40 depression-relevant abstracts may '16 newsletter

(Lindhiem, Bennett et al. 2015; Chisholm, Sweeny et al. 2016; Chisolm and Payne 2016; Coupland, Hill et al. 2016; Curtin, Warner et al. 2016; Delitala, Terracciano et al. 2016; Durgam, Earley et al. 2016; Edmondson, Brennan et al. 2016; Erlich and Psychopathology 2016; Geddes, Gardiner et al. 2016; Granek, Danan et al. 2016; Guidi, Tomba et al. 2016; Haugen, Haavet et al. 2016; Hughes, Cardno et al. 2016; Infurna, Reichl et al. 2016; Jakubovski, Varigonda et al. 2016; Ketter, Miller et al. 2016; Kirov, Owen et al. 2016; Kitsune, Kuntsi et al. 2016; Legrand and Neff 2016; Li and Prigerson 2016; Marangoni, Hernandez et al. 2016; Mehta-Raghavan, Wert et al. 2016; Mirza, Wolters et al. 2016; Mojtabai 2016; O'Neil, Fisher et al. 2016; O'Hare, O'Sullivan et al. 2016; Oud, Mayo-Wilson et al. 2016; Richards, Bower et al. 2016; Robinson and Jorge 2016; Rodríguez-Cano, López-Durán et al. 2016; Rosenblat, Kakar et al. 2016; Sarris, Murphy et al. 2016; Sharma, Guski et al. 2016; Traffanstedt, Mehta et al. 2016; Uher and Pavlova 2016; Vigod, Wilson et al. 2016; Wagener, Baeyens et al. 2016; Williams, Pasco et al. 2016; Yary, Lehto et al. 2016)

Chisholm, D., K. Sweeny, et al. (2016). ***"Scaling-up treatment of depression and anxiety: A global return on investment analysis."*** The Lancet Psychiatry. http://dx.doi.org/10.1016/S2215-0366(16)30024-4

(Available in free full text) Background Depression and anxiety disorders are highly prevalent and disabling disorders, which result not only in an enormous amount of human misery and lost health, but also lost economic output. Here we propose a global investment case for a scaled-up response to the public health and economic burden of depression and anxiety disorders. Methods In this global return on investment analysis, we used the mental health module of the OneHealth tool to calculate treatment costs and health outcomes in 36 countries between 2016 and 2030. We assumed a linear increase in treatment coverage. We factored in a modest improvement of 5% in both the ability to work and productivity at work as a result of treatment, subsequently mapped to the prevailing rates of labour participation and gross domestic product (GDP) per worker in each country. Findings The net present value of investment needed over the period 2016–30 to substantially scale up effective treatment coverage for depression and anxiety disorders is estimated to be US$147 billion. The expected returns to this investment are also substantial. In terms of health impact, scaled-up treatment leads to 43 million extra years of healthy life over the scale-up period. Placing an economic value on these healthy life-years produces a net present value of $310 billion. As well as these intrinsic benefits associated with improved health, scaled-up treatment of common mental disorders also leads to large economic productivity gains (a net present value of $230 billion for scaled-up depression treatment and $169 billion for anxiety disorders). Across country income groups, resulting benefit to cost ratios amount to 2·3–3·0 to 1 when economic benefits only are considered, and 3·3–5·7 to 1 when the value of health returns is also included. Interpretation Return on investment analysis of the kind reported here can contribute strongly to a balanced investment case for enhanced action to address the large and growing burden of common mental disorders worldwide.

Chisolm, M. S. and J. L. Payne (2016). ***"Management of psychotropic drugs during pregnancy."*** BMJ 352. http://www.bmj.com/content/bmj/352/bmj.h5918.full.pdf

Psychiatric conditions (including substance misuse disorders) are serious, potentially life threatening illnesses that can be successfully treated by psychotropic drugs, even during pregnancy. Because few rigorously designed prospective studies have examined the safety of these drugs during pregnancy, the default clinical recommendation has been to discontinue them, especially during the first trimester. However, in the past decade, as more evidence has accumulated, it seems that most psychotropic drugs are relatively safe to use in pregnancy and that not using them when indicated for serious psychiatric illness poses a greater risk to both mother and child, including tragic outcomes like suicide and infanticide. This review presents an up to date and careful examination of the most rigorous scientific studies on the effects of psychotropic drugs in pregnancy. The lack of evidence in several areas means that definite conclusions cannot be made about the risks and benefits of all psychotropic drug use in pregnancy.

Coupland, C., T. Hill, et al. (2016). ***"Antidepressant use and risk of cardiovascular outcomes in people aged 20 to 64: Cohort study using primary care database."*** BMJ 352. http://www.bmj.com/content/bmj/352/bmj.i1350.full.pdf

Objective To assess associations between different antidepressant treatments and rates of three cardiovascular outcomes (myocardial infarction, stroke or transient ischaemic attack, and arrhythmia) in people with depression.Design Cohort study.Setting UK general practices contributing to the QResearch primary care database.Participants 238 963 patients aged 20 to 64 years with a first diagnosis of depression between 1 January 2000 and 31 July 2011.Exposures Antidepressant class (tricyclic and related antidepressants, selective serotonin reuptake inhibitors, other antidepressants), dose, duration of use, and commonly prescribed individual antidepressant drugs.Main outcome measures First diagnoses of myocardial infarction, stroke or transient ischaemic attack, and arrhythmia during five years' follow-up. Cox proportional hazards models were used to estimate hazard ratios, adjusting for potential confounding variables.Results During five years of follow-up, 772 patients had a myocardial infarction, 1106 had a stroke or transient ischaemic attack, and 1452 were diagnosed as having arrhythmia. No significant associations were found between antidepressant class and myocardial infarction over five years' follow-up. In the first year of follow-up, patients treated with selective serotonin reuptake inhibitors had a significantly reduced risk of myocardial infarction (adjusted hazard ratio 0.58, 95% confidence interval 0.42 to 0.79) compared with no use of antidepressants; among individual drugs, fluoxetine was associated with a significantly reduced risk (0.44, 0.27 to 0.72) and lofepramine with a significantly increased risk (3.07, 1.50 to 6.26). No significant associations were found between antidepressant class or individual drugs and risk of stroke or transient ischaemic attack. Antidepressant class was not significantly associated with arrhythmia over five years' follow-up, although the risk was significantly increased during the first 28 days of treatment with tricyclic and related antidepressants (adjusted hazard ratio 1.99, 1.27 to 3.13). Fluoxetine was associated with a significantly reduced risk of arrhythmia (0.74, 0.59 to 0.92) over five years, but citalopram was not significantly associated with risk of arrhythmia even at high doses (1.11, 0.72 to 1.71 for doses ≥40 mg/day).Conclusions This study found no evidence that selective serotonin reuptake inhibitors are associated with an increased risk of arrhythmia or stroke/transient ischaemic attack in people diagnosed as having depression between the ages of 20 to 64 or that citalopram is associated with a significantly increased risk of arrhythmia. It found some indication of a reduced risk of myocardial infarction with selective serotonin reuptake inhibitors, particularly fluoxetine, and of an increased risk with lofepramine.

Curtin, S. C., M. Warner, et al. (2016). ***Increase in suicide in the united states, 1999-2014***. U. S. D. o. H. a. H. Services. NCHS Data Brief**:** 1-8.

Data from the National Vital Statistics System - Key Findings

● From 1999 through 2014, the age-adjusted suicide rate in the United States increased 24%, from 10.5 to 13.0 per 100,000 population, with the pace of increase greater after 2006.
● Suicide rates increased from 1999 through 2014 for both males and females and for all ages 10–74.
● The percent increase in suicide rates for females was greatest for those aged 10–14, and for males, those aged 45–64.
● The most frequent suicide method in 2014 for males involved the use of firearms (55.4%), while poisoning was the most frequent method for females (34.1%).
● Percentages of suicides attributable to suffocation increased for both sexes between 1999 and 2014.

Delitala, A. P., A. Terracciano, et al. (2016). ***"Depressive symptoms, thyroid hormone and autoimmunity in a population-based cohort from sardinia."*** Journal of Affective Disorders 191: 82-87. http://www.sciencedirect.com/science/article/pii/S0165032715309125

Objective To evaluate the association between depressive symptoms and thyroid autoimmunity, and the effect of thyroid hormone on the risk of depression. Methods We included 3138 individuals from SardiNIA project, none of whom was taking thyroid medication and antidepressants. Thyrotropin (TSH), free thyroxine (FT4), and antibodies against thyroperoxidase (TPOAb) were measured in all the sample. Depressive symptoms were assessed with Center for Epidemiologic Studies Depression Scale (CES-D). Results We found no association between TPOAb and depressive symptoms and no linear association between TSH or FT4 levels and depressive symptoms. However, individuals in the lowest and highest FT4 quintiles showed a higher CES-D score compared to individuals in the middle quintile. In addition, participants in the lowest and highest FT4 quintiles had an increased risk of CES-D≥16 with odds ratios of 1.44 (95% CI=1.09–1.89) and 1.33 (95% CI=1.01−1.77), respectively. Limitations Cross-sectional design of the study. Conclusions A U-shaped relation was found between FT4 and depressive symptoms: compared to average FT4 values, both high and low thyroid function was associated with more depressive symptoms. Further studies are necessary to determine the exact cause-effect relation of this association.

Durgam, S., W. Earley, et al. (2016). ***"An 8-week randomized, double-blind, placebo-controlled evaluation of the safety and efficacy of cariprazine in patients with bipolar i depression."*** American Journal of Psychiatry 173(3): 271-281. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2015.15020164

Objective: The authors evaluated the efficacy, safety, and tolerability of cariprazine, an atypical antipsychotic candidate, in adult patients with acute bipolar I depression. Method: This was an 8-week multinational, multicenter, randomized, double-blind, placebo-controlled, parallel-group, fixed-dose study in adult patients with bipolar I disorder experiencing a current major depressive episode. Patients were randomly assigned (1:1:1:1) to receive placebo or cariprazine at 0.75, 1.5, or 3.0 mg/day. The primary and secondary efficacy parameters were change from baseline to week 6 on the Montgomery-Åsberg Depression Rating Scale (MADRS) and the Clinical Global Impressions severity subscale (CGI-S), respectively, analyzed using a mixed-effects model for repeated measures on the modified intent-to-treat population. Results: The intent-to-treat population comprised 571 patients (141 in the placebo group and 140, 145, and 145 in the cariprazine 0.75-, 1.5-, and 3.0-mg/day groups). Cariprazine at 1.5 mg/day showed significantly greater improvement on MADRS total score change from baseline to week 6 compared with placebo; the least squares mean difference was −4.0 (95% CI=−6.3, −1.6; significant after adjustment for multiple comparisons). Cariprazine at 3.0 mg/day showed greater MADRS score reduction than placebo (−2.5, 95% CI=−4.9, −0.1; not significant when adjusted for multiple comparisons). The 0.75 mg/day dosage was similar to placebo. A similar pattern for significance was observed on the CGI-S (1.5 mg/day: least squares mean difference=−0.4, 95% CI=−0.6, −0.1; 3.0 mg/day: −0.3, 95% CI=−0.5, −0.0). The most common adverse events (≥10%) in cariprazine-treated patients were akathisia and insomnia; weight gain was slightly higher with cariprazine than with placebo. Conclusions: Cariprazine at 1.5 mg/day demonstrated consistent efficacy compared with placebo across outcomes and was generally well tolerated, suggesting efficacy for the treatment of bipolar I depression.

Edmondson, A. J., C. A. Brennan, et al. (2016). ***"Non-suicidal reasons for self-harm: A systematic review of self-reported accounts."*** Journal of Affective Disorders 191: 109-117. http://www.sciencedirect.com/science/article/pii/S0165032715307485

(Available in free full text) Background Self-harm is a major public health problem yet current healthcare provision is widely regarded as inadequate. One of the barriers to effective healthcare is the lack of a clear understanding of the functions self-harm may serve for the individual. The aim of this review is to identify first-hand accounts of the reasons for self-harm from the individual's perspective. Method A systematic review of the literature reporting first-hand accounts of the reasons for self-harm other than intent to die. A thematic analysis and 'best fit' framework synthesis was undertaken to classify the responses. Results The most widely researched non-suicidal reasons for self-harm were dealing with distress and exerting interpersonal influence. However, many first-hand accounts included reasons such as self-validation, and self-harm to achieve a personal sense of mastery, which suggests individuals thought there were positive or adaptive functions of the act not based only on its social effects. Limitations Associations with different sub-population characteristics or with the method of harm were not available from most studies included in the analysis. Conclusions Our review identified a number of themes that are relatively neglected in discussions about self-harm, which we summarised as self-harm as a positive experience and defining the self. These self-reported "positive" reasons may be important in understanding and responding especially to repeated acts of self-harm.

Erlich, M. D. and f. t. G. C. o. Psychopathology (2016). ***"Envisioning zero suicide."*** Psychiatric Services 67(3): 255-255. http://ps.psychiatryonline.org/doi/abs/10.1176/appi.ps.201500334

(Available in free full text) The incidence of suicide is rising, with devastating consequences. Suicide prevention is one of the greatest challenges facing our health care system and society. Many efforts around the world—randomized controlled trials (RCTs), public information campaigns, primary care initiatives, and restriction of access to lethal means—aim to reduce suicide rates. A 2005 comprehensive analysis of 93 suicide prevention studies concluded that improving education and restricting access to lethal means were the most efficacious preventive efforts. Subsequent studies have had similar findings. For example, a 2008 five-country RCT of brief intervention and contact—assessing low-cost suicide screening and prevention efforts in acute care settings—found that professional encounters for at-risk clients enhanced protective factors and reduced suicide risk. Governmental programs have also had success. For example, Denmark's 1989 program for adolescents curbed access to over-the-counter drugs commonly used in suicide attempts, and Danish rates of suicide, which were once equivalent to U.S. rates in the early 1990s, were halved by 2012 ... Postvention efforts are heterogeneous and imperfect; moreover, there are considerably fewer postvention best practices to guide survivors. Trauma-informed therapies, psychological first aid, and bereavement counseling are effective, but they lack an operationalized approach. Most postvention resources exist to manage school-age and adolescent suicide in order to facilitate appropriate mourning and grief, teach individuals potential warning signs of their own distress, and assist with reestablishing successful coping strategies. Evidence for the success of these efforts for adolescents and their caregivers varies. Two aspects are clear: postvention efforts need to be enhanced for all age groups, and more resources need to be invested in postvention. Suicide prevention is a primary public health goal, and we seek the day

when postvention efforts are unnecessary. Until then, postvention efforts and best practices need to be strengthened. Our language is important. "Envisioning zero" acknowledges the need to vigorously intervene after a suicide until postvention is no longer relevant.

Geddes, J. R., A. Gardiner, et al. (2016). ***"Comparative evaluation of quetiapine plus lamotrigine combination versus quetiapine monotherapy (and folic acid versus placebo) in bipolar depression (cequel): A 2 × 2 factorial randomised trial."*** The Lancet Psychiatry 3(1): 31-39. http://www.sciencedirect.com/science/article/pii/S2215036615004502

(Available in free full text) Background Depressive symptoms are a major cause of disability in bipolar disorder and there are few safe and effective treatments. The combination of lamotrigine plus quetiapine potentially offers improved outcomes for people with bipolar depression. We aimed to determine if combination therapy with quetiapine plus lamotrigine leads to greater improvement in depressive symptoms over 12 weeks than quetiapine monotherapy plus lamotrigine placebo. Methods In this double-blind, randomised, placebo-controlled, parallel group, 2 × 2 factorial trial (CEQUEL), patients with DSM-IV bipolar disorder I or II, who were aged 16 years or older, and required new treatment for a depressive episode, were enrolled from 27 sites in the UK. Patients were randomly assigned (1:1) by an adaptive minimisation algorithm to lamotrigine or placebo and to folic acid or placebo. Participants and investigators were masked to the treatment groups. The primary outcome was improvement in depressive symptoms at 12 weeks with the Quick Inventory of Depressive Symptomatology—self report version 16 (QIDS-SR16). Analysis was by modified intention-to-treat. This trial is registered with EUdraCT, number 2007-004513-33. Findings Between Oct 21, 2008, and April 27, 2012, 202 participants were randomly assigned; 101 to lamotrigine and 101 to placebo. The mean difference in QIDS-SR16 total score between the group receiving lamotrigine versus the placebo group at 12 weeks was −1·73 ([95% CI −3·57 to 0·11]; p=0·066) and at 52 weeks was −2·69 ([−4·89 to −0·49]; p=0·017). Folic acid was not superior to placebo. There was a significant interaction (p=0·028), with folic acid reducing the effectiveness of lamotrigine at 12 weeks. The mean difference on QIDS-SR16 was −4·14 ([95% CI −6·90 to −1·37]; p=0·004) for patients receiving lamotrigine without folic acid compared with 0·12 ([−2·58 to 2·82]; p=0·931) for those receiving lamotrigine and folic acid. Interpretation Addition of lamotrigine to quetiapine treatment improved outcomes. Folic acid seems to nullify the effect of lamotrigine. CEQUEL should encourage clinicians and patients to consider lamotrigine for bipolar depression, but also to be aware that concurrent folic acid might reduce its effectiveness. Funding Medical Research Council.

Granek, L., D. Danan, et al. (2016). ***"Living with bipolar disorder: The impact on patients, spouses, and their marital relationship."*** Bipolar Disorders 18(2): 192-199. http://dx.doi.org/10.1111/bdi.12370

Objectives Patients with bipolar disorder are characterized by an unusually high divorce rate. As such, the purpose of the present study was to uncover information relating specifically to the impact of bipolar disorder on patients and spouses individually, and on the marital relationship from the perspectives of both patients and spouses. Methods Eleven patients with bipolar disorder and ten spouses were interviewed separately about the impact of bipolar disorder on their lives and on their marital relationship. Data were analyzed using the grounded theory method. Results The impact of bipolar disorder for spouses included self-sacrifice, caregiving burden, emotional impact, and a sense of personal evolution. The impact of bipolar disorder on patients included an emotional impact, responsibility for self-care, and struggling socially and developmentally. When comparing patient and spouse perspectives on the impact of the disorder, neither the patient nor the spouse was able to accurately assess the impact of the disorder on their partner's lives. The impact of bipolar disorder on the relationship included volatility in the relationship, strengthening the relationship, weakening the relationship, and family planning. Conclusions The research indicated that patients and partners alike struggle with the tremendous impact of bipolar disorder on their lives and on their relationships. Given the high rates of divorce and volatility in these relationships, healthcare professionals can provide (or refer to) emotional and practical support both to patients and spouses on their own, and as a couple in their clinics.

Guidi, J., E. Tomba, et al. (2016). ***"The sequential integration of pharmacotherapy and psychotherapy in the treatment of major depressive disorder: A meta-analysis of the sequential model and a critical review of the literature."*** American Journal of Psychiatry 173(2): 128-137. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2015.15040476

A number of randomized controlled trials in major depressive disorder have employed a sequential model, which consists of the use of pharmacotherapy in the acute phase and of psychotherapy in its residual phase. The aim of this review was to provide an updated meta-analysis of the efficacy of this approach in reducing the risk of relapse in major depressive disorder and to place these findings in the larger context of treatment selection. Method: Keyword searches were conducted in MEDLINE, EMBASE, PsycINFO, and Cochrane Library from inception of each database through October 2014. Randomized controlled trials examining the efficacy of the administration of psychotherapy after successful response to acute-phase pharmacotherapy in the treatment of adults with major depressive disorder were considered for inclusion in the meta-analysis. Results: Thirteen high-quality studies with 728 patients in a sequential treatment arm and 682 in a control treatment arm were included. All studies involved cognitive-behavioral therapy (CBT). The pooled risk ratio for relapse/recurrence was 0.781 (95% confidence interval [CI]=0.671–0.909; number needed to treat=8), according to the random-effects model, suggesting a relative advantage in preventing relapse/recurrence compared with control conditions. A significant effect of CBT during continuation of antidepressant drugs compared with antidepressants alone or treatment as usual (risk ratio: 0.811; 95% CI=0.685–0.961; number needed to treat=10) was found. Patients randomly assigned to CBT who had antidepressants tapered and discontinued were significantly less likely to experience relapse/recurrence compared with those assigned to either clinical management or continuation of antidepressant medication (risk ratio: 0.674; 95% CI=0.482–0.943; number needed to treat=5). Conclusions: The sequential integration of CBT and pharmacotherapy is a viable strategy for preventing relapse in major depressive disorder. The current indications for the application of psychotherapy in major depressive disorder are discussed, with special reference to its integration with pharmacotherapy.

Haugen, W., O. R. Haavet, et al. (2016). ***"Identifying depression among adolescents using three key questions: A validation study in primary care."*** British Journal of General Practice 66(643): e65-e70. http://bjgp.org/content/bjgp/66/643/e65.full.pdf

Background Depression in adolescents is a serious psychiatric illness. GPs play an important role in identifying adolescents with depression and those at risk of developing depression. Few validated tools are suitable for identifying adolescent depression in general practice.Aim To determine if three verbally asked key questions are valid for identifying depression in adolescents. Design and setting A cross-sectional, general practice multicentre, validation study was conducted in Oslo, Norway, and Aarhus, Denmark. Method A total of 294 adolescents answered three verbally asked key questions followed by a Composite International Diagnostic Interview (CIDI) for psychiatric diagnosis. Inclusion criteria were age (14–16 years) and fluency in the Norwegian or Danish language. The primary outcome was ROC curve statistics in terms of sensitivity and specificity, predictive values, and likelihood ratios of the three key questions. Secondary outcomes were Loevinger's H, Cronbach's α, and prevalence of depression. Results The three key questions met the criteria for construct and criterion validity for detecting depression among the adolescents. ROC curve statistics for the three key questions demonstrated an AUC of 0.79 for the answer 'yes' to either screening question and of 0.73 for the answer 'yes' to the help question. The positive predictive

value was 31% and the negative predictive value was 97%. Conclusion The three key questions are useful for identifying depression in adolescents in primary health care. [BMJ comment - http://www.bmj.com/content/352/bmj.i547.full - Asking three simple questions can accurately detect depression in adolescents aged 14 to 16, a Scandinavian primary care study has shown, demonstrating that the questions had comparable sensitivity to a current "gold standard" written questionnaire for diagnosing depression. Depression can have serious consequences for the health and lives of teenagers, but validated tools for GPs to diagnose depression in this age group are currently limited. Researchers investigated whether three short questions that have been validated for detecting depression in adults in general practice were also valid for identifying mild, moderate, and major depression in adolescents. The researchers interviewed 296 adolescents aged 14 to 16 (including 145 from Denmark and 149 from Norway) by telephone. The teenagers had volunteered after being sent a letter about the study inviting them to take part. Each participant was asked three key questions verbally: **During the past month have you often been bothered by feeling down, depressed, or hopeless? During the past month have you often been bothered by little interest or pleasure in doing things? Is this something with which you would like help?** After answering these three questions the teenagers completed the Composite International Diagnostic Interview—the World Health Organization's comprehensive interview for assessing mental illness—over the telephone. The researchers compared the sensitivity, specificity, and predictive value of the three key questions for diagnosing depression with the composite diagnostic interview. Reporting in the British Journal of General Practice, the researchers found that the three key questions met the criteria for construct validity, which examines how well a test measures what it claims to be measuring, and the criterion validity, which is how well a new test matches an established test. The receiver operating characteristics (ROC) curve plotting the sensitivity (true positive rate) against the false positive rate gave an area under the curve of 0.79 for the answer "yes" to either or both of the first two questions and 0.73 after adding the answer "yes" to the third question about wanting help. The positive predictive value of these three questions for depression was 31%, and the negative predictive value was 97%. "The validity of the three questions makes them attractive for identifying depression in adolescents in primary healthcare," said the researchers, led by Wenche Haugen, of the Research Unit for General Practice in Aarhus, Denmark. The team added, "The three key questions asked verbally offer a new form of assessment tool compared with the available written questionnaires." They suggested that GPs ask the three key questions at any time during a consultation as a case finding method, followed up with a clinical assessment for depression].

Hughes, T., A. Cardno, et al. (2016). ***"Unrecognised bipolar disorder among uk primary care patients prescribed antidepressants: An observational study."*** British Journal of General Practice.
http://bjgp.org/content/bjgp/early/2016/01/05/bjgp16X683437.full.pdf

(Available in free full text) Bipolar disorder is not uncommon, is associated with high disability and risk of suicide, often presents with depression, and can go unrecognised. Aim To determine the prevalence of unrecognised bipolar disorder among those prescribed antidepressants for depressive or anxiety disorder in UK primary care; whether those with unrecognised bipolar disorder have more severe depression than those who do not; and the accuracy of a screening questionnaire for bipolar disorder, the Mood Disorder Questionnaire (MDQ), in this setting. Design and setting Observational primary care study of patients on the lists of 21 general practices in West Yorkshire aged 16–40 years and prescribed antidepressant medication. Method Participants were recruited using primary care databases, interviewed using a diagnostic interview, and completed the screening questionnaire and rating scales of symptoms and quality of life. Results The prevalence of unrecognised bipolar disorder was 7.3%. Adjusting for differences between the sample and a national database gives a prevalence of 10.0%. Those with unrecognised bipolar disorder were younger and had greater lifetime depression. The predictive value of the MDQ was poor. Conclusion Among people aged 16–40 years prescribed antidepressants in primary care for depression or anxiety, there is a substantial proportion with unrecognised bipolar disorder. When seeing patients with depression or anxiety disorder, particularly when they are young or not doing well, clinicians should review the life history for evidence of unrecognised bipolar disorder. Some clinicians might find the MDQ to be a useful supplement to non-standardised questioning.

Infurna, M. R., C. Reichl, et al. (2016). ***"Associations between depression and specific childhood experiences of abuse and neglect: A meta-analysis."*** Journal of Affective Disorders 190: 47-55.
http://www.sciencedirect.com/science/article/pii/S0165032715305309

Background Research documents a strong relationship between childhood maltreatment and depression. However, only few studies have examined the specific effects of various types of childhood abuse/neglect on depression. This meta-analysis estimated the associations between depression and different types of childhood maltreatment (antipathy, neglect, physical abuse, sexual abuse, and psychological abuse) assessed with the same measure, the Childhood Experience of Care and Abuse (CECA) interview. Method A systematic search in scientific databases included use of CECA interview and strict clinical assessment for major depression as criteria. Our meta-analysis utilized Cohen's d and relied on a random-effects model. Results The literature search yielded 12 primary studies (reduced from 44), with a total of 4372 participants and 34 coefficients. Separate meta-analyses for each type of maltreatment revealed that psychological abuse and neglect were most strongly associated with the outcome of depression. Sexual abuse, although significant, was less strongly related. Furthermore, the effects of specific types of childhood maltreatment differed across adult and adolescent samples. Limitations Our strict criteria for selecting the primary studies resulted in a small numbers of available studies. It restricted the analyses for various potential moderators. Conclusion This meta-analysis addressed the differential effects of type of childhood maltreatment on major depression, partially explaining between-study variance. The findings clearly highlight the potential impact of the more "silent" types of childhood maltreatment (other than physical and sexual abuse) on the development of depression.

Jakubovski, E., A. L. Varigonda, et al. (2016). ***"Systematic review and meta-analysis: Dose-response relationship of selective serotonin reuptake inhibitors in major depressive disorder."*** American Journal of Psychiatry 173(2): 174-183.
http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2015.15030331

Objective: Previous studies suggested that the treatment response to selective serotonin reuptake inhibitors (SSRIs) in major depressive disorder follows a flat response curve within the therapeutic dose range. The present study was designed to clarify the relationship between dosage and treatment response in major depressive disorder. Method: The authors searched PubMed for randomized placebo-controlled trials examining the efficacy of SSRIs for treating adults with major depressive disorder. Trials were also required to assess improvement in depression severity at multiple time points. Additional data were collected on treatment response and all-cause and side effect-related discontinuation. All medication doses were transformed into imipramine-equivalent doses. The longitudinal data were analyzed with a mixed-regression model. Endpoint and tolerability analyses were analyzed using meta-regression and stratified subgroup analysis by predefined SSRI dose categories in order to assess the effect of SSRI dosing on the efficacy and tolerability of SSRIs for major depressive disorder. Results: Forty studies involving 10,039 participants were included. Longitudinal modeling (dose-by-time interaction=0.0007, 95% CI=0.0001–0.0013) and endpoint analysis (meta-regression: β=0.00053, 95% CI=0.00018–0.00088, z=2.98) demonstrated a small but statistically significant positive association between SSRI dose and efficacy. Higher doses of SSRIs were associated with an increased likelihood of dropouts due to side effects (meta-regression: β=0.00207, 95% CI=0.00071–0.00342, z=2.98) and decreased

likelihood of all-cause dropout (meta-regression: β=−0.00093, 95% CI=−0.00165 to −0.00021, z=−2.54). Conclusions: Higher doses of SSRIs appear slightly more effective in major depressive disorder. This benefit appears to plateau at around 250 mg of imipramine equivalents (50 mg of fluoxetine). The slightly increased benefits of SSRIs at higher doses are somewhat offset by decreased tolerability at high doses.

Ketter, T. A., S. Miller, et al. (2016). ***"Treatment of bipolar disorder: Review of evidence regarding quetiapine and lithium."*** Journal of Affective Disorders 191: 256-273. http://www.sciencedirect.com/science/article/pii/S0165032715307722

Background: Lithium, the prototypical mood stabilizer, and quetiapine, a second-generation antipsychotic, are widely used acute and maintenance pharmacotherapies for bipolar disorder. The Clinical and Health Outcomes Initiative in Comparative Effectiveness for Bipolar Disorder (Bipolar CHOICE) study was the first comparative effectiveness assessment of lithium versus quetiapine (in combination with adjunctive personalized treatment), and found no overall significant differences in efficacy and safety/tolerability outcomes between lithium and quetiapine. Completion of Bipolar CHOICE offers a timely opportunity to review the evidence regarding lithium and quetiapine for bipolar disorder. Methods Controlled clinical trials and real-world observational studies that included quetiapine and lithium as monotherapy or as combination therapy were identified by literature search. Selected studies were reviewed in detail. Results Review of the available trials suggested comparable efficacy of quetiapine and lithium in acute mania, and possibly greater efficacy for quetiapine compared with lithium in acute bipolar depression and in prevention of recurrent (particularly depressive) episodes. Combination therapy including quetiapine and lithium was generally more effective than either agent alone in acute mania and bipolar maintenance, although adding lithium to quetiapine did not increase efficacy in acute bipolar depression. Safety data for quetiapine and lithium were consistent with the established profiles of the two treatments. Limitations Limitations include those of the available efficacy and effectiveness trial data. Conclusions Quetiapine and lithium have overlapping but distinctive roles in different phases of bipolar disorder, and further studies of these agents (particularly in combination with one another) are warranted.

Kirov, G. G., L. Owen, et al. (2016). ***"Evaluation of cumulative cognitive deficits from electroconvulsive therapy."*** The British Journal of Psychiatry 208(3): 266-270. http://bjp.rcpsych.org/content/bjprcpsych/208/3/266.full.pdf

Background Electroconvulsive therapy (ECT) is the most effective acute treatment for severe depression, but widely held concerns about memory problems may limit its use. Aims To find out whether repeated or maintenance courses of ECT cause cumulative cognitive deterioration. Method Analysis of the results of 10 years of cognitive performance data collection from patients who have received ECT. The 199 patients had a total of 498 assessments, undertaken after a mean of 15.3 ECT sessions (range 0–186). A linear mixed-effect regression model was used, testing whether an increasing number of ECT sessions leads to deterioration in performance. Results The total number of previous ECT sessions had no effect on cognitive performance. The major factors affecting performance were age, followed by the severity of depression at the time of testing and the number of days since the last ECT session. Conclusions Repeated courses of ECT do not lead to cumulative cognitive deficits. This message is reassuring for patients, carers and prescribers who are concerned about memory problems and confusion during ECT.

Kitsune, G. L., J. Kuntsi, et al. (2016). ***"Delineating adhd and bipolar disorder: A comparison of clinical profiles in adult women."*** Journal of Affective Disorders 192: 125-133. http://www.sciencedirect.com/science/article/pii/S0165032715303712

(Free full text available) Objective Overlapping symptoms can make the diagnostic differentiation of attention-deficit/hyperactivity disorder (ADHD) and bipolar disorder (BD) challenging in adults using current clinical assessments. This study sought to determine if current clinical measures delineate ADHD from BD in adults, comparing relative levels of ADHD, BD and emotional lability (EL) symptoms. Methods Sixty adult women with ADHD, BD or controls were compared on self-report and interview measures for ADHD symptoms, mania, depression, EL, and impairment. Results ADHD interview measures and self-ratings of ADHD symptoms best discriminated between ADHD and BD. Self-report measures of EL and depression showed non-specific enhancement in both clinical groups. BD-specific items may distinguish BD from ADHD if a retrospective time-frame is adopted. Conclusions Using measures which capture specific symptoms of ADHD and chronicity/episodicity of symptoms facilitates the delineation of ADHD from BD in adult women.

Legrand, F. D. and E. M. Neff (2016). ***"Efficacy of exercise as an adjunct treatment for clinically depressed inpatients during the initial stages of antidepressant pharmacotherapy: An open randomized controlled trial."*** Journal of Affective Disorders 191: 139-144. http://www.sciencedirect.com/science/article/pii/S0165032715307783

Background Physical exercise as adjunctive treatment for hospitalized patients with major depressive disorder (MDD) has been of increasing interest in the past few years. While preliminary findings are promising, these prior studies have been plagued by inclusion of participants at different stages of medication use at study entry. The present study evaluates the effects of a short (10-days) add-on endurance-training intervention in hospitalized MDD patients on antidepressant medication for less than two weeks. Method Thirty-five participants were randomly assigned to one of three study groups: aerobic exercise (n=14), placebo (stretching) exercise (n=11), or no intervention (control; n=10). The study outcome was the change in the Beck Depression Inventory (BDI-II) total score from baseline to the end of the study period. Results The intent-to-treat analysis showed significant improvements in BDI-II scores for both the aerobic and the stretching groups. However, comparing pre- to post-study depression changes in these two groups, we found a large effect size in favor of aerobic exercise (Cohen's d=−1.06). No significant change in depressive symptoms was found in the control group. Limitations The nature of the intervention (i.e., exercise) meant blinding participants to treatments was not possible. Precise information on medication dosage was not available, and the short duration of interventions and lack of follow-up assessment were all limitations. Conclusions Endurance-training can be a helpful adjunct treatment for hospitalized patients with severe affective disorders in the initial stages of pharmacotherapy.

Li, J. and H. G. Prigerson (2016). ***"Assessment and associated features of prolonged grief disorder among chinese bereaved individuals."*** Comprehensive Psychiatry 66: 9-16. http://www.sciencedirect.com/science/article/pii/S0010440X1530095X

Background Most research on the assessment and characteristics of prolonged grief disorder (PGD) has been conducted in Western bereaved samples. Limited information about PGD in Chinese samples exists. This study aims to validate the Chinese version of the Inventory of Complicated grief (ICG), examine the distinctiveness of PGD symptoms from symptoms of bereavement-related depression and anxiety, and explore the prevalence of PGD in a Chinese sample. Methods Responses from 1358 bereaved Chinese adults were collected through an on-line survey. They completed the Chinese version of ICG and a questionnaire measuring depression and anxiety symptoms. Results The findings indicate that Chinese ICG has sound validity and high internal consistency. The ICG cut-off score for PGD "caseness"in this large Chinese sample was 48. The distinctiveness of PGD symptoms from those of depression and anxiety was supported by the results of the confirmatory factor analysis and the fact that PGD occurred in isolation in the studied sample. The prevalence of PGD was13.9%. Conclusion ICG is a valid instrument for use in the Chinese context. Several key characteristics of PGD in Chinese, either different from or comparable to

findings in Western samples, may stimulate further research and clinical interest in the concept by providing empirical evidence from an large and influential Eastern country.

Lindhiem, O., C. B. Bennett, et al. (2015). ***"Mobile technology boosts the effectiveness of psychotherapy and behavioral interventions: A meta-analysis."*** Behavior Modification 39(6): 785-804. http://bmo.sagepub.com/content/39/6/785.abstract

We conducted a meta-analysis on the effects of mobile technology on treatment outcome for psychotherapy and other behavioral interventions. Our search of the literature resulted in 26 empirical articles describing 25 clinical trials testing the benefits of smartphone applications, personal digital assistants (PDAs), or text messaging systems either to supplement treatment or substitute for direct contact with a clinician. Overall, mobile technology use was associated with superior treatment outcome across all study designs and control conditions, effect size (ES) = .34, $p < .0001$. For the subset of 10 studies that looked specifically at the added benefit of mobile technology using a rigorous "Treatment" versus "Treatment + Mobile" design, effect sizes were only slightly more modest (ES = .27) and still significant ($p < .05$). Overall, the results support the role of mobile technology for the delivery of psychotherapy and other behavioral interventions.

Marangoni, C., M. Hernandez, et al. (2016). ***"The role of environmental exposures as risk factors for bipolar disorder: A systematic review of longitudinal studies."*** Journal of Affective Disorders 193: 165-174. http://www.sciencedirect.com/science/article/pii/S0165032715309939

Abstract Background The role of environmental risk factors in the development of bipolar disorder (BD) is not well characterized. We evaluate the prevalence, duration, and predictive value of environmental exposures for BD in longitudinal studies. Methods We conducted a systematic search of PubMed, Scopus and PsychINFO databases until April 01, 2015, using the following words in combination: prenatal exposure; maternal exposure; trauma; childhood abuse; alcoholism; cannabis; smoking; cocaine; central stimulants; opioids; uv light; pollution; global warming; vitamin d AND bipolar disorder. Additional references were obtained through cross-referencing. We included (1) longitudinal cohort studies or case-control studies nested within longitudinal designs; (2) studies of subjects without lifetime BD diagnoses at initial assessment and a diagnosis of BD at follow-up by clinical or structured assessment. Familial-risk studies were excluded. We tabulated details of study-design, exposure, diagnostic criteria, risk of bipolar disorder expressed as odd ratio (OR), relative risk (RR) or hazard ratio (HR). Results Of 2119 studies found, 22 met inclusion criteria. Risk factors identified can be grouped in 3 clusters: neurodevelopment (maternal influenza during pregnancy; indicators of fetal development), substances (cannabis, cocaine, other drugs – opioids, tranquilizers, stimulants, sedatives), physical/psychological stress (parental loss, adversities, abuses, brain injury). Limitations Heterogeneity of designs and methodology prevented the use of meta-analysis of the findings; studies did not provide sensitivity, specificity and predictive value of the risk factors identified; case-control studies classify cases based on diagnostic membership, but do not control for familial or genetic liability; methods for determining the exposures varied among studies. Conclusion Only preliminary evidence exists that exposure to viral infection, substances or trauma increase the likelihood of BD. Given the limited data available, the specificity, sensitivity and predictive value could not be computed. As exposures are sometimes amenable to prevention, further research is needed.

Mehta-Raghavan, N. S., S. L. Wert, et al. (2016). ***"Nature and nurture: Environmental influences on a genetic rat model of depression."*** Transl Psychiatry 6: e770. http://dx.doi.org/10.1038/tp.2016.28

(Available in free full text) In this study, we sought to learn whether adverse events such as chronic restraint stress (CRS), or /`nurture/' in the form of environmental enrichment (EE), could modify depression-like behavior and blood biomarker transcript levels in a genetic rat model of depression. The Wistar Kyoto More Immobile (WMI) is a genetic model of depression that aided in the identification of blood transcriptomic markers, which successfully distinguished adolescent and adult subjects with major depressive disorders from their matched no-disorder controls. Here, we followed the effects of CRS and EE in adult male WMIs and their genetically similar control strain, the Wistar Kyoto Less Immobile (WLI), that does not show depression-like behavior, by measuring the levels of these transcripts in the blood and hippocampus. In WLIs, increased depression-like behavior and transcriptomic changes were present in response to CRS, but in WMIs no behavioral or additive transcriptomic changes occurred. Environmental enrichment decreased both the inherent depression-like behavior in the WMIs and the behavioral difference between WMIs and WLIs, but did not reverse basal transcript level differences between the strains. The inverse behavioral change induced by CRS and EE in the WLIs did not result in parallel inverse expression changes of the transcriptomic markers, suggesting that these behavioral responses to the environment work via separate molecular pathways. In contrast, /`trait/' transcriptomic markers with expression differences inherent and unchanging between the strains regardless of the environment suggest that in our model, environmental and genetic etiologies of depression work through independent molecular mechanisms.

Mirza, S. S., F. J. Wolters, et al. (2016). ***"10-year trajectories of depressive symptoms and risk of dementia: A population-based study."*** The Lancet Psychiatry. http://dx.doi.org/10.1016/S2215-0366(16)00097-3

Background Late-life depressive symptoms have been extensively studied for their relationship with incident dementia, but have been typically assessed at a single timepoint. Such an approach neglects the course of depression, which, given its remitting and relapsing nature, might provide further insights into the complex association of depression with dementia. We therefore repeatedly measured depressive symptoms in a population of adults over a decade to study the subsequent risk of dementia. Methods Our study was embedded in the Rotterdam Study, a population-based study of adults aged 55 years or older in Rotterdam (Netherlands), ongoing since 1990. The cohort is monitored continuously for major events by data linkage between the study database and general practitioners. We examined a cohort of participants who were free from dementia, but had data for depressive symptoms from at least one examination round in 1993–95, 1997–99, or 2002–04. We assessed depressive symptoms with the validated Dutch version of the Center for Epidemiology Depression Scale (CES-D) and the Hospital Anxiety and Depression Scale-Depression. We used these data to identify 11-year trajectories of depressive symptoms by latent class trajectory modelling. We screened participants for dementia at each examination round and followed up participants for 10 years for incident dementia by latent trajectory from the third examination round to 2014. We calculated hazard ratios (HR) for dementia by assigned trajectory using two Cox proportional hazards models (model 1 adjusted for age and sex only, and model 2 adjusted additionally for APOEε4 carrier status, educational level, body-mass index, smoking, alcohol consumption, cognitive score, use of antidepressants, and prevalent disease status at baseline). We repeated the analyses censoring for incident stroke, restricting to Alzheimer's disease as an outcome, and accounting for mortality as a competing risk for dementia. Findings From 1993–2004, we obtained data for depressive symptoms from at least one examination round for 3325 participants (median age: 74·88 years [IQR 70·62–80·06], 1995 [60%] women). We identified five trajectories of depressive symptoms in these 3325 individuals, characterised by maintained low CES-D scores (low; 2441 [73%]); moderately high starting scores but then remitting (decreasing; 369 [11%]); low starting scores, increasing, then remitting (remitting; 170 [5%]); low starting scores that steadily increased (increasing; 255 [8%]); and maintained high scores (high; 90 [3%]). During 26 330 person-years, 434 participants developed incident dementia. Only the trajectory with increasing depressive symptoms

was associated with a higher risk of dementia compared with the low depressive symptom trajectory, using model 2 (HR 1·42, 95% CI 1·05–1·94; p=0·024). Additionally, only the increasing trajectory was associated with a higher risk of dementia compared with the low trajectory after censoring for incident stroke (1·58, 1·15–2·16; p=0·0041), restricting to Alzheimer's disease as an outcome (1·44, 1·03–2·02; p=0·034), and accounting for mortality as a competing risk (1·45, 1·06–1·97; p=0·019). Interpretation Risk of dementia differed with different courses of depression, which could not be captured by a single assessment of depressive symptoms. The higher risk of dementia only in the increasing trajectory suggests depression might be a prodrome of dementia.

Mojtabai, R. (2016). ***"Depressed mood in middle-aged and older adults in europe and the united states: A comparative study using anchoring vignettes."*** Journal of Aging and Health 28(1): 95-117. http://jah.sagepub.com/content/28/1/95.abstract

Objective: To compare self-ratings of depressed mood in middle-aged and older adults in the United States and nine European countries after adjustment by anchoring vignettes. Method: Samples were drawn from three large surveys of middle-aged and older adults: the U.S. Health and Retirement Study, the English Longitudinal Study of Aging (ELSA), and the Survey of Health, Ageing and Retirement in Europe. Self-ratings of depressed mood were compared across countries before and after adjustment by anchoring vignettes depicting cases with different levels of depressed mood. Results: Compared with Europeans as a group, Americans rated both the cases presented in the vignettes and themselves as more depressed. However, after adjustment by vignette ratings, Americans appeared to be less depressed than their counterparts in all but two European countries. Discussion: Cultural differences in mental health norms reflected in vignette rating may partly explain between-country differences in self-reported depressive symptoms and perhaps other psychiatric complaints.

O'Neil, A., A. J. Fisher, et al. (2016). ***"Depression is a risk factor for incident coronary heart disease in women: An 18-year longitudinal study."*** J Affect Disord 196: 117-124. http://www.ncbi.nlm.nih.gov/pubmed/26921864

BACKGROUND: According to a recent position paper by the American Heart Association, it remains unclear whether depression is a risk factor for incident Coronary Heart Disease (CHD). We assessed whether a depressive disorder independently predicts 18-year incident CHD in women. METHOD: A prospective longitudinal study of 860 women enrolled in the Geelong Osteoporosis Study (1993-2011) was conducted. Participants were derived from an age-stratified, representative sample of women (20-94 years) randomly selected from electoral rolls in South-Eastern Australia. The exposure was a diagnosis of a depressive disorder using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders. Outcomes data were collected from hospital medical records: (1) PRIMARY OUTCOME: a composite measure of cardiac death, non-fatal Myocardial Infarction or coronary intervention. (2) Secondary outcome: any cardiac event (un/stable angina, cardiac event not otherwise defined) occurring over the study period. RESULTS: Seven participants were excluded based on CHD history. Eighty-three participants (9.6%) recorded >/=1 cardiac event over the study period; 47 had a diagnosis that met criteria for inclusion in the primary analysis. Baseline depression predicted 18-year incidence, adjusting for (1) anxiety (adj. OR:2.39; 95% CIs:1.19-4.82), plus (2) typical risk factors (adj. OR:3.22; 95% CIs:1.45-6.93), plus (3) atypical risk factors (adj. OR:3.28; 95% CIs:1.36-7.90). This relationship held when including all cardiac events. No relationship was observed between depression and recurrent cardiac events. CONCLUSION: The results of this study support the contention that depression is an independent risk factor for CHD incidence in women. Moreover, the strength of association between depression and CHD incidence was of a greater magnitude than any typical and atypical risk factor.

O'Hare, C., V. O'Sullivan, et al. (2016). ***"Seasonal and meteorological associations with depressive symptoms in older adults: A geo-epidemiological study."*** Journal of Affective Disorders 191: 172-179. http://www.sciencedirect.com/science/article/pii/S0165032715305929

Background Given increased social and physiological vulnerabilities, older adults may be particularly susceptible to environmental influences on mood. Whereas the impact of season on mood is well described for adults, studies rarely extend to elders or include objective weather data. We investigated the impact of seasonality and meteorological factors on risk of current depressive symptoms in older adults. Methods We used data on 8027 participants from the first wave of The Irish Longitudinal Study of Ageing, a population-representative cohort of adults aged 50+. Depressive symptoms were recorded using the Centre for Epidemiological Studies Depression Scale. Season was defined according to the World Meteorological Organisation. Data on climate over the preceding thirty years, and temperature and rain over the preceding month, were provided by the Irish Meteorological Service and linked using Geographic Information Systems techniques to participant's geo-coded locations at a resolution of one kilometre. Results The highest levels of depressive symptoms were reported in winter and the lowest in spring (mean 6.56 [CI95% 6.09, 7.04] vs. 5.81 [CI95%: 5.40, 6.22]). In fully adjusted linear regression models, participants living in areas with higher levels of rainfall in the preceding and/or current calendar month had greater depressive symptoms (0.04 SE 0.02; p=0.039 per 10 mm additional rainfall per month) while those living in areas with sunnier climates had fewer depressive symptoms (−2.67 SE 0.88; p=0.003 for every additional hour of average annual daily sunshine). Limitations This was a cross-sectional analysis thus causality cannot be inferred; monthly rain and temperature averages were available only on a calendar month basis while monthly local levels of sunshine data were not available. Conclusions Environmental cues may influence mood in older adults and thus have relevance for the recognition and treatment of depression in this age group.

Oud, M., E. Mayo-Wilson, et al. (2016). ***"Psychological interventions for adults with bipolar disorder: Systematic review and meta-analysis."*** The British Journal of Psychiatry 208(3): 213-222. http://bjp.rcpsych.org/content/bjprcpsych/208/3/213.full.pdf

Psychological interventions may be beneficial in bipolar disorder. Aims To evaluate the efficacy of psychological interventions for adults with bipolar disorder. Method A systematic review of randomised controlled trials was conducted. Outcomes were meta-analysed using RevMan and confidence assessed using the GRADE method. Results We included 55 trials with 6010 participants. Moderate-quality evidence associated individual psychological interventions with reduced relapses at post-treatment (risk ratio (RR) = 0.66, 95% CI 0.48–0.92) and follow-up (RR = 0.74, 95% CI 0.63–0.87), and collaborative care with a reduction in hospital admissions (RR = 0.68, 95% CI 0.49–0.94). Low-quality evidence associated group interventions with fewer depression relapses at post-treatment and follow-up, and family psychoeducation with reduced symptoms of depression and mania. Conclusions There is evidence that psychological interventions are effective for people with bipolar disorder. Much of the evidence was of low or very low quality thereby limiting our conclusions. Further research should identify the most effective (and cost-effective) interventions for each phase of this disorder.

Richards, D. A., P. Bower, et al. (2016). ***"Clinical effectiveness and cost-effectiveness of collaborative care for depression in uk primary care (cadet): A cluster randomised controlled trial."*** Health Technol Assess 20(14): 1-192. http://www.ncbi.nlm.nih.gov/pubmed/26910256

(Free full text available) BACKGROUND: Collaborative care is effective for depression management in the USA. There is little UK evidence on its clinical effectiveness and cost-effectiveness. OBJECTIVE: To determine the clinical effectiveness and

cost-effectiveness of collaborative care compared with usual care in the management of patients with moderate to severe depression. DESIGN: Cluster randomised controlled trial. SETTING: UK primary care practices (n = 51) in three UK primary care districts. PARTICIPANTS: A total of 581 adults aged >/= 18 years in general practice with a current International Classification of Diseases, Tenth Edition depressive episode, excluding acutely suicidal people, those with psychosis, bipolar disorder or low mood associated with bereavement, those whose primary presentation was substance abuse and those receiving psychological treatment. INTERVENTIONS: Collaborative care: 14 weeks of 6-12 telephone contacts by care managers; mental health specialist supervision, including depression education, medication management, behavioural activation, relapse prevention and primary care liaison. Usual care was general practitioner standard practice. MAIN OUTCOME MEASURES: Blinded researchers collected depression [Patient Health Questionnaire-9 (PHQ-9)], anxiety (General Anxiety Disorder-7) and quality of life (European Quality of Life-5 Dimensions three-level version), Short Form questionnaire-36 items) outcomes at 4, 12 and 36 months, satisfaction (Client Satisfaction Questionnaire-8) outcomes at 4 months and treatment and service use costs at 12 months. RESULTS: In total, 276 and 305 participants were randomised to collaborative care and usual care respectively. Collaborative care participants had a mean depression score that was 1.33 PHQ-9 points lower [n = 230; 95% confidence interval (CI) 0.35 to 2.31; p = 0.009] than that of participants in usual care at 4 months and 1.36 PHQ-9 points lower (n = 275; 95% CI 0.07 to 2.64; p = 0.04) at 12 months after adjustment for baseline depression (effect size 0.28, 95% CI 0.01 to 0.52; odds ratio for recovery 1.88, 95% CI 1.28 to 2.75; number needed to treat 6.5). Quality of mental health but not physical health was significantly better for collaborative care at 4 months but not at 12 months. There was no difference for anxiety. Participants receiving collaborative care were significantly more satisfied with treatment. Differences between groups had disappeared at 36 months. Collaborative care had a mean cost of pound272.50 per participant with similar health and social care service use between collaborative care and usual care. Collaborative care offered a mean incremental gain of 0.02 (95% CI -0.02 to 0.06) quality-adjusted life-years (QALYs) over 12 months at a mean incremental cost of pound270.72 (95% CI -pound202.98 to pound886.04) and had an estimated mean cost per QALY of pound14,248, which is below current UK willingness-to-pay thresholds. Sensitivity analyses including informal care costs indicated that collaborative care is expected to be less costly and more effective. The amount of participant behavioural activation was the only effect mediator. CONCLUSIONS: Collaborative care improves depression up to 12 months after initiation of the intervention, is preferred by patients over usual care, offers health gains at a relatively low cost, is cost-effective compared with usual care and is mediated by patient activation. Supervision was by expert clinicians and of short duration and more intensive therapy may have improved outcomes. In addition, one participant requiring inpatient treatment incurred very significant costs and substantially inflated our cost per QALY estimate. Future work should test enhanced intervention content not collaborative care per se.

Robinson, R. G. and R. E. Jorge (2016). ***"Post-stroke depression: A review."*** American Journal of Psychiatry 173(3): 221-231. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2015.15030363

Poststroke depression (PSD) has been recognized by psychiatrists for more than 100 years, but controlled systematic studies did not begin until the 1970s. Meta-analyses addressing almost all major clinical issues in the field have emerged because of the relatively small number of patients included in some stroke studies. In order to build large databases, these meta-analyses have merged patients with rigorously assessed mood disorders with major depressive features with patients scoring above arbitrary cutoff points on depression rating scales, thus missing important findings such as cognitive impairment associated with major but not minor depression. Nevertheless, PSD occurs in a significant number of patients and constitutes an important complication of stroke, leading to greater disability as well as increased mortality. The most clinically important advances, however, have been in the treatment and prevention of PSD. Recent meta-analyses of randomized controlled trials for the treatment of PSD have demonstrated the efficacy of antidepressants. Similarly, randomized controlled trials for prevention of PSD have shown that antidepressants significantly decrease the incidence of PSD compared with placebo. Early antidepressant treatment of PSD appears to enhance both physical and cognitive recovery from stroke and might increase survival up to 10 years following stroke. There has also been progress in understanding the pathophysiology of PSD. Inflammatory processes might be associated with the onset of at least some depressive symptoms. In addition, genetic and epigenetic variations, white matter disease, cerebrovascular deregulation, altered neuroplasticity, and changes in glutamate neurotransmission might be relevant etiological factors. Further elucidation of the mechanism of PSD may ultimately lead to specific targeted treatments.

Rodríguez-Cano, R., A. López-Durán, et al. (2016). ***"Smoking cessation and depressive symptoms at 1-, 3-, 6-, and 12-months follow-up."*** Journal of Affective Disorders 191: 94-99. http://www.sciencedirect.com/science/article/pii/S0165032715307461

Background The relationship between tobacco and depressive symptoms has been examined. However, there is little information on the evolution of these symptoms when an individual quits. The aim of this study was to analyze the evolution of depressive symptoms over time (pre-, post-treatment, 1-, 3-, 6-, and 12-months follow-up) in relation to smoking status 12 months after having received a psychological treatment for smoking cessation. Method The sample was made up of 242 adults who received cognitive-behavioral treatment for smoking cessation (64.4% women; mean age=41.71 years). The BDI-II was used to assess depressive symptomatology. Participants were classified into three groups according to smoking status at 12-months follow-up (abstainers, relapsers, and smokers). Results There were no significant differences in depressive symptoms among the three groups at pretreatment. At the end of treatment, abstainers and relapsers presented less depressive symptomatology than smokers. At follow-up, abstainers continued to present less depressive symptomatology than smokers, whereas in relapsers, symptoms began to increase as the relapses occurred. Regarding the evolution of depressive symptomatology, the abstainer and relapser groups showed a significant reduction at the end of treatment. Only in the group of abstainers did the decrease continue during 12 months follow-up. Limitations The decrease of the initial sample size from 562 to 242 participants. Variables such as self-esteem and self-efficacy were not assessed. Conclusions Smoking cessation is associated with a decrease in depressive symptomatology, that is maintained over time. In contrast, relapse is associated with an increase of such symptoms. These findings signify the potential importance of addressing depressive symptomatology in smoking cessation treatment.

Rosenblat, J. D., R. Kakar, et al. (2016). ***"Anti-inflammatory agents in the treatment of bipolar depression: A systematic review and meta-analysis."*** Bipolar Disorders 18(2): 89-101. http://dx.doi.org/10.1111/bdi.12373

Objective Inflammation has been implicated in the risk, pathophysiology, and progression of mood disorders and, as such, has become a target of interest in the treatment of bipolar disorder (BD). Therefore, the objective of the current qualitative and quantitative review was to determine the overall antidepressant effect of adjunctive anti-inflammatory agents in the treatment of bipolar depression. Methods Completed and ongoing clinical trials of anti-inflammatory agents for BD published prior to 15 May 15 2015 were identified through searching the PubMed, Embase, PsychINFO, and Clinicaltrials.gov databases. Data from randomized controlled trials (RCTs) assessing the antidepressant effect of adjunctive mechanistically diverse anti-inflammatory agents were pooled to determine standard mean differences (SMDs) compared with standard therapy alone. Results Ten RCTs were identified for qualitative review. Eight RCTs (n = 312) assessing adjunctive nonsteroidal anti-inflammatory drugs (n = 53), omega-3 polyunsaturated fatty acids (n = 140), N-acetylcysteine (n = 76), and pioglitazone (n =

44) in the treatment of BD met the inclusion criteria for quantitative analysis. The overall effect size of adjunctive anti-inflammatory agents on depressive symptoms was −0.40 (95% confidence interval −0.14 to −0.65, p = 0.002), indicative of a moderate and statistically significant antidepressant effect. The heterogeneity of the pooled sample was low (I^2 = 14%, p = 0.32). No manic/hypomanic induction or significant treatment-emergent adverse events were reported. Conclusions Overall, a moderate antidepressant effect was observed for adjunctive anti-inflammatory agents compared with conventional therapy alone in the treatment of bipolar depression. The small number of studies, diversity of agents, and small sample sizes limited interpretation of the current analysis.

Sarris, J., J. Murphy, et al. (2016). ***"Adjunctive nutraceuticals for depression: A systematic review and meta-analyses."*** American Journal of Psychiatry 0(0): appi.ajp.2016.15091228. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2016.15091228

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

Sharma, T., L. S. Guski, et al. (2016). ***"Suicidality and aggression during antidepressant treatment: Systematic review and meta-analyses based on clinical study reports."*** BMJ 352. http://www.bmj.com/content/bmj/352/bmj.i65.full.pdf

Objective To study serious harms associated with selective serotonin and serotonin-norepinephrine reuptake inhibitors. Design Systematic review and meta-analysis. Main outcome measures Mortality and suicidality. Secondary outcomes were aggressive behaviour and akathisia. Data sources Clinical study reports for duloxetine, fluoxetine, paroxetine, sertraline, and venlafaxine obtained from the European and UK drug regulators, and summary trial reports for duloxetine and fluoxetine from Eli Lilly's website. Eligibility criteria for study selection Double blind placebo controlled trials that contained any patient narratives or individual patient listings of harms. Data extraction and analysis Two researchers extracted data independently; the outcomes were meta-analysed by Peto's exact method (fixed effect model). Results We included 70 trials (64 381 pages of clinical study reports) with 18 526 patients. These trials had limitations in the study design and discrepancies in reporting, which may have led to serious under-reporting of harms. For example, some outcomes appeared only in individual patient listings in appendices, which we had for only 32 trials, and we did not have case report forms for any of the trials. Differences in mortality (all deaths were in adults, odds ratio 1.28, 95% confidence interval 0.40 to 4.06), suicidality (1.21, 0.84 to 1.74), and akathisia (2.04, 0.93 to 4.48) were not significant, whereas patients taking antidepressants displayed more aggressive behaviour (1.93, 1.26 to 2.95). For adults, the odds ratios were 0.81 (0.51 to 1.28) for suicidality, 1.09 (0.55 to 2.14) for aggression, and 2.00 (0.79 to 5.04) for akathisia. The corresponding values for children and adolescents were 2.39 (1.31 to 4.33), 2.79 (1.62 to 4.81), and 2.15 (0.48 to 9.65). In the summary trial reports on Eli Lilly's website, almost all deaths were noted, but all suicidal ideation events were missing, and the information on the remaining outcomes was incomplete. Conclusions Because of the shortcomings identified and having only partial access to appendices with no access to case report forms, the harms could not be estimated accurately. In adults there was no significant increase in all four outcomes, but in children and adolescents the risk of suicidality and aggression doubled. To elucidate the harms reliably, access to anonymised individual patient data is needed.

Traffanstedt, M. K., S. Mehta, et al. (2016). ***"Major depression with seasonal variation: Is it a valid construct?"*** Clinical Psychological Science. http://cpx.sagepub.com/content/early/2016/01/18/2167702615615867.abstract

Seasonal affective disorder (SAD) is based on the theory that some depressions occur seasonally in response to reduced sunlight. SAD has attracted cultural and research attention for more than 30 years and influenced the DSM through inclusion of the seasonal variation modifier for the major depression diagnosis. This study was designed to determine if a seasonally related pattern of occurrence of major depression could be demonstrated in a population-based study. A cross-sectional U.S. survey of adults completed the Patient Health Questionnaire–8 Depression Scale. Regression models were used to determine if depression was related to measures of sunlight exposure. Depression was unrelated to latitude, season, or sunlight. Results do not support the validity of a seasonal modifier in major depression. The idea of seasonal depression may be strongly rooted in folk psychology, but it is not supported by objective data. Consideration should be given to discontinuing seasonal variation as a diagnostic modifier of major depression.

Uher, R. and B. Pavlova (2016). ***"Long-term effects of depression treatment."*** The Lancet Psychiatry 3(2): 95-96. http://www.sciencedirect.com/science/article/pii/S2215036615005787

(Available in free full text) In most cases, depression is a recurrent or chronic condition that affects individuals over the course of their lifetime.1 The realisation that depression needs long-term treatment2 has not been matched by adequate evidence of the long-term effects of specific treatments, leaving a major gap in evidence for the clinical practice of psychiatry. The most commonly used long-term treatment is maintenance antidepressants. However, for most antidepressant drugs, the efficacy of treatment lasting more than 1 year is unknown. The absence of evidence of the long-term therapeutic effects of antidepressant drugs leaves uncertainty and invites controversy. In The Lancet Psychiatry, the Article by Nicola Wiles and colleagues 3 brings perhaps the most substantial body of evidence of the long-term effects of a treatment of major depressive disorder: a comprehensive report of the effectiveness and cost-effectiveness of adjunctive cognitive behavioural therapy (CBT) in a 3·5 year follow-up of the CoBalT trial. In the CoBalT trial, 469 primary care patients with depressive symptoms of at least moderate severity despite adherence to antidepressant treatment were randomly allocated to be offered a course of 12 to 18 sessions of individual CBT or to continue their usual care that included antidepressants. Most participants had chronic and severe depression with comorbid anxiety disorders. Those who were offered the adjunctive CBT had fewer depressive symptoms and were more likely to fulfil criteria for response at 6 and 12 month follow-up.4 In the present study, Wiles and colleagues report the results of a 46 months follow-up. Outcomes were available from roughly 60% of participants. They showed that the benefits of CBT were fully maintained. More than 3 years after the end of treatment, participants who were allocated to CBT continued to

do better on several self-reported outcomes and the effect sizes were similar to those at 6 and 12 months. Participants who received CBT scored roughly four points lower on the Beck Depression Inventory (mean score of 19·2 with CBT vs 23·4 without CBT), two points lower on the Patient Health Questionnaire, had fewer anxiety symptoms, and were twice as likely to meet criteria for response or remission. These differences in outcomes were maintained for more than 3 years whereas four-fifths of participants in both groups continued to take antidepressant drugs. An accompanying health economic analysis shows that add-on individual CBT provides exceptionally good value for money.

Vigod, S. N., C. A. Wilson, et al. (2016). ***"Depression in pregnancy."*** BMJ 352. http://www.bmj.com/content/bmj/352/bmj.i1547.full.pdf

What you need to know: Offer all women education about mental health problems in pregnancy, treatment options, and the effect on themselves and their offspring. Offer women with mild or moderate depression psychological treatments if they have access to them and can commit time to therapy. Consider antidepressant drugs such as selective serotonin reuptake inhibitors (SSRIs) for women with current or past severe or recurrent depression. For pregnant women who have not used antidepressants, any SSRI (with the exception of paroxetine) is a reasonable first choice. For former antidepressant users, information on efficacy and tolerability must be considered when selecting an antidepressant during pregnancy. Switching antidepressants during pregnancy or lactation is not recommended (even with paroxetine) as there is no clear evidence that the safety profile of one drug is superior to that of another. Switching away from an effective drug could increase the risk of relapse. Depression in pregnancy affects up to 10% of women, with higher rates in low and middle income countries, a rate only slightly lower than in the postpartum period. Yet, as few as 20% of pregnant women with depression receive adequate treatment. This is problematic because depression can profoundly affect a woman's sense of wellbeing, relationships, and quality of life. Untreated or incompletely treated depression can also have adverse consequences for the offspring. Systematic reviews show an increase in markers of infant morbidity such as preterm birth, childhood emotional difficulties, behaviour problems, and, in some studies, poor cognitive development. Antenatal depression also is one of the strongest risk factors for postnatal depression, a condition linked to developmental problems in children. Severe depression can result in suicide, a major cause of maternal death. Perinatal suicides have been associated with lack of active treatment. Barriers to treatment include stigma, lack of provider training on perinatal mental health, and limited access to the evidence based psychological treatments that patients prefer. Women report that conflicting information from professional and non-professional sources about antidepressant drugs in pregnancy impedes decision making and may reduce treatment uptake. This review presents evidence for health professionals to enable shared management of depression in pregnancy with patients.

Wagener, A., C. Baeyens, et al. (2016). ***"Depressive symptomatology and the influence of the behavioral avoidance and activation: A gender-specific investigation."*** Journal of Affective Disorders 193: 123-129. http://www.sciencedirect.com/science/article/pii/S0165032715311277

Abstract Background Depression is a highly prevalent disorder which is usually considered as differentially experienced depending on gender. Behavioral theories of depression pinpoint the importance of the behavioral avoidance in the maintenance of depression. However, little is known about the specific impact of the behavioral avoidance and activation on each depressive symptom as well as on gender differences on the behavioral features of depression. Methods This study's aim was two-fold: (1) to assess the presence of gender differences on the BDI-II; (2) to investigate the respective predictive value of behavioral avoidance and of behavioral activation on each depressive symptom assessed by the BDI-II depending on gender. Community adults and adults attending mental healthcare composed the sample. Results Results showed differences in symptomatology profiles depending on gender (e.g. higher scores of sadness, self-criticalness in women, higher scores of past failure and loss of pleasure in men). Behavioral avoidance positively predicted almost all depressive symptoms in women and in men while behavioral activation negatively predicted almost all symptoms in both gender. Nevertheless, the strengths of these relationships were different for some symptoms (e.g. pessimism). Limitations The use of self-report instruments; the lack of assessment of causal or precipitating factors of the depressive symptomatology; the higher number of women in the sample. Conclusions Results are discussed with respect to previous findings and present clinical implications: (1) to underline the relevance of the combination of gender-specific assessment tools; (2) to highlight the need of tailored psychological intervention.

Williams, L. J., J. A. Pasco, et al. (2016). ***"Depression as a risk factor for fracture in women: A 10 year longitudinal study."*** Journal of Affective Disorders 192: 34-40. http://www.sciencedirect.com/science/article/pii/S0165032715306728

Background Previous research has demonstrated deficits in bone mineral density (BMD) among individuals with depression. While reduced BMD is a known risk for fracture, a direct link between depression and fracture risk is yet to be confirmed. Methods A population-based sample of women participating in the Geelong Osteoporosis Study was studied using both nested case-control and retrospective cohort study designs. A lifetime history of depression was identified using a semi-structured clinical interview (SCID-I/NP). Incident fractures were identified from radiological reports and BMD was measured at the femoral neck using dual energy absorptiometry. Anthropometry was measured and information on medication use and lifestyle factors was obtained via questionnaire. Results Among 179 cases with incident fracture and 914 controls, depression was associated with increased odds of fracture (adjusted odds ratio (OR) 1.57, 95%CI 1.04–2.38); further adjustment for psychotropic medication use appeared to attenuate this association (adjusted OR 1.52, 95%CI 0.98–2.36). Among 165 women with a history of depression at baseline and 693 who had no history of depression, depression was associated with a 68% increased risk of incident fracture (adjusted hazard ratio (HR) 1.68, 95%CI 1.02–2.76), with further adjustment for psychotropic medication use also appearing to attenuate this association (adjusted HR 1.58, 95%CI 0.95–2.61). Limitations Potential limitations include recall bias, unrecognised confounding and generalizability. Conclusions This study provides both cross-sectional and longitudinal evidence to suggest that clinical depression is a risk factor for radiologically-confirmed incident fracture, independent of a number of known risk factors. If there is indeed a clinically meaningful co-morbidity between mental and bone health, potentially worsened by psychotropic medications, the issue of screening at-risk populations needs to become a priority.

Yary, T., S. M. Lehto, et al. (2016). ***"Dietary magnesium intake and the incidence of depression: A 20-year follow-up study."*** Journal of Affective Disorders 193: 94-98. http://www.sciencedirect.com/science/article/pii/S0165032715311824

Abstract Background Depression is a major global public health concern. The aetiology of depression is partly unclear; however, intake of nutrients, such as magnesium, have been suggested to affect depressive symptoms and modify depression risk. Methods This research is a part of the Kuopio Ischemic Heart Disease Risk Factor (KIHD) Study, conducted on a sample of 2320 Eastern Finnish men aged 42–61 years old at the baseline. Magnesium intake was assessed by a 4-day food record. Hospital discharge diagnosis of unipolar depressive disorder was used as an outcome variable. Results Participants in the middle tertile of dietary magnesium intake had a statistically significantly decreased risk of getting a hospital discharge diagnosis of depression compared to participants in the lowest tertile of magnesium intake (HR 0.49, CI 0.25–0.95, P=0.035) in the prospective setting after multivariable adjustments. In addition, an inverse association between magnesium intake and the risk

of depression was found when the combined middle and highest tertiles of magnesium intake were compared with the lowest tertile (HR 0.53, CI 0.29–0.95, P=0.033). Limitations Our findings may not be generalizable to individuals below middle-age or women. Moreover, we were unable to consider cases with mild depression in the longitudinal setting. Conclusions The results of this study suggest that magnesium intake may have an effect on the risk to develop depression. Further studies are needed to investigate whether sufficient magnesium intake could have implications for prevention or treatment of depression.