# 22 action on depression abstracts, nov '12

(Boden, Lundgren et al. 2012; Bufferd, Dougherty et al. 2012; Cheavens, Strunk et al. 2012; Fekadu, Rane et al. 2012; Gentile 2012; Gibbons, Weiss et al. 2012; Hilderink, Burger et al. 2012; Hoge, Ivkovic et al. 2012; Hunkeler, Hargreaves et al. 2012; Kilbourne 2012; Kuyken, Crane et al. 2012; Luby, Lenze et al. 2012; Luby 2012; McLaughlin, Greif Green et al. 2012; Nulman, Koren et al. 2012; Otte, Zhao et al. 2012; Parikh, Zaretsky et al. 2012; Steiner 2012; Tohen, McDonnell et al. 2012; van der Lem, de Wever et al. 2012; Wiles, Thomas et al. 2012; Wilkinson and Izmeth 2012)

Boden, R., M. Lundgren, et al. (2012). ***"Risks of adverse pregnancy and birth outcomes in women treated or not treated with mood stabilisers for bipolar disorder: Population based cohort study."*** BMJ 345: e7085. http://www.ncbi.nlm.nih.gov/pubmed/23137820

OBJECTIVE: To investigate the risks of adverse pregnancy and birth outcomes for treated and untreated bipolar disorder during pregnancy. DESIGN: Population based cohort study using data from national health registers. SETTING: Sweden. PARTICIPANTS: 332 137 women with a last menstrual period anytime after 1 July 2005 and giving birth anytime before the end of 31 December 2009. Women with a record of at least two bipolar diagnoses were identified and grouped as treated (n=320)-those who had filled a prescription for mood stabilisers (lithium, antipsychotics, or anticonvulsants) during pregnancy-or untreated (n=554). Both groups were compared with all other women giving birth (n=331 263). MAIN OUTCOME MEASURES: Preterm birth, mode of labour initiation, gestational diabetes, infants born small or large for gestational age, neonatal morbidity, and congenital malformations. RESULTS: Of the untreated women, 30.9% (n=171) were induced or had a planned caesarean delivery compared with 20.7% (n=68 533) without bipolar disorder (odds ratio 1.57, 95% confidence interval 1.30 to 1.90). The corresponding values for the treated women were 37.5% (n=120) (2.12, 1.68 to 2.67). The risks of preterm birth in both treated and untreated women were increased by 50%. Of the untreated women, 3.9% (n=542) had a microcephalic infant compared with 2.3% (324 844) of the women without bipolar disorder (1.68, 1.07 to 2.62). The corresponding values for the treated women were 3.3% (n=311) (1.26, 0.67 to 2.37). Similar trends were observed for risks of infants being small for gestational age infants for weight and length. Among infants of untreated women, 4.3% (n=24) had neonatal hypoglycaemia compared with 2.5% (n=8302) among infants of women without bipolar disorder (1.51, 1.04 to 2.43), and 3.4% (n=11) of the treated women (1.18, 0.64 to 2.16). The analyses of variation in outcomes did not support any significant differences between treated and untreated women. CONCLUSIONS: Bipolar disorder in women during pregnancy, whether treated or not, was associated with increased risks of adverse pregnancy outcomes.

Bufferd, S. J., L. R. Dougherty, et al. (2012). ***"Psychiatric disorders in preschoolers: Continuity from ages 3 to 6."*** Am J Psychiatry 169(11): 1157-1164. http://ajp.psychiatryonline.org/article.aspx?articleid=1389518

OBJECTIVE Recent studies indicate that many preschoolers meet diagnostic criteria for psychiatric disorders. However, data on the continuity of these diagnoses are limited, particularly from studies examining a broad range of disorders in community samples. Such studies are necessary to elucidate the validity and clinical significance of psychiatric diagnoses in young children. The authors examined the continuity of specific psychiatric disorders in a large community sample of preschoolers from the preschool period (age 3) to the beginning of the school-age period (age 6). METHOD Eligible families with a 3-year child were recruited from the community through commercial mailing lists. For 462 children, the child's primary caretaker was interviewed at baseline and again when the child was age 6, using the parent-report Preschool Age Psychiatric Assessment, a comprehensive diagnostic interview. The authors examined the continuity of DSM-IV diagnoses from ages 3 to 6. RESULTS Three-month rates of disorders were relatively stable from age 3 to age 6. Children who met criteria for any diagnosis at age 3 were nearly five times as likely as the others to meet criteria for a diagnosis at age 6. There was significant homotypic continuity from age 3 to age 6 for anxiety, attention deficit hyperactivity disorder (ADHD), and oppositional defiant disorder, and heterotypic continuity between depression and anxiety, between anxiety and oppositional defiant disorder, and between ADHD and oppositional defiant disorder. CONCLUSIONS These results indicate that preschool psychiatric disorders are moderately stable, with rates of disorders and patterns of homotypic and heterotypic continuity similar to those observed in samples of older children.

Cheavens, J. S., D. R. Strunk, et al. (2012). ***"The compensation and capitalization models: A test of two approaches to individualizing the treatment of depression."*** Behaviour Research and Therapy 50(11): 699-706. http://www.sciencedirect.com/science/article/pii/S0005796712001222

Despite long-standing calls for the individualization of treatments for depression, modest progress has been made in this effort. The primary objective of this study was to test two competing approaches to personalizing cognitive-behavioral treatment of depression (viz., capitalization and compensation). Thirty-four adults meeting criteria for Major Depressive Disorder (59% female, 85% Caucasian) were randomized to 16-weeks of cognitive-behavioral treatment in which strategies used were selected based on either the capitalization approach (treatment matched to relative strengths) or the compensation approach (treatment matched to relative deficits). Outcome was assessed with a composite measure of both self-report (i.e., Beck Depression Inventory) and observer-rated (i.e., Hamilton Rating Scale for Depression) depressive symptoms. Hierarchical linear modeling revealed a significant treatment approach by time interaction indicating a faster rate of symptom change for the capitalization approach compared to the compensation approach (d = .69, p = .03). Personalizing treatment to patients' relative strengths led to better outcome than treatment personalized to patients' relative deficits. If replicated, these findings would suggest a significant change in thinking about how therapists might best adapt cognitive-behavioral interventions for depression for particular patients.

Fekadu, A., L. J. Rane, et al. (2012). ***"Prediction of longer-term outcome of treatment-resistant depression in tertiary care."*** British Journal of Psychiatry 201(5): 369-375. http://bjp.rcpsych.org/content/201/5/369.abstract

Background: Systematic studies on the outcome of treatment-resistant depression are scarce.AimsTo describe the longer-term outcome and predictors of outcome in treatment-resistant depression. Method: Out of 150 patients approached, 118 participants with confirmed treatment-resistant depression (unipolar, n = 77; bipolar, n = 27; secondary, n = 14) treated in a specialist in-patient centre were followed-up for between 8 and 84 months (mean = 39, s.d. = 22). Results: The majority of participants attained full remission (60.2%), most of whom (48.3% of total sample) showed sustained recovery (full remission for at least 6 months). A substantial minority had persistent subsyndromal depression (19.5%) or persistent depressive episode (20.3%). Diagnosis of bipolar treatment-resistant depression and poorer social support were associated with early relapse, whereas strong social support, higher educational status and milder level of treatment resistance measured with the Maudsley Staging Method were associated with achieving quicker remission. Exploratory analysis of treatment found positive associations between treatment with a monoamine oxidase inhibitor (MAOI) in unipolar treatment-resistant depression and attaining remission at discharge and at final follow-up, and duloxetine use predicted attainment of remission at final follow-up.

Conclusions: Although many patients with treatment-resistant depression experience persistent symptomatology even after intensive, specialist treatment, most can achieve remission. The choice of treatment and presence of good social support may affect remission rates, whereas those with low social support and a bipolar diathesis should be considered at higher risk of early relapse. We suggest that future work to improve the long-term outcome in this disabling form of depression might focus on social interventions to improve support, and the role of neglected pharmacological interventions such as MAOIs.

Gentile, S. (2012). ***"Bipolar disorder in pregnancy: To treat or not to treat?"*** BMJ 345. http://www.bmj.com/content/345/bmj.e7367

Bodén and colleagues found that both treated and untreated women with bipolar disorder were at greater risk of adverse pregnancy outcomes than women without mental illness. It is important to remember the potential consequences of bipolar relapse in pregnancy and the puerperium: a woman's mental state may preclude her from caring for herself or for her child adequately and this may lead to offspring being removed from maternal care. Given the current study's findings, it is clear that prophylactic treatment with psychotropic drugs should be actively encouraged for all pregnant women with bipolar disorder.7 The question is not "to treat or not to treat?" but "how to treat optimally?" Because no drug is without risks, clinicians cannot hope to identify a "safe choice," but merely a "less harmful" one. Furthermore, drug treatment is only one part of the overall management of pregnant women diagnosed with severe and persistent psychiatric disorders. An integrated tailored approach to management must be provided for these vulnerable mothers. It is vital to anticipate that the stigma associated with mental illness may lead to refusal to engage with psychiatric services and to ensure that barriers to engagement are attenuated. Patients must be properly counselled about the risks of treatment versus the risks associated with the untreated psychiatric disorder. Wherever possible ensure that patients are offered available financial support and help to engage with medical services. Discuss with patients, partners, and family the changes to lifestyle and challenges that come with being a parent, and help identify supportive care givers for the mother-infant pair. Encourage and facilitate social integration, especially for women from disadvantaged social groups and those who are isolated. Drug treatment will undoubtedly improve maternal adherence to these adjunctive interventions.

Gibbons, R. D., D. J. Weiss, et al. (2012). ***"Development of a computerized adaptive test for depression."*** Archives of General Psychiatry 69(11): 1104-1112. http://dx.doi.org/10.1001/archgenpsychiatry.2012.14

Context Unlike other areas of medicine, psychiatry is almost entirely dependent on patient report to assess the presence and severity of disease; therefore, it is particularly crucial that we find both more accurate and efficient means of obtaining that report.Objective To develop a computerized adaptive test (CAT) for depression, called the Computerized Adaptive Test–Depression Inventory (CAT-DI), that decreases patient and clinician burden and increases measurement precision.Design Case-control study.Setting A psychiatric clinic and community mental health center.Participants A total of 1614 individuals with and without minor and major depression were recruited for study.Main Outcome Measures The focus of this study was the development of the CAT-DI. The 24-item Hamilton Rating Scale for Depression, Patient Health Questionnaire 9, and the Center for Epidemiologic Studies Depression Scale were used to study the convergent validity of the new measure, and the Structured Clinical Interview for DSM-IV was used to obtain diagnostic classifications of minor and major depressive disorder.Results A mean of 12 items per study participant was required to achieve a 0.3 SE in the depression severity estimate and maintain a correlation of r = 0.95 with the total 389-item test score. Using empirically derived thresholds based on a mixture of normal distributions, we found a sensitivity of 0.92 and a specificity of 0.88 for the classification of major depressive disorder in a sample consisting of depressed patients and healthy controls. Correlations on the order of r = 0.8 were found with the other clinician and self-rating scale scores. The CAT-DI provided excellent discrimination throughout the entire depressive severity continuum (minor and major depression), whereas the traditional scales did so primarily at the extremes (eg, major depression).Conclusions Traditional measurement fixes the number of items administered and allows measurement uncertainty to vary. In contrast, a CAT fixes measurement uncertainty and allows the number of items to vary. The result is a significant reduction in the number of items needed to measure depression and increased precision of measurement.

Hilderink, P. H., H. Burger, et al. (2012). ***"The temporal relation between pain and depression: Results from the longitudinal aging study amsterdam."*** Psychosomatic Medicine 74(9): 945-951. http://www.psychosomaticmedicine.org/content/74/9/945.abstract

Objective Pain and depression are both common in old age, but their (long-term) temporal relationship remains unknown. This study is designed to determine whether pain predicts the onset of depression and vice versa.Methods This is a prospective, population-based cohort study with 12-year follow-up and 3-year intervals in the Netherlands (Longitudinal Aging Study Amsterdam). At baseline, participants were aged 55 to 85 years (n = 2028). Main measurements outcomes were incident depression defined as crossing the cutoff of 16 and showing a relevant change (≥5 points) on the Center for Epidemiological Studies–Depression Scale among nondepressed participants and incident pain defined as a score of 2 or higher on the pain scale of the 5-item Nottingham Health Profile in pain-free participants. Multiple imputations were adopted to estimate missing values.Results In nondepressed participants (n= 1769), a higher level of pain was predictive of incident depression in multiple extended Cox regression analyses (hazard rate [HR] = 1.13 [95% confidence interval {CI}: 1.05–1.22], p = .001), which all remained significant after correction for sociodemographic characteristics, life-style characteristics, functional limitations, and chronic diseases (HR = 1.09 [95% CI = 1.01–1.18], p = .035). In the pain-free participants (n = 1420), depressive symptoms at baseline predicted incident pain (HR = 1.02 [95% CI: 1.01–1.04], p = .006). This depression measure did not independently predicted the onset of pain in the fully adjusted models.Conclusions As pain precedes the onset of depression, strategies to prevent depression in chronic pain patients are warranted. In contrast, no effects of depression on the development of subsequent pain were found when adjusting for covariates.

Hoge, E. A., A. Ivkovic, et al. (2012). ***"Generalized anxiety disorder: Diagnosis and treatment."*** BMJ 345: e7500. http://www.bmj.com/content/345/bmj.e7500

This is a good overview of current understanding & treatment of GAD. Summary points: Generalized anxiety disorder (GAD) is associated with substantial distress and disability. GAD is often associated with other medical and psychiatric disorders. Antidepressants, such as sertraline, are generally first line medical treatment options. Psychotherapy and other psychosocial treatments can also be effective. GAD increases the risk of major depression, so preventive approaches should be put in place

Hunkeler, E. M., W. A. Hargreaves, et al. (2012). ***"A web-delivered care management and patient self-management program for recurrent depression: A randomized trial."*** Psychiatr Serv. http://ps.psychiatryonline.org/article.aspx?articleid=1360356

OBJECTIVE This study assessed the impact of an Internet-delivered care management and patient self-management program, eCare for Moods, on patients treated for recurrent or chronic depression. METHODS Patients with recurrent or chronic depression were randomly assigned to eCare (N=51) or usual specialty mental health care (N=52). The 12-month eCare

program integrates with ongoing depression care, links to patients' electronic medical records, and provides clinicians with panel management and decision support. Participants were interviewed at baseline and six, 12, 18, and 24 months after enrollment. Telephone interviewers blind to treatment used a timeline follow-back method to estimate depression severity on a 6-point scale for each of the 105 study weeks (including the baseline). Differences between groups in weekly severity over two years were examined by generalized estimating equations. RESULTS Participants in eCare experienced more reduction in depressive symptoms (estimate=-.74 on the 6-point scale over two years; 95% confidence interval [CI]=-1.38 to -.09, p=.025) and were less often depressed (-.24 over two years; CI=-.46 to -.03, p=.026). At 24 months, 43% of eCare and 30% of usual-care participants were depression free; the number needed to treat to attain one additional depression-free participant was 8. eCare participants had other favorable outcomes: improved general mental health (p=.002), greater satisfaction with specialty care (p=.003) and with learning new coping skills (p<.001), and more confidence in managing depression (p=.006). CONCLUSIONS Internet-delivered care management can help improve outcomes of patients treated for recurrent or chronic depression.

Kilbourne, A. M. (2012). ***"E-health and the transformation of mental health care."*** Psychiatr Serv 63(11): 1059. http://ps.psychiatryonline.org/article.aspx?articleid=1386873

This month's issue highlights important research milestones regarding e-health technologies and their potential to enhance access to psychosocial interventions and improve outcomes for persons with mental disorders. Hunkeler and colleagues conducted a randomized controlled trial of an Internet-delivered chronic care model for persons with chronic depression enrolled in a staff-model health maintenance organization. The program involves a Web-based self-management program supported by electronic medical record–enhanced panel management and provider decision support. Deen and coauthors report on a national assessment of telehealth use in the U.S. Department of Veterans Affairs, which found substantial increases in individual and group telepsychotherapy encounters in recent years. These e-health technologies have great potential to extend the reach of psychosocial interventions beyond the clinic walls, especially for persons in rural settings or who are reluctant to seek mental health specialty care.

Kuyken, W., R. Crane, et al. (2012). ***"Does mindfulness based cognitive therapy prevent relapse of depression?"*** BMJ 345: e7194. http://www.ncbi.nlm.nih.gov/pubmed/23144206

Depression typically runs a relapsing and recurrent course.1 Without ongoing treatment people with recurrent depression have a very high risk of repeated depressive relapses throughout their life, even after successful acute treatment. Major inroads into the substantial health burden attributable to depression could be offset through interventions that prevent depressive relapse among people at high risk of recurrent episodes.2 If the factors that make people vulnerable to depressive relapse can be attenuated, the relapsing course of depression could potentially be broken. Currently, most depression is treated in primary care, and maintenance antidepressants are the mainstay approach to preventing relapse.3 The UK's National Institute for Health and Clinical Excellence (NICE) recommends that to stay well, people with a history of recurrent depression should continue taking antidepressants for at least two years. However, many patients experience side effects, and some express a preference for psychosocial interventions, which provide long term protection against relapse.4 Mindfulness based cognitive therapy (MBCT)5 was developed as a psychosocial intervention for teaching people with a history of depression the skills to stay well in the long term. A recent systematic review and meta-analysis of six randomised controlled trials (n=593) suggests that MBCT significantly reduces the rates of depressive relapse compared with usual care or placebo, corresponding to a relative risk reduction of 34% (risk ratio 0.66, 95% confidence interval 0.53 to 0.82).6 However, despite the emerging evidence base6 and widespread clinical enthusiasm for MBCT,7 several uncertainties remain. Firstly, it is not clear how MBCT compares with other approaches to preventing depressive relapse—most notably, maintenance antidepressants. Evidence from two of the six randomised controlled trials included in systematic review mentioned above suggests that MBCT was at least as efficacious as maintenance antidepressants in preventing relapse (risk ratio 0.80, 95% confidence interval 0.60 to 1.08),6 but the sample sizes were small and the confidence intervals were wide. Even though antidepressants are the first line approach to preventing depressive relapse, no trials have yet evaluated whether the combination of antidepressants and MBCT provides added benefit over either treatment alone. There are also no head to head trials comparing MBCT with other psychosocial approaches known to help people stay well in the long term (such as cognitive behavioural therapy and interpersonal therapy). Secondly, although the six randomised controlled trials have not yet reported adverse effects, neither have studies explicitly explored in any depth MBCT's acceptability in a broad range of populations. The earliest two trials of MBCT provided evidence through retrospective analyses suggesting that MBCT may be effective only for people who had had three or more episodes of depression.6 As a result, subsequent trials have restricted their sample to patients with three or more previous episodes. Future research is needed to establish how acceptable MBCT is to a broad range of patients. Thirdly, even though it is nearly 10 years since NICE first recommended MBCT and even though the 2009 NICE update identified the therapy as a key priority for implementation, there is a substantial gap between the efficacy research and implementation in routine practice settings. A recent survey suggests that only a small number of mental health services in the UK have systematically built MBCT into their depression care pathways ... How do I know when to refer someone for cognitive behavioural therapy, interpersonal therapy, or mindfulness based cognitive therapy? All three psychosocial treatments are recommended by NICE, but cognitive behavioural and interpersonal therapies aim to help patients with current depression get well and stay well. MBCT might therefore be considered for people who are well but still at substantial risk of relapse—that is, those who have experienced three or more previous episodes of depression. This includes people who have relapsed despite antidepressant treatment; who cannot or choose not to continue antidepressant treatment; and/or who have residual symptoms. Such patients may present asking for long term support in the management of their depression or feel at risk of having future relapses after drug or psychological treatment. MBCT is best suited to people interested in a psychosocial approach to preventing future episodes of depression who are open and willing to learn new ways of thinking and behaving and to learn within a group based context, and who can invest the time both to attend the groups and to do the home practice.

Luby, J., S. Lenze, et al. (2012). ***"A novel early intervention for preschool depression: Findings from a pilot randomized controlled trial."*** J Child Psychol Psychiatry 53(3): 313-322. http://www.ncbi.nlm.nih.gov/pubmed/22040016

BACKGROUND: Validation for depression in preschool children has been established; however, to date no empirical investigations of interventions for the early onset disorder have been conducted. Based on this and the modest efficacy of available treatments for childhood depression, the need for novel early interventions has been emphasized. Large effect sizes (ES) for preschool psychotherapies for several Axis I disorders suggest that earlier intervention in depression may also be promising. Therefore, a novel form of treatment for preschool depression, Parent-Child Interaction Therapy Emotion Development (PCIT-ED) was developed and tested. METHODS: A preliminary randomized controlled trial (RCT) was conducted comparing PCIT-ED to psycho-education in depressed 3- to 7-year-olds and their caregivers. A total of 54 patients met symptom criteria for DSM-IV major depressive disorder and were randomized, 19 patients completed the active treatment (n = 8 dropouts) and 10 completed psycho-education (n = 17 dropouts). RESULTS: Both groups showed significant improvement in several domains, with PCIT-ED showing significance in a greater number of domains. An intent-to-treat analysis suggested that

PCIT-ED was significantly more effective than psycho-education on executive functioning (p = .011, ES = 0.12) and emotion recognition skills (p = .002, ES = 0.83). CONCLUSIONS: The RCT proved feasible and suggests an individual control condition should be used in future trials to minimize differential dropout. These pilot data, although limited by power, suggest that PCIT-ED may be a promising early intervention for depression. Larger scale randomized controlled trials of PCIT-ED for depressed preschoolers are now warranted.

Luby, J. L. (2012). ***"Dispelling the "they'll grow out of it" myth: Implications for intervention."*** Am J Psychiatry 169(11): 1127-1129. http://ajp.psychiatryonline.org/article.aspx?articleid=1389511

(Free full text available): Although the field of infant/preschool mental health is not young, it has been met with high levels of skepticism and has yet to be well integrated into mainstream psychiatry. As outlined by Bufferd et al. in their landmark paper in this issue (1), efforts to empirically investigate and validate mental disorders in early childhood have faced a number of impediments. These have included concern that diagnostic labels might stigmatize young children; the lack—until recently—of developmentally sensitive, age-appropriate measures of psychopathology that make accurate distinctions from developmental norms; and, perhaps most importantly, a long-held underlying belief that early emotional and behavioral problems represent normative extremes that young children simply grow out of. Bufferd and colleagues' longitudinal study of a large community sample adds to the literature and provides some of the most rigorous broad-based data to date refuting this notion. Building on the growing body of literature validating the onset of numerous axis I psychiatric disorders as early as age 3 (2–5), Bufferd et al. provide findings from a relatively large community sample of 3-year-old children assessed using a comprehensive interviewer-based diagnostic interview (among other measures) and followed longitudinally to age 6. As the authors point out, unique features of the study design included the community-based sampling and the use of a rigorous and comprehensive diagnostic interview designed specifically to assess discrete disorders in preschoolers (as opposed to more commonly used generic checklist measures). The study findings clearly demonstrated that the manifestation of symptoms meeting DSM-IV criteria for clinical disorders at age 3 was a robust marker of risk for disorders at age 6. Both homotypic and heterotypic continuity were demonstrated. Notably, having a disorder at age 3 was associated with an almost fivefold greater risk of having a disorder at age 6. Conversely, more than 50% of children who met criteria for a disorder at age 6 already had clinically significant symptoms by age 3. One limitation of the study was that the age 6 assessment was done by telephone rather than in person as was done at the age 3 assessment. Another was that the diagnosis was based on parental report and was not supplemented by observational data, thereby introducing possible bias that cannot be offset by child report (since young children have a limited ability to self-report on symptoms directly). It should be noted, however, that the use of parent informants in research diagnostic assessments of young children stands as the state of the art today, despite some promising efforts to develop feasible valid and reliable observational tools that map onto diagnostic algorithms (6). Notwithstanding these limitations, the study findings clearly add broad evidence supporting the relative stability, rather than transience, of early forms of psychopathology and therefore the importance of early identification and intervention ... The field of psychiatry, facing the need to develop more powerful and effective treatments, has been searching for new models to conceptualize disorders and to understand mechanisms of risk (11). Along this line, there has been an increasing focus on understanding the developmental underpinnings of disorders so that they may be identified before they are full-blown and, in some cases, on the path to chronicity. In this light, the findings of Bufferd et al. should blow new wind into the sails of efforts to identify and define the earliest-onset forms of mental disorders. Such work may help us understand the developmental pathways of adult disorders and develop new methods for intervening earlier in life, during periods of greater developmental change and plasticity.

McLaughlin, K. A., J. Greif Green, et al. (2012). ***"Childhood adversities and first onset of psychiatric disorders in a national sample of US adolescents."*** Archives of General Psychiatry 69(11): 1151-1160. http://dx.doi.org/10.1001/archgenpsychiatry.2011.2277

Context Although childhood adversities (CAs) are known to be highly co-occurring, most research examines their associations with psychiatric disorders one at a time. However, recent evidence from adult studies suggests that the associations of multiple CAs with psychiatric disorders are nonadditive, arguing for the importance of multivariate analysis of multiple CAs. To our knowledge, no attempt has been made to perform a similar kind of analysis among children or adolescents. Objective To examine the multivariate associations of 12 CAs with first onset of psychiatric disorders in a national sample of US adolescents. Design A US national survey of adolescents (age range, 13-17 years) assessing DSM-IV anxiety, mood, behavior, and substance use disorders and CAs. The CAs include parental loss (death, divorce, and other separations), maltreatment (neglect and physical, sexual, and emotional abuse), and parental maladjustment (violence, criminality, substance abuse, and psychopathology), as well as economic adversity. Setting Dual-frame household-school samples. Participants In total, 6483 adolescent-parent pairs. Main Outcome Measures Lifetime DSM-IV disorders assessed using the World Health Organization Composite International Diagnostic Interview. Results Overall, exposure to at least 1 CA was reported by 58.3% of adolescents, among whom 59.7% reported multiple CAs. The CAs reflecting maladaptive family functioning were more strongly associated than other CAs with the onset of psychiatric disorders. The best-fitting model included terms for the type and number of CAs and distinguished between maladaptive family functioning and other CAs. The CAs predicted behavior disorders most strongly and fear disorders least strongly. The joint associations of multiple CAs were subadditive. The population-attributable risk proportions across DSM-IV disorder classes ranged from 15.7% for fear disorders to 40.7% for behavior disorders. The CAs were associated with 28.2% of all onsets of psychiatric disorders. Conclusions Childhood adversities are common, highly co-occurring, and strongly associated with the onset of psychiatric disorders among US adolescents. The subadditive multivariate associations of CAs with the onset of psychiatric disorders have implications for targeting interventions to reduce exposure to CAs and to mitigate the harmful effects of CAs to improve population mental health.

Nulman, I., G. Koren, et al. (2012). ***"Neurodevelopment of children following prenatal exposure to venlafaxine, selective serotonin reuptake inhibitors, or untreated maternal depression."*** Am J Psychiatry 169(11): 1165-1174. http://ajp.psychiatryonline.org/article.aspx?articleid=1389519

OBJECTIVE Effects on child neurodevelopment of neurotransmitter reuptake inhibitors used as antidepressants during pregnancy have not been adequately studied. The authors compared the effects of prenatal exposure to venlafaxine (serotonin-norepinephrine reuptake inhibitor), selective serotonin reuptake inhibitors (SSRIs), and maternal depression. METHOD A cohort derived from a prospectively collected database included four groups of children born to 1) depressed women who took venlafaxine during pregnancy (N=62), 2) depressed women who took SSRIs during pregnancy (N=62), 3) depressed women who were untreated during pregnancy (N=54), and 4) nondepressed, healthy women (N=62). The children's intelligence and behavior outcomes were evaluated with standardized instruments at one time point between the ages of 3 years and 6 years, 11 months. RESULTS The children exposed to venlafaxine, SSRIs, and maternal depression during pregnancy had similar full-scale IQs (105, 105, and 108, respectively). The IQs of the venlafaxine and SSRI groups were significantly lower than that of the children of nondepressed mothers (112). The three groups exposed to maternal depression had consistently, but nonsignificantly, higher rates of most problematic behaviors than the children of nondepressed mothers. Severity of maternal depression in pregnancy and at testing predicted child behavior. Maternal IQ and child sex predicted child IQ. Antidepressant

dose and duration during pregnancy did not predict any cognitive or behavioral outcome. CONCLUSIONS Factors other than antidepressant exposure during pregnancy strongly predict children's intellect and behavior. Depression during pregnancy is a significant risk factor for postpartum depression. Children of depressed mothers may be at risk of future psychopathology.

Otte, C., S. Zhao, et al. (2012). ***"Statin use and risk of depression in patients with coronary heart disease: Longitudinal data from the heart and soul study."*** J Clin Psychiatry 73(5): 610-615. http://www.ncbi.nlm.nih.gov/pubmed/22394433

BACKGROUND: Statins are among the most commonly prescribed medications worldwide. Although their benefits for cardiovascular disease are well established, the effects of statins on depressive symptoms are unknown. METHOD: We examined the association between baseline statin use (2000-2002) and subsequent depressive symptoms in a prospective cohort study of 965 outpatients with coronary disease from 12 outpatient clinics in the San Francisco Bay Area. Depressive symptoms were assessed annually for 6 years using the Patient Health Questionnaire (PHQ) (primary outcome measure). We evaluated the cross-sectional association between statin use and risk of depressive symptoms at baseline and the longitudinal association between baseline statin use and risk of depressive symptoms during follow-up. RESULTS: Of the 965 participants, 629 (65%) used statins. At baseline, statin users had lower mean +/- SE PHQ depression scores than nonusers (4.8 +/- 0.2 vs 5.9 +/- 0.3, P < .01). Statin users were less likely than nonusers to have depression (PHQ score >/= 10) at baseline (17% vs 24%; P = .02) and during follow-up (28% vs 40%; P < .01). Among the 776 patients without depressive symptoms at baseline (PHQ < 10), statin use was associated with a 48% decreased odds of developing depression during follow-up (odds ratio [OR], 0.52; 95% CI, 0.38-0.73; P < .01). After we adjusted for potentially confounding variables, statin use remained associated with a 38% decreased odds of subsequent depression (adjusted OR, 0.62; 95% CI, 0.41-0.95; P = .02). CONCLUSIONS: We found that statin use was associated with a decreased risk of subsequent depressive symptoms in patients with coronary heart disease. Whether use of statins prevents depressive symptoms deserves further study.

Parikh, S. V., A. Zaretsky, et al. (2012). ***"A randomized controlled trial of psychoeducation or cognitive-behavioral therapy in bipolar disorder: A Canadian network for mood and anxiety treatments (CANMAT) study [CME]."*** J Clin Psychiatry 73(6): 803-810. http://www.ncbi.nlm.nih.gov/pubmed/22795205

OBJECTIVE: Bipolar disorder is insufficiently controlled by medication, so several adjunctive psychosocial interventions have been tested. Few studies have compared these psychosocial treatments, all of which are lengthy, expensive, and difficult to disseminate. We compared the relative effectiveness of a brief psychoeducation group intervention to a more comprehensive and longer individual cognitive-behavioral therapy intervention, measuring longitudinal outcome in mood burden in bipolar disorder. METHOD: This single-blind randomized controlled trial was conducted between June 2002 and September 2006. A total of 204 participants (ages 18-64 years) with DSM-IV bipolar disorder type I or II participated from 4 Canadian academic centers. Subjects were recruited via advertisements or physician referral when well or minimally symptomatic, with few exclusionary criteria to enhance generalizability. Participants were assigned to receive either 20 individual sessions of cognitive-behavioral therapy or 6 sessions of group psychoeducation. The primary outcome of symptom course and morbidity was assessed prospectively over 72 weeks using the Longitudinal Interval Follow-up Evaluation, which yields depression and mania symptom burden scores for each week. RESULTS: Both treatments had similar outcomes with respect to reduction of symptom burden and the likelihood of relapse. Eight percent of subjects dropped out prior to receiving psychoeducation, while 64% were treatment completers; rates were similar for cognitive-behavioral therapy (6% and 66%, respectively). Psychoeducation cost $180 per subject compared to cognitive-behavioral therapy at $1,200 per subject. CONCLUSIONS: Despite longer treatment duration and individualized treatment, cognitive-behavioral therapy did not show a significantly greater clinical benefit compared to group psychoeducation. Psychoeducation is less expensive to provide and requires less clinician training to deliver, suggesting its comparative attractiveness. TRIAL REGISTRATION: ClinicalTrials.gov identifier: NCT00188838.

Steiner, M. (2012). ***"Prenatal exposure to antidepressants: How safe are they?"*** Am J Psychiatry 169(11): 1130-1132. http://ajp.psychiatryonline.org/article.aspx?articleid=1389512

(Free full text available): The question of whether maternal antidepressant treatment during pregnancy is better or worse for the offspring than untreated maternal depression is still mostly unanswered. The majority of studies addressing this issue have focused on the risks of neonatal malformation and on immediate postpartum neonatal discontinuation syndrome (also known as neonatal withdrawal or adaptation syndrome). Several guidelines have been published over the past 5 years, by the American Psychiatric Association and the American College of Obstetricians and Gynecologists, Great Britain's National Institute for Health and Clinical Excellence, the Scottish Intercollegiate Guidelines Network, and the Black Dog Institute of Australia. They all end with a cautionary statement that the decision to use medication during pregnancy must take into account any possible risk associated with using antidepressants at this time. Monitoring of a specific malformation and/or postpartum neonatal discontinuation syndrome among antidepressant-exposed pregnancies is based on retrospective case-control surveillance, which has obvious limitations. Based on recent data from the Metropolitan Atlanta Congenital Defects Program, the risk of major structural or genetic birth defects in the United States is approximately 3% of all births (5). To date, there is no report suggesting that the use of antidepressants during pregnancy increases that risk above the general population risk of 2%–3%, nor is there evidence to indicate that they might cause organ-specific defects. The only exception is the reports suggesting that paroxetine use early in pregnancy is associated with an increased risk of atrium septum defects. More recently, several larger cohort databases have presented a more optimistic view when comparing the ill effects of untreated maternal depression to the outcomes for neonates born to mothers exposed to antidepressants during pregnancy. Works by Spinelli and by Diav-Citrin and Ornoy are also informative. My colleagues and I recently completed a large systematic review and meta-analysis of pregnancy and delivery outcomes after exposure to antidepressants. We focused on gestational age, birth weight, and APGAR scores among infants exposed to antidepressants in utero. Although the results showed statistically significant associations for all three outcomes, the effects found were small in magnitude (gestational age approximately 3 days shorter, birth weight 75 g lower, and difference in APGAR scores at 1 and 5 minutes less than half a point), and the values in the exposed group typically fell within the normal range. There are a handful of studies that examined the impact of antidepressant exposure during pregnancy on developmental milestones in the offspring. These include both testing for cognitive and behavioral functioning in preschoolers and long-term follow-up into adolescence and adulthood. None suggests any significant negative impact; see data from the Danish National Birth Cohort and the Norwegian Mother and Child Cohort Study . There is, however, ample evidence that anxiety, depression, and in particular, stress during pregnancy, especially early in gestation, can have adverse effects on fetal maturation, cognitive performance during infancy, and learning and memory in 6- to 8-year-old children. In this issue, Nulman and colleagues present data on the effects of prenatal exposure to venlafaxine, selective serotonin reuptake inhibitors (SSRIs), and maternal depression on long-term child neurodevelopment. The results failed to show an effect of antidepressant medication on children's intellectual or behavioral outcomes. Instead, the results showed that untreated depression is associated with a higher risk for postpartum depression and that prenatal and childhood exposure to maternal depression is associated with behavioral problems in the offspring and may increase the risk for long-term psychopathology. The same group, from the Motherisk Program at the Hospital for Sick Children in Toronto, under the directorship of Gideon Koren, was the first to publish,

10 years ago, results along the same lines. In a prospective, controlled study, Nulman and colleagues found that exposure to tricyclic antidepressants or fluoxetine throughout gestation was not associated with poor cognition, nor did it affect language development or temperament of preschool and early-school children, whereas maternal depression was associated with less cognitive and language achievement in the offspring. Regardless of this encouraging perspective, health care providers should keep in mind that in order to prescribe antidepressants during pregnancy, the indication must be compelling. Not only is it crucial to establish an axis I diagnosis, it is also important to assess the degree of distress and the burden of illness that the pregnant woman is experiencing. It is also paramount to have a frank discussion with the patient (and whenever possible, with her partner in attendance) on the pros and cons of using antidepressants during pregnancy based on the most recent available evidence and to obtain her or their consent.

Tohen, M., D. P. McDonnell, et al. (2012). ***"Randomised, double-blind, placebo-controlled study of olanzapine in patients with bipolar i depression."*** British Journal of Psychiatry 201(5): 376-382. http://bjp.rcpsych.org/content/201/5/376.abstract

Background: Atypical antipsychotics are widely used in bipolar mania. However, the efficacy of atypical antipsychotics in bipolar depression has not been comprehensively explored. Aims: To evaluate olanzapine monotherapy in patients with bipolar depression. Method: Patients with bipolar depression received olanzapine (5–20 mg/day, n = 343) or placebo (n = 171) for 6 weeks. The primary outcome was change from baseline to end-point in Montgomery–Åsberg Depression Rating Scale (MADRS) total score. Secondary outcomes included: Clinical Global Impression – Bipolar Version (CGI-BP) scale, 17-item Hamilton Rating Scale for Depression (HRSD-17) and Young Mania Rating Scale (YMRS) scores, and the rate of response (⩾50% reduction in MADRS at end-point), recovery (MADRS ⩽12 for ⩾4 weeks plus treatment completion) and remission (MADRS ⩽8). The trial was registered with ClinicalTrials.gov (NCT00510146).ResultsOlanzapine demonstrated: significantly greater (P<0.04) improvements on MADRS (least-squares mean change −13.82 v. −11.67), HRSD-17 and YMRS total scores and all CGI-BP subscale scores v. placebo; significantly (P⩽0.05) more response and remission, but not recovery; significantly (P<0.01) greater mean increases in weight, fasting cholesterol and triglycerides; and significantly more (P<0.001) patients gained ⩾7% body weight. Conclusions: Olanzapine monotherapy appears to be efficacious in bipolar depression. Additional long-term studies are warranted to confirm these results. Safety findings were consistent with the known safety profile of olanzapine.

van der Lem, R., W. de Wever, et al. (2012). ***"The generalizability of psychotherapy efficacy trials in major depressive disorder: An analysis of the influence of patient selection in efficacy trials on symptom outcome in daily practice."*** BMC Psychiatry 12(1): 192. http://www.biomedcentral.com/1471-244X/12/192

(Free full text available) BACKGROUND:Treatment guidelines for major depressive disorder (MDD) are based on results from randomized clinical trials, among others in psychotherapy efficacy trials. However, patients in these trials differ from routine practice patients since trials use stringent criteria for patient selection. It is unknown whether the exclusion criteria used in psychotherapy efficacy trials (PETs) influence symptom outcome in clinical practice. We first explored which exclusion criteria are used in PETs. Second, we investigated the influence of commonly used exclusion criteria on symptom outcome in routine clinical practice. METHODS:We performed an extensive literature search in PubMed, PsycInfo and additional databases for PETs for MDD. From these, we identified commonly used exclusion criteria. We investigated the influence of exclusion criteria on symptom outcome by multivariate regression models in a sample of patients suffering from MDD according to the MINIplus from a routine clinical practice setting (n=598). Data on routine clinical practice patients were gathered through Routine Outcome Monitoring. RESULTS:We selected 20 PETs and identified the following commonly used exclusion criteria: 'a baseline severity threshold of HAM-D<=14', 'current or past abuse or dependence of alcohol and/or drugs' and 'previous use of medication or ECT'. In our routine clinical practice sample of patients suffering from MDD (n=598), presence of 'current or past abuse of or dependence on alcohol and/or drugs' had no significant influence on outcome.'Meeting a baseline severity threshold of HAM-D<=14' and 'previous use of medication or ECT' were associated with better outcome, but the explained variance of the models was very small (R2=2-11%). CONCLUSIONS:The most consistently used exclusion criteria are not a major threat to the generalizability of results found in PETs. However, PETs do somewhat improve their results by exclusion of patients with minor depression and patients who used antidepressants prior to psychotherapy.

Wiles, N., L. Thomas, et al. (2012). ***"Cognitive behavioural therapy as an adjunct to pharmacotherapy for primary care based patients with treatment resistant depression: Results of the COBALT randomised controlled trial."*** Lancet. http://www.ncbi.nlm.nih.gov/pubmed/23219570

BACKGROUND: Only a third of patients with depression respond fully to antidepressant medication but little evidence exists regarding the best next-step treatment for those whose symptoms are treatment resistant. The CoBalT trial aimed to examine the effectiveness of cognitive behavioural therapy (CBT) as an adjunct to usual care (including pharmacotherapy) for primary care patients with treatment resistant depression compared with usual care alone. METHODS: This two parallel-group multicentre randomised controlled trial recruited 469 patients aged 18-75 years with treatment resistant depression (on antidepressants for >/=6 weeks, Beck depression inventory [BDI] score >/=14 and international classification of diseases [ICD]-10 criteria for depression) from 73 UK general practices. Participants were randomised, with a computer generated code (stratified by centre and minimised according to baseline BDI score, whether the general practice had a counsellor, previous treatment with antidepressants, and duration of present episode of depression) to one of two groups: usual care or CBT in addition to usual care, and were followed up for 12 months. Because of the nature of the intervention it was not possible to mask participants, general practitioners, CBT therapists, or researchers to the treatment allocation. Analyses were by intention to treat. The primary outcome was response, defined as at least 50% reduction in depressive symptoms (BDI score) at 6 months compared with baseline. This trial is registered, ISRCTN38231611. FINDINGS: Between Nov 4, 2008, and Sept 30, 2010, we assigned 235 patients to usual care, and 234 to CBT plus usual care. 422 participants (90%) were followed up at 6 months and 396 (84%) at 12 months, finishing on Oct 31, 2011. 95 participants (46%) in the intervention group met criteria for response at 6 months compared with 46 (22%) in the usual care group (odds ratio 3.26, 95% CI 2.10-5.06, p<0.001). INTERPRETATION: Before this study, no evidence from large-scale randomised controlled trials was available for the effectiveness of augmentation of antidepressant medication with CBT as a next-step for patients whose depression has not responded to pharmacotherapy. Our study has provided robust evidence that CBT as an adjunct to usual care that includes antidepressants is an effective treatment, reducing depressive symptoms in this population.

Wilkinson, P. and Z. Izmeth (2012). ***"Continuation and maintenance treatments for depression in older people."*** Cochrane Database Syst Rev 11: CD006727. http://www.ncbi.nlm.nih.gov/pubmed/23152240

BACKGROUND: Depressive illness in older people causes significant suffering and health service utilisation. Relapse and recurrence rates are high. OBJECTIVES: To examine the efficacy of antidepressants and psychological therapies in preventing the relapse and recurrence of depression in older people. SEARCH METHODS: Search of the Cochrane Depression, Anxiety and Neurosis Review Group's specialized register (the CCDANCTR) up to 22 June 2012. The CCDANCTR includes relevant randomised

controlled trials from the following bibliographic databases: The Cochrane Library (all years), EMBASE, (1974 to date) MEDLINE (1950 to date) and PsycINFO (1967 to date). We handsearched relevant journals, contacted experts in the field and examined reference lists, conference proceedings and bibliographies. SELECTION CRITERIA: Both review authors independently selected studies. We included randomised controlled trials (RCTs) involving people aged 60 and over successfully treated for an episode of depression and randomised to receive continuation and maintenance treatment with antidepressants, psychological therapies, or combination. DATA COLLECTION AND ANALYSIS: Data were extracted independently by the two authors.The primary outcome was relapse/recurrence rate of depression (reaching a cut-off on any depression rating scale) at six-monthly intervals. Secondary outcomes included global impression of change, social functioning, and deaths. Meta-analysis was performed using risk ratio for dichotomous outcomes and mean differences (MD) for continuous outcomes, with 95% confidence intervals. MAIN RESULTS: Seven studies met the inclusion criteria (803 participants). Six compared antidepressant medication with placebo; two involved psychological therapies. There was marked heterogeneity between the studies.Comparing antidepressants with placebo, at six months follow-up there was no significant difference. At 12 months follow-up there was a statistically significant difference favouring antidepressants in reducing recurrence compared with placebo (three RCTs, N = 247, RR = 0.67, 95% CI 0.55 to 0.82; NNTB = five). At 24 months there was no significant difference for antidepressants overall, however, for the subgroup of tricyclic antidepressants there was significant benefit (three RCTs, N = 169, RR = 0.70, 95% CI 0.50 to 0.99; NNTB = five). At 36 months there was no significant difference for antidepressants overall. There was no difference in treatment acceptability or death rates between antidepressant and placebo.There was no significant difference between psychological treatment and antidepressant in recurrence rates at 12, 24, and 36 months (one RCT, N = 53) or between combination and antidepressant alone. Overall, the included studies were at low risk of bias. AUTHORS' CONCLUSIONS: The long-term benefits of continuing antidepressant medication in the prevention of recurrence of depression in older people are not clear and no firm treatment recommendations can be made on the basis of this review. Continuing antidepressant medication for 12 months appears to be helpful but this is based on only three small studies with relatively few participants using differing classes of antidepressants in clinically heterogeneous populations. Comparisons at other time points did not reach statistical significance. Data on psychological therapies and combined treatments are too limited to draw any conclusions.