

22 action on depression abstracts, feb '13

(Martiny, Refsgaard et al. 2012; Akbaraly, Sabia et al. 2013; Bolton Jm and et al. 2013; Bower, Kontopantelis et al. 2013; Cable, Bartley et al. 2013; Castro, Clements et al. 2013; Di Florio, Forty et al. 2013; Gilman, Trinh et al. 2013; Hans and Hiller 2013; Jeste, Savla et al. 2013; Kok, Waugh et al. 2013; Kuramoto, Runeson et al. 2013; Morgan, Mackinnon et al. 2013; Niemeyer, Musch et al. 2013; Nolen and Weisler 2013; Sienaert, Lambrichts et al. 2013; Skapinakis, Rai et al. 2013; van der Schaaf, Dusseldorp et al. 2013; Watts, Mackenzie et al. 2013; Weinstock, Strong et al. 2013; Yatham, Kennedy et al. 2013; Yatham, Kennedy et al. 2013)

Akbaraly, T. N., S. Sabia, et al. (2013). **"Adherence to healthy dietary guidelines and future depressive symptoms: Evidence for sex differentials in the Whitehall II study."** *Am J Clin Nutr* 97(2): 419-427.

<http://ajcn.nutrition.org/content/97/2/419.abstract>

(Free full text available) Background: It has been suggested that dietary patterns are associated with future risk of depressive symptoms. However, there is a paucity of prospective data that have examined the temporality of this relation. Objective: We examined whether adherence to a healthy diet, as defined by using the Alternative Healthy Eating Index (AHEI), was prospectively associated with depressive symptoms assessed over a 5-y period. Design: Analyses were based on 4215 participants in the Whitehall II Study. AHEI scores were computed in 1991-1993 and 2003-2004. Recurrent depressive symptoms were defined as having a Center for Epidemiologic Studies Depression Scale score ≥ 16 or self-reported use of antidepressants in 2003-2004 and 2008-2009. Results: After adjustment for potential confounders, the AHEI score was inversely associated with recurrent depressive symptoms in a dose-response fashion in women (P-trend < 0.001 ; for 1 SD in AHEI score; OR: 0.59; 95% CI: 0.47, 0.75) but not in men. Women who maintained high AHEI scores or improved their scores during the 10-y measurement period had 65% (OR: 0.35%; 95% CI: 0.19%, 0.64%) and 68% (OR: 0.32%; 95% CI: 0.13%, 0.78%) lower odds of subsequent recurrent depressive symptoms than did women who maintained low AHEI scores. Among AHEI components, vegetable, fruit, trans fat, and the ratio of polyunsaturated fat to saturated fat components were associated with recurrent depressive symptoms in women. Conclusion: In the current study, there was a suggestion that poor diet is a risk factor for future depression in women.

Bolton Jm, A. W. L. W. D. and et al. (2013). **"Parents bereaved by offspring suicide: A population-based longitudinal case-control study."** *JAMA Psychiatry* 70(2): 158-167. <http://dx.doi.org/10.1001/jamapsychiatry.2013.275>

Context Suicide bereavement remains understudied and poorly understood. Objectives To examine outcomes of parents bereaved by the suicide death of their offspring and to compare these with both nonbereaved parent controls and parents who had offspring die in a motor vehicle crash (MVC). Design Population-based case-control study. Suicide-bereaved parents were compared with nonbereaved matched control parents in the general population (n = 1415) and with MVC-bereaved parents (n = 1132) on the rates of physician-diagnosed mental and physical disorders, social factors, and treatment use in the 2 years after death of the offspring. Adjusted relative rates (ARRs) were generated by generalized estimating equation models and adjusted for confounding factors. Setting Manitoba, Canada. Participants All identifiable parents who had an offspring die by suicide between 1996 and 2007 (n = 1415). Main Outcome Measures Mental and physical disorders, social factors, and treatment use. Results Suicide bereavement was associated with an increased rate of depression (ARR, 2.14; 95% CI, 1.88-2.43), anxiety disorders (ARR, 1.41; 95% CI, 1.24-1.60), and marital breakup (ARR, 1.18; 95% CI, 1.13-1.23) in the 2 years after the suicide of an offspring, as compared with the 2 years prior to the death. Suicide-bereaved and MVC-bereaved parents had very few differences on predeath to postdeath outcomes. Depression rate increases were greater for MVC-bereaved parents (19.9%) compared with suicide-bereaved parents (15.9%; P = .005), whereas suicide-bereaved parents had higher rate increases of hospitalization for mental illness (P = .049). Suicide-bereaved parents were more likely than their MVC-bereaved counterparts to have depression (ARR, 1.30; 95% CI, 1.06-1.61), physical disorders (ARR, 1.32; 95% CI, 1.19-1.45), and low income (ARR, 1.34; 95% CI, 1.18-1.51) before their offspring's death. Conclusions Suicide bereavement is associated with adverse mental health and social outcomes. These consequences appear similar to those associated with MVC bereavement. Parents who lose offspring to suicide appear to be a vulnerable group even prior to their offspring's death.

Bower, P., E. Kontopantelis, et al. (2013). **"Influence of initial severity of depression on effectiveness of low intensity interventions: Meta-analysis of individual patient data."** *BMJ* 346: f540. <http://www.ncbi.nlm.nih.gov/pubmed/23444423>

OBJECTIVE: To assess how initial severity of depression affects the benefit derived from low intensity interventions for depression. DESIGN: Meta-analysis of individual patient data from 16 datasets comparing low intensity interventions with usual care. SETTING: Primary care and community settings. PARTICIPANTS: 2470 patients with depression. INTERVENTIONS: Low intensity interventions for depression (such as guided self help by means of written materials and limited professional support, and internet delivered interventions). MAIN OUTCOME MEASURES: Depression outcomes (measured with the Beck Depression Inventory or Center for Epidemiologic Studies Depression Scale), and the effect of initial depression severity on the effects of low intensity interventions. RESULTS: Although patients were referred for low intensity interventions, many had moderate to severe depression at baseline. We found a significant interaction between baseline severity and treatment effect (coefficient -0.1 (95% CI -0.19 to -0.002)), suggesting that patients who are more severely depressed at baseline demonstrate larger treatment effects than those who are less severely depressed. However, the magnitude of the interaction (equivalent to an additional drop of around one point on the Beck Depression Inventory for a one standard deviation increase in initial severity) was small and may not be clinically significant. CONCLUSIONS: The data suggest that patients with more severe depression at baseline show at least as much clinical benefit from low intensity interventions as less severely depressed patients and could usefully be offered these interventions as part of a stepped care model.

Cable, N., M. Bartley, et al. (2013). **"Friends are equally important to men and women, but family matters more for men's well-being."** *J Epidemiol Community Health* 67(2): 166-171. <http://jech.bmj.com/content/67/2/166.abstract>

Background People with larger social networks are known to have better well-being; however, little is known about (1) the association with socio-demographic factors that may predict the size and composition of social networks and (2) whether the association with well-being is independent of pre-existing psychological health or socio-demographic factors. Methods The authors used information collected from 3169 men and 3512 women who were born in Great Britain in 1958. First, age on leaving full-time education, partnership and employment status at age 42 were used to predict the size and composition of cohort members' social networks at age 45 using ordered logistic regression. Second, using multiple linear regression, the associations between social network size by composition (relatives and friends) and psychological well-being at age 50 were assessed, adjusting for socio-demographic factors and psychological health at age 42. Results Not having a partner and staying in full-time education after age 16 was associated with a smaller kinship network in adults. Having a smaller friendship network at age 45 was associated with poorer psychological well-being among adults at age 50, over and above socio-demographic

factors and previous psychological health. Additionally, having a smaller kinship network was associated with poorer psychological well-being among men. Conclusions Having a well-integrated friendship network is a source of psychological well-being among middle-aged adults, while kinship networks appear to be more important for men's well-being than for women's. These relationships are independent of education, material status and prior psychological health.

Castro, V. M., C. C. Clements, et al. (2013). **"QT interval and antidepressant use: A cross sectional study of electronic health records."** *BMJ* 346: f288. <http://www.bmj.com/content/346/bmj.f288>

OBJECTIVE: To quantify the impact of citalopram and other selective serotonin reuptake inhibitors on corrected QT interval (QTc), a marker of risk for ventricular arrhythmia, in a large and diverse clinical population. **DESIGN:** A cross sectional study using electrocardiographic, prescribing, and clinical data from electronic health records to explore the relation between antidepressant dose and QTc. Methadone, an opioid known to prolong QT, was included to demonstrate assay sensitivity. **SETTING:** A large New England healthcare system comprising two academic medical centres and outpatient clinics. **PARTICIPANTS:** 38,397 adult patients with an electrocardiogram recorded after prescription of antidepressant or methadone between February 1990 and August 2011. **MAIN OUTCOME MEASURES:** Relation between antidepressant dose and QTc interval in linear regression, adjusting for potential clinical and demographic confounding variables. For a subset of patients, change in QTc after drug dose was also examined. **RESULTS:** Dose-response association with QTc prolongation was identified for citalopram (adjusted beta 0.10 (SE 0.04), $P < 0.01$), escitalopram (adjusted beta 0.58 (0.15), $P < 0.001$), and amitriptyline (adjusted beta 0.11 (0.03), $P < 0.001$), but not for other antidepressants examined. An association with QTc shortening was identified for bupropion (adjusted beta 0.02 (0.01) $P < 0.05$). Within-subject paired observations supported the QTc prolonging effect of citalopram (10 mg to 20 mg, mean QTc increase 7.8 (SE 3.6) ms, adjusted $P < 0.05$; and 20 mg to 40 mg, mean QTc increase 10.3 (4.0) ms, adjusted $P < 0.01$). **CONCLUSIONS:** This study confirmed a modest prolongation of QT interval with citalopram, and identified additional antidepressants with similar observed risk. Pharmacovigilance studies using electronic health record data may be a useful method of identifying potential risk associated with treatments. *(The authors also wrote under "Implications of this study": The implications for clinicians merit careful consideration. One notable finding is that nearly one in five patients treated with these antidepressants who underwent electrocardiography had QT intervals which would be considered abnormal. The clinical significance of this prolongation, including the risk of induction of torsades de pointes, is unknown. However, the incidence of torsades de pointes is low among general clinical populations and is similar among patients treated with antidepressants. For this reason, QTc is often used as a proxy measure for risk of torsades associated with medication, recognising that it is an imperfect surrogate. Indeed, the FDA warning for citalopram was issued in spite of the epidemiological data showing no difference in risk for arrhythmia. The question of whether patients for whom antidepressants will be prescribed should routinely have electrocardiograms before and/or after treatment starts cannot be addressed directly by this study. However, in terms of treatment selection, our results do suggest some variation within treatment class in terms of risk. For example, selective serotonin reuptake inhibitors such as sertraline may be associated with less risk than citalopram, and therefore might be preferred in individuals with other risk factors. For escitalopram, our data are less definitive, but suggest that some risk may need to be considered for this drug as well. Of interest, bupropion is routinely used as an augmentation strategy when initial antidepressant treatment fails to achieve remission, though it is not approved by the FDA for this indication. Our results suggest that, given its capacity to shorten QT interval, bupropion treatment might be a reasonable next step for patients partially responsive to citalopram who would otherwise require a dose increase.)*

Di Florio, A., L. Forty, et al. (2013). **"Perinatal episodes across the mood disorder spectrum."** *JAMA Psychiatry* 70(2): 168-175. <http://dx.doi.org/10.1001/jamapsychiatry.2013.279>

Context Affective disorders are common in women, with many episodes having an onset in pregnancy or during the postpartum period. **Objective** To investigate the occurrence and timing of perinatal mood episodes in women with bipolar I disorder, bipolar II disorder, and recurrent major depression (RMD). **Setting and Patients** Women were recruited in our ongoing research on the genetic and nongenetic determinants of major affective disorders. Participants were interviewed and case notes were reviewed. **Best-estimate diagnoses** were made according to DSM-IV criteria. The 1785 parous women identified included 1212 women with bipolar disorder (980 with type I and 232 with type II) and 573 with RMD. Data were available on 3017 live births. **Main Outcome Measures** We report the lifetime occurrence of perinatal mood episodes, the rates of perinatal episodes per pregnancy/postpartum period, and the timing of the onset of episodes in relation to delivery. **Results** More than two-thirds of all diagnostic groups reported at least 1 lifetime episode of illness during pregnancy or the postpartum period. Women with bipolar I disorder reported an approximately 50% risk of a perinatal major affective episode per pregnancy/postpartum period. Risks were lower in women with RMD or bipolar II disorder, at approximately 40% per pregnancy/postpartum period. Mood episodes were significantly more common in the postpartum period in bipolar I disorder and RMD. Most perinatal episodes occurred within the first postpartum month, with mania or psychosis having an earlier onset than depression. **Conclusions** Although episodes of postpartum mood disorder are more common in bipolar I disorder and manic and psychotic presentations occur earlier in the postpartum period, perinatal episodes are highly prevalent across the mood disorder spectrum.

Gilman, S. E., N.-H. Trinh, et al. (2013). **"Psychosocial stressors and the prognosis of major depression: A test of axis IV."** *Psychological Medicine* 43(02): 303-316. <http://dx.doi.org/10.1017/S0033291712001080>

Background Axis IV is for reporting 'psychosocial and environmental problems that may affect the diagnosis, treatment and prognosis of mental disorders'. No studies have examined the prognostic value of Axis IV in DSM-IV. **Method** We analyzed data from 2497 participants in the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) with major depressive episode (MDE). We hypothesized that psychosocial stressors predict a poor prognosis of MDE. **Secondarily**, we hypothesized that psychosocial stressors predict a poor prognosis of anxiety and substance use disorders. **Stressors** were defined according to DSM-IV's taxonomy, and empirically using latent class analysis (LCA). **Results** Primary support group problems, occupational problems and childhood adversity increased the risks of depressive episodes and suicidal ideation by 20-30%. Associations of the empirically derived classes of stressors with depression were larger in magnitude. Economic stressors conferred a 1.5-fold increase in risk for a depressive episode [95% confidence interval (CI) 1.2-1.9]; financial and interpersonal instability conferred a 1.3-fold increased risk of recurrent depression (95% CI 1.1-1.6). These two classes of stressors also predicted the recurrence of anxiety and substance use disorders. **Stressors** were not related to suicidal ideation independent from depression severity. **Conclusions** Psychosocial and environmental problems are associated with the prognosis of MDE and other Axis I disorders. Although DSM-IV's taxonomy of stressors stands to be improved, these results provide empirical support for the prognostic value of Axis IV. **Future work** is needed to determine the reliability of Axis IV assessments in clinical practice, and the usefulness of this information to improving the clinical course of mental disorders.

Hans, E. and W. Hiller (2013). **"Effectiveness of and dropout from outpatient cognitive behavioral therapy for adult unipolar depression: A meta-analysis of nonrandomized effectiveness studies."** *J Consult Clin Psychol* 81(1): 75-88. <http://www.ncbi.nlm.nih.gov/pubmed/23379264>

OBJECTIVE: The primary aim of this study was to assess the overall effectiveness of and dropout from individual and group outpatient cognitive behavioral therapy (CBT) for adults with a primary diagnosis of unipolar depressive disorder in routine clinical practice. **METHOD:** We conducted a random effects meta-analysis of 34 nonrandomized effectiveness studies on outpatient individual and group CBT for adult unipolar depressive disorder. Standardized mean gain effect sizes are reported for end-of-treatment and 6-month follow-up effects for depression severity, dysfunctional cognitions, general anxiety, psychological distress, and functional impairment. The mean dropout rate from CBT is reported. We benchmarked our results against high-quality randomized controlled trials (RCTs). **RESULTS:** Outpatient CBT was effective in reducing depressive severity in completer ($d = 1.13$) and intention-to-treat (ITT) samples ($d = 1.06$). Moderate to large posttreatment effect sizes ($d = 0.67-0.88$) were found for secondary outcomes. The weighted mean dropout rate was 24.63%. Posttreatment gains for depression were maintained at 6 months after completion of therapy. Effect sizes for depression were inferior to those of benchmark RCTs. **CONCLUSIONS:** Although clinical practice patients show lesser improvements in depressive symptoms than RCT patients, individual and group outpatient CBT can be effectively transported to routine clinical practice. The considerable treatment dropout rate, especially in individual CBT, must be improved. The small number of available studies and low quality of some reports stress the need for high-quality effectiveness studies.

Jeste, D. V., G. N. Savla, et al. (2013). **"Association between older age and more successful aging: Critical role of resilience and depression."** *Am J Psychiatry* 170(2): 188-196. <http://ajp.psychiatryonline.org/Article.aspx?ArticleID=1478351>

OBJECTIVE: There is growing public health interest in understanding and promoting successful aging. While there has been some exciting empirical work on objective measures of physical health, relatively little published research combines physical, cognitive, and psychological assessments in large, randomly selected, community-based samples to assess self-rated successful aging. **METHOD:** In the Successful Aging Evaluation (SAGE) study, the authors used a structured multicohort design to assess successful aging in 1,006 community-dwelling adults in San Diego County, ages 50-99 years, with oversampling of people over 80. A modified version of random-digit dialing was used to recruit subjects. Evaluations included a 25-minute telephone interview followed by a comprehensive mail-in survey of physical, cognitive, and psychological domains, including positive psychological traits and self-rated successful aging, scaled from 1 (lowest) to 10 (highest). **RESULTS:** The mean age of the respondents was 77.3 years. Their mean self-rating of successful aging was 8.2, and older age was associated with a higher rating, despite worsening physical and cognitive functioning. The best multiple regression model achieved, using all the potential correlates, accounted for 30% of the variance in the score for self-rated successful aging and included resilience, depression, physical functioning, and age (entering the regression model in that order). **CONCLUSIONS:** Resilience and depression had significant associations with self-rated successful aging, with effects comparable in size to that for physical health. While no causality can be inferred from cross-sectional data, increasing resilience and reducing depression might have effects on successful aging as strong as that of reducing physical disability, suggesting an important role for psychiatry in promoting successful aging.

Kok, B. E., C. E. Waugh, et al. (2013). **"Meditation and health: The search for mechanisms of action."** *Social and Personality Psychology Compass* 7(1): 27-39. <http://dx.doi.org/10.1111/spc3.12006>

(Free full text available) Psychological interest in the impact of mental states on biological functioning is growing rapidly, driving a need for new methods for inducing mental states that last long enough, and are sufficiently impactful, to have significant effects on physical health. The many traditions of meditative practice are one potential pathway for studying mind-body interactions. The purpose of this review is to introduce personality and social psychologists to the field of meditation research. Beginning with a brief introduction to meditation and the heterogeneity of meditative practices, we showcase research linking meditative practice to changes in immune and cardiovascular functioning and pain perception. We then discuss theoretical and empirical evidence that meditation works by inducing changes in psychological capacities such as emotion regulation and self-regulation or through repeated induction of specific mental states such as love or meta-cognitive awareness. At the frontier of the science of meditation is the need to empirically test whether meditation-driven changes in cognitive and affective processes are the cause of improvements in physical health. Emerging challenges in meditation research include a need for large studies using randomized controlled and dual-blind designs with active control groups and an increased focus on measuring mechanisms of action as well as outcomes. Meditation represents a potentially powerful tool for generating new knowledge of mind-body interactions.

Kuramoto, S., B. Runeson, et al. (2013). **"Time to hospitalization for suicide attempt by the timing of parental suicide during offspring early development."** *JAMA Psychiatry* 70(2): 149-157. <http://dx.doi.org/10.1001/jamapsychiatry.2013.274>

Context Previous studies have suggested that children who experience parental suicide at earlier ages are at higher risk of future hospitalization for suicide attempt. However, how the trajectories of risk differ by offspring age at the time of parental suicide is currently unknown. **Objective** To study time at risk to suicide attempt hospitalization among offspring of suicide decedents as compared with offspring of unintentional injury decedents by their developmental period at the time of parental death. **Design** Population-based retrospective cohort study. **Setting** Sweden. **Participants** Twenty-six thousand ninety-six offspring who experienced parental suicide and 32 395 offspring of unintentional injury decedents prior to age 25 years between the years 1973 and 2003. **Main Outcome Measure** Parametric survival analysis was used to model the time to hospitalization for suicide attempt among offspring who lost a parent during early childhood (0-5 years old), later childhood (6-12 years old), adolescence (13-17 years old), and young adulthood (18-24 years old). **Results** The risk in offspring who lost a parent to suicide or an unintentional injury during childhood surpassed the other age groups' risk approximately 5 years after the origin and, for the youngest group, continued to rise over decades. Offspring who lost a parent during adolescence or young adulthood were at greatest risk within 1 to 2 years after parental death, and risk declined over time. Offspring who lost a parent to suicide in childhood and young adulthood had earlier onset of hospitalization for suicide attempt compared with offspring who lost a parent to an unintentional injury. **Conclusions** The hospitalization risk for suicide attempt in offspring who lost a parent during their childhood is different from those who lost a parent later in development. The results suggest critical windows for careful monitoring and intervention for suicide attempt risk, especially 1 to 2 years after parental death for the older age groups and over decades for childhood survivors of parental death.

Martiny, K., E. Refsgaard, et al. (2012). **"A 9-week randomized trial comparing a chronotherapeutic intervention (wake and light therapy) to exercise in major depressive disorder patients treated with duloxetine."** *J Clin Psychiatry* 73(9): 1234-1242. <http://www.ncbi.nlm.nih.gov/pubmed/23059149>

OBJECTIVE: The onset of action of antidepressants often takes 4 to 6 weeks. The antidepressant effect of wake therapy (sleep deprivation) comes within hours but carries a risk of relapse. The objective of this study was to investigate whether a new chronotherapeutic intervention combining wake therapy with bright light therapy and sleep time stabilization could induce a rapid and sustained augmentation of response and remission in major depressive disorder. **METHOD:** 75 adult patients with DSM-IV major depressive disorder, recruited from psychiatric wards, psychiatric specialist practices, or general medical practices

between September 2005 and August 2008, were randomly assigned to a 9-week chronotherapeutic intervention using wake therapy, bright light therapy, and sleep time stabilization (n = 37) or a 9-week intervention using daily exercise (n = 38). Patients were evaluated at a psychiatric research unit. The study period had a 1-week run-in phase in which all patients began treatment with duloxetine. This phase was followed by a 1-week intervention phase in which patients in the wake therapy group did 3 wake therapies in combination with daily morning light therapy and sleep time stabilization and patients in the exercise group began daily exercise. This phase was followed by a 7-week continuation phase with daily light therapy and sleep time stabilization or daily exercise. The 17-item Hamilton Depression Rating Scale was the primary outcome measure, and the assessors were blinded to patients' treatment allocation. RESULTS: Both groups responded well to treatment. Patients in the wake therapy group did, however, have immediate and clinically significantly better response and remission compared to the exercise group. Thus, immediately after the intervention phase (week 2), response was obtained in 41.4% of wake therapy patients versus 12.8% of exercise patients (odds ratio [OR] = 4.8; 95% CI, 1.7-13.4; P = .003), and remission was obtained in 23.9% of wake therapy patients versus 5.4% of exercise patients (OR = 5.5; 95% CI, 1.7-17.8; P = .004). These superior response and remission rates obtained by the wake therapy patients were sustained for the whole study period. At week 9, response was obtained in 71.4% of wake therapy patients versus 47.3% of exercise patients (OR = 2.8; 95% CI, 1.1-7.3; P = .04), and remission was obtained in 45.6% of wake therapy patients and 23.1% of exercise patients (OR = 2.8; 95% CI, 1.1-7.3, P = .04). All treatment elements were well tolerated. CONCLUSIONS: Patients treated with wake therapy in combination with bright light therapy and sleep time stabilization had an augmented and sustained antidepressant response and remission compared to patients treated with exercise, who also had a clinically relevant antidepressant response.

Morgan, A. J., A. J. Mackinnon, et al. (2013). **"Behavior change through automated e-mails: Mediation analysis of self-help strategy use for depressive symptoms."** *Behaviour Research and Therapy* 51(2): 57-62.

<http://www.sciencedirect.com/science/article/pii/S0005796712001726>

Objective To evaluate whether automated e-mails promoting effective self-help strategies for depressive symptoms were effective in changing self-help behavior, and whether this improved depression outcomes. Method 568 adults with sub-threshold depression participated in a randomized controlled trial and provided complete data. A series of 12 e-mails promoting the use of evidence-based self-help strategies was compared with e-mails providing non-directive depression information. Depression symptoms were assessed with the Patient Health Questionnaire depression scale (PHQ-9) and use of self-help strategies was assessed at baseline and post-intervention. We hypothesized that those receiving the self-help e-mails would increase their use of evidence-based self-help and this would be associated with improvements in depression. Mediation analyses were conducted using a non-parametric bootstrapping procedure. Results Total use of the self-help strategies promoted in the e-mails significantly mediated the effect of the intervention on depressive symptoms (B = -0.75, SE = 0.16, 95% CI: -1.06 to -0.48). The direct effect of the intervention on depressive symptoms was much smaller and not significant when the mediation path was included. The majority of the individual strategies also had a significant indirect effect on depressive symptoms. Conclusions In adults with sub-threshold depression, automated e-mails based on behavior change principles can successfully increase use of self-help strategies, leading to a reduction in depressive symptoms.

Niemeyer, H., J. Musch, et al. (2013). **"Publication bias in meta-analyses of the efficacy of psychotherapeutic interventions for depression."** *J Consult Clin Psychol* 81(1): 58-74. <http://www.ncbi.nlm.nih.gov/pubmed/23244368>

OBJECTIVE: The aim of this study was to assess whether systematic reviews investigating psychotherapeutic interventions for depression are affected by publication bias. Only homogeneous data sets were included, as heterogeneous data sets can distort statistical tests of publication bias. METHOD: We applied Begg and Mazumdar's adjusted rank correlation test, Egger's regression analysis, and the trim and fill procedure to assess the presence and magnitude of publication bias in all homogeneous data sets of systematic reviews published up to September 2010. RESULTS: Thirty-one data sets reported in 19 meta-analyses fulfilled our inclusion criteria. Significant bias was detected in 5 (16.13%; rank correlation test) and 6 (19.35%; Egger's regression analysis) of these data sets. Applying the trim and fill procedure to amend presumably missing studies rarely changed the assessment of the efficacy of therapeutic interventions, with 2 exceptions. In 1 data set psychotherapy was no longer found to be significantly more efficacious than pharmacotherapy in reducing dropout at posttreatment when publication bias was taken into account. In the 2nd data set, after correcting for publication bias, there was no longer evidence that depressed patients without comorbid personality disorder profited more from psychotherapy and pharmacotherapy than patients with comorbid personality disorder. CONCLUSIONS: The results suggest that taken together, psychotherapy research for depression is only marginally affected by the selective reporting of positive outcomes. With 2 notable exceptions, correcting for publication bias did not change the evaluation of the efficacy of psychotherapeutic interventions.

Nolen, W. A. and R. H. Weisler (2013). **"The association of the effect of lithium in the maintenance treatment of bipolar disorder with lithium plasma levels: A post hoc analysis of a double-blind study comparing switching to lithium or placebo in patients who responded to quetiapine (trial 144)."** *Bipolar Disorders* 15(1): 100-109.

<http://dx.doi.org/10.1111/bdi.12027>

(Free full text available) Objectives: There is no robust proof that the efficacy of lithium in the prevention of manic and depressive episodes in bipolar disorder depends on its plasma level. This analysis aimed to compare the effect of lithium within the presumed therapeutic range of 0.6–1.2 mEq/L and below 0.6 mEq/L with that of placebo. Methods: We carried out a post hoc analysis of a double-blind trial in which patients aged ≥18 years with bipolar I disorder (DSM-IV) who had achieved stabilization from a manic, depressive, or mixed episode during open-label treatment with quetiapine were randomized to continue quetiapine or to switch to lithium or placebo for up to 104 weeks. Of patients randomized to lithium, 201 obtained median lithium levels between 0.6 and 1.2 mEq/L, and 137 obtained median lithium levels <0.6 mEq/L. Their outcomes were compared with those of patients receiving placebo (n = 404). The primary outcome was time to recurrence of any mood event; additional outcomes included time to recurrence of a manic or depressive event. Results: Times to recurrence of any mood event as well as a manic or depressive event were significantly longer for the lithium 0.6–1.2 mEq/L group versus placebo and versus lithium <0.6 mEq/L, with no differences between lithium <0.6 mEq/L and placebo. Conclusions: The results support and expand previous findings that lithium should be dosed high enough to achieve plasma levels ≥0.6 mEq/L in order to achieve an effect in the prevention of both manic and depressive recurrences of bipolar I disorder. A major limitation is that the composition of the two lithium groups was not based on randomization.

Sienaert, P., L. Lambrichts, et al. (2013). **"Evidence-based treatment strategies for treatment-resistant bipolar depression: A systematic review."** *Bipolar Disorders* 15(1): 61-69. <http://dx.doi.org/10.1111/bdi.12026>

(Free full text available) Objectives: Treatment resistance in bipolar depression is a common clinical problem that constitutes a major challenge for the treating clinician as there is a paucity of treatment options. The objective of this paper was to review the evidence for treatment options in treatment-resistant bipolar depression, as found in randomized controlled trials and with special attention to the definition and assessment of treatment resistance. Methods: A Medline search (from database inception to May 2012) was performed using the search terms treatment resistance or treatment refractory, and bipolar

depression or bipolar disorder, supplemented with 43 separate searches using the various pharmacologic agents or technical interventions as search terms. Results: Only seven studies met our inclusion criteria. These studies examined the effects of ketamine (n = 1), (ar)modafinil (n = 2), pramipexole (n = 1), lamotrigine (n = 1), inositol (n = 1), risperidone (n = 1), and electroconvulsive therapy (ECT) (n = 2). Conclusions: The available level I evidence for treatment strategies in resistant bipolar depression is extremely scarce, and although the response rates reported are reassuring, most of the strategies remain experimental. There is an urgent need for further study in homogeneous patient samples using a clear concept of treatment resistance.

Skapinakis, P., D. Rai, et al. (2013). **"Sleep disturbances and depressive symptoms: An investigation of their longitudinal association in a representative sample of the UK general population."** *Psychological Medicine* 43(02): 329-339. <http://dx.doi.org/10.1017/S0033291712001055>

Background It has been argued that sleep disturbances are a risk factor for depression but previous longitudinal studies have had limitations and not addressed alternative explanations. The aim of this study was to examine the longitudinal association between sleep disturbances and depressive symptoms in a nationally representative sample. Method Data from the 18-month follow-up of the UK National Psychiatric Morbidity survey were used (n = 2406). Sleep disturbances, depressive and other psychiatric symptoms (fatigue, concentration problems, irritability, anxiety and pain symptoms) were assessed using the Revised Clinical Interview Schedule (CIS-R). The bidirectional association between symptoms was investigated with logistic regression analyses and path analysis. Results Sleep disturbances and depressive symptoms were correlated with each other cross-sectionally (r = 0.52, p < 0.001). In the longitudinal analysis, sleep disturbances at baseline did not predict depressive symptoms at follow-up [odds ratio (OR) 1.27, 95% confidence interval (CI) 0.51–3.19] and the same was observed for the reciprocal association (OR 0.87, 95% CI 0.56–1.35). In the path analysis, the reciprocal model did not have a better fit compared to the simpler first-order model without cross-lagged paths. The path from sleep disturbances at baseline to depressive symptoms at follow-up had a minimal contribution to the explained variance of the latter (<1%). Conclusions Previous studies may have overestimated the importance of sleep disturbances as an independent risk factor of depression. The strong cross-sectional association is compatible with sleep disturbances being either a prodromal or a residual symptom of depression and this may have implications for recognition and treatment of depression.

van der Schaaf, P. S., E. Dusseldorp, et al. (2013). **"Impact of the physical environment of psychiatric wards on the use of seclusion."** *British Journal of Psychiatry* 202(2): 142-149. <http://bjp.rcpsych.org/content/202/2/142.abstract>

Background The physical environment is presumed to have an effect on aggression and also on the use of seclusion on psychiatric wards. Multicentre studies that include a broad variety of design features found on psychiatric wards and that control for patient, staff and general ward characteristics are scarce. Aims To explore the effect of design features on the risk of being secluded, the number of seclusion incidents and the time in seclusion, for patients admitted to locked wards for intensive psychiatric care. Method Data on the building quality and safety of psychiatric as well as forensic wards (n = 199) were combined with data on the frequency and type of coercive measures per admission (n = 23 868 admissions of n = 14 834 patients) on these wards, over a 12-month period. We used non-linear principal components analysis (CATPCA) to reduce the observed design features into a smaller number of uncorrelated principal components. Two-level multilevel (logistic) regression analyses were used to explore the relationship with seclusion. Admission was the first level in the analyses and ward was the second level. Results Overall, 14 design features had a significant effect on the risk of being secluded during admission. The 'presence of an outdoor space', 'special safety measures' and a large 'number of patients in the building' increased the risk of being secluded. Design features such as more 'total private space per patient', a higher 'level of comfort' and greater 'visibility on the ward', decreased the risk of being secluded. Conclusions A number of design features had an effect on the use of seclusion and restraint. The study highlighted the need for a greater focus on the impact of the physical environment on patients, as, along with other interventions, this can reduce the need for seclusion and restraint.

Watts, S., A. Mackenzie, et al. (2013). **"CBT for depression: A pilot RCT comparing mobile phone vs. Computer."** *BMC Psychiatry* 13(1): 49. <http://www.biomedcentral.com/1471-244X/13/49>

(Free full text available) BACKGROUND: This paper reports the results of a pilot randomized controlled trial comparing the delivery modality (mobile phone/tablet or fixed computer) of a cognitive behavioural therapy intervention for the treatment of depression. The aim was to establish whether a previously validated computerized program (The Sadness Program) remained efficacious when delivered via a mobile application. METHOD: 35 participants were recruited with Major Depression (80% female) and randomly allocated to access the program using a mobile app (on either a mobile phone or iPad) or a computer. Participants completed 6 lessons, weekly homework assignments, and received weekly email contact from a clinical psychologist or psychiatrist until completion of lesson 2. After lesson 2 email contact was only provided in response to participant request, or in response to a deterioration in psychological distress scores. The primary outcome measure was the Patient Health Questionnaire 9 (PHQ-9). Of the 35 participants recruited, 68.6% completed 6 lessons and 65.7% completed the 3-months follow up. Attrition was handled using mixed-model repeated-measures ANOVA. RESULTS: Both the Mobile and Computer Groups were associated with statistically significant benefits in the PHQ-9 at post-test. At 3 months follow up, the reduction seen for both groups remained significant. CONCLUSIONS: These results provide evidence to indicate that delivering a CBT program using a mobile application, can result in clinically significant improvements in outcomes for patients with depression.

Weinstock, L. M., D. Strong, et al. (2013). **"Differences in depression symptom endorsement between bipolar disorder and major depressive disorder: Lessons learned from the national epidemiologic survey on alcohol and related conditions."** *Bipolar Disorders* 15(1): 110-111. <http://dx.doi.org/10.1111/bdi.12029>

(Free full text available) The recent paper by Moreno et al. (1) drew data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (2) to evaluate clinical features and course of major depressive episodes (MDEs) in bipolar I disorder (BD-I), bipolar II disorder (BD-II), and major depressive disorder (MDD). Although findings concerning course characteristics (e.g., age of onset) were somewhat mixed, results generally supported a spectrum of MDE severity between disorders, with greatest endorsement of depressive symptoms, psychiatric comorbidity, and positive family history in the BD-I group, followed by BD-II and then by MDD.

Yatham, L. N., S. H. Kennedy, et al. (2013). **"The evolution of CANMAT bipolar disorder guidelines: Past, present, and future."** *Bipolar Disorders* 15(1): 58-60. <http://dx.doi.org/10.1111/bdi.12038>

Good downloadable free full text commentary on these helpful guidelines.

Yatham, L. N., S. H. Kennedy, et al. (2013). **"Canadian network for mood and anxiety treatments (CANMAT) and international society for bipolar disorders (ISBD) collaborative update of CANMAT guidelines for the management of patients with bipolar disorder: Update 2013."** *Bipolar Disorders* 15(1): 1-44. <http://dx.doi.org/10.1111/bdi.12025>

(Free full text available) The Canadian Network for Mood and Anxiety Treatments published guidelines for the management of bipolar disorder in 2005, with updates in 2007 and 2009. This third update, in conjunction with the International Society for Bipolar Disorders, reviews new evidence and is designed to be used in conjunction with the previous publications. The recommendations for the management of acute mania remain largely unchanged. Lithium, valproate, and several atypical antipsychotic agents continue to be first-line treatments for acute mania. Monotherapy with asenapine, paliperidone extended release (ER), and divalproex ER, as well as adjunctive asenapine, have been added as first-line options. For the management of bipolar depression, lithium, lamotrigine, and quetiapine monotherapy, as well as olanzapine plus selective serotonin reuptake inhibitor (SSRI), and lithium or divalproex plus SSRI/bupropion remain first-line options. Lurasidone monotherapy and the combination of lurasidone or lamotrigine plus lithium or divalproex have been added as second-line options. Ziprasidone alone or as adjunctive therapy, and adjunctive levetiracetam have been added as not-recommended options for the treatment of bipolar depression. Lithium, lamotrigine, valproate, olanzapine, quetiapine, aripiprazole, risperidone long-acting injection, and adjunctive ziprasidone continue to be first-line options for maintenance treatment of bipolar disorder. Asenapine alone or as adjunctive therapy have been added as third-line options.