36 depression-relevant abstracts july '17 newsletter

(Andreas, Schulz et al. 2017; Berk, Daglas et al. 2017; Brown, Ray et al. 2017; Cowlishaw, Gale et al. 2017; Danese and S 2017; de Jonge, Dekker et al. 2017; Dean, Kanchanatawan et al. 2017; Dell'Osso, Gesi et al. 2017; Dunlop, Kelley et al. 2017; Feltes, Doorduin et al. 2017; Fuller-Thomson, Jayanthikumar et al. 2017; Genovese, Dalrymple et al. 2017; Green, Goldstein-Piekarski et al. 2017; Hirschtritt, Bloch et al. 2017; Horvath, Łukasik et al. 2017; Jacka 2017; Kendler, Lönn et al. 2017; Lori L. Altshuler, Catherine A. Sugar et al. 2017; MacQueen, Surette et al. 2017; Man, Chan et al. 2017; Mazahery, Stonehouse et al. 2017; McGorry, Nelson et al. 2017; Nelson and Spyker 2017; Ng, Venkatanarayanan et al. 2017; Opie, Itsiopoulos et al. 2017; Opie, O'Neil et al. 2017; Pinto-Sanchez, Hall et al. 2017; Siahbazi, Behboudi-Gandevani et al. 2017; Slyepchenko, Maes et al. 2017; Sujan, Rickert et al. 2017; Thornicroft, Chatterji et al. 2017; Ustun, Adler et al. 2017; Viktorin, Rydén et al. 2017; Walkup 2017; Wallace and Milev 2017; Wiens, Williams et al. 2017)

Andreas, S., H. Schulz, et al. (2017). ***"Prevalence of mental disorders in elderly people: The european mentdis_icf65+ study."*** The British Journal of Psychiatry 210(2): 125-131 http://bjp.rcpsych.org/content/210/2/125

Background Except for dementia and depression, little is known about common mental disorders in elderly people. Aims To estimate current, 12-month and lifetime prevalence rates of mental disorders in different European and associated countries using a standardised diagnostic interview adapted to measure the cognitive needs of elderly people. Method The MentDis_ICF65+ study is based on an age-stratified, random sample of 3142 older men and women (65–84 years) living in selected catchment community areas of participating countries. Results One in two individuals had experienced a mental disorder in their lifetime, one in three within the past year and nearly one in four currently had a mental disorder. The most prevalent disorders were anxiety disorders, followed by affective and substance-related disorders. Conclusions Compared with previous studies we found substantially higher prevalence rates for most mental disorders. These findings underscore the need for improving diagnostic assessments adapted to the cognitive capacity of elderly people. There is a need to raise awareness of psychosocial problems in elderly people and to deliver high-quality mental health services to these individuals.

Berk, M., R. Daglas, et al. (2017). ***"Quetiapine v. Lithium in the maintenance phase following a first episode of mania: Randomised controlled trial."*** The British Journal of Psychiatry 210(6): 413-421 http://bjp.rcpsych.org/content/210/6/413

Background Lithium and quetiapine are considered standard maintenance agents for bipolar disorder yet it is unclear how their efficacy compares with each other. Aims To investigate the differential effect of lithium and quetiapine on symptoms of depression, mania, general functioning, global illness severity and quality of life in patients with recently stabilised first-episode mania. Method Maintenance trial of patients with first-episode mania stabilised on a combination of lithium and quetiapine, subsequently randomised to lithium or quetiapine monotherapy (up to 800 mg/day) and followed up for 1 year. (Trial registration: Australian and New Zealand Clinical Trials Registry – ACTRN12607000639426.) Results In total, 61 individuals were randomised. Within mixed-model repeated measures analyses, significant omnibus treatment × visit interactions were observed for measures of overall psychopathology, psychotic symptoms and functioning. Planned and post hoc comparisons further demonstrated the superiority of lithium treatment over quetiapine. Conclusions In people with first-episode mania treated with a combination of lithium and quetiapine, continuation treatment with lithium rather than quetiapine is superior in terms of mean levels of symptoms during a 1-year evolution.

Brown, H. K., J. G. Ray, et al. (2017). ***"Association between serotonergic antidepressant use during pregnancy and autism spectrum disorder in children."*** JAMA 317(15): 1544-1552. http://dx.doi.org/10.1001/jama.2017.3415

Importance Previous observations of a higher risk of child autism spectrum disorder with serotonergic antidepressant exposure during pregnancy may have been confounded.Objective To evaluate the association between serotonergic antidepressant exposure during pregnancy and child autism spectrum disorder. Design, Setting, and Participants Retrospective cohort study. Health administrative data sets were used to study children born to mothers who were receiving public prescription drug coverage during pregnancy in Ontario, Canada, from 2002-2010, reflecting 4.2% of births. Children were followed up until March 31, 2014. Exposures Serotonergic antidepressant exposure was defined as 2 or more consecutive maternal prescriptions for a selective serotonin or serotonin-norepinephrine reuptake inhibitor between conception and delivery. Main Outcomes and Measures Child autism spectrum disorder identified after the age of 2 years. Exposure group differences were addressed by inverse probability of treatment weighting based on derived high-dimensional propensity scores (computerized algorithm used to select a large number of potential confounders) and by comparing exposed children with unexposed siblings. Results There were 35 906 singleton births at a mean gestational age of 38.7 weeks (50.4% were male, mean maternal age was 26.7 years, and mean duration of follow-up was 4.95 years). In the 2837 pregnancies (7.9%) exposed to antidepressants, 2.0% (95% CI, 1.6%-2.6%) of children were diagnosed with autism spectrum disorder. The incidence of autism spectrum disorder was 4.51 per 1000 person-years among children exposed to antidepressants vs 2.03 per 1000 person-years among unexposed children (between-group difference, 2.48 [95% CI, 2.33-2.62] per 1000 person-years; hazard ratio [HR], 2.16 [95% CI, 1.64-2.86]; adjusted HR, 1.59 [95% CI, 1.17-2.17]). After inverse probability of treatment weighting based on the high-dimensional propensity score, the association was not significant (HR, 1.61 [95% CI, 0.997-2.59]). The association was also not significant when exposed children were compared with unexposed siblings (incidence of autism spectrum disorder was 3.40 per 1000 person-years vs 2.05 per 1000 person-years, respectively; adjusted HR, 1.60 [95% CI, 0.69-3.74]). Conclusions and Relevance In children born to mothers receiving public drug coverage in Ontario, Canada, in utero serotonergic antidepressant exposure compared with no exposure was not associated with autism spectrum disorder in the child. Although a causal relationship cannot be ruled out, the previously observed association may be explained by other factors.

Cowlishaw, S., L. Gale, et al. (2017). ***"Gambling problems among patients in primary care: A cross-sectional study of general practices."*** British Journal of General Practice 67(657): e274-e279

(Available in free full text) Background Primary care is an important context for addressing health-related behaviours, and may provide a setting for identification of gambling problems. Aim To indicate the extent of gambling problems among patients attending general practices, and explore settings or patient groups that experience heightened vulnerability. Design and setting Cross-sectional study of patients attending 11 general practices in Bristol, South West England. Method Adult patients (n = 1058) were recruited from waiting rooms of practices that were sampled on the basis of population characteristics. Patients completed anonymous questionnaires comprising measures of mental health problems (for example, depression) and addictive behaviours (for example, risky alcohol use). The Problem Gambling Severity Index (PGSI) measured gambling problems, along with a single-item measure of gambling problems among family members. Estimates of extent and variability

according to practice and patient characteristics were produced. Results There were 0.9% of all patients exhibiting problem gambling (PGSI ≥5), and 4.3% reporting problems that were low to moderate in severity (PGSI 1–4). Around 7% of patients reported gambling problems among family members. Further analyses indicated that rates of any gambling problems (PGSI ≥1) were higher among males and young adults, and more tentatively, within a student healthcare setting. They were also elevated among patients exhibiting drug use, risky alcohol use, and depression. Conclusion There is need for improved understanding of the burden of, and responses to, patients with gambling problems in general practices, and new strategies to increase identification to facilitate improved care and early intervention.

Danese, A. and J. L. S (2017). ***"Psychoneuroimmunology of early-life stress: The hidden wounds of childhood trauma?"*** Neuropsychopharmacology 42(1): 99-114. https://www.ncbi.nlm.nih.gov/pubmed/27629365

The brain and the immune system are not fully formed at birth, but rather continue to mature in response to the postnatal environment. The two-way interaction between the brain and the immune system makes it possible for childhood psychosocial stressors to affect immune system development, which in turn can affect brain development and its long-term functioning. Drawing from experimental animal models and observational human studies, we propose that the psychoneuroimmunology of early-life stress can offer an innovative framework to understand and treat psychopathology linked to childhood trauma. Early-life stress predicts later inflammation, and there are striking analogies between the neurobiological correlates of early-life stress and of inflammation. Furthermore, there are overlapping trans-diagnostic patterns of association of childhood trauma and inflammation with clinical outcomes. These findings suggest new strategies to remediate the effect of childhood trauma before the onset of clinical symptoms, such as anti-inflammatory interventions and potentiation of adaptive immunity. Similar strategies might be used to ameliorate the unfavorable treatment response described in psychiatric patients with a history of childhood trauma.

de Jonge, M., J. J. M. Dekker, et al. (2017). ***"The role of affect in predicting depressive symptomatology in remitted recurrently depressed patients."*** Journal of Affective Disorders 210: 66-71. http://www.sciencedirect.com/science/article/pii/S0165032716311880

Abstract Background Major depressive disorder is an emotional disorder. It is important to improve our understanding of the role of affect in relapse/recurrence of depression. Therefore, this study examines whether affect plays a role in prospectively predicting depressive symptomatology and if there are indications for emotional scarring as a consequence of undergoing depressive episodes. Methods In 107 patients remitted from recurrent depression affect was examined in predicting depressive symptomatology as measured with the Inventory of Depressive Symptomatology – Self Report. Affect was measured with the Positive and Negative Affect Schedule and with a one item Visual Analogue Mood Scale. Indication of emotional scarring was examined by comparing number of previous depressive episodes to levels of affect. Results Less positive affect as assessed after remission predicted increased depressive symptomatology six months later, even after we controlled for baseline symptomatology. Negative affect also predicted depressive symptomatology six months later, but not after controlling for baseline depressive symptomatology. No relationship was found between affect and number of previous episodes. Limitations All participants in this study had two or more previous depressive episodes and received CBT during the acute phase of their depression. The instruments that measured mood and affect were administered within 4 weeks of each other. Conclusions Positive affect and negative affect as assessed after remission in recurrent depression can predict depressive symptomatology. Especially positive affect seems to play an independent role in predicting depressive symptomatology. Directly targeting positive affect in relapse prevention during remission might be a way to enhance treatment effects.

Dean, O. M., B. Kanchanatawan, et al. (2017). ***"Adjunctive minocycline treatment for major depressive disorder: A proof of concept trial."*** Australian & New Zealand Journal of Psychiatry 0(0): 0004867417709357. http://journals.sagepub.com/doi/abs/10.1177/0004867417709357

Objective: Conventional antidepressant treatments result in symptom remission in 30% of those treated for major depressive disorder, raising the need for effective adjunctive therapies. Inflammation has an established role in the pathophysiology of major depressive disorder, and minocycline has been shown to modify the immune-inflammatory processes and also reduce oxidative stress and promote neuronal growth. This double-blind, randomised, placebo-controlled trial examined adjunctive minocycline (200 mg/day, in addition to treatment as usual) for major depressive disorder. This double-blind, randomised, placebo-controlled trial investigated 200 mg/day adjunctive minocycline (in addition to treatment as usual) for major depressive disorder. Methods: A total of 71 adults with major depressive disorder (Diagnostic and Statistical Manual of Mental Disorders–Fourth Edition) were randomised to this 12-week trial. Outcome measures included the Montgomery–Asberg Depression Rating Scale (primary outcome), Clinical Global Impression–Improvement and Clinical Global Impression–Severity, Hamilton Anxiety Rating Scale, Quality of Life Enjoyment and Satisfaction Questionnaire, Social and Occupational Functioning Scale and the Range of Impaired Functioning Tool. The study was registered on the Australian and New Zealand Clinical Trials Register: www.anzctr.org.au, #ACTRN12612000283875. Results: Based on mixed-methods repeated measures analysis of variance at week 12, there was no significant difference in Montgomery–Asberg Depression Rating Scale scores between groups. However, there were significant differences, favouring the minocycline group at week 12 for Clinical Global Impression–Improvement score – effect size (95% confidence interval) = −0.62 [−1.8, −0.3], p = 0.02; Quality of Life Enjoyment and Satisfaction Questionnaire score – effect size (confidence interval) = −0.12 [0.0, 0.2], p < 0.001; and Social and Occupational Functioning Scale and the Range of Impaired Functioning Tool score – 0.79 [−4.5, −1.4], p < 0.001. These effects remained at follow-up (week 16), and Patient Global Impression also became significant, effect size (confidence interval) = 0.57 [−1.7, −0.4], p = 0.017. Conclusion: While the primary outcome was not significant, the improvements in other comprehensive clinical measures suggest that minocycline may be a useful adjunct to improve global experience, functioning and quality of life in people with major depressive disorder. Further studies are warranted to confirm the potential of this accessible agent to optimise treatment outcomes.

Dell'Osso, L., C. Gesi, et al. (2017). ***"Adult autism subthreshold spectrum (adas spectrum): Validation of a questionnaire investigating subthreshold autism spectrum."*** Comprehensive Psychiatry 73: 61-83. http://www.sciencedirect.com/science/article/pii/S0010440X1630339X

Abstract Aim Increasing literature has shown the usefulness of a dimensional approach to autism. The present study aimed to determine the psychometric properties of the Adult Autism Subthreshold Spectrum (AdAS Spectrum), a new questionnaire specifically tailored to assess subthreshold forms of autism spectrum disorder (ASD) in adulthood. Methods 102 adults endorsing at least one DSM-5 symptom criterion for ASD (ASDc), 143 adults diagnosed with a feeding and eating disorder (FED), and 160 subjects with no mental disorders (CTL), were recruited from 7 Italian University Departments of Psychiatry and administered the following: SCID-5, Autism-Spectrum Quotient (AQ), Ritvo Autism and Asperger Diagnostic Scale 14-item version (RAADS-14), and AdAS Spectrum. Results The AdAS Spectrum demonstrated excellent internal consistency for the total score (Kuder–Richardson's coefficient=.964) as well as for five out of seven domains (all coefficients>.80) and sound test–retest reliability (ICC=.976). The total and domain AdAS Spectrum scores showed a moderate to strong (>.50) positive

correlation with one another and with the AQ and RAADS-14 total scores. ASDc subjects reported significantly higher AdAS Spectrum total scores than both FED (p<.001) and CTL (p<.001), and significantly higher scores on the Childhood/adolescence, Verbal communication, Empathy, Inflexibility and adherence to routine, and Restricted interests and rumination domains (all p<.001) than FED, while on all domains compared to CTL. CTL displayed significantly lower total and domain scores than FED (all p<.001). A significant effect of gender emerged for the Hyper– and hyporeactivity to sensory input domain, with women showing higher scores than men (p=.003). A Diagnosis* Gender interaction was also found for the Verbal communication (p=.019) and Empathy (p=.023) domains. When splitting the ASDc in subjects with one symptom criterion (ASD1) and those with a ASD, and the FED in subjects with no ASD symptom criteria (FED0) and those with one ASD symptom criterion (FED1), a gradient of severity in AdAS Spectrum scores from CTL subjects to ASD patients, across FED0, ASD1, FED1 was shown. Conclusions The AdAS Spectrum showed excellent internal consistency and test–retest reliability and strong convergent validity with alternative dimensional measures of ASD. The questionnaire performed differently among the three diagnostic groups and enlightened some significant effects of gender in the expression of autistic traits.

Dunlop, B. W., M. E. Kelley, et al. (2017). ***"Effects of patient preferences on outcomes in the predictors of remission in depression to individual and combined treatments (predict) study."*** American Journal of Psychiatry 174(6): 546-556. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2016.16050517

Objective: The Predictors of Remission in Depression to Individual and Combined Treatments [PReDICT] study aimed to identify clinical and biological factors predictive of treatment outcomes in major depressive disorder among treatment-naive adults. The authors evaluated the efficacy of cognitive-behavioral therapy (CBT) and two antidepressant medications (escitalopram and duloxetine) in patients with major depression and examined the moderating effect of patients' treatment preferences on outcomes. Method: Adults aged 18–65 with treatment-naive major depression were randomly assigned with equal likelihood to 12 weeks of treatment with escitalopram (10–20 mg/day), duloxetine (30–60 mg/day), or CBT (16 50-minute sessions). Prior to randomization, patients indicated whether they preferred medication or CBT or had no preference. The primary outcome was change in the 17-item Hamilton Depression Rating Scale (HAM-D), administered by raters blinded to treatment. Results: A total of 344 patients were randomly assigned, with a mean baseline HAM-D score of 19.8 (SD=3.8). The mean estimated overall decreases in HAM-D score did not significantly differ between treatments (CBT: 10.2, escitalopram: 11.1, duloxetine: 11.2). Last observation carried forward remission rates did not significantly differ between treatments (CBT: 41.9%, escitalopram: 46.7%, duloxetine: 54.7%). Patients matched to their preferred treatment were more likely to complete the trial but not more likely to achieve remission. Conclusions: Treatment guidelines that recommend either an evidence-based psychotherapy or antidepressant medication for nonpsychotic major depression can be extended to treatment-naive patients. Treatment preferences among patients without prior treatment exposure do not significantly moderate symptomatic outcomes.

Feltes, P. K., J. Doorduin, et al. (2017). ***"Anti-inflammatory treatment for major depressive disorder: Implications for patients with an elevated immune profile and non-responders to standard antidepressant therapy."*** Journal of Psychopharmacology 0(0): 0269881117711708. http://journals.sagepub.com/doi/abs/10.1177/0269881117711708

(Available in free full text) Major depressive disorder (MDD) is a prevalent and disabling psychiatric disease with rates of non-responsiveness to antidepressants ranging from 30–50%. Historically, the monoamine depletion hypothesis has dominated the view on the pathophysiology of depression. However, the lack of responsiveness to antidepressants and treatment resistance suggests that additional mechanisms might play a role. Evidence has shown that a subgroup of depressive patients may have an underlying immune deregulation that could explain the lack of therapeutic benefit from antidepressants. Stimuli like inflammation and infection can trigger the activation of microglia to release pro-inflammatory cytokines, acting on two main pathways: (1) activation of the hypothalamic–pituitary adrenal axis, generating an imbalance in the serotonergic and noradrenergic circuits; (2) increased activity of the enzyme indoleamine-2,3-dioxygenase, resulting in depletion of serotonin levels and the production of quinolinic acid. If this hypothesis is proven true, the subgroup of MDD patients with increased levels of pro-inflammatory cytokines, mainly IL-6, TNF-α and IL-1β, might benefit from an anti-inflammatory intervention. Here, we discuss the pre-clinical and clinical studies that have provided support for treatment with non-steroidal anti-inflammatory drugs in depressed patients with inflammatory comorbidities or an elevated immune profile, as well as evidences for anti-inflammatory properties of standard antidepressants.

Fuller-Thomson, E., J. Jayanthikumar, et al. (2017). ***"Untangling the association between migraine, pain, and anxiety: Examining migraine and generalized anxiety disorders in a canadian population based study."*** Headache: The Journal of Head and Face Pain 57(3): 375-390. http://dx.doi.org/10.1111/head.13010

Objective: The aims of this study were to investigate: (1) the prevalence and unadjusted and adjusted odds of 12-month generalized anxiety disorder (GAD) among adults with migraine in comparison to those without migraine; (2) If debilitating pain and/or limitations in instrumental activities of daily living (IADLs) are mediators of the migraine-GAD association; and (3) Factors associated with past year GAD among adults with migraine. Methods: Secondary data analysis of the nationally representative 2012 Canadian Community Health Survey-Mental Health (CCHS-MS), a population-based survey of community dwellers with a response rate of 68.9%. The first subsample included those with (n = 2232) and without migraine (n = 19,270), and the second subsample was restricted to those with migraine (n = 2232). GAD was based on the WHO-CIDI scale. Results: Fully, 6% of those with migraines had past year GAD in comparison of 2.1% of those without migraine (P < .001). The socio-demographically adjusted odds of past year GAD were two and a half times higher among those with migraine than those without (OR= 2.46; 95% CI = 2.00, 3.02). A path analysis indicated that debilitating pain and limitations in IADLs were mediators in the relationship between migraine and GAD. In the sample restricted to migraineurs, the factors associated with higher odds of 12-month GAD included having a university degree, having low income, being without a confidant, and being male. Conclusions: Generalized anxiety disorder is robustly associated with migraine and targeted outreach and interventions are warranted.

Genovese, T., K. Dalrymple, et al. (2017). ***"Subjective anger and overt aggression in psychiatric outpatients."*** Comprehensive Psychiatry 73: 23-30. http://www.sciencedirect.com/science/article/pii/S0010440X16302978

Abstract Background The attention given to anger and aggression in psychiatric patients pales in comparison to the attention given to depression and anxiety. Most studies have focused on a limited number of psychiatric disorders, and results have been inconsistent. The present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project sought to replicate and extend prior findings examining which psychiatric disorders and demographic characteristics were independently associated with elevated levels of anger and aggression. Method 3800 individuals presenting to the Rhode Island Hospital Department of Psychiatry outpatient practice underwent a semi-structured interview to determine current Axis I (N = 3800) and Axis II (N = 2151) pathology. Severity of subjective anger and overt aggression within the past week were also assessed for each patient, and odds ratios were determined for each disorder. Multiple regression analyses were conducted to determine which diagnoses independently contributed to increased levels of anger and aggression. Results Almost

half of the sample reported moderate-to-severe levels of current subjective anger, and more than 20% endorsed moderate-to-severe levels of current overt aggression. The frequency of anger was similar to the frequencies of depressed mood and psychic anxiety. Anger and aggression were elevated across all diagnoses except adjustment disorder. Anger and aggression were most elevated in patients with major depressive disorder, panic disorder with agoraphobia, post-traumatic stress disorder, intermittent explosive disorder, and cluster B personality disorders. Conclusions Anger is as common as depressed mood and psychic anxiety amongst psychiatric outpatients, and problems with anger cut across diagnostic categories. Given the high prevalence of problems with anger in psychiatric patients, more research should be directed towards its effective treatment.

Green, E., A. N. Goldstein-Piekarski, et al. (2017). ***"Personalizing antidepressant choice by sex, body mass index, and symptom profile: An ispot-d report."*** Personalized Medicine in Psychiatry 1: 65-73. http://dx.doi.org/10.1016/j.pmip.2016.12.001

(Available in free full text) Antidepressants are efficacious but we do not know which antidepressant is best suited to which person. We investigated the working hypothesis that obesity and sex may together be differential predictors of acute remission of specific symptoms for commonly used antidepressant medications. Data were acquired for 659 outpatients (18?65years of age) who completed the iSPOT-D practical randomized controlled clinical trial. We measured adiposity by body mass index (BMI). By WHO criteria, 42% of patients were normal weight, 28% overweight and 31%, obese [class I (15%), II (10%) and III (6%)]. Patients were randomly assigned to 8-weeks of treatment with escitalopram, sertraline or venlafaxine extended-release (venlafaxine-XR) and then defined as remitters (17-item Hamilton Rating Scale for Depression score ?7) or non-remitters. In logistic regression models, BMI was a differential predictor of remission according to antidepressant type. Morbidly obese patients, compared to those with normal weight, were more likely to remit on venlafaxine-XR in particular. This effect was driven by a reduction specifically in physical symptoms, including sleep disturbance, somatic anxiety and appetite. The number needed to treat to achieve remission with venlafaxine-XR in obese III participants was 6. Higher BMI females but not males were more likely to remit regardless of medication type; this effect was related to a change in cognitive symptoms, including suicidal ideation, guilt, and psychomotor changes. Our findings suggest that considering BMI and sex, and assessing specific symptoms, could help tailor antidepressant choices to improve remission from depression in specialty and primary care settings.

Hirschtritt, M. E., M. H. Bloch, et al. (2017). ***"Obsessive-compulsive disorder: Advances in diagnosis and treatment."*** JAMA 317(13): 1358-1367. http://dx.doi.org/10.1001/jama.2017.2200

Importance Obsessive-compulsive disorder (OCD) is a neuropsychiatric disorder associated with significant impairment and a lifetime prevalence of 1% to 3%; however, it is often missed in primary care settings and frequently undertreated.Objective To review the most current data regarding screening, diagnosis, and treatment options for OCD. Evidence Review We searched PubMed, EMBASE, and PsycINFO to identify randomized controlled trials (RCTs), meta-analyses, and systematic reviews that addressed screening and diagnostic and treatment approaches for OCD among adults (≥18 years), published between January 1, 2011, and September 30, 2016. We subsequently searched references of retrieved articles for additional reports. Meta-analyses and systematic reviews were prioritized; case series and reports were included only for interventions for which RCTs were not available. Findings Among 792 unique articles identified, 27 (11 RCTs, 11 systematic reviews or meta-analyses, and 5 reviews/guidelines) were selected for this review. The diagnosis of OCD was revised for the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, which addresses OCD separately from anxiety disorders and contains specifiers to delineate the presence of tics and degree of insight. Treatment advances include increasing evidence to support the efficacy of online-based dissemination of cognitive behavioral therapies, which have demonstrated clinically significant decreases in OCD symptoms when conducted by trained therapists. Current evidence continues to support the use of selective serotonin reuptake inhibitors as first-line pharmacologic interventions for OCD; however, more recent data support the adjunctive use of neuroleptics, deep-brain stimulation, and neurosurgical ablation for treatment-resistant OCD. Preliminary data suggest safety of other agents (eg, riluzole, ketamine, memantine, N-acetylcysteine, lamotrigine, celecoxib, ondansetron) either in combination with selective serotonin reuptake inhibitors or as monotherapy in the treatment of OCD, although their efficacy has not yet been established. Conclusions and Relevance The dissemination of computer-based cognitive behavioral therapy and improved evidence supporting it represent a major advancement in treatment of OCD. Although cognitive behavioral therapy with or without selective serotonin reuptake inhibitors remains a preferred initial treatment strategy, increasing evidence that supports the safety and efficacy of neuroleptics and neuromodulatory approaches in treatment-resistant cases provides alternatives for patients whose condition does not respond to first-line interventions.

Horvath, A., J. Łukasik, et al. (2017). ***"Ω-3 fatty acid supplementation does not affect autism spectrum disorder in children: A systematic review and meta-analysis."*** The Journal of Nutrition 147(3): 367-376. http://jn.nutrition.org/content/147/3/367.abstract

Background: Effective treatments for the core symptoms of autism spectrum disorder (ASD) are still lacking.Objective: We aimed to update the data on the effectiveness of ω-3 (n–3) fatty acid (FA) supplementation as a treatment for ASD.Methods: The Cochrane Library, MEDLINE, and EMBASE databases were systematically searched up until August 2016 with no language restrictions for randomized controlled trials (RCTs) comparing ω-3 FA supplementation with placebo or with no supplementation. Participants were children diagnosed with ASD. All functional outcome measures reported were considered. For dichotomous outcomes, the results for individual studies and pooled statistics were reported as RRs. Mean differences (MDs) were calculated for continuous outcomes.Results: Five RCTs (183 participants) were included. With 4 exceptions, there were no statistically significant differences in ASD symptoms between groups measured by validated scales. Among studies that used the Aberrant Behavior Checklist, parents' ratings indicated significant improvement in lethargy symptoms in the ω-3 FA group compared with the placebo group (2 RCTs) (pooled MD: 1.98; 95% CI: 0.32, 3.63). Among studies that used the Behavioral Assessment System for Children, parents' ratings indicated significant worsening of both externalizing behavior (2 RCTs) (pooled MD: −6.22; 95% CI: −10.9, −1.59) and social skills (1 RCT) (MD: −7; 95% CI: −13.62, −0.38) in the ω-3 FA group compared with the placebo group. One RCT reported a significant improvement in the ω-3 FA group for the daily-living component of the Vineland Adaptive Behavior Scale (MD: 6.2; 95% CI: 0.37, 12.03). Adverse effects were similar in both groups.Conclusions: Because of the limited number of included studies and small sample sizes, no firm conclusions can be drawn. However, the limited data currently available suggest that ω-3 FA supplementation does not enhance the performance of children with ASD.

Jacka, F. N. (2017). ***"Nutritional psychiatry: Where to next?"*** EBioMedicine 17: 24-29. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5360575/

(Available in free full text) The nascent field of 'Nutritional Psychiatry' offers much promise for addressing the large disease burden associated with mental disorders. A consistent evidence base from the observational literature confirms that the quality of individuals' diets is related to their risk for common mental disorders, such as depression. This is the case across countries and age groups. Moreover, new intervention studies implementing dietary changes suggest promise for the prevention and treatment of depression. Concurrently, data point to the utility of selected nutraceuticals as adjunctive treatments for

mental disorders and as monotherapies for conditions such as ADHD. Finally, new studies focused on understanding the biological pathways that mediate the observed relationships between diet, nutrition and mental health are pointing to the immune system, oxidative biology, brain plasticity and the microbiome-gut-brain axis as key targets for nutritional interventions. On the other hand, the field is currently limited by a lack of data and methodological issues such as heterogeneity, residual confounding, measurement error, and challenges in measuring and ensuring dietary adherence in intervention studies. Key challenges for the field are to now: replicate, refine and scale up promising clinical and population level dietary strategies; identify a clear set of biological pathways and targets that mediate the identified associations; conduct scientifically rigorous nutraceutical and 'psychobiotic' interventions that also examine predictors of treatment response; conduct observational and experimental studies in psychosis focused on dietary and related risk factors and treatments; and continue to advocate for policy change to improve the food environment at the population level.

Kendler, K. S., S. L. Lönn, et al. (2017). ***"Divorce and the onset of alcohol use disorder: A swedish population-based longitudinal cohort and co-relative study."*** American Journal of Psychiatry 174(5): 451-458. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2016.16050589

Objective: The purpose of this study was to clarify the magnitude and nature of the relationship between divorce and risk for alcohol use disorder (AUD). Method: In a population-based Swedish sample of married individuals (N=942,366), the authors examined the association between divorce or widowhood and risk for first registration for AUD. AUD was assessed using medical, criminal, and pharmacy registries. Results: Divorce was strongly associated with risk for first AUD onset in both men (hazard ratio=5.98, 95% CI=5.65–6.33) and women (hazard ratio=7.29, 95% CI=6.72–7.91). The hazard ratio was estimated for AUD onset given divorce among discordant monozygotic twins to equal 3.45 and 3.62 in men and women, respectively. Divorce was also associated with an AUD recurrence in those with AUD registrations before marriage. Furthermore, widowhood increased risk for AUD in men (hazard ratio=3.85, 95% CI=2.81–5.28) and women (hazard ratio=4.10, 95% CI=2.98–5.64). Among divorced individuals, remarriage was associated with a large decline in AUD in both sexes (men: hazard ratio=0.56, 95% CI=0.52–0.64; women: hazard ratio=0.61, 95% CI=0.55–0.69). Divorce produced a greater increase in first AUD onset in those with a family history of AUD or with prior externalizing behaviors. Conclusions: Spousal loss through divorce or bereavement is associated with a large enduring increased AUD risk. This association likely reflects both causal and noncausal processes. That the AUD status of the spouse alters this association highlights the importance of spouse characteristics for the behavioral health consequences of spousal loss. The pronounced elevation in AUD risk following divorce or widowhood, and the protective effect of remarriage against subsequent AUD, speaks to the profound impact of marriage on problematic alcohol use.

Lori L. Altshuler, Catherine A. Sugar, et al. (2017). ***"Switch rates during acute treatment for bipolar ii depression with lithium, sertraline, or the two combined: A randomized double-blind comparison."*** American Journal of Psychiatry 174(3): 266-276. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2016.15040558

Objective:The authors compared medication-induced mood switch risk (primary outcome), as well as treatment response and side effects (secondary outcomes) with three acute-phase treatments for bipolar II depression. Method:In a 16-week, double-blind, multisite comparison study, 142 participants with bipolar II depression were randomly assigned to receive lithium monotherapy (N=49), sertraline monotherapy (N=45), or combination treatment with lithium and sertraline (N=48). At each visit, mood was assessed using standardized rating scales. Rates of switch were compared, as were rates of treatment response and the presence and severity of treatment-emergent side effects. Results:Twenty participants (14%) experienced a switch during the study period (hypomania, N=17; severe hypomania, N=3). Switch rates did not differ among the three treatment groups, even after accounting for dropout. No patient had a manic switch or was hospitalized for a switch. Most switches occurred within the first 5 weeks of treatment. The treatment response rate for the overall sample was 62.7% (N=89), without significant differences between groups after accounting for dropout. The lithium/sertraline combination group had a significantly higher overall dropout rate than the monotherapy groups but did not have an accelerated time to response. Conclusions:Lithium monotherapy, sertraline monotherapy, and lithium/sertraline combination therapy were associated with similar switch and treatment response rates in participants with bipolar II depression. The dropout rate was higher in the lithium/sertraline combination treatment group, without any treatment acceleration advantage.

MacQueen, G., M. Surette, et al. (2017). ***"The gut microbiota and psychiatric illness."*** Journal of Psychiatry & Neuroscience : JPN 42(2): 75-77. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5373703/

(Available in free full text) The global market for probiotics is projected to be worth almost $USD 100 billion by 2020,1 reflecting growing acceptance that our intestinal microbiota can influence physiologic systems, including but not limited to the gut. Many lay publications enthusiastically tout the potential health benefits of an optimized microbiome — or conversely, the risks of dysbiosis. Depression, stress, anxiety and autism are all proposed to be at least partially sensitive to manipulation of the gut microbiome. Studies have suggested that a variety of conditions are influenced by the microbiome, including obesity, functional gastrointestinal (GI) disorders, chronic fatigue syndrome and inflammatory illnesses. All of these disorders also have an important central nervous system component. It is likely that a substantial portion of people who consume prebiotics or probiotics will do so with the aim of improving symptoms related to the brain … There is interest among both the research and lay communities in understanding the effects of the microbiome on the brain. Patients and clinicians alike are keen to understand whether modifying the microbiome might provide a treatment avenue for various neuropsychiatric conditions. Despite a relative abundance of reviews of the microbiome in human mental health and disease, actual data are sparse, and the widespread use of probiotics is not currently supported by randomized controlled trial data. Research programs that are comprehensive and bring together investigators from various disciplines may provide the best opportunity to move this exciting but challenging field forward in the next decade.

Man, K. K. C., E. W. Chan, et al. (2017). ***"Prenatal antidepressant use and risk of attention-deficit/hyperactivity disorder in offspring: Population based cohort study."*** BMJ 357

Objective To assess the potential association between prenatal use of antidepressants and the risk of attention-deficit/hyperactivity disorder (ADHD) in offspring.Design Population based cohort study.Setting Data from the Hong Kong population based electronic medical records on the Clinical Data Analysis and Reporting System.Participants 190 618 children born in Hong Kong public hospitals between January 2001 and December 2009 and followed-up to December 2015.Main outcome measure Hazard ratio of maternal antidepressant use during pregnancy and ADHD in children aged 6 to 14 years, with an average follow-up time of 9.3 years (range 7.4-11.0 years).Results Among 190 618 children, 1252 had a mother who used prenatal antidepressants. 5659 children (3.0%) were given a diagnosis of ADHD or received treatment for ADHD. The crude hazard ratio of maternal antidepressant use during pregnancy was 2.26 (P<0.01) compared with non-use. After adjustment for potential confounding factors, including maternal psychiatric disorders and use of other psychiatric drugs, the adjusted hazard ratio was reduced to 1.39 (95% confidence interval 1.07 to 1.82, P=0.01). Likewise, similar results were observed when comparing children of mothers who had used antidepressants before pregnancy with those who were never users (1.76, 1.36 to

2.30, P<0.01). The risk of ADHD in the children of mothers with psychiatric disorders was higher compared with the children of mothers without psychiatric disorders even if the mothers had never used antidepressants (1.84, 1.54 to 2.18, P<0.01). All sensitivity analyses yielded similar results. Sibling matched analysis identified no significant difference in risk of ADHD in siblings exposed to antidepressants during gestation and those not exposed during gestation (0.54, 0.17 to 1.74, P=0.30).Conclusions The findings suggest that the association between prenatal use of antidepressants and risk of ADHD in offspring can be partially explained by confounding by indication of antidepressants. If there is a causal association, the size of the effect is probably smaller than that reported previously.

Mazahery, H., W. Stonehouse, et al. (2017). ***"Relationship between long chain n-3 polyunsaturated fatty acids and autism spectrum disorder: Systematic review and meta-analysis of case-control and randomised controlled trials."*** Nutrients 9(2): 155. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5331586/

(Available in free full text) Omega-3 long chain polyunsaturated fatty acid supplementation (n-3 LCPUFA) for treatment of Autism Spectrum Disorder (ASD) is popular. The results of previous systematic reviews and meta-analyses of n-3 LCPUFA supplementation on ASD outcomes were inconclusive. Two meta-analyses were conducted; meta-analysis 1 compared blood levels of LCPUFA and their ratios arachidonic acid (ARA) to docosahexaenoic acid (DHA), ARA to eicosapentaenoic acid (EPA), or total n-6 to total n-3 LCPUFA in ASD to those of typically developing individuals (with no neurodevelopmental disorders), and meta-analysis 2 compared the effects of n-3 LCPUFA supplementation to placebo on symptoms of ASD. Case-control studies and randomised controlled trials (RCTs) were identified searching electronic databases up to May, 2016. Mean differences were pooled and analysed using inverse variance models. Heterogeneity was assessed using I(2) statistic. Fifteen case-control studies (n = 1193) were reviewed. Compared with typically developed, ASD populations had lower DHA (−2.14 [95% CI −3.22 to −1.07]; p < 0.0001; I(2) = 97%), EPA (−0.72 [95% CI −1.25 to −0.18]; p = 0.008; I(2) = 88%), and ARA (−0.83 [95% CI, −1.48 to −0.17]; p = 0.01; I(2) = 96%) and higher total n-6 LCPUFA to n-3 LCPUFA ratio (0.42 [95% CI 0.06 to 0.78]; p = 0.02; I(2) = 74%). Four RCTs were included in meta-analysis 2 (n = 107). Compared with placebo, n-3 LCPUFA improved social interaction (−1.96 [95% CI −3.5 to −0.34]; p = 0.02; I(2) = 0) and repetitive and restricted interests and behaviours (−1.08 [95% CI −2.17 to −0.01]; p = 0.05; I(2) = 0). Populations with ASD have lower n-3 LCPUFA status and n-3 LCPUFA supplementation can potentially improve some ASD symptoms. Further research with large sample size and adequate study duration is warranted to confirm the efficacy of n-3 LCPUFA.

McGorry, P. D., B. Nelson, et al. (2017). ***"Effect of ω-3 polyunsaturated fatty acids in young people at ultrahigh risk for psychotic disorders: The neurapro randomized clinical trial."*** JAMA Psychiatry 74(1): 19-27. http://dx.doi.org/10.1001/jamapsychiatry.2016.2902

Importance A promising treatment to prevent onset and improve outcomes in patients at ultrahigh risk for psychosis is dietary supplementation with long-chain ω-3 polyunsaturated fatty acids (PUFAs).Objective To determine whether treatment with ω-3 PUFAs in combination with a high-quality psychosocial intervention (cognitive behavioral case management [CBCM]) is more effective than placebo plus CBCM.Design, Setting, and Participants NEURAPRO, a double-blind, placebo-controlled, randomized clinical trial, was conducted from March 1, 2010, to September 30, 2014, in 10 specialized early psychosis treatment services in Australia, Asia, and Europe. The primary analysis used the intention-to-treat approach.Interventions A daily dose of 1.4 g of ω-3 PUFAs or placebo (paraffin oil), plus 20 or fewer sessions of CBCM over the 6-month study period.Main Outcomes and Measures The primary outcome was transition to psychosis status at 6 months. The secondary outcomes were general levels of psychopathology and functioning, as assessed by the Brief Psychiatric Rating Scale (BPRS) (range, 24-168), Scale for the Assessment of Negative Symptoms (SANS) (range, 0-125), Montgomery-Åsberg Depression Rating Scale (MADRS) (range, 0-60), Young Mania Rating Scale (YMRS) (range, 0-44), Social and Occupational Functioning Assessment Scale (SOFAS) (range, 0-100), and the Global Functioning: Social and Role scale (range, 0-10). For SOFAS and Global Functioning: Social and Role scale, higher scores were better; for other measures, lower scores were better.Results In this study of 304 adults at ultrahigh risk for psychotic disorders, 153 (50.3%) received ω-3 PUFAs and 151 (49.7%) received placebo. In all, 139 (45.7%) were male; mean (SD) age was 19.1 (4.6) years. The Kaplan-Meier–estimated 6-month transition rates were 5.1% (95% CI, 1.3%-8.7%) in the control group and 6.7% (95% CI, 2.3%-10.8%) in the ω-3 PUFA group. At 12 months, the rates were 11.2% (95% CI, 5.5%-16.7%) in the control group and 11.5% (95% CI, 5.8%-16.9%) in the ω-3 PUFA group. No significant difference was observed between the transition rates of both groups (hazard ratio, 1.1; 95% CI, 0.55-2.23; P = .76, stratified log-rank test).Conclusions and Relevance This trial clearly failed to replicate the findings of the original single-center trial. The most likely explanation is that ω-3 PUFAs lack efficacy under these conditions. However, the lower-than-expected transition rate may have prevented a test of the main hypothesis. Given the substantial symptomatic and functional improvement in both groups, the other treatments received (ie, CBCM and antidepressants) likely produced a ceiling effect beyond which ω-3 PUFAs, even if effective, could not be shown to confer additional benefits. Nevertheless, the main conclusion is that ω-3 PUFAs are not effective under conditions where good quality, evidence-based psychosocial treatment is available.

Nelson, J. C. and D. A. Spyker (2017). ***"Morbidity and mortality associated with medications used in the treatment of depression: An analysis of cases reported to u.S. Poison control centers, 2000–2014."*** American Journal of Psychiatry 174(5): 438-450. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2016.16050523

Objective: The authors sought to determine the relative morbidity and mortality associated with drugs used to treat depression and to examine specific clinical effects associated with serious outcomes. Method: The National Poison Data System, which receives exposure reports from regional poison centers serving the United States, Puerto Rico, and the District of Columbia, was queried for single drug exposures in individuals 12 years and older during the period 2000–2014. Medications included were antidepressants, atypical antipsychotics, anticonvulsants, lithium, and other medications used in the treatment of depression. The main outcomes were the morbidity index (the number of serious outcomes per 1,000 exposures) and the mortality index (the number of fatal outcomes per 10,000 exposures). Results: During this 15-year period, there were 962,222 single substance exposures to the 48 medications studied. Serious outcomes rose 2.26-fold and in linear fashion over the 15 years. While tricyclic and monoamine oxidase inhibitor medications were associated with high morbidity and mortality, several newer agents also appeared hazardous. Lithium, quetiapine, olanzapine, bupropion, and carbamazepine were associated with high morbidity indices. Lithium, venlafaxine, bupropion, quetiapine, olanzapine, ziprasidone, valproic acid, carbamazepine, and citalopram were associated with higher mortality indices. Conclusions: Serious outcomes after overdose or nonintentional exposures to medications used to treat depression have risen dramatically over the past 15 years. The present data suggest that the morbidity and mortality risks vary substantially among these medications. These differences become important when selecting treatments for patients with depression, especially those at increased risk for suicide.

Ng, Q. X., N. Venkatanarayanan, et al. (2017). ***"Clinical use of hypericum perforatum (st john's wort) in depression: A meta-analysis."*** Journal of Affective Disorders 210: 211-221. http://www.sciencedirect.com/science/article/pii/S0165032716315920

Abstract Introduction St John's wort is a popular herbal remedy recommended by Traditional Chinese Medicine (TCM) practitioners and licensed and widely prescribed for depression in many European countries. However, conflicting data regarding its benefits and risks exist, and the last large meta-analysis on St John's wort use for depression was done in 2008, with no updated meta-analysis available. Methods Using the keywords [St John's Wort OR Hypericum perforatum OR hypericin OR hyperforin OR johanniskraut OR圣约翰草] AND [depression OR antidepressant OR SSRI], a preliminary search (without language restriction) on the PubMed, Ovid, Clinical Trials Register of the Cochrane Collaboration Depression, Anxiety and Neurosis Group, Cochrane Field for Complementary Medicine, China National Knowledge Infrastructure and WanFang database yielded 5428 papers between 1-Jan-1960 and 1-May-2016. Results 27 clinical trials with a total of 3808 patients were reviewed, comparing the use of St John's wort and SSRI. In patients with depression, St John's wort demonstrated comparable response (pooled RR 0.983, 95% CI 0.924–1.042, p<0.001) and remission (pooled RR 1.013, 95% CI 0.892–1.134, p<0.001) rate, and significantly lower discontinuation/dropout (pooled OR 0.587, 95% CI 0.478–0.697, p<0.001) rate compared to standard SSRIs. The pooled SMD from baseline HAM-D scores (pooled SMD −0.068, 95% CI −0.127 to 0.021, p<0.001) also support its significant clinical efficacy in ameliorating depressive symptoms. Limitations Evidence on the long-term efficacy and safety of St. John's wort is limited as the duration of all available studies ranged from 4 to 12 weeks. It is also unclear if St John's wort would be beneficial for patients with severe depression, high suicidality or suicide risk. Conclusion For patients with mild-to-moderate depression, St John's wort has comparable efficacy and safety when compared to SSRIs. Follow-up studies carried out over a longer duration should be planned to ascertain its benefits.

Opie, R. S., C. Itsiopoulos, et al. (2017). ***"Dietary recommendations for the prevention of depression."*** Nutr Neurosci 20(3): 161-171. http://www.tandfonline.com/doi/abs/10.1179/1476830515Y.0000000043?journalCode=ynns20

BACKGROUND: Major depressive disorder is a common, chronic condition that imposes a substantial burden of disability globally. As current treatments are estimated to address only one-third of the disease burden of depressive disorders, there is a need for new approaches to prevent depression or to delay its progression. While in its early stages, converging evidence from laboratory, population research, and clinical trials now suggests that dietary patterns and specific dietary factors may influence the risk for depression. However, largely as a result of the recency of the nutritional psychiatry field, there are currently no dietary recommendations for depression. AIM: The aim of this paper is to provide a set of practical dietary recommendations for the prevention of depression, based on the best available current evidence, in order to inform public health and clinical recommendations. RESULTS: Five key dietary recommendations for the prevention of depression emerged from current published evidence. These comprise: (1) follow 'traditional' dietary patterns, such as the Mediterranean, Norwegian, or Japanese diet; (2) increase consumption of fruits, vegetables, legumes, wholegrain cereals, nuts, and seeds; (3) include a high consumption of foods rich in omega-3 polyunsaturated fatty acids; (4) replace unhealthy foods with wholesome nutritious foods; (5) limit your intake of processed-foods, 'fast' foods, commercial bakery goods, and sweets. CONCLUSION: Although there are a number of gaps in the scientific literature to date, existing evidence suggests that a combination of healthful dietary practices may reduce the risk of developing depression. It is imperative to remain mindful of any protective effects that are likely to come from the cumulative and synergic effect of nutrients that comprise the whole-diet, rather than from the effects of individual nutrients or single foods. As the body of evidence grows from controlled intervention studies on dietary patterns and depression, these recommendations should be modified accordingly.

Opie, R. S., A. O'Neil, et al. (2017). ***"A modified mediterranean dietary intervention for adults with major depression: Dietary protocol and feasibility data from the smiles trial."*** Nutritional Neuroscience: 1-15. http://dx.doi.org/10.1080/1028415X.2017.1312841

(Available in free full text) Background: The SMILES trial was the first randomized controlled trial (RCT) explicitly designed to evaluate a dietary intervention, conducted by qualified dietitians, for reducing depressive symptomatology in adults with clinical depression.Objectives: Here we detail the development of the prescribed diet (modified Mediterranean diet (ModiMedDiet)) for individuals with major depressive disorders (MDDs) that was designed specifically for the SMILES trial. We also present data demonstrating the extent to which this intervention achieved improvements in diet quality.Methods: The ModiMedDiet was designed using a combination of existing dietary guidelines and scientific evidence from the emerging field of nutritional psychiatric epidemiology. Sixty-seven community dwelling individuals (Melbourne, Australia) aged 18 years or over, with current poor quality diets, and MDDs were enrolled into the SMILES trial. A retention rate of 93.9 and 73.5% was observed for the dietary intervention and social support control group, respectively. The dietary intervention (ModiMedDiet) consisted of seven individual nutrition counselling sessions delivered by a qualified dietitian. The control condition comprised a social support protocol matched to the same visit schedule and length.Results: This manuscript details the first prescriptive individualized dietary intervention delivered by dietitians for adults with major depression. Significant improvements in dietary quality were observed among individuals randomized to the ModiMedDiet group. These dietary improvements were also found to be associated with changes in depressive symptoms.Discussion/Conclusion: The ModiMedDiet, a novel and individually tailored intervention designed specifically for adults with major depression, can be effectively implemented in clinical practice to manage this highly prevalent and debilitating condition.

Pinto-Sanchez, M. I., G. B. Hall, et al. (2017). ***"Probiotic bifidobacterium longum ncc3001 reduces depression scores and alters brain activity: A pilot study in patients with irritable bowel syndrome."*** Gastroenterology. http://dx.doi.org/10.1053/j.gastro.2017.05.003

Background & Aims Probiotics can reduce symptoms of irritable bowel syndrome (IBS), but little is known about their effects on psychiatric comorbidities. We performed a prospective study to evaluate the effects of Bifidobacterium longum NCC3001 (BL) on anxiety and depression in patients with IBS. Methods We performed a randomized, double-blind, placebo-controlled study of 44 adults with IBS and diarrhea or a mixed-stool pattern (based on Rome III criteria) and mild to moderate anxiety and/or depression (based on the Hospital Anxiety and Depression scale) at McMaster University in Canada, from March 2011 to May 2014. At the screening visit, clinical history and symptoms were assessed and blood samples were collected. Patients were then randomly assigned to groups and given daily BL (n = 22) or placebo (n = 22) for 6 weeks. At weeks 0, 6, and 10, we determined patients' levels of anxiety and depression, IBS symptoms, quality of life, and somatization using validated questionnaires. At weeks 0 and 6, stool, urine and blood samples were collected, and functional magnetic resonance imaging (fMRI) test was performed. We assessed brain activation patterns, fecal microbiota, urine metabolome profiles, serum markers of inflammation, neurotransmitters, and neurotrophin levels. Results At week 6, 14 of 22 patients in the BL group had reduction in depression scores of 2 points or more on the Hospital Anxiety and Depression scale, vs 7 of 22 patients in the placebo group (P = .04). BL had no significant effect on anxiety or IBS symptoms. Patients in the BL group had a mean increase in quality of life score compared with the placebo group. The fMRI analysis showed that BL reduced responses to negative emotional stimuli in multiple brain areas, including amygdala and fronto-limbic regions, compared with placebo. The groups had similar fecal microbiota profiles, serum markers of inflammation, and levels of neurotrophins and neurotransmitters, but the BL group had reduced urine levels of methylamines and aromatic amino acids metabolites. At week 10, depression scores were

reduced in patients given BL vs placebo. Conclusion In a placebo-controlled trial, we found that the probiotic BL reduces depression but not anxiety scores and increases quality of life in patients with IBS. These improvements were associated with changes in brain activation patterns that indicate that this probiotic reduces limbic reactivity.

Siahbazi, S., S. Behboudi-Gandevani, et al. (2017). ***"Effect of zinc sulfate supplementation on premenstrual syndrome and health-related quality of life: Clinical randomized controlled trial."*** Journal of Obstetrics and Gynaecology Research 43(5): 887-894. http://dx.doi.org/10.1111/jog.13299

Aim: The purpose of study was to assess the effect of zinc sulfate (ZS) supplementation on premenstrual syndrome (PMS) and health-related quality of life (QoL). Methods: This was a double-blind randomized and placebo-controlled trial using the parallel technique conducted between June 2013 and May 2014. A total of 142 women (age, 20–35 years) with PMS were allocated to either the ZS or placebo group. The women in the intervention group received ZS 220-mg capsules (containing 50 mg elemental zinc) from the 16th day of the menstrual cycle to the second day of the next cycle. Data were collected using the Premenstrual Symptoms Screening Tool (PSST) and 12-item Short-Form Health Survey Questionnaire. Result: The prevalence of moderate to severe PMS in the ZS group significantly decreased throughout the study period (9.5% in the first, 6% in the second and 2.6% in the third month of the study, P < 0.001), but in the control placebo group this reduction was seen only in the first month of the study (14.2% in the first, 13.7% in the second and 13.5% in the third month, P = 0.08). Also, ZS improved the PSST component scores throughout the study period. The mean scores of QoL in physical and mental components were significantly improved in the ZS intervention group. However, the differences were statistically significant only 3 months after the intervention. Conclusion: Zinc sulfate, as a simple and inexpensive treatment, was associated with improvement of PMS symptoms and health-related QoL. Additional studies are warranted to confirm these findings.

Slyepchenko, A., M. Maes, et al. (2017). ***"Gut microbiota, bacterial translocation, and interactions with diet: Pathophysiological links between major depressive disorder and non-communicable medical comorbidities."*** Psychother Psychosom 86(1): 31-46. https://www.karger.com/Article/Abstract/448957

BACKGROUND: Persistent low-grade immune-inflammatory processes, oxidative and nitrosative stress (O&NS), and hypothalamic-pituitary-adrenal axis activation are integral to the pathophysiology of major depressive disorder (MDD). The microbiome, intestinal compositional changes, and resultant bacterial translocation add a new element to the bidirectional interactions of the gut-brain axis; new evidence implicates these pathways in the patho-aetiology of MDD. In addition, abnormalities in the gut-brain axis are associated with several chronic non-communicable disorders, which frequently co-occur in individuals with MDD, including but not limited to irritable bowel syndrome (IBS), chronic fatigue syndrome (CFS), obesity, and type 2 diabetes mellitus (T2DM). METHODS: We searched the PubMed/MEDLINE database up until May 1, 2016 for studies which investigated intestinal dysbiosis and bacterial translocation (the 'leaky gut') in the pathophysiology of MDD and co-occurring somatic comorbidities with an emphasis on IBS, CFS, obesity, and T2DM. RESULTS: The composition of the gut microbiota is influenced by several genetic and environmental factors (e.g. diet). Several lines of evidence indicate that gut-microbiota-diet interactions play a significant pathophysiological role in MDD and related medical comorbidities. Gut dysbiosis and the leaky gut may influence several pathways implicated in the biology of MDD, including but not limited to immune activation, O&NS, and neuroplasticity cascades. However, methodological inconsistencies and limitations limit comparisons across studies. CONCLUSIONS: Intestinal dysbiosis and the leaky gut may constitute a key pathophysiological link between MDD and its medical comorbidities. This emerging literature opens relevant preventative and therapeutic perspectives.

Sujan, A. C., M. E. Rickert, et al. (2017). ***"Associations of maternal antidepressant use during the first trimester of pregnancy with preterm birth, small for gestational age, autism spectrum disorder, and attention-deficit/hyperactivity disorder in offspring."*** JAMA 317(15): 1553-1562. http://dx.doi.org/10.1001/jama.2017.3413

Importance Prenatal antidepressant exposure has been associated with adverse outcomes. Previous studies, however, may not have adequately accounted for confounding.Objective To evaluate alternative hypotheses for associations between first-trimester antidepressant exposure and birth and neurodevelopmental problems.Design, Setting, and Participants This retrospective cohort study included Swedish offspring born between 1996 and 2012 and followed up through 2013 or censored by death or emigration. Analyses controlling for pregnancy, maternal and paternal covariates, as well as sibling comparisons, timing of exposure comparisons, and paternal comparisons, were used to examine the associations.Exposures Maternal self-reported first-trimester antidepressant use and first-trimester antidepressant dispensations. Main Outcomes and Measures Preterm birth (<37 gestational weeks), small for gestational age (birth weight <2 SDs below the mean for gestational age), and first inpatient or outpatient clinical diagnosis of autism spectrum disorder and attention-deficit/hyperactivity disorder in offspring.Results Among 1 580 629 offspring (mean gestational age, 279 days; 48.6% female; 1.4% [n = 22 544] with maternal first-trimester self-reported antidepressant use) born to 943 776 mothers (mean age at childbirth, 30 years), 6.98% of exposed vs 4.78% of unexposed offspring were preterm, 2.54% of exposed vs 2.19% of unexposed were small for gestational age, 5.28% of exposed vs 2.14% of unexposed were diagnosed with autism spectrum disorder by age 15 years, and 12.63% of exposed vs 5.46% of unexposed were diagnosed with attention-deficit/hyperactivity disorder by age 15 years. At the population level, first-trimester exposure was associated with all outcomes compared with unexposed offspring (preterm birth odds ratio [OR], 1.47 [95% CI, 1.40-1.55]; small for gestational age OR, 1.15 [95% CI, 1.06-1.25]; autism spectrum disorder hazard ratio [HR], 2.02 [95% CI, 1.80-2.26]; attention-deficit/hyperactivity disorder HR, 2.21 [95% CI, 2.04-2.39]). However, in models that compared siblings while adjusting for pregnancy, maternal, and paternal traits, first-trimester antidepressant exposure was associated with preterm birth (OR, 1.34 [95% CI, 1.18-1.52]) but not with small for gestational age (OR, 1.01 [95% CI, 0.81-1.25]), autism spectrum disorder (HR, 0.83 [95% CI, 0.62-1.13]), or attention-deficit/hyperactivity disorder (HR, 0.99 [95% CI, 0.79-1.25]). Results from analyses assessing associations with maternal dispensations before pregnancy and with paternal first-trimester dispensations were consistent with findings from the sibling comparisons. Conclusions and Relevance Among offspring born in Sweden, after accounting for confounding factors, first-trimester exposure to antidepressants, compared with no exposure, was associated with a small increased risk of preterm birth but no increased risk of small for gestational age, autism spectrum disorder, or attention-deficit/hyperactivity disorder.

Thornicroft, G., S. Chatterji, et al. (2017). ***"Undertreatment of people with major depressive disorder in 21 countries."*** The British Journal of Psychiatry 210(2): 119-124. http://bjp.rcpsych.org/content/210/2/119

Background Major depressive disorder (MDD) is a leading cause of disability worldwide. Aims To examine the: (a) 12-month prevalence of DSM-IV MDD; (b) proportion aware that they have a problem needing treatment and who want care; (c) proportion of the latter receiving treatment; and (d) proportion of such treatment meeting minimal standards.MethodRepresentative community household surveys from 21 countries as part of the World Health Organization World Mental Health Surveys. Results Of 51 547 respondents, 4.6% met 12-month criteria for DSM-IV MDD and of these 56.7% reported needing treatment. Among those who recognised their need for treatment, most (71.1%) made at least one visit to a service provider. Among those who received treatment, only 41.0% received treatment that met minimal standards. This

resulted in only 16.5% of all individuals with 12-month MDD receiving minimally adequate treatment. Conclusions Only a minority of participants with MDD received minimally adequate treatment: 1 in 5 people in high-income and 1 in 27 in low-/lower-middle-income countries. Scaling up care for MDD requires fundamental transformations in community education and outreach, supply of treatment and quality of services.

Ustun, B., L. A. Adler, et al. (2017). ***"The world health organization adult attention-deficit/hyperactivity disorder self-report screening scale for dsm-5."*** JAMA Psychiatry. http://dx.doi.org/10.1001/jamapsychiatry.2017.0298

Importance Recognition that adult attention-deficit/hyperactivity disorder (ADHD) is common, seriously impairing, and usually undiagnosed has led to the development of adult ADHD screening scales for use in community, workplace, and primary care settings. However, these scales are all calibrated to DSM-IV criteria, which are narrower than the recently developed DSM-5 criteria.Objectives To update for DSM-5 criteria and improve the operating characteristics of the widely used World Health Organization Adult ADHD Self-Report Scale (ASRS) for screening.Design, Setting, and Participants Probability subsamples of participants in 2 general population surveys (2001-2003 household survey [n = 119] and 2004-2005 managed care subscriber survey [n = 218]) who completed the full 29-question self-report ASRS, with both subsamples over-sampling ASRS-screened positives, were blindly administered a semistructured research diagnostic interview for DSM-5 adult ADHD. In 2016, the Risk-Calibrated Supersparse Linear Integer Model, a novel machine-learning algorithm designed to create screening scales with optimal integer weights and limited numbers of screening questions, was applied to the pooled data to create a DSM-5 version of the ASRS screening scale. The accuracy of the new scale was then confirmed in an independent 2011-2012 clinical sample of patients seeking evaluation at the New York University Langone Medical Center Adult ADHD Program (NYU Langone) and 2015-2016 primary care controls (n = 300). Data analysis was conducted from April 4, 2016, to September 22, 2016.Main Outcomes and Measures The sensitivity, specificity, area under the curve (AUC), and positive predictive value (PPV) of the revised ASRS.Results Of the total 637 participants, 44 (37.0%) household survey respondents, 51 (23.4%) managed care respondents, and 173 (57.7%) NYU Langone respondents met DSM-5 criteria for adult ADHD in the semistructured diagnostic interview. Of the respondents who met DSM-5 criteria for adult ADHD, 123 were male (45.9%); mean (SD) age was 33.1 (11.4) years. A 6-question screening scale was found to be optimal in distinguishing cases from noncases in the first 2 samples. Operating characteristics were excellent at the diagnostic threshold in the weighted (to the 8.2% DSM-5/Adult ADHD Clinical Diagnostic Scale population prevalence) data (sensitivity, 91.4%; specificity, 96.0%; AUC, 0.94; PPV, 67.3%). Operating characteristics were similar despite a much higher prevalence (57.7%) when the scale was applied to the NYU Langone clinical sample (sensitivity, 91.9%; specificity, 74.0%; AUC, 0.83; PPV, 82.8%). Conclusions and Relevance The new ADHD screening scale is short, easily scored, detects the vast majority of general population cases at a threshold that also has high specificity and PPV, and could be used as a screening tool in specialty treatment settings.

Viktorin, A., E. Rydén, et al. (2017). ***"The risk of treatment-emergent mania with methylphenidate in bipolar disorder."*** American Journal of Psychiatry 174(4): 341-348. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2016.16040467

Objective: The authors sought to determine the risk of treatment-emergent mania associated with methylphenidate, used in monotherapy or with a concomitant mood-stabilizing medication, in patients with bipolar disorder. Method: Using linked Swedish national registries, the authors identified 2,307 adults with bipolar disorder who initiated therapy with methylphenidate between 2006 and 2014. The cohort was divided into two groups: those with and those without concomitant mood-stabilizing treatment. To adjust for individual-specific confounders, including disorder severity, genetic makeup, and early environmental factors, Cox regression analyses were used, conditioning on individual to compare the rate of mania (defined as hospitalization for mania or a new dispensation of stabilizing medication) 0–3 months and 3–6 months after medication start following nontreated periods. Results: Patients on methylphenidate monotherapy displayed an increased rate of manic episodes within 3 months of medication initiation (hazard ratio=6.7, 95% CI=2.0–22.4), with similar results for the subsequent 3 months. By contrast, for patients taking mood stabilizers, the risk of mania was lower after starting methylphenidate (hazard ratio=0.6, 95% CI=0.4–0.9). Comparable results were observed when only hospitalizations for mania were counted. Conclusions: No evidence was found for a positive association between methylphenidate and treatment-emergent mania among patients with bipolar disorder who were concomitantly receiving a mood-stabilizing medication. This is clinically important given that up to 20% of people with bipolar disorder suffer from comorbid ADHD. Given the markedly increased hazard ratio of mania following methylphenidate initiation in bipolar patients not taking mood stabilizers, careful assessment to rule out bipolar disorder is indicated before initiating monotherapy with psychostimulants.

Walkup, J. T. (2017). ***"Antidepressant efficacy for depression in children and adolescents: Industry- and nimh-funded studies."*** American Journal of Psychiatry 174(5): 430-437. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2017.16091059

Significant controversy surrounds the efficacy of the newer antidepressants for children and adolescents with depression. The controversy largely hinges on meta-analyses of studies that suggest that antidepressants are minimally effective, not effective, or equivalent to placebo. In this review, the author discusses several scientific and clinical complexities that are important to understand in reviewing the antidepressant literature: the strengths and weaknesses of meta-analyses; the scientific and regulatory context for the large number of antidepressant trials in the late 1990s and early 2000s; and the distinction between a negative trial, where the treatment does not demonstrate efficacy, and a failed trial, where methodological problems make it impossible to draw any conclusion about efficacy. It is the premise of this review that meta-analyses that include the large number of industry-sponsored antidepressant trials distort the picture of antidepressant efficacy for teen depression. Industry-sponsored child and adolescent depression trials suffer from a number of implementation challenges and should be considered failed trials that are largely uninformative and not eligible to be included in efficacy meta-analyses. In contrast to the industry-sponsored trials, depression trials funded by the National Institute of Mental Health (NIMH) (N=2) are characterized by many methodological strengths, lower placebo response rates (30%−35%), and meaningful between-group differences (25%−30%) that support antidepressant efficacy. The NIMH-funded trials, taken together with the demonstrated efficacy of the serotonin reuptake inhibitors for childhood-onset obsessive-compulsive disorder and the anxiety disorders, suggest a broad and important role for antidepressant medications in pediatric internalizing conditions.

Wallace, C. J. K. and R. Milev (2017). ***"The effects of probiotics on depressive symptoms in humans: A systematic review."*** Annals of General Psychiatry 16: 14. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5319175/

(Available in free full text) BACKGROUND: Patients suffering from depression experience significant mood, anxiety, and cognitive symptoms. Currently, most antidepressants work by altering neurotransmitter activity in the brain to improve these symptoms. However, in the last decade, research has revealed an extensive bidirectional communication network between the gastrointestinal tract and the central nervous system, referred to as the "gut–brain axis." Advances in this field have linked psychiatric disorders to changes in the microbiome, making it a potential target for novel antidepressant treatments. The aim of this review is to analyze the current body of research assessing the effects of probiotics, on symptoms of depression in humans.

METHODS: A systematic search of five databases was performed and study selection was completed using the preferred reporting items for systematic reviews and meta-analyses process. RESULTS: Ten studies met criteria and were analyzed for effects on mood, anxiety, and cognition. Five studies assessed mood symptoms, seven studies assessed anxiety symptoms, and three studies assessed cognition. The majority of the studies found positive results on all measures of depressive symptoms; however, the strain of probiotic, the dosing, and duration of treatment varied widely and no studies assessed sleep. CONCLUSION: The evidence for probiotics alleviating depressive symptoms is compelling but additional double-blind randomized control trials in clinical populations are warranted to further assess efficacy.

Wiens, K., J. V. A. Williams, et al. (2017). ***"Is the prevalence of major depression increasing in the canadian adolescent population? Assessing trends from 2000 to 2014."*** Journal of Affective Disorders 210: 22-26. http://www.sciencedirect.com/science/article/pii/S0165032716315798

AbstractBackground Major depressive disorder is a relatively common diagnosis with onset across the lifespan. There is a recent belief that major depressive episodes (MDE) are increasing in adolescence; however, it is not clear if this is truly an increase in prevalence or reflective of other causes such as change in diagnostic patterns. This study aimed to determine whether evidence supports an epidemic of MDE in Canadian adolescents. Methods Past year MDE prevalence estimates were derived from a series of nationally representative surveys. Random effects meta-regression and graphical analyses were used to evaluate trends. A post hoc analysis compared trends in MDE prevalence to trends in self-reported mood disorder diagnosis (made by a health professional). The sample was split into 9 birth cohorts to examine whether MDE prevalence increased in more recent cohorts. Results Prevalence of MDE did not significantly change between 2000 and 2014 (β=0.001; p=0.532), and there was no modification of trends by sex or age. However, prevalence of self-reported mood disorder diagnosis by a health professional increased from 2003 to 2014 (β=0.001; p=0.024). There was no indication that MDE prevalence differed by birth cohort. Limitations Limitations include reduced precision in subgroup analyses, lack of clinical judgement in the structured diagnostic interview, and inability to differentiate mild, moderate and severe episodes of depression. Conclusion These findings do not support an epidemic of MDE in adolescents, however as more individuals report diagnoses by a health professional, future policy may need to incorporate an increase in need of mental health services.