1016/S2215-0366(17)30004-4

(Available in free full text) Adolescence is an important risk period for the development of depression, when the rates of major depressive disorder and symptoms of depression rise markedly.1 Depressive symptoms and disorders are common in adolescence and are associated with poor long-term mental health, social, and educational outcomes. Adolescent major depressive disorder is often unrecognised and untreated despite evidence that duration of untreated depressive illness is a key factor in predicting recurrence in adult life. An Article in this issue of Lancet Psychiatry shows the beneficial effect of mental health service contact during adolescence on subsequent depressive symptomatology. In a longitudinal community study, Neufeld and colleagues show that, among adolescents aged 14 years with a DSM-IV psychiatric disorder, use of mental health services substantially reduces depressive symptomatology at the 36-month follow-up. Thus, by age 17 years, the odds of adolescents who had a disorder but did not contact mental health services reporting symptoms of depression in the clinical range was seven times higher than in adolescents who did access services. Importantly, these findings were generated using statistical methods that balance confounders across intervention and control groups (similar to what is done in randomised controlled trials) … In conclusion, the study by Neufeld and colleagues is important in empirically showing the long-term beneficial effects of prompt treatment of adolescent mental health problems and provides hope that the benefits could be achieved with interventions of relatively short duration.

Riecher-Rössler, A. (2016). ***"Sex and gender differences in mental disorders."*** The Lancet Psychiatry. http://dx.doi.org/10.1016/S2215-0366(16)30348-0

Summary: Increased prevalence, severity, and burden of anxiety, trauma-related and stress-related disorders in women compared with men has been well documented. Evidence from a variety of fields has emerged suggesting that sex hormones, particularly oestradiol and progesterone, play a significant part in generation of these sex differences. In this Series paper, we aim to integrate the literature reporting on the effects of sex hormones on biological, behavioural, and cognitive pathways, to propose two broad mechanisms by which oestradiol and progesterone influence sex differences in anxiety disorders: augmentation of vulnerability factors associated with anxiety disorder development; and facilitation of the

maintenance of anxious symptoms post-development. The implications for future research, along with novel approaches to psychological and pharmacological treatment of anxiety disorders, are also considered.

Rueger, S. Y., C. K. Malecki, et al. (2016). ***"A meta-analytic review of the association between perceived social support and depression in childhood and adolescence."*** Psychol Bull 142(10): 1017-1067. http://psycnet.apa.org/journals/bul/142/10/1017/

This meta-analysis evaluated the relation between social support and depression in youth and compared the cumulative evidence for 2 theories that have been proposed to explain this association: the general benefits (GB; also known as main effects) and stress-buffering (SB) models. The study included 341 articles (19% unpublished) gathered through a search in PsycINFO, PsycARTICLES, ERIC, and ProQuest, and a hand search of 11 relevant journals. Using a random effects model, the overall effect size based on k = 341 studies and N = 273,149 participants was r = .26 (95% CI [.24, .28]), with robust support for the GB model and support for the SB model among medically ill youth. Stress-buffering analyses suggest that different stressful contexts may not allow youth to fully draw on the benefits of social support, and we propose value in seeking to better understand both stress-buffering (effects of social support are enhanced) and reverse stress-buffering (effects of social support are dampened) processes. Key findings regarding other moderators include a different pattern of effect sizes across various sources of support. In addition, gender differences were largely absent from this study, suggesting that social support may be a more critical resource for boys than is typically acknowledged. Results also demonstrated the importance of using instruments with adequate psychometric support, with careful consideration of methodological and conceptual issues. Building upon these collective findings, we provide recommendations for theory and practice, as well as recommendations for addressing limitations in the extant literature to guide future investigations.

Salk, R. H., J. L. Petersen, et al. (2016). ***"The contemporary face of gender differences and similarities in depression throughout adolescence: Development and chronicity."*** Journal of Affective Disorders 205: 28-35. //www.sciencedirect.com/science/article/pii/S0165032715311769

Background We probe the adolescent gender difference in depression, asking two critical questions. First, most longitudinal studies of gender differences in adolescent depression date from the 1980s and 1990s, raising the need for a body of evidence on whether the developmental pattern is similar or different today. Second, despite the importance of chronicity to depression, we do not know whether there is a gender difference in the chronicity burden of the disorder. Methods In a contemporary longitudinal sample of U.S. adolescents, depression symptoms were assessed at ages 11, 13, 15, and 18, and depression diagnoses were assessed at age 20. To capture the chronicity burden of clinical depression, we assessed for every depressive episode in an individual's lifetime and summed the total number of days spent in episode. Results A gender difference emerged at age 13 for depression symptoms and at ages 13–14 for diagnoses. These findings are similar to those in the 1980s and 1990s despite many social changes that have occurred. However, the magnitude of the gender difference in symptoms at ages 13 and 15 may be larger than those documented previously. Latent growth curve modeling of depression symptoms indicated that girls' symptoms accelerated early in adolescence whereas boys' symptoms accelerated later. Although more girls (24%) than boys (15%) experienced major depression or dysthymia by age 20, the chronicity burden among those with depression showed gender similarities (median=2.6% days depressed for boys and 2.4% for girls). Limitations Depression diagnoses were assessed retrospectively; however, symptom data were assessed prospectively, and symptom and diagnostic data converged. The sample was also predominantly White, limiting generalizability. Conclusions In a contemporary adolescent sample we observed gender differences in depression symptoms and diagnoses beginning at age 13. We documented distinct developmental trajectories of depression for adolescent girls and boys, suggesting different developmental windows for depression prevention programs. We also discovered a gender similarity in the chronicity burden of clinical depression.

Schaakxs, R., H. C. Comijs, et al. (2017). ***"Age-related variability in the presentation of symptoms of major depressive disorder."*** Psychological Medicine 47(3): 543-552. https://www.cambridge.org/core/article/div-class-title-age-related-variability-in-the-presentation-of-symptoms-of-major-depressive-disorder-div/B83301A906F2EC6550043672883D6ED4

Background The heterogeneous aetiology of major depressive disorder (MDD) might affect the presentation of depressive symptoms across the lifespan. We examined to what extent a range of mood, cognitive, and somatic/vegetative depressive symptoms were differentially present depending on patient's age.MethodData came from 1404 participants with current MDD (aged 18–88 years) from two cohort studies: the Netherlands Study of Depression and Anxiety (NESDA) and the Netherlands Study of Depression in Older Persons (NESDO). Associations between age (per 10 years) and 30 depressive symptoms as well as three symptom clusters (mood, cognitive, somatic/vegetative) were assessed using logistic and linear regression analyses.ResultsDepression severity was found to be stable with increasing age. Nevertheless, 20 (67%) out of 30 symptoms were associated with age. Most clearly, with ageing there was more often early morning awakening [odds ratio (OR) 1.47, 95% confidence interval (CI) 1.36–1.60], reduced interest in sex (OR 1.42, 95% CI 1.31–1.53), and problems sleeping during the night (OR 1.33, 95% CI 1.24–1.43), whereas symptoms most strongly associated with younger age were interpersonal sensitivity (OR 0.72, 95% CI 0.66–0.79), feeling irritable (OR 0.73, 95% CI 0.67–0.79), and sleeping too much (OR 0.75, 95% CI 0.68–0.83). The sum score of somatic/vegetative symptoms was associated with older age ($B = 0.23$, $p < 0.001$), whereas the mood and cognitive sum scores were associated with younger age ($B = -0.20$, $p < 0.001$; $B = -0.04$, $p = 0.004$).ConclusionsDepression severity was found to be stable across the lifespan, yet depressive symptoms tend to shift with age from being predominantly mood-related to being more somatic/vegetative. Due to the increasing somatic presentation of depression with age, diagnoses may be missed.

Shackman, A. J., D. P. Tromp, et al. (2016). ***"Dispositional negativity: An integrative psychological and neurobiological perspective."*** Psychol Bull 142(12): 1275-1314. https://www.ncbi.nlm.nih.gov/pubmed/27732016

Dispositional negativity-the propensity to experience and express more frequent, intense, or enduring negative affect-is a fundamental dimension of childhood temperament and adult personality. Elevated levels of dispositional negativity can have profound consequences for health, wealth, and happiness, drawing the attention of clinicians, researchers, and policymakers. Here, we highlight recent advances in our understanding of the psychological and neurobiological processes linking stable individual differences in dispositional negativity to momentary emotional states. Self-report data suggest that 3 key pathways-increased stressor reactivity, tonic increases in negative affect, and increased stressor exposure-explain most of the heightened negative affect that characterizes individuals with a more negative disposition. Of these 3 pathways, tonically elevated, indiscriminate negative affect appears to be most central to daily life and most relevant to the development of psychopathology. New behavioral and biological data provide insights into the neural systems underlying these 3 pathways and motivate the hypothesis that seemingly "tonic" increases in negative affect may actually reflect increased reactivity to stressors that are remote, uncertain, or diffuse. Research focused on humans, monkeys, and rodents suggests that this indiscriminate negative affect reflects trait-like variation in the activity and connectivity of several key brain regions, including the central extended amygdala and parts of the prefrontal cortex. Collectively, these observations provide an integrative psychobiological framework

for understanding the dynamic cascade of processes that bind emotional traits to emotional states and, ultimately, to emotional disorders and other kinds of adverse outcomes.

Sweeney, S. and A. MacBeth (2016). ***"The effects of paternal depression on child and adolescent outcomes: A systematic review."*** Journal of Affective Disorders 205: 44-59. //www.sciencedirect.com/science/article/pii/S0165032715312404

Background Paternal depression has been associated with suboptimal developmental outcomes in offspring. We sought to systematically review the research evidence from prospective studies for an association between paternal depression and child adolescent emotional and behavioral outcomes. We also reviewed potential mediators of this association and sources of methodological bias. Methods A systematic review was conducted using the following databases: Medline, EMBASE, PsycINFO and Google Scholar. Reference lists of the included papers were also searched. Results Twenty-one studies were included in the review. Findings suggested that paternal depression does negatively impact upon offspring development. This impact is observable when paternal depression is present in the antenatal and postnatal stages and during offspring adolescence. The strength of this association is strongly reliant upon a number of contextual mediators, namely; paternal negative expressiveness, hostility and involvement and marital conflict. A quality assessment rating showed the studies were relatively strong methodologically. Limitations Heterogeneity regarding method of assessment and the magnitude and timing of exposure hinder attempts to make strong conclusions regarding the trajectory of paternal depression and its effects on child and adolescent outcomes. Conclusions Paternal mental health screening during pregnancy is necessary in order to identify and prevent depression negatively impacting offspring functioning. Including both parents in this process should encourage the alleviation of the environmental mediators which dominate the negative association outlined within the review. Research examining gene-environment interaction is necessary to uncover more accurate details regarding paternal depression and subsequent offspring vulnerability.

Tham, A., U. Jonsson, et al. (2016). ***"Efficacy and tolerability of antidepressants in people aged 65 years or older with major depressive disorder – a systematic review and a meta-analysis."*** Journal of Affective Disorders 205: 1-12. //www.sciencedirect.com/science/article/pii/S0165032716307455

Background There has been a steady increase in the prescription of antidepressants for the elderly. This study comprises a systematic review of randomized, placebo-controlled trials of antidepressants for treatment of depressive disorder in people aged 65 years or more. Methods PubMed, EMBASE, Cochrane Library, CINAL, and PsycINFO were searched until May 2016. Where appropriate, the results were synthesized in meta-analyses. Results Twelve trials met the inclusion criteria. For patients with major depressive disorder, selective serotonin re-uptake inhibitors (SSRI) were not superior to placebo in achieving remission (OR: 0.79, 95% CI: 0.61–1.03) or response (OR=0.86, 95% CI: 0.51–1.10) after 8 weeks of treatment (three trials). However, maintenance treatment with SSRIs was superior to placebo in preventing relapse (OR: 0.22, 95% CI: 0.13–0.36; NNT=5, 95% CI: 3–6; two trials). Duloxetine was superior to placebo in achieving remission (OR: 1.78, 95% CI: 1.20–2.65; NNT=9, 95% CI: 6–20; three trials) and response (OR: 1.83, 95% CI: 1.96–4.08; two trials) in recurrent major depression after 8 weeks, but increased the risk of adverse events that can be problematic in the elderly. Limitations The quality of evidence was generally low or moderate, emphasizing the uncertainty of the results. Study populations only partly covered the heterogeneous population of elderly with depressed mood, limiting the generalizability. Conclusion The results underscore the importance of close monitoring of the effects of antidepressants in treatment of elderly patients with a depressive disorder. Methods for early detection of non-responders and effective treatment options for this group are needed.