20 action on depression abstracts, dec '12

(Alexander, Tatum et al. 2012; Almeida, Draper et al. 2012; Anderson, Haddad et al. 2012; Casanas, Catalan et al. 2012; Dakwar, Blanco et al. 2012; Del Re, Fluckiger et al. 2012; Dishman, Sui et al. 2012; Dording, Mischoulon et al. 2012; Farabaugh, Alpert et al. 2012; Lau, Colley et al. 2012; Leucht, Huhn et al. 2012; Moreno, Chong et al. 2012; Nelson 2012; Okusaga and Postolache 2012; Orriols, Queinec et al. 2012; Papakostas, Cassiello et al. 2012; Papakostas, Shelton et al. 2012; Piet, Wurtzen et al. 2012; Pinniger, Brown et al. 2012; Rethorst, Sunderajan et al. 2012)

Alexander, V., B. C. Tatum, et al. (2012). ***"A study of mindfulness practices and cognitive therapy: Effects on depression and self-efficacy."*** International Journal of Psychology and Counselling 4(9): 115-122. http://www.academicjournals.org/ijpc/abstracts/abstracts/abstracts2012/October/Alexander%20et%20al.htm

(Free full text available) Despite research findings that Cognitive Therapy (CT) reduces relapse of depression, patients often do have setbacks. Recently, CT researchers have integrated the Eastern meditative practice of mindfulness into cognitive approach. This study was a variation on research on Mindfulness Based Cognitive Therapy (the incorporation of mindfulness and CT) and relapse prevention from depression. Three tracks of participants, mindfulness training (MT), CT and treatment as usual (TAU) were studied to examine relapse rates from depression and the participants' sense of self-efficacy. The MT and CT tracks were added on to a regular outpatient treatment program. Three measures were used: the Beck Depression Inventory, the Mindfulness-Based Self Efficacy Scale and the Generalized Self-Efficacy Scale. Participants were assessed during an initial (pretest, baseline) period and again at a 3-month follow-up. Results reveal a significant decrease in depression and an increase in mindful and generalized self-efficacy in the MT track (N = 33). The results also showed a significant decrease in depression and mindfulness self-efficacy for the CT track (N = 27), but no significant change in generalized self-efficacy. The TAU track (N = 30) revealed no significant changes in any of the three measures. These trends show promise for relapse prevention of depression and improved sense of self-management through both therapeutic methodologies of mindfulness and cognitive therapy.

Almeida, O. P., B. Draper, et al. (2012). ***"Factors associated with suicidal thoughts in a large community study of older adults."*** The British Journal of Psychiatry 201(6): 466-472. http://bjp.rcpsych.org/content/201/6/466.abstract

BackgroundThoughts about death and self-harm in old age have been commonly associated with the presence of depression, but other risk factors may also be important.AimsTo determine the independent association between suicidal ideation in later life and demographic, lifestyle, socioeconomic, psychiatric and medical factors.MethodA cross-sectional study was conducted of a community-derived sample of 21 290 adults aged 60–101 years enrolled from Australian primary care practices. We considered that participants endorsing any of the four items of the Depressive Symptom Inventory –Suicidality Subscale were experiencing suicidal thoughts. We used standard procedures to collect demographic, lifestyle, psychosocial and clinical data. Anxiety and depressive symptoms were assessed with the Hospital Anxiety and Depression Scale.ResultsThe 2-week prevalence of suicidal ideation was 4.8%. Male gender, higher education, current smoking, living alone, poor social support, no religious practice, financial strain, childhood physical abuse, history of suicide in the family, past depression, current anxiety, depression or comorbid anxiety and depression, past suicide attempt, pain, poor self-perceived health and current use of antidepressants were independently associated with suicidal ideation. Poor social support was associated with a population attributable fraction of 38.0%, followed by history of depression (23.6%), concurrent anxiety and depression (19.7%), prevalent anxiety (15.1%), pain (13.7%) and no religious practice (11.4%).ConclusionsPrevalent and past mood disorders seem to be valid targets for indicated interventions designed to reduce suicidal thoughts and behaviour. However, our data indicate that social disconnectedness and stress account for a larger proportion of cases than mood disorders. Should these associations prove to be causal, then interventions that succeeded in addressing these issues would contribute the most to reducing suicidal ideation and, possibly, suicidal behaviour in later life.

Anderson, I. M., P. M. Haddad, et al. (2012). ***"Bipolar disorder."*** BMJ 345: e8508. http://www.ncbi.nlm.nih.gov/pubmed/23271744

Bipolar (affective) disorder, originally called manic depressive illness, is one of the most challenging psychiatric disorders to manage. Although it has been associated with creativity, it has a negative impact on the lives of most patients and more than 6% die through suicide in the two decades after diagnosis. Organisational change means that specialist services mostly treat acute episodes, leaving primary care with long term management. This review summarises current best practice in the diagnosis and management of bipolar disorder, signposting areas of uncertainty. Summary points: Bipolar disorder is characterised by recurrent episodes of elevated mood and depression, together with changes in activity levels. Elevated mood is severe and sustained (mania) in bipolar I disorder and less severe (hypomania) in bipolar II disorder. Depression is usually more common and longer lasting than elevated mood, and—together with inter-episode milder symptoms—contributes most to overall morbidity. Other psychiatric disorders, such as anxiety disorder and alcohol and drug misuse, are common. Risk of death from suicide and from natural causes, most often cardiovascular disease, is increased. Treatment is with drugs and supplemental psychotherapies; for both acute episodes and maintenance, treatment is guided by whether mania or depression predominates

Casanas, R., R. Catalan, et al. (2012). ***"Effectiveness of a psycho-educational group program for major depression in primary care: A randomized controlled trial."*** BMC Psychiatry 12: 230. http://www.ncbi.nlm.nih.gov/pubmed/23249399

(Free full text available) ABSTRACT: BACKGROUND: Studies show the effectiveness of group psychoeducation in reducing symptoms in people with depression. However, few controlled studies that have included aspects of personal care and healthy lifestyle (diet, physical exercise, sleep) together with cognitive-behavioral techniques in psychoeducation are proven to be effective.The objective of this study is to assess the effectiveness of a psychoeducational program, which includes aspects of personal care and healthy lifestyle, in patients with mild/moderate depression symptoms in Primary Care (PC). METHODS: In a randomized, controlled trial, 246 participants over 20 years old with ICD-10 major depression were recruited through nurses/general practitioners at 12 urban Primary Care Centers (PCCs) in Barcelona. The intervention group (IG) (n=119) received a group psychoeducational program (12 weekly, 1.5 h sessions led by two nurses) and the control group (CG) (n=112) received usual care. Patients were assessed at baseline and at, 3, 6 and 9 months. The main outcome measures were the BDI, EQ-5D and remission based upon the BDI. RESULTS: 231 randomized patients were included, of whom 85 had mild depression and 146 moderate depression. The analyses showed significant differences between groups in relation to remission of symptoms, especially in the mild depression group with a high rate of 57% (p=0.009) at post-treatment and 65% (p=0.006) at 9 month follow up, and only showed significant differences on the BDI at post-treatment (p=0.016; effect size Cohen's d'=.51) and at 6 and 9 month follow-up (p= 0.048; d'=.44).In the overall and moderate sample, the analyses only showed significant differences between groups on the BDI at post-treatment, p=0.02 (d'=.29) and p=0.010 (d'=.47), respectively.The

psychoeducation group improved significantly on the EQ-5D at short and long-term. CONCLUSIONS: This psychoeducational intervention is a short and long-term effective treatment for patients with mild depression symptoms. It results in a high remission rate, is recommended in PC and can be carried out by nurses with previous training. In moderate patients, group psychoeducation is effective in the short-term.

Dakwar, E., C. Blanco, et al. (2012). ***"Exercise and mental illness: Results from the national epidemiologic survey on alcohol and related conditions (nesarc)."*** J Clin Psychiatry 73(7): 960-966. http://www.ncbi.nlm.nih.gov/pubmed/22901347

BACKGROUND: Regular exercise is thought to be associated with low rates of mental illness, but this association has been inadequately studied. The purpose of this study was to test the hypotheses that the recommended amount of self-reported vigorous exercise would be cross-sectionally associated with reduced prevalence and incidence of various DSM-IV psychiatric disorders, as well as increased rates of remission. METHOD: Data were collected from 2001 to 2005 as part of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a 2-wave face-to-face survey conducted by the National Institute on Alcohol Abuse and Alcoholism. For this study, the sample consisted of 23,505 nondisabled adults aged between 18 and 65 years. RESULTS: Individuals who engaged in vigorous exercise at Wave 2 were significantly more likely than were nonexercisers to be diagnosed with a current psychiatric disorder (adjusted odds ratio [AOR] = 1.22, 95% CI, 1.12-1.34 for the nationally recommended amount vs no exercise), significantly less likely to attain remission from a psychiatric disorder between waves (AOR = 0.77, 95% CI, 0.65-0.91), and significantly more likely to relapse or be newly diagnosed with a psychiatric disorder between waves (AOR = 1.15, 95% CI, 1.02-1.30). Alcohol dependence and bipolar II disorder were the disorders most strongly associated with exercise. CONCLUSIONS: This investigation suggests that the pursuit of vigorous exercise is associated with a vulnerability to mental illness. This surprising finding may be due to reward-related factors that influence both exercise engagement and the expression of certain psychiatric disorders. Prospective trials will be helpful in further clarifying the associations between exercise and mental illness, as the relationships between the 2 are more complex than previously believed.

Del Re, A. C., C. Fluckiger, et al. (2012). ***"Therapist effects in the therapeutic alliance-outcome relationship: A restricted-maximum likelihood meta-analysis."*** Clin Psychol Rev 32(7): 642-649. http://www.ncbi.nlm.nih.gov/pubmed/22922705

OBJECTIVE: Although the relationship between the therapeutic alliance and outcome has been supported consistently across several studies and meta-analyses, there is less known about how the patient and therapist contribute to this relationship. The purpose of this present meta-analysis was to (1) test for therapist effects in the alliance-outcome correlation and (2) extend the findings of previous research by examining several potential confounds/covariates of this relationship. METHOD: A random effects analysis examined several moderators of the alliance-outcome correlation. These included (a) patient-therapist ratio (patient N divided by therapist N), (b) alliance and outcome rater (patient, therapist, and observer), (c) alliance measure, (d) research design and (e) DSM IV Axis II diagnosis. RESULTS: The patient-therapist ratio (PTR) was a significant moderator of the alliance-outcome correlation. Controlling for several potential confounds in a multi-predictor meta-regression, including rater of alliance, research design, percentage of patient Axis II diagnoses, rater of outcome and alliance measure, PTR remained a significant moderator of the alliance-outcome correlation. CONCLUSION: Corroborating previous research, therapist variability in the alliance appears to be more important than patient variability for improved patient outcomes. This relationship remains significant even when simultaneously controlling for several potential covariates of this relationship.

Dishman, R. K., X. Sui, et al. (2012). ***"Decline in cardiorespiratory fitness and odds of incident depression."*** Am J Prev Med 43(4): 361-368. http://www.ncbi.nlm.nih.gov/pubmed/22992353

BACKGROUND: Studies of physical activity and incidence of physician-diagnosed depression have been limited to a single estimate of self-reported physical activity exposure, despite follow-up periods lasting many years. PURPOSE: To examine longitudinal change in cardiorespiratory fitness, an objective marker of habitual physical activity, and incident depression complaints made to a physician. METHODS: Cardiorespiratory fitness assessed at four clinic visits between 1971 and 2006, each separated by an average of 2-3 years, was used to objectively measure cumulative physical activity exposure in cohorts of 7936 men and 1261 women, aged 20-85 years, from the Aerobics Center Longitudinal Study who did not complain of depression at their first clinic visit in 1971-2003. Data were analyzed in August 2010. RESULTS: Across subsequent visits, there were 446 incident cases in men and 153 cases in women. After adjustment for age, time between visits, BMI at each visit, and fitness at Visit 1, each 1-minute decline in treadmill endurance (i.e., a decline in cardiorespiratory fitness of approximately 1 half-MET) between ages 51 and 55 years in men and ages 53 and 56 years in women, increased the odds of incident depression complaints by approximately 2% and 9.5%, respectively. The increased odds remained significant but were attenuated to 1.3% and 5.4% after further adjustment at each visit for smoking, alcohol use, chronic medical conditions, anxiety, and sleep problems. CONCLUSIONS: Maintenance of cardiorespiratory fitness during late middle age, when decline in fitness typically accelerates, helps protect against the onset of depression complaints made to a physician.

Dording, C. M., D. Mischoulon, et al. (2012). ***"Same and sexual functioning."*** Eur Psychiatry 27(6): 451-454. http://www.ncbi.nlm.nih.gov/pubmed/21398094

BACKGROUND: Sexual dysfunction is a known side effect of antidepressant treatment (ADT), affecting up to 58-73% of those who receive ADT, potentially affecting antidepressant adherence. Consequently, it is vital to develop novel treatments that target antidepressant-induced sexual dysfunction. METHODS: We examined whether adjunctive S-adenosyl-l-methionine (SAMe) is associated with greater improvement in sexual functioning than adjunctive placebo by measuring changes in sexual functioning using the Massachusetts General Hospital-Sexual Functioning Questionnaire (MGH-SFQ) during a 6-week, single-center, randomized, double-blind trial of SAMe augmentation for SSRI/SNRI- nonresponders. RESULTS: Controlling for the degree of arousal dysfunction at baseline as well as the degree of change in HDRS-17 scale scores during the course of the study, men treated with adjunctive SAMe demonstrated significantly lower arousal dysfunction at endpoint than those treated with adjunctive placebo. In addition, controlling for the degree of erectile dysfunction at baseline as well as the degree of change in HDRS-17 scale scores, men treated with adjunctive SAMe demonstrated significantly lower erectile dysfunction at endpoint than those treated with adjunctive placebo. CONCLUSIONS: In the present study, we have observed that adjunctive SAMe can have positive benefit on male arousal and erectile dysfunction, independent of improvement in depressive symptoms. These findings are preliminary, and warrant replication.

Farabaugh, A., J. Alpert, et al. (2012). ***"Cognitive therapy for anxious depression in STAR(*)D: What have we learned?"*** J Affect Disord 142(1-3): 213-218. http://www.ncbi.nlm.nih.gov/pubmed/22877961

BACKGROUND: Anxious depression, defined as MDD with high levels of anxiety symptoms, has been associated with lower rates of antidepressant response and remission as well as greater chronicity, suicidality and antidepressant side-effect burden. The primary aim of this study was to assess the effectiveness of cognitive therapy (CT) alone or in combination with

medications for anxious versus non-anxious depression. METHODS: We assessed the STAR()D study participants who were partial or non-responders to citalopram. Subjects were then either switched (n=696) to a new antidepressant or to CT alone, or they were kept on citalopram and augmented (n=577) with another antidepressant or CT. We compared response and remission rates, across treatment conditions, between those who met criteria for anxious depression and those who did not. RESULTS: Those with anxious depression had significantly lower remission rates based on the QIDS, whether assigned to switch or augmentation, compared to those with non-anxious depression. Those with anxious depression, compared to those without, had significantly lower response rates based on the QIDS only in the switch group. There was no significant interaction between anxious depression and treatment assignment. LIMITATIONS: Limitations include the use of citalopram as the only Level 1 pharmacotherapy and medication augmentation option, the relatively small size of the CT arms, use of depression-focused CT rather than anxiety-focused CT, and focus on acute treatment outcomes. CONCLUSIONS: Individuals with anxious depression appear to experience higher risk of poorer outcome following pharmacotherapy and/or CT after an initial course of citalopram and continued efforts to target this challenging form of depression are needed.

Lau, M., L. Colley, et al. (2012). ***"Employee's preferences for access to mindfulness-based cognitive therapy to reduce the risk of depressive relapse - a discrete choice experiment."*** Mindfulness (N Y) 3(4): 318-326. http://dx.doi.org/10.1007/s12671-012-0108-3

Disseminating mindfulness-based cognitive therapy (MBCT), an evidence-based group treatment, in the workplace may help employees who have recovered from depression to prevent depressive relapse and stay well. Employees' potential confidentiality concerns about participating in a group-based workplace MBCT intervention may be alleviated by delivering MBCT in alternative formats that would maintain the employees' anonymity. The aim of the current study was to determine the stated preferences of employees from large healthcare organizations for four different MBCT delivery methods (i.e., group, online group, individual, and individual via the telephone). We determined the stated preferences of 151 health authority employees for the four MBCT delivery methods using a discrete choice experiment comprised of 18 choice sets of five attributes. A latent class model was used to evaluate the heterogeneity of respondents' preferences. This analysis suggested that four classes existed in the sample. The most important preferences were the effectiveness of MBCT, the type of interaction, face-to-face delivery, and receipt of MBCT on their own time. These results suggest strong preferences for the four different MBCT delivery methods. The presence of latent classes also shows that preferences for alternative modes of delivery vary in association with differences in sociodemographic variables between groups of employees. The overall findings of this study have the potential to influence the development of institutional programs that could make workplace MBCT more appealing to a greater number of employees, thereby improving participant uptake, decreasing the potential for depressive relapse, and minimizing absenteeism.

Leucht, C., M. Huhn, et al. (2012). ***"Amitriptyline versus placebo for major depressive disorder."*** Cochrane Database Syst Rev 12: CD009138. http://www.ncbi.nlm.nih.gov/pubmed/23235671

BACKGROUND: Amitriptyline is a tricyclic antidepressant that was synthesised in 1960 and introduced as early as 1961 in the USA, but is still regularly used. It has also been frequently used as an active comparator in trials on newer antidepressants and can therefore be called a 'benchmark' antidepressant. However, its efficacy and safety compared to placebo in the treatment of major depression has not been assessed in a systematic review and meta-analysis. OBJECTIVES: To assess the effects of amitriptyline compared to placebo or no treatment for major depressive disorder in adults. SEARCH METHODS: We searched the Cochrane Depression, Anxiety and Neurosis Group's Specialised Register (CCDANCTR-Studies and CCDANCTR-References) to August 2012. This register contains relevant randomised controlled trials from: The Cochrane Library (all years), EMBASE (1974 to date), MEDLINE (1950 to date) and PsycINFO (1967 to date). The reference lists of reports of all included studies were screened and manufacturers of amitriptyline contacted for details of additional studies. SELECTION CRITERIA: All randomised controlled trials (RCTs) comparing amitriptyline with placebo or no treatment in patients with major depressive disorder as diagnosed by operationalised criteria. DATA COLLECTION AND ANALYSIS: Two review authors independently extracted data. For dichotomous data, we calculated the odds ratio (OR) with 95% confidence intervals (CI). We analysed continuous data using standardised mean differences (with 95% CI). We used a random-effects model throughout. MAIN RESULTS: The review includes 39 trials with a total of 3509 participants. Study duration ranged between three and 12 weeks. Amitriptyline was significantly more effective than placebo in achieving acute response (18 RCTs, n = 1987, OR 2.67, 95% CI 2.21 to 3.23). Significantly fewer participants allocated to amitriptyline than to placebo withdrew from trials due to inefficacy of treatment (19 RCTs, n = 2017, OR 0.20, 95% CI 0.14 to 0.28), but more amitriptyline-treated participants withdrew due to side effects (19 RCTs, n = 2174, OR 4.15, 95% CI 2.71 to 6.35). Amitriptyline also caused more anticholinergic side effects, tachycardia, dizziness, nervousness, sedation, tremor, dyspepsia, sedation, sexual dysfunction and weight gain. In subgroup and meta-regression analyses the results of the primary outcome were robust towards publication year (1971 to 1997), mean participant age at baseline, mean amitriptyline dose, study duration in weeks, pharmaceutical sponsor, inpatient versus outpatient setting and two-arm versus three-arm design. However, higher severity at baseline was associated with higher superiority of amitriptyline (P = 0.02), while higher responder rates in the placebo groups were associated with lower superiority of amitriptyline (P = 0.05). The results of the primary outcome were rather homogeneous, reflecting comparability of the trials. However, methods of randomisation, allocation concealment and blinding were usually poorly reported. Not all studies used intention-to-treat analyses and in many of them standard deviations were not reported and often had to be imputed. Funnel plots suggested a possible publication bias, but the trim and fill method did not change the overall effect size much (seven adjusted studies, OR 2.64, 95% CI 2.24 to 3.10). AUTHORS' CONCLUSIONS: Amitriptyline is an efficacious antidepressant drug. It is, however, also associated with a number of side effects. Degree of placebo response and severity of depression at baseline may moderate drug-placebo efficacy differences.

Moreno, F. A., J. Chong, et al. (2012). ***"Use of standard webcam and internet equipment for telepsychiatry treatment of depression among underserved hispanics."*** Psychiatr Serv 63(12): 1213-1217. http://www.ncbi.nlm.nih.gov/pubmed/23026854

OBJECTIVE: Depression affects nearly one in five Americans at some time in their life, causing individual suffering and financial cost. The Internet has made it possible to deliver telemedicine care economically to areas and populations with limited access to specialist or culturally and linguistically congruent care. METHODS: This study compared the effectiveness for Hispanic patients of depression treatment provided by a psychiatrist through Internet videoconferencing (Webcam intervention) and treatment as usual by a primary care provider. Adults (N=167) with a diagnosis of depression were recruited from a community clinic and were randomly assigned to treatment condition. Webcam participants met remotely each month with the psychiatrist, and treatment-as-usual patients received customary care from their primary care providers, all for six months. At baseline and three and six months, analyses of variance tested differences between conditions in scores on depression rating scales and quality-of-life and functional ability measures. RESULTS: All participants experienced an improvement in depression symptoms. Ratings on the Montgomery-Asberg Depression Rating Scale by clinicians blind to treatment group and self-ratings on the nine-item Patient Health Questionnaire, Quality of Life Enjoyment and Satisfaction Questionnaire, and Sheehan Disability Scale showed a significant main effect of time. On all four measures, a significant interaction of time by intervention favoring the

Webcam group was noted. DISCUSSION: Results suggest that telepsychiatry delivered through the Internet utilizing commercially available domestic Webcams and standard Internet and computer equipment is effective and acceptable. Use of this technology may help close the gap in access to culturally and linguistically congruent specialists.

Nelson, J. C. (2012). ***"The evolving story of folate in depression and the therapeutic potential of l-methylfolate."*** Am J Psychiatry 169(12): 1223-1225. http://ajp.psychiatryonline.org/article.aspx?articleid=1461094

(Full text freely available) In this issue, Papakostas and colleagues report the successful use of adjunctive l-methylfolate in treatment-resistant patients with major depressive disorder. The study employs a novel trial design, the sequenced parallel comparison design, and adds to the growing literature suggesting that the one-carbon cycle may moderate antidepressant treatment response. The study involved two trials. The first compared l-methylfolate at 7.5 mg/day with placebo in 148 patients with nonpsychotic unipolar depression. All patients had a prior failed 8-week trial of a selective serotonin reuptake inhibitor (SSRI). l-Methylfolate at 7.5 mg/day was not more effective than placebo, but efficacy was suggested for a small group of patients in the trial who were treated with 15 mg/day. Based on that finding, a second trial was conducted in 75 patients using 15 mg/day or placebo. The difference in response rates between l-methylfolate at 15 mg/day and placebo (32.3% and 14.6%, respectively) was significant and meaningful. The number needed to treat, six, is quite respectable. Side effects were no more common with l-methylfolate than with placebo, which suggests that side effects were not likely to unblind the investigators or patients to treatment assignment ... The association of depressive symptoms and folate deficiency has been known for five decades. Numerous studies have found low serum folate levels or low RBC folate concentrations in depressed patients. Other studies suggested that low folate levels are associated with reduced response to antidepressants, which in turn suggested that folic acid might be used to augment antidepressants. Coppen and Bailey conducted a double-blind placebo-controlled study of adjunctive folic acid (500 µg/day) added to fluoxetine at the beginning of treatment in patients with major depressive disorder. They found that adjunctive folic acid was effective in women but not in men. Resler et al. also observed greater improvement with folic acid in 27 patients with major depression who were being treated with fluoxetine (20 mg/day) and were randomly assigned to receive to folic acid (10 mg/day) or placebo. Alpert et al. noted modest improvement in depressive symptoms after they administered folinic acid in an open-label study to 22 patients who had failed to respond to 4 weeks of SSRI treatment. In those three studies, patients with major depression were selected without regard to folate deficiency. Trials of both monotherapy and adjunctive l-methylfolate have been reported. Four monotherapy trials (reviewed elsewhere), suggested efficacy. Two were open trials and two were double-blind trials comparing l-methylfolate with antidepressants. The first adjunctive trial was a double-blind placebo-controlled trial in 24 patients with major depression who had deficient RBC folate levels. l-Methylfolate at 15 mg/day was added to ongoing antidepressant treatment. At 3 months and at 6 months, patients receiving adjunctive l-methylfolate exhibited greater improvement than those in the placebo group ... In summary, the Papakostas et al. study suggests that l-methylfolate is a useful treatment for depression that has proved to be resistant to a course of SSRI treatment. Previous studies of folic acid, folinic acid, and l-methylfolate support this contention. l-Methylfolate was well tolerated and may be preferred by patients for that reason. It may be particularly helpful in patients with the TT genetic variant. The efficacy of l-methylfolate in resistant depression has not been compared with that of other adjunctive agents, nor has long-term use of the agent been reported in major depression. The potential value of long-term administration of l-methylfolate in individuals with recurrent depression and the genetic enzyme deficiency is particularly intriguing.

Okusaga, O. and T. T. Postolache (2012). ***Toxoplasma gondii, the immune system, and suicidal behavior***. The neurobiological basis of suicide. Y. Dwivedi. Boca Raton (FL).

Each year suicide leads to the tragic and premature deaths of over 1 million individuals around the world with an estimated annual mortality of 14.5 per 100,000 people. This translates to one death occurring every 40 s. Suicide is the 10th leading cause of death, making up 11.5% of all deaths (Hawton and van Heeringen 2009), though this burden is probably underestimated considering many third world countries appear to underreport suicide 9-10 times the actual amount (Hawton and van Heeringen 2009). While suicide rates have remained constant for the last decade, the three greatest causes of death (heart disease, cancer, and cerebrovascular disease) have all seen a decrease in death rates in this time period. Two of the most important risk factors for suicide are history of past suicide attempt (Harris and Barraclough 1997; Mann 2003) and a history of mood disorder. Every suicide is preceded by an estimated 8-25 suicide attempts, and 4% of depressed individuals die from suicide (Hawton and van Heeringen 2009). Additionally, more than half of individuals who attempt suicide had a major depressive episode at the time of the attempt. For the past 7 years, our team at the University of Maryland School of Medicine Mood and Anxiety Program has been focused on studying triggers and vulnerabilities for suicide originating in the natural environment, that is, physical, chemical, and biological. In particular, we have been interested in the highly consistent peaks of suicide (Postolache et al. 2010) during certain seasons and their possible triggers. Specifically, we have identified (1) a relationship between atmospheric peaks of aeroallergens and suicide attempts in women (Postolache et al. 2005), confirmed in Denmark (Qin et al. 2011), (2) a relationship between suicide and allergy (Qin et al. 2011), and (3) an increased expression of allergy-related cytokines in the prefrontal cortex of suicide victims (Tonelli et al. 2008b). We have also reported that intranasal administration of allergens induces animal behaviors that are analogous to certain suicide risk factors such as aggression (Tonelli et al. 2008a) and anxiety (Tonelli et al. 2009). Our intermediate conclusion is that molecular and cellular mechanisms involved in the allergic immune response might attenuate functional capabilities of areas of the prefrontal cortex to act as behavioral breaks via multisynaptic inhibition of infralimbic centers. Following this line of thought, if allergy (a misdirected immune response against innocuous substances that were "misperceived" by the immune system as invasive pathogens) is associated with suicidal behavior, one would expect real neurotropic parasites to also be associated with suicide behavior. This led us to investigate Toxoplasma gondii and the anti-T. gondii immune response. A possible connection between T. gondii and suicidal behavior was suggested by the relatively high seroprevalence, its neurotropism (Flegr 2007), the immune activation involved in the defense against the parasite leading to elevation of cytokines previously found related to suicidal behavior (see Section 19.3.2), the occurrence of induced self-destructive behavior in rodent models (Lamberton et al. 2008; Vyas et al. 2007; Webster 2007), behavioral changes in humans (Flegr et al. 2002), and the parasite's association with mental illness (Niebuhr et al. 2008; Torrey et al. 2007). We will first briefly review the immune system and the evidence connecting immune activation with suicidal behavior, and then we will describe the immune response to T. gondii, followed by a description of the parasite and the evidence associating T. gondii infection with suicidal behavior.

Orriols, L., R. Queinec, et al. (2012). ***"Risk of injurious road traffic crash after prescription of antidepressants."*** J Clin Psychiatry 73(8): 1088-1094. http://www.ncbi.nlm.nih.gov/pubmed/22967773

OBJECTIVE: To estimate the risk of road traffic crash associated with prescription of antidepressants. METHOD: Data were extracted and matched from 3 French national databases: the national health care insurance database, police reports, and the national police database of injurious crashes. A case-control analysis comparing 34,896 responsible versus 37,789 nonresponsible drivers was conducted. Case-crossover analysis was performed to investigate the acute effect of medicine exposure. RESULTS: 72,685 drivers, identified by their national health care number, involved in an injurious crash in France from July 2005 to May 2008 were included. 2,936 drivers (4.0%) were exposed to at least 1 antidepressant on the day of the

crash. The results showed a significant association between the risk of being responsible for a crash and prescription of antidepressants (odds ratio [OR] = 1.34; 95% CI, 1.22-1.47). The case-crossover analysis showed no association with treatment prescription, but the risk of road traffic crash increased after an initiation of antidepressant treatment (OR = 1.49; 95% CI, 1.24-1.79) and after a change in antidepressant treatment (OR = 1.32; 95% CI, 1.09-1.60). CONCLUSIONS: Patients and prescribers should be warned about the risk of crash during periods of treatment with antidepressant medication and about particularly high vulnerability periods such as those when a treatment is initiated or modified.

Papakostas, G. I., C. F. Cassiello, et al. (2012). ***"Folates and s-adenosylmethionine for major depressive disorder."*** Can J Psychiatry 57(7): 406-413. http://www.ncbi.nlm.nih.gov/pubmed/22762295

Interest in nonpharmaceutical supplements for treating major depressive disorder (MDD) has increased significantly, both among patients and among clinicians during the past decades. Despite the large array of antidepressants (ADs) available, many patients continue to experience relatively modest response and remission rates, in addition to a burden of side effects that can hinder treatment compliance and acceptability. In this article, we review the literature on folates and S-adenosylmethionine (SAMe), 2 natural compounds linked in the 1-carbon cycle metabolic pathway, for which substantial evidence supports their involvement in mood disorders. Background information, efficacy data, proposed mechanisms of action, and side effects are reviewed. Based on existing data, supplementation with SAMe, as well as with various formulations of folates, appears to be efficacious and well tolerated in reducing depressive symptoms. Compared with other forms of folates, 5-methyltetrahydrofolate (L-methylfolate or 5-MTHF) may represent a preferable treatment option for MDD given its greater bioavailability in patients with a genetic polymorphism, and the lower risk of specific side effects associated with folic acid. Although further randomized controlled trials in this area appear warranted, SAMe and L-methylfolate may represent a useful addition to the AD armamentarium.

Papakostas, G. I., R. C. Shelton, et al. (2012). ***"L-methylfolate as adjunctive therapy for SSRI-resistant major depression: Results of two randomized, double-blind, parallel-sequential trials."*** Am J Psychiatry 169(12): 1267-1274. http://www.ncbi.nlm.nih.gov/pubmed/23212058

OBJECTIVE: The authors conducted two multicenter sequential parallel comparison design trials to investigate the effect of L-methylfolate augmentation in the treatment of major depressive disorder in patients who had a partial response or no response to selective serotonin reuptake inhibitors (SSRIs). METHOD: In the first trial, 148 outpatients with SSRI-resistant major depressive disorder were enrolled in a 60-day study divided into two 30-day periods. Patients were randomly assigned, in a 2:3:3 ratio, to receive L-methylfolate for 60 days (7.5 mg/day for 30 days followed by 15 mg/day for 30 days), placebo for 30 days followed by L-methylfolate (7.5 mg/day) for 30 days, or placebo for 60 days. SSRI dosages were kept constant throughout the study. In the second trial, with 75 patients, the design was identical to the first, except that the l-methylfolate dosage was 15 mg/day during both 30-day periods. RESULTS: In the first trial, no significant difference was observed in outcomes between the treatment groups. In the second trial, adjunctive L-methylfolate at 15 mg/day showed significantly greater efficacy compared with continued SSRI therapy plus placebo on both primary outcome measures (response rate and degree of change in depression symptom score) and two secondary outcome measures of symptom severity. The number needed to treat for response was approximately six in favor of adjunctive L-methylfolate at 15 mg/day. L-Methylfolate was well tolerated, with rates of adverse events no different from those reported with placebo. CONCLUSIONS: Adjunctive L-methylfolate at 15 mg/day may constitute an effective, safe, and relatively well tolerated treatment strategy for patients with major depressive disorder who have a partial response or no response to SSRIs.

Piet, J., H. Wurtzen, et al. (2012). ***"The effect of mindfulness-based therapy on symptoms of anxiety and depression in adult cancer patients and survivors: A systematic review and meta-analysis."*** J Consult Clin Psychol 80(6): 1007-1020. http://www.ncbi.nlm.nih.gov/pubmed/22563637

OBJECTIVE: The use of mindfulness-based therapy (MBT) in oncology settings has become increasingly popular, and research in the field has rapidly expanded. The objective was by means of a systematic review and meta-analysis to evaluate the current evidence for the effect of MBT on symptoms of anxiety and depression in adult cancer patients and survivors. METHOD: Electronic databases were searched, and researchers were contacted for further relevant studies. Twenty-two independent studies with a total of 1,403 participants were included. Studies were coded for quality (range: 0-4), and overall effect size analyses were performed separately for nonrandomized studies (K = 13, n = 448) and randomized controlled trials (RCTs; K = 9, n = 955). Effect sizes were combined using the random-effects model. RESULTS: In the aggregated sample of nonrandomized studies (average quality score: 0.5), MBT was associated with significantly reduced symptoms of anxiety and depression from pre- to posttreatment corresponding to moderate effect sizes (Hedges\'s g) of 0.60 and 0.42, respectively. The pooled controlled effect sizes (Hedges\'s g) of RCTs (average quality score: 2.9) were 0.37 for anxiety symptoms ($p < .001$) and 0.44 for symptoms of depression ($p < .001$). These effect sizes appeared robust. Furthermore, in RCTs, MBT significantly improved mindfulness skills (Hedges\'s g = 0.39). CONCLUSION: While the overall quality of existing clinical trials varies considerably, there appears to be some positive evidence from relatively high-quality RCTs to support the use of MBT for cancer patients and survivors with symptoms of anxiety and depression.

Pinniger, R., R. F. Brown, et al. (2012). ***"Argentine tango dance compared to mindfulness meditation and a waiting-list control: A randomised trial for treating depression."*** Complementary Therapies in Medicine 20(6): 377-384. http://www.sciencedirect.com/science/article/pii/S0965229912000891

SummaryObjectives To determine whether tango dancing is as effective as mindfulness meditation in reducing symptoms of psychological stress, anxiety and depression, and in promoting well-being. Design This study employed analysis of covariance (ANCOVA) and multiple regression analysis. Participants Ninety-seven people with self-declared depression were randomised into tango dance or mindfulness meditation classes, or to control/waiting-list. Setting classes were conducted in a venue suitable for both activities in the metropolitan area of Sydney, Australia. Interventions Participants completed six-week programmes (1½ h/week of tango or meditation). The outcome measures were assessed at pre-test and post-test. Main outcome measures Depression, Anxiety and Stress Scale; The Self Esteem Scale; Satisfaction with Life Scale, and Mindful Attention Awareness Scale. Results Sixty-six participants completed the program and were included in the statistical analysis. Depression levels were significantly reduced in the tango (effect size d = 0.50, p = .010), and meditation groups (effect size d = 0.54, p = .025), relative to waiting-list controls. Stress levels were significantly reduced only in the tango group (effect size d = 0.45, p = .022). Attending tango classes was a significant predictor for the increased levels of mindfulness R2 = .10, adjusted R2 = .07, F (2,59) = 3.42, p = .039. Conclusion Mindfulness-meditation and tango dance could be effective complementary adjuncts for the treatment of depression and/or inclusion in stress management programmes. Subsequent trials are called to explore the therapeutic mechanisms involved.

Rethorst, C. D., P. Sunderajan, et al. (2012). ***"Does exercise improve self-reported sleep quality in non-remitted major depressive disorder?"*** Psychol Med: 1-11. http://www.ncbi.nlm.nih.gov/pubmed/23171815

BACKGROUND: Sleep disturbances are persistent residual symptoms following remission of major depressive disorder (MDD) and are associated with an increased risk of MDD recurrence. The purpose of the current study was to examine the effect of exercise augmentation on self-reported sleep quality in participants with non-remitted MDD. Method Participants were randomized to receive selective serotonin reuptake inhibitor (SSRI) augmentation with one of two doses of exercise: 16 kilocalories per kilogram of body weight per week (KKW) or 4 KKW for 12 weeks. Depressive symptoms were assessed using the clinician-rated Inventory of Depressive Symptomatology (IDS-C). The four sleep-related items on the IDS-C (Sleep Onset Insomnia, Mid-Nocturnal Insomnia, Early Morning Insomnia, and Hypersomnia) were used to assess self-reported sleep quality. RESULTS: Significant decreases in total insomnia ($p<0.0001$) were observed, along with decreases in sleep onset, mid-nocturnal and early-morning insomnia (p's <0.002). Hypersomnia did not change significantly ($p=0.38$). Changes in total, mid-nocturnal and early-morning insomnia were independent of changes in depressive symptoms. Higher baseline hypersomnia predicted a greater decrease in depression severity following exercise treatment ($p=0.0057$). No significant moderating effect of any baseline sleep on change in depression severity was observed. There were no significant differences between exercise treatment groups on total insomnia or any individual sleep item. CONCLUSIONS: Exercise augmentation resulted in improvements in self-reported sleep quality in patients with non-remitted MDD. Given the prevalence of insomnia as a residual symptom following MDD treatment and the associated risk of MDD recurrence, exercise augmentation may have an important role in the treatment of MDD.