48 depression-relevant abstracts august '16 newsletter

(Hallford and Mellor 2015; Al-Karawi and Jubair 2016; Amsterdam, Lorenzo-Luaces et al. 2016; Armitage, Rahim et al. 2016; Beard, Hsu et al. 2016; Bukh, Andersen et al. 2016; Buntrock, Ebert et al. 2016; Cattaneo, Ferrari et al. 2016; Charles, Lambert et al. 2016; Christensen, Batterham et al. 2016; Cipriani, Zhou et al. 2016; Clarke, DeBar et al. 2016; Coimbra, Pereira e Silva et al. 2016; Davidson, Dowrick et al. 2016; Delgadillo, Moreea et al. 2016; Eckerd, Barnett et al. 2016; Fava, Memisoglu et al. 2016; Fernandes, Dean et al. 2016; Fornaro, Orsolini et al. 2016; Fountoulakis, Savopoulos et al. 2016; Gibson, Cartwright et al. 2016; Goracci, Rucci et al. 2016; Grant, Chamberlain et al. 2016; Hallford and Mellor 2016; Hartig and Viola 2016; Hawton, Witt et al. 2016; Henriksen, Skrede et al. 2016; Huijbers, Spinhoven et al. 2016; Johnson and Dunbar 2016; Karyotaki, Smit et al. 2016; Keefe, Webb et al. 2016; Louzon, Bossarte et al. 2016; Luong, Wrzus et al. 2016; Mansur, Rizzo et al. 2016; Martin, Ul-Haq et al. 2016; McLeod, Horwood et al. 2016; McNamara and Welge 2016; Melo, Daher et al. 2016; Mithoefer, Grob et al. 2016; Nitzburg, Russo et al. 2016; Papakostas, Martinson et al. 2016; Passos, Mwangi et al. 2016; Rong, Liu et al. 2016; Salagre, Fernandes et al. 2016; Spinhoven, Drost et al. 2016; Suppes, Silva et al. 2016; White, Zaninotto et al. 2016; Yovell, Bar et al. 2016)

Al-Karawi, D. and L. Jubair (2016). ***"Bright light therapy for nonseasonal depression: Meta-analysis of clinical trials."*** Journal of Affective Disorders 198: 64-71. http://www.sciencedirect.com/science/article/pii/S0165032716300076

Abstract Background Bright light therapy (BLT) is a well-established treatment for seasonal depression. In the last two decades, the interest in BLT has expanded to involve other nonseasonal types of depression. The role of BLT for nonseasonal depression remains unsettled. In view of the growing number of studies in this area, this review aimed to assess the efficacy of BLT in nonseasonal depression. Methods We searched Pubmed; Scopus; PsychINFO; Evidence Based Medicine Guidelines and Cochrane Library until December 2015. The Standardized mean difference was calculated to assess the efficacy of BLT in nonseasonal depression. Data were subgrouped according to different study characteristics. Heterogeneity was assessed by examining the I2 index. Results Nine trials met the inclusion criteria. After employing the more conservative random-effects model, the overall model showed a significant reduction of depressive symptoms after BLT administration (SMD=−0.62, P<0.001, I2=37%). In particular, BLT appears to be efficacious when administered for 2-5 weeks (SMD=−0.78, P<0.001, I2=0%), and as monotherapy (SMD=−0.71, P<0.001, I2=18%). Studies of BLT for perinatal depression have found statistically insignificant improvement (SMD=−0.17, P>0.05, I2=44%). Limitations The overall heterogeneity of the included trials was moderate. The participants were not adequately blinded to the intervention. The sample size was small for certain subgroups. The long-term effect of BLT on depression was not explored. Conclusions BLT appears to be efficacious, particularly when administered for 2–5 weeks' duration and as monotherapy. There is an obvious need to optimize the duration and intensity of exposure, the timing and the duration of treatment sessions.

Amsterdam, J. D., L. Lorenzo-Luaces, et al. (2016). ***"Short-term venlafaxine v. Lithium monotherapy for bipolar type ii major depressive episodes: Effectiveness and mood conversion rate."*** The British Journal of Psychiatry 208(4): 359-365. http://bjp.rcpsych.org/content/bjprcpsych/208/4/359.full.pdf

Background Controversy exists over antidepressant use in bipolar II depression.AimsTo compare the safety and effectiveness of antidepressant v. mood stabiliser monotherapy for bipolar type II major depressive episodes. Method Randomised, double-blind, parallel-group, 12-week comparison of venlafaxine (n = 65) v. lithium (n = 64) monotherapy in adult out-patients (trial registration number NCT00602537). Results Primary outcome – venlafaxine produced a greater response rate (67.7%) v. lithium (34.4%, P<;0.001). Secondary outcomes – venlafaxine produced a greater remission rate (58.5% v. 28.1%, P<0.001); greater decline in depression symptom scores over time (β = −5.32, s.e. = 1.16, χ2 = 21.19, P<0.001); greater reduction in global severity scores over time (β = −1.05, s.e. = 0.22, w2 = 22.33, P<0.001); and greater improvement in global change scores (β = −1.31, s.e. = 0.32, χ2 = 16.95, P<0.001) relative to lithium. No statistically significant or clinically meaningful differences in hypomanic symptoms were observed between treatments. Conclusions These findings suggest that short-term venlafaxine monotherapy may provide effective antidepressant treatment for bipolar II depression without a statistically significant increase in hypomanic symptoms relative to lithium.

Armitage, C. J., W. A. Rahim, et al. (2016). ***"An exploratory randomised trial of a simple, brief psychological intervention to reduce subsequent suicidal ideation and behaviour in patients admitted to hospital for self-harm."*** The British Journal of Psychiatry 208(5): 470-476. http://bjp.rcpsych.org/content/bjprcpsych/208/5/470.full.pdf

Background Implementation intentions link triggers for self-harm with coping skills and appear to create an automatic tendency to invoke coping responses when faced with a triggering situation. Aims To test the effectiveness of implementation intentions in reducing suicidal ideation and behaviour in a high-risk group. Method Two hundred and twenty-six patients who had self-harmed were randomised to: (a) forming implementation intentions with a 'volitional help sheet'; (b) self-generating implementation intentions without help; or (c) thinking about triggers and coping, but not forming implementation intentions. We measured self-reported suicidal ideation and behaviour, threats of suicide and likelihood of future suicide attempt at baseline and then again at the 3-month follow-up. Results All suicide-related outcome measures were significantly lower at follow-up among patients forming implementation intentions compared with those in the control condition (ds > 0.35). The volitional help sheet resulted in fewer suicide threats (d = 0.59) and lowered the likelihood of future suicide attempts (d = 0.29) compared with patients who self-generated implementation intentions. Conclusions Implementation intention-based interventions, particularly when supported by a volitional help sheet, show promise in reducing future suicidal ideation and behaviour.

Beard, C., K. J. Hsu, et al. (2016). ***"Validation of the phq-9 in a psychiatric sample."*** Journal of Affective Disorders 193: 267-273. http://www.sciencedirect.com/science/article/pii/S0165032715310272

Background The PHQ-9 was originally developed as a screener for depression in primary care and is commonly used in medical settings. However, surprisingly little is known about its psychometric properties and utility as a severity measure in psychiatric populations. We examined the full range of psychometric properties of the PHQ-9 in patients with a range of psychiatric disorders (i.e., mood, anxiety, personality, psychotic). Methods Patients (n=1023) completed the PHQ-9 upon admission and discharge from a partial hospital, as well as other self-report measures of depression, anxiety, well-being, and a structured diagnostic interview. Results Internal consistency was good (α=.87). The PHQ-9 demonstrated a strong correlation with a well-established measure of depression, moderate correlations with related constructs, a weak correlation with a theoretically unrelated construct (i.e., disgust sensitivity), and good sensitivity to change, with a large pre- to post-treatment effect size. Using a cut-off of ≥13, the PHQ-9 demonstrated good sensitivity (.83) and specificity (.72). A split-half exploratory factor analysis/confirmatory factor analysis suggested a two-factor solution with one factor capturing cognitive and affective

symptoms and a second factor reflecting somatic symptoms. Psychometric properties did not differ between male and female participants. Limitations No clinician-rated measure of improvement, and the sample lacked ethnoracial diversity. Conclusions This first comprehensive validation of the PHQ-9 in a large, psychiatric sample supported its use as a severity measure and as a measure of treatment outcome. It also performed well as a screener for a current depressive episode using a higher cut-off than previously recommended for primary care samples.

Bukh, J. D., P. K. Andersen, et al. (2016). ***"Rates and predictors of remission, recurrence and conversion to bipolar disorder after the first lifetime episode of depression – a prospective 5-year follow-up study."*** Psychological Medicine 46(06): 1151-1161. http://dx.doi.org/10.1017/S0033291715002676

Background In depression, non-remission, recurrence of depressive episodes after remission and conversion to bipolar disorder are crucial determinants of poor outcome. The present study aimed to determine the cumulative incidences and clinical predictors of these long-term outcomes after the first lifetime episode of depression. Method A total of 301 in- or out-patients aged 18–70 years with a validated diagnosis of a single depressive episode were assessed from 2005 to 2007. At 5 years of follow-up, 262 patients were reassessed by means of the life chart method and diagnostic interviews from 2011 to 2013. Cumulative incidences and the influence of clinical variables on the rates of remission, recurrence and conversion to bipolar disorder, respectively, were estimated by survival analysis techniques. Results Within 5 years, 83.3% obtained remission, 31.5% experienced recurrence of depression and 8.6% converted to bipolar disorder (6.3% within the first 2 years). Non-remission increased with younger age, co-morbid anxiety and suicidal ideations. Recurrence increased with severity and treatment resistance of the first depression, and conversion to bipolar disorder with treatment resistance, a family history of affective disorder and co-morbid alcohol or drug abuse. Conclusions The identified clinical characteristics of the first lifetime episode of depression should guide patients and clinicians for long-term individualized tailored treatment.

Buntrock, C., D. Ebert, et al. (2016). ***"Effect of a web-based guided self-help intervention for prevention of major depression in adults with subthreshold depression: A randomized clinical trial."*** JAMA 315(17): 1854-1863. http://dx.doi.org/10.1001/jama.2016.4326

Importance Evidence-based treatments for major depressive disorder (MDD) are not very successful in improving functional and health outcomes. Attention has increasingly been focused on the prevention of MDD. Objective To evaluate the effectiveness of a web-based guided self-help intervention for the prevention of MDD. Design, Setting, and Participants Two-group randomized clinical trial conducted between March 1, 2013, and March 4, 2015. Participants were recruited in Germany from the general population via a large statutory health insurance company (ie, insurance funded by joint employer-employee contributions). Participants included 406 self-selected adults with subthreshold depression (Centre for Epidemiologic Studies Depression Scale score ≥16, no current MDD according to Diagnostic and Statistical Manual of Mental Disorders [Fourth Edition, Text Revision] criteria).Interventions All participants had unrestricted access to usual care (visits to the primary care clinician) and were randomized to either a web-based guided self-help intervention (cognitive-behavioral and problem-solving therapy supported by an online trainer; n = 202) or a web-based psychoeducation program (n = 204). Main Outcomes and Measures The primary outcome was time to onset of MDD in the intervention group relative to the control group over a 12-month follow-up period as assessed by blinded diagnostic raters using the telephone-administered Structured Clinical Interview for DSM-IV Axis Disorders at 6- and 12-month follow-up, covering the period to the previous assessment. Results Among 406 randomized patients (mean age, 45 years; 73.9% women), 335 (82%) completed the telephone follow-up at 12 months. Fifty-five participants (27%) in the intervention group experienced MDD compared with 84 participants (41%) in the control group. Cox regression analyses controlling for baseline depressive symptom severity revealed a hazard ratio of 0.59 (95% CI, 0.42-0.82; P = .002) at 12-month follow-up. The number needed to treat to avoid 1 new case of MDD was 5.9 (95% CI, 3.9-14.6). Conclusions and Relevance Among patients with subthreshold depression, the use of a web-based guided self-help intervention compared with enhanced usual care reduced the incidence of MDD over 12 months. Further research is needed to understand whether the effects are generalizable to both first onset of depression and depression recurrence as well as efficacy without the use of an online trainer.

Cattaneo, A., C. Ferrari, et al. (2016). ***"Absolute measurements of macrophage migration inhibitory factor and interleukin-1-β mrna levels accurately predict treatment response in depressed patients."*** International Journal of Neuropsychopharmacology. http://ijnp.oxfordjournals.org/content/ijnp/early/2016/06/02/ijnp.pyw045.full.pdf

(Available in free full text) Background: Increased levels of inflammation have been associated with a poorer response to antidepressants in several clinical samples, but these findings have had been limited by low reproducibility of biomarker assays across laboratories, difficulty in predicting response probability on an individual basis, and unclear molecular mechanisms.Methods: Here we measured absolute mRNA values (a reliable quantitation of number of molecules) of Macrophage Migration Inhibitory Factor and interleukin-1β in a previously published sample from a randomized controlled trial comparing escitalopram vs nortriptyline (GENDEP) as well as in an independent, naturalistic replication sample. We then used linear discriminant analysis to calculate mRNA values cutoffs that best discriminated between responders and nonresponders after 12 weeks of antidepressants. As Macrophage Migration Inhibitory Factor and interleukin-1β might be involved in different pathways, we constructed a protein-protein interaction network by the Search Tool for the Retrieval of Interacting Genes/Proteins.Results: We identified cutoff values for the absolute mRNA measures that accurately predicted response probability on an individual basis, with positive predictive values and specificity for nonresponders of 100% in both samples (negative predictive value=82% to 85%, sensitivity=52% to 61%). Using network analysis, we identified different clusters of targets for these 2 cytokines, with Macrophage Migration Inhibitory Factor interacting predominantly with pathways involved in neurogenesis, neuroplasticity, and cell proliferation, and interleukin-1β interacting predominantly with pathways involved in the inflammasome complex, oxidative stress, and neurodegeneration.Conclusion: We believe that these data provide a clinically suitable approach to the personalization of antidepressant therapy: patients who have absolute mRNA values above the suggested cutoffs could be directed toward earlier access to more assertive antidepressant strategies, including the addition of other antidepressants or antiinflammatory drugs. [The BMJ - http://www.bmj.com/content/353/bmj.i3203?etoc= - comments *"Scientists have developed a blood test to predict whether depressed patients will respond to common antidepressants. They said that this could herald a new area of personalised treatment for people with depression, where patients who have blood inflammation above a certain threshold could receive more aggressive treatment. The research, published in the International Journal of Neuropsychopharmacology,1 focused on two biomarkers that measure blood inflammation: macrophage migration inhibitory factor and interleukin 1β. Previous research has shown that patients with depression who are resistant to conventional antidepressants have higher concentrations of inflammatory biomarkers in plasma or serum. The researchers measured absolute mRNA values of these two markers in a sample of 74 patients with moderately severe depression who were taking part in a randomised drug trial comparing the tricyclic nortriptyline with the selective serotonin reuptake inhibitor escitalopram. They also measured the two markers in a second independent sample of 68 patients who were drug-free at baseline and then took a range of antidepressant drugs. The study, which was funded by the UK Medical Research Council, found that patients whose levels of the two biomarkers were above a specified threshold level showed a 100% chance of not responding to conventional*

antidepressants. But those with inflammation below the same threshold were found to respond to first line antidepressants. About half of all patients with depression do not respond to first line antidepressants, and a third are resistant to all available drug treatments. Until now it has not been established whether a patient will respond to common antidepressants, meaning that patients are treated with a trial and error approach, which can take months. The two biomarkers examined in the study are involved in several brain mechanisms relevant to depression, including the birth of new brain cells, as well as the death of brain cells through oxidative stress. The researchers said the findings meant that patients with blood inflammation above a certain level could be directed towards more assertive antidepressant strategies, which could include a combination of more than one drug. They are recruiting for a clinical trial to test whether adding an anti-inflammatory drug to an antidepressant improves depression. Annamaria Cattaneo, study author at the Institute of Psychiatry, Psychology and Neuroscience at King's College, London, said, "This is the first time a blood test has been used to precisely predict, in two independent clinical groups of depressed patients, the response to a range of commonly prescribed antidepressants. These results also confirm and extend the mounting evidence that high levels of inflammation induce a more severe form of depression, which is less likely to respond to common antidepressants." She added, "This study moves us a step closer to providing personalised antidepressant treatment at the earliest signs of depression."]

Charles, E. F., C. G. Lambert, et al. (2016). ***"Bipolar disorder and diabetes mellitus: Evidence for disease-modifying effects and treatment implications."*** International Journal of Bipolar Disorders 4(1): 1-11. http://dx.doi.org/10.1186/s40345-016-0054-4

(Available in free full text) Background: Bipolar disorder refers to a group of chronic psychiatric disorders of mood and energy levels. While dramatic psychiatric symptoms dominate the acute phase of the diseases, the chronic course is often determined by an increasing burden of co-occurring medical conditions. High rates of diabetes mellitus in patients with bipolar disorder are particularly striking, yet unexplained. Treatment and lifestyle factors could play a significant role, and some studies also suggest shared pathophysiology and risk factors. Objective: In this systematic literature review, we explored data around the relationship between bipolar disorder and diabetes mellitus in recently published population-based cohort studies with special focus on the elderly. Methods: A systematic search in the PubMed database for the combined terms "bipolar disorder" AND "elderly" AND "diabetes" in papers published between January 2009 and December 2015 revealed 117 publications; 7 studies were large cohort studies, and therefore, were included in our review. Results: We found that age- and gender-adjusted risk for diabetes mellitus was increased in patients with bipolar disorder and vice versa (odds ratio range between 1.7 and 3.2). Discussion: Our results in large population-based cohort studies are consistent with the results of smaller studies and chart reviews. Even though it is likely that heterogeneous risk factors may play a role in diabetes mellitus and in bipolar disorder, growing evidence from cell culture experiments and animal studies suggests shared disease mechanisms. Furthermore, disease-modifying effects of bipolar disorder and diabetes mellitus on each other appear to be substantial, impacting both treatment response and outcomes. Conclusions: The risk of diabetes mellitus in patients with bipolar disorder is increased. Our findings add to the growing literature on this topic. Increasing evidence for shared disease mechanisms suggests new disease models that could explain the results of our study. A better understanding of the complex relationship between bipolar disorder and diabetes mellitus could lead to novel therapeutic approaches and improved outcomes.

Christensen, H., P. J. Batterham, et al. (2016). ***"Effectiveness of an online insomnia program (shuti) for prevention of depressive episodes (the goodnight study): A randomised controlled trial."*** The Lancet Psychiatry 3(4): 333-341. http://www.sciencedirect.com/science/article/pii/S2215036615005362

Summary Background In view of the high co-occurrence of depression and insomnia, a novel way to reduce the risk of escalating depression might be to offer an insomnia intervention. We aimed to assess whether an online self-help insomnia program could reduce depression symptoms. Methods We did this randomised controlled trial at the Australian National University in Canberra, Australia. Internet users (aged 18–64 years) with insomnia and depression symptoms, but who did not meet criteria for major depressive disorder, were randomly assigned (1:1), via computer-generated randomisation, to receive SHUTi, a 6 week, modular, online insomnia program based on cognitive behavioural therapy for insomnia, or HealthWatch, an interactive, attention-matched, internet-based placebo control program. Randomisation was stratified by age and sex. Telephone-based interviewers, statisticians, and chief investigators were masked to group allocation. The primary outcome was depression symptoms at 6 months, as measured with the Patient Health Questionnaire (PHQ-9). The primary analysis was by intention to treat. This trial is registered with the Australian New Zealand Clinical Trials Registry, number ACTRN12611000121965. Findings Between April 30, 2013, and June 9, 2014, we randomly assigned 1149 participants to receive SHUTi (n=574) or HealthWatch (n=575), of whom 581 (51%) participants completed the study program assessments at 6 weeks and 504 (44%) participants completed 6 months' follow-up. SHUTi significantly lowered depression symptoms on the PHQ-9 at 6 weeks and 6 months compared with HealthWatch (F[degrees of freedom 2,640·1]=37·2, p<0·0001). Major depressive disorder was diagnosed in 22 (4%) participants at 6 months (n=9 in the SHUTi group and n=13 in the HealthWatch group), with no superior effect of SHUTi versus HealthWatch (Fisher's exact test=0·52; p=0·32). No adverse events were reported. Interpretation Online cognitive behaviour therapy for insomnia treatment is a practical and effective way to reduce depression symptoms and could be capable of reducing depression at the population level by use of a fully automatised system with the potential for wide dissemination. Funding Australian National Health and Medical Research Council.

Cipriani, A., X. Zhou, et al. (2016). ***"Comparative efficacy and tolerability of antidepressants for major depressive disorder in children and adolescents: A network meta-analysis."*** The Lancet. http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)30385-3/abstract

(Free linked 13 minute podcast) Summary: Background Major depressive disorder is one of the most common mental disorders in children and adolescents. However, whether to use pharmacological interventions in this population and which drug should be preferred are still matters of controversy. Consequently, we aimed to compare and rank antidepressants and placebo for major depressive disorder in young people. Methods We did a network meta-analysis to identify both direct and indirect evidence from relevant trials. We searched PubMed, the Cochrane Library, Web of Science, Embase, CINAHL, PsycINFO, LiLACS, regulatory agencies' websites, and international registers for published and unpublished, double-blind randomised controlled trials up to May 31, 2015, for the acute treatment of major depressive disorder in children and adolescents. We included trials of amitriptyline, citalopram, clomipramine, desipramine, duloxetine, escitalopram, fluoxetine, imipramine, mirtazapine, nefazodone, nortriptyline, paroxetine, sertraline, and venlafaxine. Trials recruiting participants with treatment-resistant depression, treatment duration of less than 4 weeks, or an overall sample size of less than ten patients were excluded. We extracted the relevant information from the published reports with a predefined data extraction sheet, and assessed the risk of bias with the Cochrane risk of bias tool. The primary outcomes were efficacy (change in depressive symptoms) and tolerability (discontinuations due to adverse events). We did pair-wise meta-analyses using the random-effects model and then did a random-effects network meta-analysis within a Bayesian framework. We assessed the quality of evidence contributing to each network estimate using the GRADE framework. This study is registered with PROSPERO, number CRD42015016023. Findings We deemed 34 trials eligible, including 5260 participants and 14 antidepressant treatments. The quality of evidence was rated

as very low in most comparisons. For efficacy, only fluoxetine was statistically significantly more effective than placebo (standardised mean difference −0·51, 95% credible interval [CrI] −0·99 to −0·03). In terms of tolerability, fluoxetine was also better than duloxetine (odds ratio [OR] 0·31, 95% CrI 0·13 to 0·95) and imipramine (0·23, 0·04 to 0·78). Patients given imipramine, venlafaxine, and duloxetine had more discontinuations due to adverse events than did those given placebo (5·49, 1·96 to 20·86; 3·19, 1·01 to 18·70; and 2·80, 1·20 to 9·42, respectively). In terms of heterogeneity, the global I2 values were 33·21% for efficacy and 0% for tolerability. Interpretation When considering the risk–benefit profile of antidepressants in the acute treatment of major depressive disorder, these drugs do not seem to offer a clear advantage for children and adolescents. Fluoxetine is probably the best option to consider when a pharmacological treatment is indicated.

Clarke, G., L. L. DeBar, et al. (2016). ***"Cognitive behavioral therapy in primary care for youth declining antidepressants: A randomized trial."*** Pediatrics 137(5).
http://pediatrics.aappublications.org/content/pediatrics/137/5/e20151851.full.pdf

BACKGROUND AND OBJECTIVE: Health care providers have few alternatives for youth depression other than antidepressants. We examined whether brief cognitive behavioral therapy (CBT) is a viable alternative in primary care. METHODS: A total of 212 adolescents aged 12 to 18 with major depression who had recently declined or quickly discontinued new antidepressant treatment were randomized to self-selected treatment as usual (TAU) control condition or TAU plus brief individual CBT. Blinded evaluators followed youth for 2 years. The primary outcome was time to major depression diagnostic recovery. RESULTS: CBT was superior to the control condition on the primary outcome of time to diagnostic recovery from major depression, with number needed to treat from 4 to 10 across follow-up. A similar CBT advantage was found for time to depression diagnosis response, with number needed to treat of 5 to 50 across time points. We observed a significant advantage for CBT on many secondary outcomes over the first year of follow-up but not the second year. Cohen's d effect sizes for significant continuous measures ranged from 0.28 to 0.44, in the small to medium effect range. Most TAU health care services did not differ across conditions, except for psychiatric hospitalizations, which occurred at a significantly higher rate in the control condition through the first year of follow-up. CONCLUSIONS: Observed results were consistent with recent meta-analyses of CBT for youth depression. The initial year of CBT superiority imparted an important clinical benefit and may reduce the risk of future recurrent depression episodes.

Coimbra, D. G., A. C. Pereira e Silva, et al. (2016). ***"Do suicide attempts occur more frequently in the spring too? A systematic review and rhythmic analysis."*** Journal of Affective Disorders 196: 125-137.
http://www.sciencedirect.com/science/article/pii/S0165032715309083

Abstract Background Seasonal variations in suicides have been reported worldwide, however, there may be a different seasonal pattern in suicide attempts. The aim of this study was to perform a systematic review on seasonality of suicide attempts considering potential interfering variables, and a statistical analysis for seasonality with the collected data. Method Observational epidemiological studies about seasonality in suicide attempts were searched in PubMed, Web of Science, LILACS and Cochrane Library databases with terms attempted suicide, attempt and season. Monthly or seasonal data available were evaluated by rhythmic analysis softwares. Results Twenty-nine articles from 16 different countries were included in the final review. It was observed different patterns of seasonality, however, suicide attempts in spring and summer were the most frequent seasons reported. Eight studies indicated differences in sex and three in the method used for suicide attempts. Three articles did not find a seasonal pattern in suicide attempts. Cosinor analysis identified an overall pattern of seasonal variation with a suggested peak in spring, considering articles individually or grouped and independent of sex and method used. A restricted analysis with self-poisoning in hospital samples demonstrated the same profile. Limitations Grouping diverse populations and potential analytical bias due to lack of information are the main limitations. Conclusions The identification of a seasonal profile suggests the influence of an important environmental modulator that can reverberate to suicide prevention strategies. Further studies controlling interfering variables and investigating the biological substrate for this phenomenon would be helpful to confirm our conclusion.

Davidson, S. K., C. F. Dowrick, et al. (2016). ***"Impact of functional and structural social relationships on two year depression outcomes: A multivariate analysis."*** Journal of Affective Disorders 193: 274-281.
http://www.sciencedirect.com/science/article/pii/S016503271530803X

Background High rates of persistent depression highlight the need to identify the risk factors associated with poor depression outcomes and to provide targeted interventions to people at high risk. Although social relationships have been implicated in depression course, interventions targeting social relationships have been disappointing. Possibly, interventions have targeted the wrong elements of relationships. Alternatively, the statistical association between relationships and depression course is not causal, but due to shared variance with other factors. We investigated whether elements of social relationships predict major depressive episode (MDE) when multiple relevant variables are considered. Method Data is from a longitudinal study of primary care patients with depressive symptoms. 494 participants completed questionnaires at baseline and a depression measure (PHQ-9) two years later. Baseline measures included functional (i.e. quality) and structural (i.e. quantity) social relationships, depression, neuroticism, chronic illness, alcohol abuse, childhood abuse, partner violence and sociodemographic characteristics. Logistic regression with generalised estimating equations was used to estimate the association between social relationships and MDE. Results Both functional and structural social relationships predicted MDE in univariate analysis. Only functional social relationships remained significant in multivariate analysis (OR: 0.87; 95%CI: 0.79–0.97; p=0.01). Other unique predictors of MDE were baseline depression severity, neuroticism, childhood sexual abuse and intimate partner violence. Limitations We did not assess how a person's position in their depression trajectory influenced the association between social relationships and depression. Conclusions Interventions targeting relationship quality may be part of a personalised treatment plan for people at high risk due of persistent depression due to poor social relationships.

Delgadillo, J., O. Moreea, et al. (2016). ***"Different people respond differently to therapy: A demonstration using patient profiling and risk stratification."*** Behaviour Research and Therapy 79: 15-22.
http://www.sciencedirect.com/science/article/pii/S0005796716300249

Background This study aimed to identify patient characteristics associated with poor outcomes in psychological therapy, and to develop a patient profiling method. Method Clinical assessment data for 1347 outpatients was analysed. Final treatment outcome was based on reliable and clinically significant improvement (RCSI) in depression (PHQ-9) and anxiety (GAD-7) measures. Thirteen patient characteristics were explored as potential outcome predictors using logistic regression in a cross-validation design. Results Disability, employment status, age, functional impairment, baseline depression and outcome expectancy predicted post-treatment RCSI. Regression coefficients for these factors were used to derive a weighting scheme called Leeds Risk Index (LRI), used to assign risk scores to individual cases. After stratifying cases into three levels of LRI scores, we found significant differences in RCSI and treatment completion rates. Furthermore, LRI scores were significantly correlated with the proportion of treatment sessions classified as 'not on track'. Conclusions The LRI tool can identify cases at risk of poor progress to inform personalized treatment recommendations for low and high intensity psychological interventions.

Eckerd, L. M., J. E. Barnett, et al. (2016). ***"Grief following pet and human loss: Closeness is key."*** Death Stud 40(5): 275-282. http://www.tandfonline.com/doi/abs/10.1080/07481187.2016.1139014?journalCode=udst20

The authors compared grief severity and its predictors in two equivalent college student samples who had experienced the death of a pet (n = 211) or a person (n = 146) within the past 2 years. The human death sample reported higher grief severity, p < .01, but effect sizes were small (ds = .28–.30). For both samples, closeness to the deceased was overwhelmingly the strongest predictor of grief severity; other predictors generally dropped out with closeness added to the model. Results highlight the importance of including closeness to deceased in grief research, and its centrality in understanding grief counseling clients.

Fava, M., A. Memisoglu, et al. (2016). ***"Opioid modulation with buprenorphine/samidorphan as adjunctive treatment for inadequate response to antidepressants: A randomized double-blind placebo-controlled trial."*** American Journal of Psychiatry 173(5): 499-508. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2015.15070921

Objective: Major depressive disorder has been associated with dysregulation of the endogenous opioid system. The authors sought to determine whether opioid modulation achieved through administration of ALKS 5461, a combination of a μ- and κ-opioid partial agonist, buprenorphine, and a μ-opioid antagonist, samidorphan, would exhibit antidepressant activity in patients with major depression. Method: A multicenter, randomized, double-blind, placebo-controlled, two-stage sequential parallel comparison design study was conducted in adults with major depression who had an inadequate response to one or two courses of antidepressant treatment. Participants were randomly assigned to receive adjunctive treatment with 2 mg/2 mg of buprenorphine/samidorphan (the 2/2 dosage group), 8 mg/8 mg of buprenorphine/samidorphan (the 8/8 dosage group), or placebo. Antidepressant effect was measured based on change from baseline to the end of 4 weeks of treatment on the 17-item Hamilton Depression Rating Scale (HAM-D), the Montgomery-Åsberg Depression Rating Scale (MADRS), and the Clinical Global Impressions severity scale (CGI-S). Results: Compared with the placebo group, there were significantly greater improvements in the 2/2 dosage group across the three depression outcome measures (HAM-D: −2.8, 95% CI=−5.1, −0.6; MADRS: −4.9, 95% CI=−8.2, −1.6; CGI-S: −0.5, 95% CI=−0.9, −0.1). There was also evidence of improvement in the 8/8 dosage group, although it did not achieve statistical significance. Overall, the buprenorphine/samidorphan combinations were well tolerated, and there was no evidence of opioid withdrawal on treatment discontinuation. Conclusions: The buprenorphine/samidorphan combination is a novel and promising candidate for treatment of major depressive disorder in patients who have an inadequate response to standard antidepressants.

Fernandes, B. S., O. M. Dean, et al. (2016). ***"N-acetylcysteine in depressive symptoms and functionality: A systematic review and meta-analysis."*** J Clin Psychiatry 77(4): e457-466. http://www.ncbi.nlm.nih.gov/pubmed/27137430

OBJECTIVE: To assess the utility of N-acetylcysteine administration for depressive symptoms in subjects with psychiatric conditions using a systematic review and meta-analysis. DATA SOURCES: A computerized literature search was conducted in MEDLINE, Embase, the Cochrane Library, SciELO, PsycINFO, Scopus, and Web of Knowledge. No year or country restrictions were used. The Boolean terms used for the electronic database search were (NAC OR N-acetylcysteine OR acetylcysteine) AND (depression OR depressive OR depressed) AND (trial). The last search was performed in November 2014. STUDY SELECTION: The literature was searched for double-blind, randomized, placebo-controlled trials using N-acetylcysteine for depressive symptoms regardless of the main psychiatric condition. Using keywords and cross-referenced bibliographies, 38 studies were identified and examined in depth. Of those, 33 articles were rejected because inclusion criteria were not met. Finally, 5 studies were included. DATA EXTRACTION: Data were extracted independently by 2 investigators. The primary outcome measure was change in depressive symptoms. Functionality, quality of life, and manic and anxiety symptoms were also examined. A full review and meta-analysis were performed. Standardized mean differences (SMDs) and odds ratios (ORs) with 95% CIs were calculated. RESULTS: Five studies fulfilled our inclusion criteria for the meta-analysis, providing data on 574 participants, of whom 291 were randomized to receive N-acetylcysteine and 283 to placebo. The follow-up varied from 12 to 24 weeks. Two studies included subjects with bipolar disorder and current depressive symptoms, 1 included subjects with MDD in a current depressive episode, and 2 included subjects with depressive symptoms in the context of other psychiatric conditions (1 trichotillomania and 1 heavy smoking). Treatment with N-acetylcysteine improved depressive symptoms as assessed by Montgomery-Asberg Depression Rating Scale and Hamilton Depression Rating Scale when compared to placebo (SMD = 0.37; 95% CI = 0.19 to 0.55; P < .001). Subjects receiving N-acetylcysteine had better depressive symptoms scores on the Clinical Global Impressions-Severity of Illness scale at follow-up than subjects on placebo (SMD = 0.22; 95% CI = 0.03 to 0.41; P < .001). In addition, global functionality was better in N-acetylcysteine than in placebo conditions. There were no changes in quality of life. With regard to adverse events, only minor adverse events were associated with N-acetylcysteine (OR = 1.61; 95% CI = 1.01 to 2.59; P = .049). CONCLUSIONS: Administration of N-acetylcysteine ameliorates depressive symptoms, improves functionality, and shows good tolerability.

Fornaro, M., L. Orsolini, et al. (2016). ***"The prevalence and predictors of bipolar and borderline personality disorders comorbidity: Systematic review and meta-analysis."*** Journal of Affective Disorders 195: 105-118. http://www.sciencedirect.com/science/article/pii/S016503271531291X

AbstractI ntroduction Data about the prevalence of borderline personality (BPD) and bipolar (BD) disorders comorbidity are scarce and the boundaries remain controversial. We conducted a systematic review and meta-analysis investigating the prevalence of BPD in BD and BD in people with BPD. Methods Two independent authors searched MEDLINE, Embase, PsycINFO and the Cochrane Library from inception till November 4, 2015. Articles reporting the prevalence of BPD and BD were included. A random effects meta-analysis and meta-regression were conducted. Results Overall, 42 papers were included: 28 considering BPD in BD and 14 considering BD in BPD. The trim and fill adjusted analysis demonstrated the prevalence of BPD among 5273 people with BD (39.94±11.78 years, 44% males) was 21.6% (95% CI 17.0–27.1). Higher comorbid BPD in BD were noted in BD II participants (37.7%, 95% CI 21.9–56.6, studies=6) and North American studies (26.2%, 95% CI 18.7–35.3, studies=11). Meta regression established that a higher percentage of males and higher mean age significantly (p<0.05) predicted a lower prevalence of comorbid BPD in BD participants. The trim and fill adjusted prevalence of BD among 1814 people with BPD (32.22±7.35 years, 21.5% male) was 18.5% (95% CI 12.7–26.1). Limitations Paucity of longitudinal/control group studies and accurate treatment records. Conclusions BPD-BD comorbidity is common, with approximately one in five people experiencing a comorbid diagnosis. Based on current diagnostic constructs, and a critical interpretation of results, both qualitative and quantitative syntheses of the evidence prompt out the relevance of differences rather similarities between BD and BPD.

Fountoulakis, K. N., C. Savopoulos, et al. (2016). ***"Climate change but not unemployment explains the changing suicidality in thessaloniki greece (2000–2012)."*** Journal of Affective Disorders 193: 331-338. http://www.sciencedirect.com/science/article/pii/S0165032715313069

Introduction Recently there was a debate concerning the etiology behind attempts and completed suicides. The aim of the current study was to search for possible correlations between the rates of attempted and completed suicide and climate

variables and regional unemployment per year in the county of Thessaloniki, Macedonia, northern Greece, for the years 2000–12. Material and methods The regional rates of suicide and attempted suicide as well as regional unemployment were available from previous publications of the authors. The climate variables were calculated from the daily E-OBS gridded dataset which is based on observational data Results Only the male suicide rates correlate significantly with high mean annual temperature but not with unemployment. The multiple linear regression analysis results suggest that temperature is the only variable that determines male suicides and explains 51% of their variance. Unemployment fails to contribute significantly to the model. There seems to be a seasonal distribution for attempts with mean rates being higher for the period from May to October and the rates clearly correlate with temperature. The highest mean rates were observed during May and August and the lowest during December and February. Multiple linear regression analysis suggests that temperature also determines the female attempts rate although the explained variable is significant but very low (3–5%) Conclusion Climate variables and specifically high temperature correlate both with suicide and attempted suicide rates but with a different way between males and females. The climate effect was stronger than the effect of unemployment.

Gibson, K., C. Cartwright, et al. (2016). ***"'In my life antidepressants have been…': A qualitative analysis of users' diverse experiences with antidepressants."*** BMC Psychiatry 16(1): 1-7. http://dx.doi.org/10.1186/s12888-016-0844-3

(Available in free full text) Background: While mental health professionals have focused on concerns about whether antidepressants work on a neurochemical level it is important to understand the meaning this medication holds in the lives of people who use it. This study explores diversity in the experience of antidepressant users. Methods: One thousand seven hundred forty-seven New Zealand antidepressant users responded to an open-ended question about their experience of antidepressants. This was analysed using content and thematic analysis. Results: There was considerable diversity in participants' responses including positive (54 %), negative (16 %) and mixed (28 %) experiences with antidepressants. Those with positive experiences saw antidepressants as a necessary treatment for a 'disease', a life saver, a way of meeting social obligations, dealing with difficult circumstances or a stepping stone to further help. Negative themes described antidepressants as being ineffective, having unbearable side effects, undermining emotional authenticity, masking real problems and reducing the experience of control. Mixed experience themes showed how participants weighed up the unpleasant side effects against the benefits, felt calmer but less like themselves, struggled to find the one or dosage and felt stuck with continuing on antidepressants when they wished to stop. Conclusions: Mental health professions need to recognize that antidepressants are not a 'one size fits all' solution.

Goracci, A., P. Rucci, et al. (2016). ***"Development, acceptability and efficacy of a standardized healthy lifestyle intervention in recurrent depression."*** Journal of Affective Disorders 196: 20-31. http://www.sciencedirect.com/science/article/pii/S0165032715308715

Abstract Background Research evidence on the effects of integrated multifaceted lifestyle interventions for depression is scanty. The aim of the present study is to report on the development, acceptability and efficacy of a standardized healthy lifestyle intervention, including exercise, eating habits, sleep hygiene and smoking cessation in preventing relapses. Methods One hundred-sixty outpatients with recurrent unipolar depression or bipolar disorder were recruited after achieving full remission or recovery from the most recent depressive episode. Patients were randomized to 3-months of usual care or to an intervention aimed at promoting a healthy lifestyle (HLI), as an augmentation of pharmacological maintenance treatment. Usual care consisted of clinical management visits. At the end of the intervention, follow-up visits were scheduled at 3,6,9 and 12 months. Results During the intervention phase, 1 relapse occurred in the HLI group and 4 in the control group. Over the 12 months of follow-up, relapses were 5 in the HLI group and 16 in control group. Using an intent-to-treat approach, the overall percentage of relapses was 6/81 (7.4%) in the HLI group vs. 20/79 (25.3%) in the control group. In a Kaplan-Meier survival analysis the risk of relapse was significantly lower in patients receiving the HLI intervention (log-rank test, p=0.003) over the 60 weeks of observation. The majority of patients assigned to HLI adhered to the program, and were highly motivated throughout the intervention. Limitations The retention rate was low because patients were recruited during the maintenance phase and the 1-year follow-up was relatively short to detect a long-term effect of HLI. Conclusions The HLI program proved to be efficacious in preventing relapses. Given the absence of contraindications and its cost-effectiveness in routine practice, the use of HLI should be encouraged to promote the well-being of patients with recurrent depression.

Grant, J. E., S. R. Chamberlain, et al. (2016). ***"N-acetylcysteine in the treatment of excoriation disorder: A randomized clinical trial."*** JAMA Psychiatry 73(5): 490-496. http://dx.doi.org/10.1001/jamapsychiatry.2016.0060

Importance Excoriation (skin-picking) disorder (SPD) is a disabling, underrecognized condition in which individuals repeatedly pick at their skin, leading to noticeable tissue damage. To date, there has been no clearly effective pharmacologic or psychological treatment for SPD.Objective To determine whether N-acetylcysteine, an amino acid that appears to restore extracellular glutamate concentration in the nucleus accumbens, will be more effective than placebo in reducing compulsive picking behavior.Design, Setting, and Participants A randomized, double-blind trial was conducted at ambulatory care centers at the University of Minnesota (September 12, 2011, to June 15, 2012) and the University of Chicago (December 17, 2012, to June 26, 2015) and included 66 adults with SPD. Data analysis was performed from July 16 to September 9, 2015.Interventions N-acetylcysteine (dosing range, 1200-3000 mg/d) or placebo was administered for 12 weeks.Main Outcomes and Measures Participants were assessed using measures of skin-picking severity, including the modified Yale-Brown Obsessive Compulsive Scale (NE-YBOCS); total scores range from 0 to 40, with higher scores reflective of greater symptom severity. Another measure of skin-picking severity was the Clinical Global Impression-Severity Scale; total scores range from 1 (normal) to 7 (among the most extremely ill patients), and improvement ratings range from 7 (very much worse) to 1 (very much improved). Selected cognitive tasks included the Intra-dimensional/Extra-dimensional Shift Task to examine cognitive flexibility, with the key outcome measures being the number of errors, and Stop-Signal Reaction Time task, which evaluates motor inhibition. Outcomes were examined using a linear mixed-effects model.Results Of the 66 participants (31 randomized to placebo and 35 to N-acetylcysteine) included in the analysis, 59 (89%) were women; mean (SD) age was 34.8 (11.0) years. Compared with placebo, N-acetylcysteine treatment was associated with significant improvements in the NE-YBOCS. At baseline, NE-YBOCS scores were 18.9 and 17.9 for the treatment and placebo groups, respectively, and at 12 weeks, the scores were 11.5 and 14.1 for the treatment and placebo groups, respectively (P = .048). For the Clinical Global Impression-Severity scale, baseline scores were 3.5 and 4.0 and 12-week scores were 3.0 and 4.2, respectively (P = .003). These effects were significant both in terms of treatment by time interactions and post hoc tests at 1 or more individual time points. At the study's end point, of the 53 participants who completed the study, 15 of the 32 participants (47%) receiving N-acetylcysteine were much or very much improved compared with 4 of the 21 participants (19%) receiving placebo (P = .03). There were no significant differences between the active and placebo arms in terms of psychosocial functioning.Conclusions and Relevance N-acetylcysteine treatment resulted in significant reductions in skin-picking symptoms and was well tolerated. The glutamate system may prove a beneficial target in treating SPD and other compulsive behaviors.

Hallford, D. J. and D. Mellor (2015). ***"Brief reminiscence activities improve state well-being and self-concept in young adults: A randomised controlled experiment."*** Memory: 1-10. http://www.ncbi.nlm.nih.gov/pubmed/26522498

Reminiscence-based psychotherapies have been demonstrated to have robust effects on a range of therapeutic outcomes. However, little research has been conducted on the immediate effects of guided activities they are composed of, or how these might differ dependent on the type of reminiscence. The current study utilised a controlled experimental design, whereby 321 young adults (mean age = 25.5 years, SD = 3.0) were randomised to one of four conditions of online reminiscence activity: problem-solving (successful coping experiences), identity (self-defining events contributing to a meaningful and continuous personal identity), bitterness revival (negative or adverse events), or a control condition (any memory from their past). Participants recalled autobiographical memories congruent with the condition, and answered questions to facilitate reflection on the memories. The results indicated that problem-solving and identity reminiscence activities caused significant improvements in self-esteem, meaning in life, self-efficacy and affect, whereas no effects were found in the bitterness revival and control conditions. Problem-solving reminiscence also caused a small effect in increasing perceptions of a life narrative/s. Differences between the conditions did not appear to be explained by the positive-valence of memories. These results provide evidence for the specific effects of adaptive types of problem-solving and identity reminiscence in young adults.

Hallford, D. J. and D. Mellor (2016). ***"Autobiographical memory and depression: Identity-continuity and problem-solving functions indirectly predict symptoms over time through psychological well-being."*** Applied Cognitive Psychology 30(2): 152-159. http://dx.doi.org/10.1002/acp.3169

(Available in free full text) The aim of this study was to assess the longitudinal associations between adaptive autobiographical memory functions and depressive symptoms. Consistent with the proposed mechanisms of change underpinning cognitive-reminiscence therapy (CRT), it was hypothesised that more frequent adaptive reminiscence would lead to increases in psychological resources over time and indirectly affect depressive symptoms through this pathway. A sample of 171 young adults (mean age = 25.9 years, SD = 3.5) completed measures of how frequently they utilised autobiographical memory for identity-continuity and problem-solving purposes, depressive symptoms and personal resources (self-esteem, self-efficacy, meaning in life and optimism) at two time-points. The results of structural equation modelling supported the model of indirect influence between reminiscence functions and depression through these psychological resources. These findings clarify the effects of adaptive autobiographical memory on depressive symptoms in young adults and indicate potential benefits of interventions such as CRT. *[The excellent BPS Research Digest* - http://digest.bps.org.uk/2016/04/looking-back-on-your-past-can-make-you.html - *comments "Is spending time looking back on our lives good for our mental health? A lot of research suggests it is, but these studies have been cross-sectional, making it hard to form a clear causal story – for example, perhaps being happier makes it more likely that people will reminisce. On the other hand, there are therapeutic trials that show purposeful reminiscence can bring about clinically meaningful decreases in depression. Now, a longitudinal investigation in Applied Cognitive Psychology provides further evidence for the benefits of the right kind of looking back, and it shows that reminiscence has this effect by building up our psychological resources. The work, from Deakin University's David Hallford and David Mellor, recruited 171 adult US participants (average age 26) using Amazon's Mechanical Turk survey website. At two time points a week apart, the participants rated their levels of depression symptoms and they reflected on the past week, reporting how much they had thought or talked about their personal history during that time, and whether they had done it to achieve either of two specific goals: to help define who they are today – the identity function of reminiscence – or to remind themselves that they have the skills or character to deal with present challenges, which is the problem-solving function. Past research suggests these adaptive uses of reminiscence are what seem to have the clinical effects over time. The current study clarified that these kinds of reminiscence were not associated with lower levels of depression in the same week that the reminiscence took place, but were associated with less depression one week later. So, you're not necessarily in a better state during periods when you are being reflective, but reminiscing now is likely to protect you against depression in the future. Note, the effects of reminiscence on next week's depression symptoms were not direct. Rather, reminiscence affected a set of positive psychological resources: self esteem, confidence in own ability, optimism and meaning in life. And where these resources were enhanced, depression dropped. Although the participants in this study reported a range of depression symptoms, they were not diagnosed with clinical depression. Nonetheless, the results do suggest a cognitive explanation for how reminiscence-based therapy is effective for people with more serious depression. Rather than reminiscence activating brain pathways that somehow flush out depression, it provides sense, meaning and ways of thinking to free the individual from feelings of joylessness or despair. Prior evidence (albeit cross-sectional) has suggested that reminiscence can cut both ways – dwelling on bitter experiences can increase our psychological distress, and I should emphasise that this new research focused on adaptive reminiscence. Casting your mind back through the past to reflect on the person you are, or are constantly becoming; treating your experience as a testimonial to what you are capable of. By these activities, we can nourish the psyche and protect our wellbeing."].*

Hartig, J. and J. Viola (2016). ***"Online grief support communities: Therapeutic benefits of membership."*** OMEGA - Journal of Death and Dying 73(1): 29-41. http://ome.sagepub.com/content/73/1/29.abstract

Online grief support communities have become popular in recent years for those seeking information and empathetic others following the death of someone close to them. Hundreds of Facebook pages and Web sites are now devoted to bereavement—and health-care professionals need to assess what therapeutic benefits virtual communities might offer to help people manage grief and integrate death into their lives. In the current study of online grief support networks (N = 185), individuals report less psychological distress as a result of joining these groups—and this psychosocial benefit increased over time. Individuals who were members for a year or more characterized their grief as less severe compared with those who had a shorter tenure in the community. Additional findings and implications are discussed.

Hawton, K., K. G. Witt, et al. (2016). ***"Psychosocial interventions following self-harm in adults: A systematic review and meta-analysis."*** The Lancet Psychiatry 3(8): 740-750. http://dx.doi.org/10.1016/S2215-0366(16)30070-0

Background Self-harm (intentional acts of non-fatal self-poisoning or self-injury) is common, particularly in young adults aged 15–35 years, often repeated, and strongly associated with suicide. Effective aftercare of individuals who self-harm is therefore important. We have undertaken a Cochrane systematic review and meta-analysis of the effectiveness of psychosocial interventions for self-harm in adults. Methods We searched five electronic databases (CCDANCTR-Studies and References, CENTRAL, MEDLINE, Embase, and PsycINFO) between Jan 1, 1998, and April 29, 2015, for randomised controlled trials of psychosocial interventions for adults after a recent (within 6 months) episode of self-harm. Most interventions were assessed in single trials. We report results for interventions for which at least three randomised controlled trials comparing interventions with treatment as usual have been published and hence might contribute to clinical guidance. The primary outcome was repetition of self-harm at the conclusion of treatment and at 6, 12, and 24 months' follow-up analysed, when available, with the intention-to-treat method; if this was not possible, we analysed with all available case data. Findings We identified 29 non-overlapping randomised controlled trials with three independent trials of the same intervention. Cognitive-behavioural-based psychotherapy (CBT; comprising cognitive-behavioural and problem-solving therapy) was associated with fewer participants repeating self-harm at 6 months' (odds ratio 0·54, 95% CI 0·34–0·85; 12 trials; n=1317) and at 12 months' follow-up (0·80,

0·65–0·98; ten trials; n=2232). There were also significant improvements in the secondary outcomes of depression, hopelessness, suicidal ideation, and problem solving. Patients receiving dialectical behaviour therapy (in three trials) were not less likely to repeat self-harm compared with those provided with treatment as usual at 6 months (odds ratio [OR] 0·59, 95% CI 0·16–2·15; n=267, three trials) or at 12 months (0·36, 0·05–2·47; n=172, two trials). However, the secondary endpoint of frequency of self-harm was associated with a significant reduction with use of dialectical behaviour therapy (mean difference −18·82, 95% CI −36·68 to −0·95). Four trials each of case management (OR 0·78, 95% CI 0·47–1·30; n=1608) and sending regular postcards (OR 0·87, 95% CI 0·62–1·23; n=3277) did not reduce repetition of self-harm. Interpretation CBT seems to be effective in patients after self-harm. Dialectical behaviour therapy did not reduce the proportion of patients repeating self-harm but did reduce the frequency of self-harm. However, aside from CBT, there were few trials of other promising interventions, precluding firm conclusions as to their effectiveness.

Henriksen, T. E. G., S. Skrede, et al. (2016). ***"Blue-blocking glasses as additive treatment for mania: A randomized placebo-controlled trial."*** Bipolar Disorders 18(3): 221-232. http://dx.doi.org/10.1111/bdi.12390

(Available in free full text) Objectives The discovery of the blue lightsensitive retinal photoreceptor responsible for signaling daytime to the brain suggested that light to the circadian system could be inhibited by using blue-blocking orange tinted glasses. Blue-blocking (BB) glasses are a potential treatment option for bipolar mania. We examined the effectiveness of BB glasses in hospitalized patients with bipolar disorder in a manic state. Methods In a single-blinded, randomized, placebo-controlled trial (RCT), eligible patients (with bipolar mania; age 18–70 years) were recruited from five clinics in Norway. Patients were assigned to BB glasses or placebo (clear glasses) from 6 p.m. to 8 a.m. for 7 days, in addition to treatment as usual. Symptoms were assessed daily by use of the Young Mania Rating Scale (YMRS). Motor activity was assessed by actigraphy, and compared to data from a healthy control group. Wearing glasses for one evening/night qualified for inclusion in the intention-to-treat analysis. Results From February 2012 to February 2015, 32 patients were enrolled. Eight patients dropped out and one was excluded, resulting in 12 patients in the BB group and 11 patients in the placebo group. The mean decline in YMRS score was 14.1 [95% confidence interval (CI): 9.7–18.5] in the BB group, and 1.7 (95% CI: −4.0 to 7.4) in the placebo group, yielding an effect size of 1.86 (Cohen's d). In the BB group, one patient reported headache and two patients experienced easily reversible depressive symptoms. Conclusions This RCT shows that BB glasses are effective and feasible as add-on treatment for bipolar mania.

Huijbers, M. J., P. Spinhoven, et al. (2016). ***"Discontinuation of antidepressant medication after mindfulness-based cognitive therapy for recurrent depression: Randomised controlled non-inferiority trial."*** The British Journal of Psychiatry 208(4): 366-373. http://bjp.rcpsych.org/content/bjprcpsych/208/4/366.full.pdf

(Available in free full text) Background Mindfulness-based cognitive therapy (MBCT) and maintenance antidepressant medication (mADM) both reduce the risk of relapse in recurrent depression, but their combination has not been studied. Aims To investigate whether MBCT with discontinuation of mADM is non-inferior to MBCT+mADM. Method A multicentre randomised controlled non-inferiority trial (ClinicalTrials.gov: NCT00928980). Adults with recurrent depression in remission, using mADM for 6 months or longer (n = 249), were randomly allocated to either discontinue (n = 128) or continue (n = 121) mADM after MBCT. The primary outcome was depressive relapse/recurrence within 15 months. A confidence interval approach with a margin of 25% was used to test non-inferiority. Key secondary outcomes were time to relapse/recurrence and depression severity. Results The difference in relapse/recurrence rates exceeded the non-inferiority margin and time to relapse/recurrence was significantly shorter after discontinuation of mADM. There were only minor differences in depression severity. Conclusions Our findings suggest an increased risk of relapse/recurrence in patients withdrawing from mADM after MBCT.

Johnson, K. V. and R. I. Dunbar (2016). ***"Pain tolerance predicts human social network size."*** Sci Rep 6: 25267. http://www.ncbi.nlm.nih.gov/pubmed/27121297

Personal social network size exhibits considerable variation in the human population and is associated with both physical and mental health status. Much of this inter-individual variation in human sociality remains unexplained from a biological perspective. According to the brain opioid theory of social attachment, binding of the neuropeptide beta-endorphin to mu-opioid receptors in the central nervous system (CNS) is a key neurochemical mechanism involved in social bonding, particularly amongst primates. We hypothesise that a positive association exists between activity of the mu-opioid system and the number of social relationships that an individual maintains. Given the powerful analgesic properties of beta-endorphin, we tested this hypothesis using pain tolerance as an assay for activation of the endogenous mu-opioid system. We show that a simple measure of pain tolerance correlates with social network size in humans. Our results are in line with previous studies suggesting that mu-opioid receptor signalling has been elaborated beyond its basic function of pain modulation to play an important role in managing our social encounters. The neuroplasticity of the mu-opioid system is of future research interest, especially with respect to psychiatric disorders associated with symptoms of social withdrawal and anhedonia, both of which are strongly modulated by endogenous opioids.

Karyotaki, E., Y. Smit, et al. (2016). ***"Combining pharmacotherapy and psychotherapy or monotherapy for major depression? A meta-analysis on the long-term effects."*** Journal of Affective Disorders 194: 144-152. http://www.sciencedirect.com/science/article/pii/S0165032715310387

Background The present meta-analysis aimed to examine to what extent combined pharmacotherapy with psychotherapy results in a different response to treatment compared to psychotherapy or pharmacotherapy alone in adults with major depression at six months or longer postrandomization. Methods A systematic literature search resulted in 23 randomized controlled trials with 2184 participants. Combined treatment was compared to either psychotherapy or anti-depressant medication alone in both the acute phase and the maintenance phase. Odds ratios of a positive outcome were calculated for all comparisons. Results In acute phase treatment, combined psychotherapy with antidepressants outperformed antidepressants alone at six months or longer postrandomization in patients with major depressive disorder (OR=2.93, 95%CI 2.15–3.99, $p < 0.001$). Heterogeneity was zero (95%CI 0–57%, $p < 0.05$). However, combined therapy resulted in equal response to treatment compared to psychotherapy alone at six months or longer postrandomization. As for the maintenance treatment, combined maintenance psychotherapy with antidepressants resulted in better-sustained treatment response compared to antidepressants at six months or longer postrandomization (OR=1.61, 95%CI 1.14–2.27, $p < 0.05$). Heterogeneity was zero (95%CI 0–68%, $p < 0.05$). Conclusions Combined therapy results in a superior enduring effect compared to antidepressants alone in patients with major depression. Psychotherapy is an adequate alternative for combined treatment in the acute phase as it is as effective as combined treatment in the long-term.

Keefe, J. R., C. A. Webb, et al. (2016). ***"In cognitive therapy for depression, early focus on maladaptive beliefs may be especially efficacious for patients with personality disorders."*** J Consult Clin Psychol 84(4): 353-364. http://www.ncbi.nlm.nih.gov/pubmed/26727410

OBJECTIVE: Patients with major depressive disorder (MDD) and a comorbid personality disorder (PD) have been found to exhibit relatively poor outcomes in cognitive therapy (CT) and other treatments. Adaptations of CT focusing heavily on patients' core beliefs have yielded promising findings in the treatment of PD. However, there have been no investigations that have specifically tested whether increased focus on maladaptive beliefs contributes to CT's efficacy for these patients. METHOD: CT technique use from an early CT session was assessed for 59 patients (33 without PD, 26 with PD-predominantly Cluster C) who participated in a randomized controlled trial for moderate to severe MDD. Scores were calculated for directive CT techniques (CT-Concrete) and a set of belief-focused items (CT-Belief) as rated by the Collaborative Study Process Rating Scale. Robust regressions were conducted to estimate relations between scores on each of these measures and change in depressive and PD symptoms. A PD status by CT-Belief use interaction tested the hypothesis that therapist use of CT-Belief techniques would exhibit a stronger association with symptom change in the PD group relative to the non-PD group. RESULTS: As hypothesized, a significant interaction between PD status and use of CT-Belief techniques emerged in the prediction of depressive and PD symptom change. Among PD patients, higher early CT-Belief interventions were found to predict significantly greater improvement. CT-Belief use did not predict greater symptom change among those without PD. CONCLUSIONS: Early focus on CT-Belief interventions may facilitate changes in depression and PD symptoms for patients with MDD-PD comorbidity.

Louzon, S. A., R. Bossarte, et al. (2016). ***"Does suicidal ideation as measured by the phq-9 predict suicide among va patients?"*** Psychiatric Services 67(5): 517-522. http://ps.psychiatryonline.org/doi/abs/10.1176/appi.ps.201500149

Objective: Frequency of suicidal ideation in the past two weeks, assessed by item 9 of the nine-item Patient Health Questionnaire (PHQ-9), has been positively associated with suicide mortality among patients in a setting other than the Veterans Health Administration (VHA). To inform suicide prevention activities at the VHA, it is important to evaluate whether item 9 is associated with suicide risk among patients in the VHA system. Methods: PHQ-9 assessments (N=447,245) conducted by the VHA between October 1, 2009, and September 30, 2010, were collected. National Death Index data were used to ascertain suicide mortality from the date of PHQ-9 assessment through September 30, 2011. Multivariable proportional hazards regressions were used to evaluate associations between responses to item 9 and suicide mortality. Results: After the analyses adjusted for covariates, a response of "several days" for item 9 was associated with a 75% increased risk of suicide (hazard ratio [HR]=1.75, 95% confidence interval [CI]=1.24–2.46), a response of "more than half the days" was associated with a 115% increased risk of suicide (HR=2.15, CI=1.32–3.51), and a response of "nearly every day" was associated with a 185% increased risk of suicide (HR=2.85, CI=1.81–4.47), compared with a response of "not at all." However, 71.6% of suicides during the study period occurred among patients who responded "not at all" to item 9 from their most recent PHQ-9. Conclusions: Higher levels of suicidal ideation, indicated by item 9 of the PHQ-9, were associated with increased risk of suicide among patients in the VHA system.

Luong, G., C. Wrzus, et al. (2016). ***"When bad moods may not be so bad: Valuing negative affect is associated with weakened affect-health links."*** Emotion 16(3): 387-401. http://www.ncbi.nlm.nih.gov/pubmed/26571077

Bad moods are considered "bad" not only because they may be aversive experiences in and of themselves, but also because they are associated with poorer psychosocial functioning and health. We propose that people differ in their negative affect valuation (NAV; the extent to which negative affective states are valued as pleasant, useful/helpful, appropriate, and meaningful experiences) and that affect-health links are moderated by NAV. These predictions were tested in a life span sample of 365 participants ranging from 14-88 years of age using reports of momentary negative affect and physical well-being (via experience sampling) and assessments of NAV and psychosocial and physical functioning (via computer-assisted personal interviews and behavioral measures of hand grip strength). Our study demonstrated that the more individuals valued negative affect, the less pronounced (and sometimes even nonexistent) were the associations between everyday experiences of negative affect and a variety of indicators of poorer psychosocial functioning (i.e., emotional health problems, social integration) and physical health (i.e., number of health conditions, health complaints, hand grip strength, momentary physical well-being). Exploratory analyses revealed that valuing positive affect was not associated with the analogous moderating effects as NAV. These findings suggest that it may be particularly important to consider NAV in models of affect-health links.

Mansur, R. B., L. B. Rizzo, et al. (2016). ***"Impaired glucose metabolism moderates the course of illness in bipolar disorder."*** Journal of Affective Disorders 195: 57-62. http://www.sciencedirect.com/science/article/pii/S0165032715312994

AbstractBackground The longitudinal course of bipolar disorder (BD) is highly heterogeneous, and is moderated by the presence of general medical comorbidities. This study aimed to investigate the moderating effects of impaired glucose metabolism (IGM) on variables of illness course and severity in a BD population. Methods Fifty-five patients with BD were evaluated. All subjects were evaluated with respect to current and past psychiatric and medical disorders, as well as lifetime use of any medication. Body mass index (BMI) and metabolic parameters were obtained. IGM was operationalized as pre-diabetes or type 2 diabetes mellitus. Results Thirty (54.5%) individuals had IGM. After adjustment for age, gender, ethnicity, alcohol use, smoking, BMI and past and current exposure to psychotropic medications, individuals with IGM, when compared to euglycemic participants, had an earlier age of onset (RR: 0.835, p=0.024), longer illness duration (RR: 1.754, p=0.007), a higher number of previous manic/hypomanic episodes (RR: 1.483, p=0.002) and a higher ratio of manic/hypomanic to depressive episodes (RR: 1.753, p=0.028). Moreover, we observed a moderating effect of IGM on the association between number of mood episodes and other variables of illness course, with the correlation between lifetime mood episodes and frequency of episodes being significantly greater in the IGM subgroup (RR: 1.027, p=0.029). All associations observed herein remained significant after adjusting for relevant confounding factors (e.g. age, alcohol and tobacco use, exposure to psychotropic agents, BMI). Limitations Cross-sectional design, small sample size. Conclusions Comorbid IGM may be a key moderator of illness progression in BD.

Martin, D. J., Z. Ul-Haq, et al. (2016). ***"Cardiometabolic disease and features of depression and bipolar disorder: Population-based, cross-sectional study."*** The British Journal of Psychiatry 208(4): 343-351. http://bjp.rcpsych.org/content/bjprcpsych/208/4/343.full.pdf

Background The relative contribution of demographic, lifestyle and medication factors to the association between affective disorders and cardiometabolic diseases is poorly understood. Aims To assess the relationship between cardiometabolic disease and features of depresion and bipolar disorder within a large population sample. Method Cross-sectional study of 145 991 UK Biobank participants: multivariate analyses of associations between features of depression or bipolar disorder and five cardiometabolic outcomes, adjusting for confounding factors.ResultsThere were significant associations between mood disorder features and 'any cardiovascular disease' (depression odds ratio (OR) = 1.15, 95% CI 1.12–1.19; bipolar OR = 1.28, 95% CI 1.14–1.43) and with hypertension (depression OR = 1.15, 95% CI 1.13–1.18; bipolar OR = 1.26, 95% CI 1.12–1.42). Individuals with features of mood disorder taking psychotropic medication were significantly more likely than controls not on psychotropics to report myocardial infarction (depression OR = 1.47, 95% CI 1.24–1.73; bipolar OR = 2.23, 95% CI 1.53–3.57) and stroke (depression OR = 2.46, 95% CI 2.10–2.80; bipolar OR = 2.31, 95% CI 1.39–3.85). Conclusions Associations between features of depression or bipolar disorder and cardiovascular disease outcomes were statistically independent of

demographic, lifestyle and medication confounders. Psychotropic medication may also be a risk factor for cardiometabolic disease in individuals without a clear history of mood disorder.

McLeod, G. F. H., L. J. Horwood, et al. (2016). ***"Adolescent depression, adult mental health and psychosocial outcomes at 30 and 35 years."*** Psychological Medicine 46(07): 1401-1412. http://dx.doi.org/10.1017/S0033291715002950

Background There is limited information on long-term outcomes of adolescent depression. This study examines the associations between severity of depression in adolescence and a broad array of adult functional outcomes. Method Data were gathered as part of the Christchurch Health and Development Study, a 35-year longitudinal study of a birth cohort of 1265 children born in Christchurch, New Zealand in 1977. Severity of depression at age 14–16 years was classified into three levels according to DSM symptom criteria for major depression (no depression/sub-threshold symptoms/major depression). This classification was related to adult functional outcomes assessed at ages 30 and 35 years using a generalized estimating equation modeling approach. Outcome measures spanned domains of mental disorder, education/economic circumstances, family circumstances and partner relationships. Results There were modest but statistically significant bivariate associations between adolescent depression severity and most outcomes. After covariate adjustment there remained weak but significant ($p < 0.05$) associations with rates of major depression, anxiety disorder, illicit substance abuse/dependence, any mental health problem and intimate partner violence (IPV) victimization. Estimates of attributable risk for these outcomes ranged from 3.8% to 7.8%. For two outcomes there were significant ($p < 0.006$) gender interactions such that depression severity was significantly related to increased rates of unplanned pregnancy and IPV victimization for females but not for males. Conclusions The findings reinforce the importance of the individual/family context in which adolescent depression occurs. When contextual factors and probable maturational effects are taken into account the direct effects of adolescent depression on functioning in mature adulthood appear to be very modest.

McNamara, R. K. and J. A. Welge (2016). ***"Meta-analysis of erythrocyte polyunsaturated fatty acid biostatus in bipolar disorder."*** Bipolar Disorders 18(3): 300-306. http://dx.doi.org/10.1111/bdi.12386

Objectives Dietary deficiency in polyunsaturated fatty acids (PUFAs), including the omega-3 fatty acids eicosapentaenoic acid (EPA; 20:5n-3) and docosahexaenoic acid (DHA; 22:6n-3), and excesses in omega-6 fatty acids, including linoleic acid (LA; 18:2n-6) and arachidonic acid (AA; 20:4n-6), may be associated with the pathophysiology of bipolar disorder. In an effort to provide clarification regarding the relationship between PUFA biostatus and bipolar disorder, this meta-analysis investigated studies comparing erythrocyte (red blood cell) membrane PUFA composition in patients with bipolar disorder and healthy controls. Methods A meta-analysis was performed on case–control studies comparing erythrocyte PUFA (EPA, DHA, LA and AA) levels in patients with bipolar I disorder and healthy controls. Standardized effect sizes were calculated and combined using a random effects model. Results Six eligible case-control studies comprising $n = 118$ bipolar I patients and $n = 147$ healthy controls were included in the analysis. Compared with healthy controls, patients with bipolar I disorder exhibited robust erythrocyte DHA deficits ($p = 0.0008$) and there was a trend for lower EPA ($p = 0.086$). There were no significant differences in LA ($p = 0.42$) or AA ($p = 0.64$). Conclusions Bipolar I disorder is associated with robust erythrocyte DHA deficits. These findings add to a growing body of evidence implicating omega-3 PUFA deficiency in the pathophysiology of bipolar disorder.

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

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

Mithoefer, M. C., C. S. Grob, et al. (2016). ***"Novel psychopharmacological therapies for psychiatric disorders: Psilocybin and mdma."*** The Lancet Psychiatry 3(5): 481-488. http://www.sciencedirect.com/science/article/pii/S2215036615005763

Summary 4-phosphorloxy-N,N-dimethyltryptamine (psilocybin) and methylenedioxymethamfetamine (MDMA), best known for their illegal use as psychedelic drugs, are showing promise as therapeutics in a resurgence of clinical research during the past 10 years. Psilocybin is being tested for alcoholism, smoking cessation, and in patients with advanced cancer with anxiety. MDMA is showing encouraging results as a treatment for refractory post-traumatic stress disorder, social anxiety in autistic adults, and anxiety associated with a life-threatening illness. Both drugs are studied as adjuncts or catalysts to psychotherapy, rather than as stand-alone drug treatments. This model of drug-assisted psychotherapy is a possible alternative to existing pharmacological and psychological treatments in psychiatry. Further research is needed to fully assess the potential of these compounds in the management of these common disorders that are difficult to treat with existing methods.

Nitzburg, G. C., M. Russo, et al. (2016). ***"Coping strategies and real-world functioning in bipolar disorder."*** Journal of Affective Disorders 198: 185-188. http://www.sciencedirect.com/science/article/pii/S016503271531363X

Abstract Background Bipolar disorder (BD) patients encounter significant life adversity, which has contributed to bipolar disorder being a leading cause of disability worldwide. Studies suggest BD patients have more maladaptive coping strategies, some of which can impact their illness course. Yet research on which coping strategies most influence disability is lacking. Such research could inform cognitive-behavioral targets to improve functional outcomes. Thus, we sought to identify relations between coping strategies and real-world function in BD. Methods In 92 affectively-stable BD outpatients, we measured coping strategies via the Brief COPE, real-world disability via the World Health Organization Disability Assessment Schedule, current symptoms, illness chronicity, and neurocognitive functioning via the MATRICS. Multiple regression analysis served to identify the neurocognitive domains predictive of disability for entry into subsequent analyses. Multiple regressions assessed how adaptive and maladaptive coping strategies influenced disability. Results Only one neurocognitive domain, verbal learning, significantly predicted disability and was included in subsequent analyses. Maladaptive coping significantly predicted disability while adaptive

coping did not. Behavioral disengagement (giving up) and self-blame were the only remaining predictors of disability, after controlling for age, sex, illness chronicity, current symptoms, and neurocognitive functioning. Limitations The study was limited by the use of a self-report disability measure and a brief-form coping scale. Conclusions Results suggest that giving up and self-blame are significant predictors of real-world functioning beyond sub-threshold depressive symptoms. Our results in BD expand upon recent schizophrenia studies suggesting that defeatist beliefs negatively influence functional outcomes across the range of major psychiatric disorders.

Papakostas, G. I., M. A. Martinson, et al. (2016). ***"Demographic variables, design characteristics, and effect sizes of randomized, placebo-controlled, monotherapy trials of major depressive disorder and bipolar depression."*** J Clin Psychiatry 77(5): e619-624. http://www.ncbi.nlm.nih.gov/pubmed/27249092

OBJECTIVE: The aim of this work is to compare the efficacy of pharmacologic agents for the treatment of major depressive disorder (MDD) and bipolar depression. DATA SOURCES: MEDLINE/PubMed databases were searched for studies published in English between January 1980 and September 2014 by cross-referencing the search term placebo with each of the antidepressant agents identified and with bipolar. The search was supplemented by manual bibliography review. STUDY SELECTION: We selected double-blind, randomized, placebo-controlled trials of antidepressant monotherapies for the treatment of MDD and of oral drug monotherapies for the treatment of bipolar depression. 196 trials in MDD and 19 trials in bipolar depression were found eligible for inclusion in our analysis. DATA EXTRACTION: Data were extracted by one of the authors and checked for accuracy by a second one. Data extracted included year of publication, number of patients randomized, probability of receiving placebo, duration of the trial, baseline symptom severity, dosing schedule, study completion rates, and clinical response rates. RESULTS: Response rates for drug versus placebo in trials of MDD and bipolar depression were 52.7% versus 37.5% and 54.7% versus 40.5%, respectively. The random-effects meta-analysis indicated that drug therapy was more effective than placebo in both MDD (risk ratio for response = 1.373; $P < .001$) and bipolar depression (risk ratio = 1.257; $P < .001$) trials. The meta-regression analysis suggested a statistically significant difference in the risk ratio of responding to drug versus placebo between MDD and bipolar depression trials in favor of MDD ($P = .008$). CONCLUSIONS: Although a statistically significantly greater treatment effect size was noted in MDD relative to bipolar depression studies, the absolute magnitude of the difference was numerically small. Therefore, the present study suggests no clinically significant differences in the overall short-term efficacy of pharmacologic monotherapies for MDD and bipolar depression.

Passos, I. C., B. Mwangi, et al. (2016). ***"Identifying a clinical signature of suicidality among patients with mood disorders: A pilot study using a machine learning approach."*** Journal of Affective Disorders 193: 109-116. http://www.sciencedirect.com/science/article/pii/S0165032715310922

Objective A growing body of evidence has put forward clinical risk factors associated with patients with mood disorders that attempt suicide. However, what is not known is how to integrate clinical variables into a clinically useful tool in order to estimate the probability of an individual patient attempting suicide. Method A total of 144 patients with mood disorders were included. Clinical variables associated with suicide attempts among patients with mood disorders and demographic variables were used to 'train' a machine learning algorithm. The resulting algorithm was utilized in identifying novel or 'unseen' individual subjects as either suicide attempters or non-attempters. Three machine learning algorithms were implemented and evaluated. Results All algorithms distinguished individual suicide attempters from non-attempters with prediction accuracy ranging between 65% and 72% ($p < 0.05$). In particular, the relevance vector machine (RVM) algorithm correctly predicted 103 out of 144 subjects translating into 72% accuracy (72.1% sensitivity and 71.3% specificity) and an area under the curve of 0.77 ($p < 0.0001$). The most relevant predictor variables in distinguishing attempters from non-attempters included previous hospitalizations for depression, a history of psychosis, cocaine dependence and post-traumatic stress disorder (PTSD) comorbidity. Conclusion Risk for suicide attempt among patients with mood disorders can be estimated at an individual subject level by incorporating both demographic and clinical variables. Future studies should examine the performance of this model in other populations and its subsequent utility in facilitating selection of interventions to prevent suicide.

Rong, P., J. Liu, et al. (2016). ***"Effect of transcutaneous auricular vagus nerve stimulation on major depressive disorder: A nonrandomized controlled pilot study."*** Journal of Affective Disorders 195: 172-179. http://www.sciencedirect.com/science/article/pii/S0165032715309332

AbstractBackground Depression presents a significant burden to both patients and society. One treatment that has emerged is vagus nerve stimulation (VNS), an FDA-approved physical treatment for depressive disorders. However, the application of this intervention has been limited by the involvement of surgery and potential side effects. The aim of this study is to explore the effectiveness of stimulating the superficial branches of the vagus nerve as a solo treatment for MDD. Methods This is a nonrandomized, controlled study. The first cohort of patients (n=91) only received transcutaneous auricular VNS (taVNS) for 12 weeks. In the second cohort (n=69), patients first received 4 weeks of sham taVNS followed by 8 weeks of taVNS. All treatments were self-administered by the patients at home after they received training from the hospitals. The primary outcome measurement was the 24-item Hamilton Depression Rating Scale measured at weeks 0, 4, 8, and 12. Data analysis included a timelag analysis comparing (1) real and sham taVNS groups at week 4; (2) the real taVNS group at week 4 vs the sham taVNS group at week 8 (fourth week of real taVNS following 4 weeks of sham); and (3) the real taVNS group at week 8 vs the sham taVNS group at week 12 (eighth week of real taVNS following sham). Results After four weeks of treatment, MDD patients in the taVNS group showed greater improvement than patients in the sham taVNS group as indicated by Hamilton score changes as well as response and remission rates at week four. In addition, we also found that the clinical improvements continued until week 12 during taVNS. Limitations Patients were not randomized in this study. Conclusions Our results suggest that taVNS is a promising, safe, and cost-effective therapeutic method for mild and moderate MDD.

Salagre, E., B. S. Fernandes, et al. (2016). ***"Statins for the treatment of depression: A meta-analysis of randomized, double-blind, placebo-controlled trials."*** J Affect Disord 200: 235-242. http://www.ncbi.nlm.nih.gov/pubmed/27148902

BACKGROUND: In epidemiological studies, statins appear to benefit mood, and there are now some randomized controlled trials examining the efficacy of statins. However, the role of statins in depression remains uncertain. Thus the aim of this paper was to assess the effect of statins on depressive symptoms by performing a meta-analysis of all double-blind, randomized, placebo controlled clinical trials (RCT) conducted in subjects with depression. METHODS: A systematic search was executed using PubMed and ClinicalTrials.gov in November 30th, 2015 for all double-blind, RCT of statins versus placebo in persons with depressive symptoms. Sixty-seven potential articles were identified through search of electronic databases, of those three met inclusion criteria and were included in the meta-analysis. The outcome measure was change in Hamilton Depression Rating Scale (HDRS) scores associated with statin use. A meta-analysis was conducted and standardized mean differences (SMDs) with 95% confidence intervals (CIs) were calculated. GRADE was used to assess study quality. RESULTS: The three articles included provided data on 165 participants with moderate to severe depression. Of these, 82 were randomized to statins as an adjuvant therapy to antidepressant treatment (i.e., citalopram or fluoxetine) and 83 to the placebo arm. All studies were double-blind RCTs, with a follow-up of 6-12 weeks. The statin agents evaluated were lovastatin, atorvastatin, and

simvastatin. When compared to placebo, statins, as add-on to treatment as usual, largely improved depressive symptoms as assessed by the HDRS (SMD=-0.73, 95% IC -1.04 to -0.42, p<0.001, 3 between-group comparisons, n=165). No serious adverse effects were reported. CONCLUSIONS: Our results suggest that adjunctive treatment with statins could be useful for the treatment of depressive symptoms. Additional double-blind, randomised, placebo-controlled trials are necessary to settle the matter.

Spinhoven, P., J. Drost, et al. (2016). ***"Is experiential avoidance a mediating, moderating, independent, overlapping, or proxy risk factor in the onset, relapse and maintenance of depressive disorders?"*** Cognitive Therapy and Research 40(2): 150-163. http://dx.doi.org/10.1007/s10608-015-9747-8

(Available in free full text) Our study aim was to investigate how experiential avoidance 'works together' with bordering psychological constructs (i.e., rumination, worry and neuroticism) in predicting the onset, relapse and maintenance of depressive disorders. We performed a longitudinal cohort study with repeated assessments after 2 and 4 years in a sample of 737 persons with a 6-month recency dysthymic and/or major depressive disorder, a sample of 1150 remitted persons with a history of previous depressive disorders; and a sample of 626 persons with no 6-month recency depressive or anxiety disorders and no previous depressive disorders. Experiential avoidance predicted onset, relapse as well as maintenance of depressive disorders during the 4-year follow-up period. However, after controlling for rumination, worry and neuroticism, experiential avoidance no longer significantly predicted onset, relapse or maintenance of depressive disorders in contrast to repetitive thinking in the form of rumination or worry. Experiential avoidance also did not mediate or moderate the effect of rumination, worry and neuroticism.

Suppes, T., R. Silva, et al. (2016). ***"Lurasidone for the treatment of major depressive disorder with mixed features: A randomized, double-blind, placebo-controlled study."*** American Journal of Psychiatry 173(4): 400-407. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2015.15060770

Objective: Accumulating evidence indicates that manic symptoms below the threshold for hypomania (mixed features) are common in individuals with major depressive disorder. This form of depression is often severe and is associated with an increased risk for recurrence, suicide attempts, substance abuse, and functional disability. This study evaluated the efficacy and safety of lurasidone in major depressive disorder with mixed features. Methods: Patients meeting DSM-IV-TR criteria for major depressive disorder who presented with two or three protocol-defined manic symptoms were randomly assigned to 6 weeks of double-blind treatment with either lurasidone at 20–60 mg/day (N=109) or placebo (N=100). Changes from baseline in Montgomery-Åsberg Depression Rating Scale score (MADRS; primary outcome measure) and Clinical Global Impressions severity subscale score (CGI-S; key secondary outcome measure) were evaluated using a mixed model for repeated-measures analysis. Results: Lurasidone significantly improved depressive symptoms and overall illness severity, assessed by least squares mean change at week 6 in the MADRS and CGI-S scores: −20.5 compared with −13.0 (effect size, 0.80) and −1.8 compared with −1.2 (effect size, 0.60), respectively. Significant improvement in manic symptoms, assessed by the Young Mania Rating Scale, was also observed, in addition to other secondary efficacy endpoints. Rates of discontinuation due to adverse events were low. The most common adverse events were nausea (6.4% and 2.0% in the lurasidone and placebo groups, respectively) and somnolence (5.5% and 1.0%). Conclusions: Lurasidone was effective and well tolerated in this study involving patients with major depressive disorder associated with subthreshold hypomanic symptoms (mixed features).

White, J., P. Zaninotto, et al. (2016). ***"Duration of depressive symptoms and mortality risk: The english longitudinal study of ageing (elsa)."*** The British Journal of Psychiatry 208(4): 337-342. http://bjp.rcpsych.org/content/bjprcpsych/208/4/337.full.pdf

(Available in free full text) Background The relationship between the duration of depressive symptoms and mortality remains poorly understood. Aims To examine whether the duration of depressive symptoms is associated with mortality risk. Method Data (n = 9560) came from the English Longitudinal Study of Ageing (ELSA). We assessed depressive symptom duration as the sum of examinations with an eight-item Center for Epidemiologic Studies Depression Scale score of ⩾3; we ascertained mortality from linking our data to a national register. Results Relative to those participants who never reported symptoms, the age- and gender-adjusted hazard ratios for elevated depressive symptoms over 1, 2, 3 and 4 examinations were 1.41 (95% CI 1.15–1.74), 1.80 (95% CI 1.44–2.26), 1.97 (95% CI 1.57–2.47) and 2.48 (95% CI 1.90–3.23), respectively (P for trend < 0.001). This graded association can be explained largely by differences in physical activity, cognitive function, functional impairments and physical illness. Conclusions In this cohort of older adults, the duration of depressive symptoms was associated with mortality in a dose–response manner.

Yovell, Y., G. Bar, et al. (2016). ***"Ultra-low-dose buprenorphine as a time-limited treatment for severe suicidal ideation: A randomized controlled trial."*** American Journal of Psychiatry 173(5): 491-498. http://ajp.psychiatryonline.org/doi/abs/10.1176/appi.ajp.2015.15040535

Objective: Suicidal ideation and behavior currently have no quick-acting pharmacological treatments that are suitable for independent outpatient use. Suicidality is linked to mental pain, which is modulated by the separation distress system through endogenous opioids. The authors tested the efficacy and safety of very low dosages of sublingual buprenorphine as a time-limited treatment for severe suicidal ideation. Method: This was a multisite randomized double-blind placebo-controlled trial of ultra-low-dose sublingual buprenorphine as an adjunctive treatment. Severely suicidal patients without substance abuse were randomly assigned to receive either buprenorphine or placebo (in a 2:1 ratio), in addition to their ongoing individual treatments. The primary outcome measure was change in suicidal ideation, as assessed by the Beck Suicide Ideation Scale at the end of each of 4 weeks of treatment. Results: Patients who received ultra-low-dose buprenorphine (initial dosage, 0.1 mg once or twice daily; mean final dosage=0.44 mg/day; N=40) had a greater reduction in Beck Suicide Ideation Scale scores than patients who received placebo (N=22), both after 2 weeks (mean difference −4.3, 95% CI=−8.5, −0.2) and after 4 weeks (mean difference=−7.1, 95% CI=−12.0, −2.3). Concurrent use of antidepressants and a diagnosis of borderline personality disorder did not affect the response to buprenorphine. No withdrawal symptoms were reported after treatment discontinuation at the end of the trial. Conclusions: The time-limited, short-term use of very low dosages of sublingual buprenorphine was associated with decreased suicidal ideation in severely suicidal patients without substance abuse. Further research is needed to establish the efficacy, safety, dosing, and appropriate patient populations for this experimental treatment.