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*Psychiatry Research, 2015 March 30; 226(1):73–7*

Impact of childhood life events and childhood trauma on the onset and recurrence of depressive and anxiety disorders
*The Journal of Clinical Psychiatry, 2015 February 17; Epub ahead of print*

Effects of adjunctive exercise on physiological and psychological parameters in depression: a randomized pilot trial
*Journal of Affective Disorders, 2015 May 15; 177:1–6*

Metabolic syndrome in patients with bipolar disorder: comparison with major depressive disorder and non-psychiatric controls
*Journal of Psychosomatic Research, 2015 April; 78(4):391–8*

Clinical effectiveness of cognitive therapy v. interpersonal psychotherapy for depression: results of a randomized controlled trial
*Psychological Medicine, 2015 July; 45(10):2095–110*

Driving performance and psychomotor function in depressed patients treated with agomelatine or venlafaxine
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Insomnia and somnolence associated with second-generation antidepressants during the treatment of major depression: a meta-analysis
*Journal of Clinical Psychopharmacology, 2015 June; 35(3):296–303*
Screen time is associated with depression and anxiety in Canadian youth
*Preventive Medicine, 2015 April; 73:133–8*

Predicting the naturalistic course of major depressive disorder using clinical and multimodal neuroimaging information: a multivariate pattern recognition study
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Antidepressant drug development: focus on triple monoamine reuptake inhibition
*Journal of Psychopharmacology, 2015 May; 29(5):526–44*

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*Clinical Psychology Review, 2015 February 26; Epub ahead of print*

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a meta-analysis of randomized controlled trials
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MAJOR DEPRESSIVE DISORDER AND SMOKING RELAPSE AMONG ADULTS IN THE UNITED STATES: A 10-YEAR, PROSPECTIVE INVESTIGATION

Psychiatry Research, 2015 March 30; 226(1):73–7

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BACKGROUND & AIM: Cigarette smoking is the major preventable cause of death in the USA. Although most smokers would like to stop smoking, the quit rate remains low. It would therefore be helpful to identify modifiable risk factors for smoking relapse among former smokers. Epidemiological evidence suggests a link between current or past depression and poor smoking cessation outcomes, but the degree to which depression affects the long-term risk of smoking relapse, and the influence of the proximity and persistence of depression on risk of relapse, remain to be determined.

The aim of this study was to determine the association between a history of major depressive disorder (MDD) and the long-term risk of smoking relapse among former smokers in the general US population. The relation between current and persistent depression and risk of relapse among former smokers compared to those without depression was also explored.

STUDY DESIGN: Cohort study.


METHOD: Data from adult participants in the Midlife Development in the United States (MIDUS) Survey Waves I & II were analysed using logistic regression to explore associations between MDD in 1994, MDD in 2005 and persistent depression (in 1994 and 2005) and risk of smoking relapse in 2005 among former smokers, adjusting for demographics, anxiety disorders, substance use problems and smoking characteristics.

RESULTS: Among former smokers, adults with depression in 1994 (n=91) were significantly more likely than those without depression in 1994 (n=608) to experience smoking relapse by 2005 (adjusted odds ratio 2.4, 95% confidence interval 1.3–4.2, p<0.05). The risk of smoking relapse in 2005 was also significantly (p<0.05) higher among adults with current depression in 2005 (n=77) than among those without current depression (n=622; adjusted OR 3.3, 95% CI 1.8–6.0) and among those with persistent depression (n=25) than among those with no depression in either 1994 or 2005 (n=556; adjusted OR 3.5, 95% CI 1.3–9.4).

CONCLUSION: MDD was associated with both a short- and long-term increased risk of smoking relapse among former smokers in the US general population.
BACKGROUND & AIM: Adverse experiences in childhood have been associated with psychopathology such as depressive and anxiety disorders in later life. However, prospective evidence for these associations is scarce. The aim of this study was to investigate the effect of childhood life events and trauma on the onset and recurrence of depressive and/or anxiety disorders over a 2-year period in participants without current psychopathology at baseline.

STUDY DESIGN: Prospective cohort study.

ENDPOINTS: Associations of childhood life events (death of a parent, divorce of parents, being placed in care) or childhood trauma (emotional neglect and psychological, physical or sexual abuse) with 2-year occurrence rates of new or recurrent depressive and/or anxiety disorders.

METHOD: Longitudinal data were collected from 1167 adults participating in the Netherlands Study of Depression and Anxiety who had no depressive or anxiety disorder at baseline (2004–2007). Depressive and/or anxiety disorders emerging during 2 years of follow-up were diagnosed using the Composite International Diagnostic Interview. Factors associated with the incidence of these disorders were identified using a multivariable logistic regression model.

RESULTS: At baseline, 172 (14.7%) participants reported having experienced at least one childhood life event and 412 (35.3%) reported a history of any childhood trauma. At 2-year follow up, 226 participants (19.4%) were diagnosed with a new (n=58) or recurrent (n=168) episode of a depressive and/or anxiety disorder. First onset or recurrence of either a depressive or comorbid disorder, but not an anxiety disorder, was significantly higher among individuals who had experienced childhood emotional neglect or psychological, physical or sexual abuse (p<0.001). On multivariate analysis, emotional neglect was the only significant independent predictor of first onset or recurrence of any depressive or comorbid disorder (p=0.002). Severe psychological and sexual abuse were both predictive of the occurrence of a comorbid disorder (p<0.05). These effects were primarily mediated by the severity of (subclinical) depressive symptoms at baseline (mediating effect 0.117, 95% confidence interval 0.077–0.173) and a prior lifetime diagnosis of a depressive and/or anxiety disorder (mediating effect 0.072, 95% CI 0.042–0.108). Childhood life events did not predict the onset or recurrence of depressive or anxiety disorders.

CONCLUSION: Childhood trauma was found to predict the occurrence of depressive and comorbid disorders within 2 years in adults without current psychopathology at baseline.
BACKGROUND & AIM: Depressed individuals show reduced physical activity and increased rates of the metabolic syndrome (MetS), a risk factor for type 2 diabetes and cardiovascular disorders. Exercise training has been shown to improve cardiorespiratory fitness and MetS factors, and to have a moderate effect on depressive symptoms. However, exercise prescription to depressive patients is challenging, and the feasibility of exercise interventions for severely depressed patients in an inpatient setting is unclear. The aims of this study were to evaluate the feasibility of an exercise intervention and its effects on depressive symptoms, cardiorespiratory fitness and MetS components in inpatients with moderate to severe depression.

STUDY DESIGN: Randomized pilot trial.

ENDPOINTS: Effect on depressive symptoms, with response to the intervention defined as ≥50% reduction from baseline in the Montgomery–Åsberg Depression Rating Scale (MADRS); improvements in MetS components (fasting blood glucose, diastolic blood pressure, waist circumference and high-density lipoprotein cholesterol, HDL-C); and improvement in exercise capacity, measured by peak oxygen uptake (VO₂ peak), ventilator anaerobic threshold (VAT) and workload expressed as Watts (W).

METHOD: A total of 42 inpatients with moderate to severe depression were randomized to receive treatment as usual only (TAU group, n=20) or combined with physician-supervised exercise training for 6 weeks (exercise group, n=22). Exercise training consisted of three 45-minute sessions of moderate-intensity exercise per week. MetS was defined according to the National Cholesterol Education Program's Adult Treatment Panel III criteria.

RESULTS: Depressive symptoms declined significantly in both groups during the study period. However, more patients in the exercise group than the TAU group were classified as responders at 6 weeks (14 versus 6, p=0.037). Both groups showed significant reduction of fasting glucose after 6 weeks. Only the exercise group showed reductions in diastolic blood pressure (p=0.049) and waist circumference (p<0.001), increased HDL-C (p=0.01) and improvement in all cardiorespiratory fitness parameters at study end.

CONCLUSIONS: The addition of exercise training to standard antidepressant treatment improved depressive symptoms, MetS factors and cardiorespiratory fitness in patients hospitalized with moderate to severe depression. Given the association of depression with cardiometabolic disorders, the authors recommend that depressed patients receive adjunctive exercise training.

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METABOLIC SYNDROME IN PATIENTS WITH BIPOLAR DISORDER: COMPARISON WITH MAJOR DEPRESSIVE DISORDER AND NON-PSYCHIATRIC CONTROLS


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BACKGROUND & AIM: Patients with bipolar disorder (BD) are at high risk for metabolic syndrome (MetS), and the co-occurrence of MetS and BD is associated with a more severe clinical presentation of BD, suicidality and decreased functional recovery. Many of the studies investigating the prevalence of MetS in BD have used either non-psychiatric controls or subjects with schizophrenia as comparison groups. The aim of this study was to investigate the prevalence of MetS and its individual components in patients with BD compared to those with major depressive disorder (MDD) and a non-psychiatric control group.

STUDY DESIGN: Cohort study.

ENDPOINTS: Prevalence of MetS and its individual components.

METHOD: The analysis included 241 individuals with BD, 1648 with MDD and 542 non-psychiatric controls. Participants were recruited from two longitudinal cohort studies in the Netherlands: the Bipolar Stress Study and the Netherlands Study of Depression and Anxiety. Diagnosis of MetS was established according to the National Cholesterol Education Program’s Adult Treatment Panel III criteria. The number of MetS components was used as an indicator of the severity of metabolic abnormalities. Multivariable analyses were adjusted for age, sex, ethnicity, level of education, smoking status and severity of depressive symptoms. In BD individuals, the adjustment also included use of psychotropic medication.

RESULTS: The prevalence of MetS was 28.4% among individuals with BD, 20.2% among those with MDD and 16.5% among non-psychiatric controls (p<0.001). The increased prevalence of MetS among BD patients remained significant after adjustment for sociodemographic and lifestyle variables (odds ratio versus the MDD group: 1.52, 95% confidence interval 1.09–2.12, p=0.02; OR versus controls: 1.79, 95% CI 1.20–2.67, p=0.005). Compared with non-psychiatric controls, BD patients had higher mean waist circumference (88.8 cm versus 91.0 cm, respectively, p=0.03) and lower mean systolic blood pressure (135.6 mmHg versus 132.7 mmHg, respectively, p=0.03). In logistic regression analyses, the difference in MetS prevalence between the BD and MDD groups was more pronounced for patients with depressive symptoms than nonsymptomatic patients (adjusted OR 1.71, 95% CI 1.12–2.61, p=0.01; and OR 1.03, 95% CI 0.56–1.90, p=0.92, respectively).

CONCLUSIONS: Patients with BD had a higher prevalence of MetS than patients with MDD or non-psychiatric controls. Abdominal obesity and symptomatic depression were strongly associated with this increased risk.
CLINICAL EFFECTIVENESS OF COGNITIVE THERAPY v. INTERPERSONAL PSYCHOTHERAPY FOR DEPRESSION: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

Psychological Medicine, 2015 July; 45(10):2095–110

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BACKGROUND & AIM: Cognitive therapy (CT) and interpersonal psychotherapy (IPT) are both effective treatments for major depressive disorder (MDD). Whether either therapy is superior to the other in terms of effects on disorder severity and course remains unclear. The aim of this study was to compare the clinical effectiveness of CT and IPT in a large cohort of depressed patients treated in an outpatient mental health clinic. The study also evaluated whether active treatment was superior to no treatment.

STUDY DESIGN: Single centre, parallel group, randomized controlled study.

ENDPOINT: Change from baseline in depression severity, assessed during the treatment phase (month 0–7) and monthly during 5 months of follow-up (month 8–12).

METHOD: Adult patients with depression were randomized to CT (n=76), IPT (n=75), or a 2-month waiting list (WLC) control condition followed by treatment of choice (n=31). Patients allocated to CT or IPT received at least 12 sessions out of 16–20 planned individual sessions lasting 45 minutes. Depression severity was assessed using the Beck Depression Inventory–II (BDI-II).

RESULTS: Both CT and IPT were associated with considerable improvement in depression severity up to 12 months from baseline, exceeding change in the WLC condition. There were no significant differences in effects between CT and IPT. The results were not influenced by individual differences in therapists, baseline depression severity, or total number of sessions.

CONCLUSIONS: In patients with depression, both CT and IPT were equally effective in relieving depressive symptoms during treatment and this effect was sustained for a further 5 months of follow-up. Both interventions were superior to no treatment.
BACKGROUND & AIM: Antidepressant prescription and use are currently growing, particularly in the elderly, and there are concerns about the safety of drivers using psychopharmacological treatment. However, only a few epidemiological studies investigating the effects of antidepressants on road safety have been conducted, and experimental data on the driving behaviour of antidepressant-treated patients are sparse. The aim of this study was to assess the effects of the newer antidepressants agomelatine and venlafaxine on psychomotor functions related to driving skills and on driving performance in patients with major depression.

STUDY DESIGN: Randomized case-control study.

ENDPOINTS: Global driving ability score and on-road test results.

METHOD: The study included 40 patients with major depression (Hamilton Rating Scale for Depression score ≥20) who were randomized 1:1 to receive agomelatine or venlafaxine at a dose selected on an individual basis by the treating psychiatrist. All patients underwent psychomotor and visual perception tests prior to treatment and at 14 days and 28 days after treatment to assess visual perception, selective attention, vigilance, reactivity and stress tolerance (global driving ability score). On day 28, participants also underwent a standardized 50-minute on-road driving test conducted by a licensed driving instructor blinded to treatment, diagnosis and test results. To control for retest effects, 20 healthy subjects underwent the same testing schedule.

RESULTS: After 4 weeks of treatment, depressive symptoms significantly improved in the patients receiving agomelatine or venlafaxine. There was a significant improvement in global driving ability score after 14 days of treatment in both the agomelatine group (z = –2.16, p < 0.05) and the venlafaxine group (z = –2.74, p < 0.01), which was sustained at day 28. After controlling for retest effects, both patient groups had significantly improved scores in their reactivity and stress-tolerance tests, and a significant improvement in concentration was observed in the agomelatine group. In the on-road test, 72.5% of patients were rated as good drivers and 22.5% as satisfactory drivers. There were no significant differences between the treatment groups in either the psychomotor or on-road tests, but neither patient group reached the same level of performance as the healthy controls.

CONCLUSION: Treatment with agomelatine or venlafaxine resulted in significantly improved performance in tasks related to driving ability in patients with major depression, with the majority being rated as fit to drive in an on-road driving test 28 days after treatment initiation.
INSOMNIA AND SOMNOLENCE ASSOCIATED WITH SECOND-GENERATION ANTIDEPRESSANTS DURING THE TREATMENT OF MAJOR DEPRESSION: A META-ANALYSIS

BACKGROUND & AIM: Second-generation antidepressant drugs, such as selective serotonin reuptake inhibitors (SSRI) and serotonin–norepinephrine reuptake inhibitors (SNRI), are frequently associated with insomnia or daytime somnolence, which can be beneficial or harmful to the patient depending on their symptom profile. However, the rates of insomnia and daytime somnolence have not been compared among the individual antidepressants. The aim of this meta-analysis was to compare the short-term rates of insomnia and somnolence associated with 14 second-generation antidepressants during treatment of major depression.

STUDY DESIGN: Meta-analysis.

ENDPOINTS: Short-term insomnia and somnolence rates.

METHOD: A systematic search of the Medline, ISI Web of Science and Cochrane databases was performed to identify controlled and uncontrolled studies published up to January 2013 that provided data on short-term (up to 12 weeks) drug-related insomnia and/or somnolence rates in adult patients with major depression treated with a second-generation antidepressant. A minimum study duration of 6 weeks was required. A total of 276 trials were included in the meta-analysis, of which 223 were randomized controlled, seven were non-randomized controlled and 46 were uncontrolled trials. Pooled odds ratios (ORs) for insomnia and somnolence rates were calculated using a random effects model, and heterogeneity was assessed.

RESULTS: Ten of the 14 antidepressants were associated with significantly higher rates of short-term insomnia compared with placebo, with bupropion and desvenlafaxine having the highest incidence rates. The only antidepressant with a lower likelihood of inducing insomnia compared with placebo was agomelatine. Eleven of the antidepressants were associated with significantly higher rates of short-term somnolence compared with placebo, with fluvoxamine and mirtazapine demonstrating the highest frequency of somnolence. Bupropion was the only antidepressant with a significantly lower risk of inducing somnolence than placebo. Sensitivity analyses of only the randomized, double-blind, placebo-controlled trials confirmed the overall results, with only a small degree of variation.

CONCLUSION: Second-generation antidepressants vary in terms of their association with insomnia or somnolence, most likely due to their different modes of action, but most are associated with a higher risk of insomnia and somnolence than placebo. Understanding the differences among antidepressant drugs in terms of their effects on sleepiness could be useful for tailoring the choice of medication to the specific needs of the individual patient.
SCREEN TIME IS ASSOCIATED WITH DEPRESSION AND ANXIETY IN CANADIAN YOUTH

Preventive Medicine, 2015 April; 73:133–8

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BACKGROUND & AIM: The use of screen-based electronic devices (such as television, video games and computers) is popular among young people in industrialized societies and is associated with obesity, cardiometabolic risk factors and diabetes. Although depression and anxiety are common among adolescents, little research has been conducted into the relationship between sedentary, screen-based activities and mental health in this age group. The evidence to date is contradictory, with some studies showing a positive association between screen time and anxiety or depression and others finding no such association. The aim of this study was to examine the relationships between sedentary screen time and symptoms of depression and anxiety in a large community sample of Canadian youth.

STUDY DESIGN: Cohort study.

ENDPOINTS: Screen time and any association with symptoms of depression and anxiety.

METHOD: Cross-sectional data were collected from 2482 English-speaking grade 7–12 Canadian students (1048 male) participating in the Research on Eating and Adolescent Lifestyles (REAL) study between 2006 and 2010. Mental health status was assessed using the Children’s Depression Inventory and the Multidimensional Anxiety Scale for Children–10. Screen time (hours/day of television, video games and computer use) was assessed using the Leisure-Time Sedentary Activities questionnaire. Associations between screen time and symptoms of depression and anxiety were identified using multiple linear regression analysis.

RESULTS: Duration of screen time was associated with the severity of both depression ($\beta=0.23$, $p<0.001$) and anxiety ($\beta=0.07$, $p<0.004$) after controlling for age, sex, ethnicity, parental education, geographic area, physical activity and body mass index. Time spent playing video games ($\beta=0.13$, $p<0.001$) and using the computer ($\beta=0.17$, $p<0.001$), but not watching television, were associated with more severe depressive symptoms. Video game playing ($\beta=0.11$, $p<0.001$) was also predictive of more severe anxiety symptoms.

CONCLUSION: Longer duration of screen time was associated with more severe symptoms of depression and anxiety in adolescents.

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PREDICTING THE NATURALISTIC COURSE OF MAJOR DEPRESSIVE DISORDER USING CLINICAL AND MULTIMODAL NEUROIMAGING INFORMATION: A MULTIVARIATE PATTERN RECOGNITION STUDY

BACKGROUND & AIM: The early identification of patients with major depressive disorder (MDD) who are at risk of experiencing a chronic disease course would enable appropriate treatment strategies to be implemented promptly. Although some clinical characteristics are known to be linked with chronic MDD, neurobiological markers are lacking. There is some evidence that neuroimaging findings could be helpful, but their relevance for predicting risk at the level of the individual patient has not been demonstrated. This study evaluated the prognostic value of different neuroimaging modalities, clinical characteristics, and their combination, for classifying MDD course trajectories in a naturalistic cohort of patients with MDD.

STUDY DESIGN: Cohort study.

ENDPOINTS: Prediction of MDD course trajectory.

METHOD: The study included 118 patients with MDD who underwent structural and functional magnetic resonance imaging (MRI), including assessments of brain activation during emotional facial processing and during executive functioning. Patients were followed up clinically for 2 years using the Life Chart Interview to measure symptoms each month, and a latent class growth analysis of these data identified three MDD trajectories: chronic (n=23), gradual improving (n=36) and fast remission (n=59). The prognostic value of neuroimaging data and clinical characteristics (including baseline MDD severity, MDD duration and comorbidity) for discriminating among these trajectories was evaluated using a multivariate pattern recognition method involving Gaussian process classifiers.

RESULTS: Functional MRI measures of the neural responses to emotional faces could be used to discriminate between patients with a chronic course and those with fast remission (based on responses to angry and happy faces; accuracy 73%), and between those with a chronic course and those with a gradually improving course (based on happy and neutral faces; accuracy 69%). MDD course trajectories could not be discriminated using structural MRI or functional MRI related to executive functioning. Clinical characteristics could be used to discriminate patients with a chronic course from those with remission (accuracy 69%), but this became non-significant when age differences were accounted for. Combining different neuroimaging modalities and clinical characteristics did not increase the accuracy for predicting course trajectories.

CONCLUSION: Neuroimaging data on responses to emotional facial expressions were useful for predicting the course of MDD, and such predictions were more accurate than those based on clinical data alone.
**BACKGROUND & AIM:** New antidepressant drugs are needed to treat major depressive disorder (MDD), as many patients only partially respond or have no clinically meaningful response to current treatments. However, industry investment in antidepressant drug development has waned for various reasons, including the high rate of failure of antidepressants in late-stage clinical trials. Triple-reuptake inhibitors (TRIs) that simultaneously inhibit serotonin, norepinephrine and dopamine reuptake would potentially have greater efficacy than currently available drugs in some patients with MDD. The author summarized the evidence for TRIs and discussed issues around their development.

**ARTICLE TYPE:** Review.

**FINDINGS:** Patients with MDD form a heterogeneous group with a wide range of overlapping symptoms. The successful development of next-generation antidepressants will require a deeper understanding of individual differences in biology and treatment response, as well as the ability to translate this knowledge into the development of drugs targeting specific subgroups of patients who share the same symptoms. Patients unresponsive to current treatment who have a high burden of decreased positive mood symptoms and comorbidities that suggest reward-network dysfunction could potentially benefit from the addition of dopamine reuptake inhibition to counteract hypodopaminergic effects.

Trials of TRIs have so far been unsuccessful, with results indicating a lack of efficacy compared with placebo or standard care in phase 2 clinical studies. However, these findings do not negate the hypothesis that a TRI could be effective in a subgroup of MDD patients, as TRI development programmes have made assumptions concerning suitable target populations and have lacked translational research studies with pharmacodynamic biomarkers and predictive animal models. Also, the optimal mix of relative inhibitory potencies for the three transporters is still unknown.

Addressing these limitations in future drug development would allow a TRI to be compared more accurately with placebo and existing antidepressants in the target population. They would also allow dose–response relationships to be established for efficacy and safety, and would indicate whether cardiovascular effects are manageable in the proposed dose range.

**CONCLUSIONS:** Cost-effective and successful drug development of TRIs should be possible with the use of relevant biomarkers, improved animal models and identification of the specific target population. Success would induce renewed investment by the pharmaceutical industry in the development of novel antidepressant medications and improve the therapeutic outlook for patients with MDD.
A LIFETIME APPROACH TO MAJOR DEPRESSIVE DISORDER:
THE CONTRIBUTIONS OF PSYCHOLOGICAL INTERVENTIONS
IN PREVENTING RELAPSE AND RECURRENCE

Clinical Psychology Review, 2015 February 26; Epub ahead of print

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BACKGROUND & AIM: Major depressive disorder (MDD) often follows a recurrent
course. Strategies for preventing relapse and recurrence include the continuation
of antidepressant medication and the use of psychological interventions. This article
considers the role of psychological interventions in the prevention of relapse and recur-
rence of MDD, based on a review of the published literature.

TYPE OF ARTICLE: Review.

FINDINGS: The mechanisms underlying the effectiveness of preventive psychological
interventions are not fully understood, but probably involve changes in dysfunctional
beliefs or the process of cognition. Preventive psychological therapies may be started
during the acute phase of the illness, may be continued in patients who have responded
to acute-phase treatment, or may be started when patients are in remission.

Acute-phase interventions: Cognitive behavioural therapy administered during
the acute phase of illness reduces the risk of relapse for a period that extends beyond
the end of treatment. There is also some evidence that it may reduce the risk of recurrence.

Continuation/maintenance interventions: Continuing treatment with
cognitive-behavioural therapy after response/remission has been achieved (con-
tinuation treatment) and after the patient has recovered fully from the index episode
(maintenance treatment) has been shown to further reduce the risk of relapse or recurrence. There is some evidence that continuation/maintenance therapy with interpersonal psychotherapy may also be effective.

Interventions started after remission: Well-being cognitive therapy, mindfulness-
based cognitive therapy and preventive cognitive therapy started in patients who
are currently in remission but who are at high risk of recurrence can be effective in
reducing the risk of relapse or recurrence. Behavioural activation also shows promise,
based on a single study.

Subgroups who benefit the most: Cognitive therapy continuation and preventive interventions started after remission appear to provide the greatest differential benefit for those patients who are at greatest risk of relapse/recurrence, including patients with unstable remission, a higher number of previous episodes, early age of onset, and more severe childhood trauma.

CONCLUSION: Psychological interventions can reduce the risk of relapse or recurrence in patients with MDD.

http://www.sciencedirect.com/science/journal/02727358
CAN ATYPICAL ANTIPSYCHOTIC AUGMENTATION REDUCE SUBSEQUENT TREATMENT FAILURE MORE EFFECTIVELY AMONG DEPRESSED PATIENTS WITH A HIGHER DEGREE OF TREATMENT RESISTANCE?

A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

BACKGROUND & AIM: Augmentation treatment with atypical antipsychotic agents has been shown to be an effective option for patients with major depressive disorder (MDD) that is resistant to standard antidepressant therapy. However, it is not known whether the degree of treatment resistance present has an impact on the effect of such augmentation therapy. The aim of this meta-analysis was to determine whether the effect size of atypical antipsychotic augmentation in MDD varies according to the degree of treatment resistance.

STUDY DESIGN: Meta-analysis.

ENDPOINTS: Response and remission rates.

METHOD: A search of the Cochrane Library, Embase, Medline and KoreaMed databases for randomized, double-blind, placebo-controlled, acute-phase trials evaluating the efficacy of atypical antipsychotic augmentation in patients with non-psychotic MDD identified 11 trials \((n=3341)\), including 9 in treatment-resistant depression and 2 in non-resistant depression. The degree of treatment resistance was classified according to the number of failed treatment trials during the index episode: one (TRD1), two (TRD2), or two to four (TRD2–4). Results were pooled using a random-effects meta-analysis. The trials in non-resistant depression were excluded from meta-analysis of response rates because only one of them produced suitable data.

RESULTS: Based on the pooled data for treatment-resistant depression, atypical antipsychotic augmentation of antidepressant therapy was more efficacious than antidepressant monotherapy in treatment-resistant depression in terms of the response rate (risk ratio \(1.38\), 95% confidence interval \(1.25–1.53\)) and the remission rate (RR \(1.62\), 95% CI \(1.42–1.85\)). Effect sizes for the response rate increased with increasing degree of treatment resistance, with risk ratios rising from 1.24 for the TRD1 subgroup to 1.58 for the TRD2–4 subgroup \((z=0.121257, p=0.05)\). Effect sizes for the remission rate did not differ significantly according to the degree of treatment resistance. Based on the pooled data for non-resistant depression, atypical antipsychotic augmentation was not superior to antidepressant monotherapy in terms of remission rates (RR \(0.89\), 95% CI \(0.69–1.14\)).

CONCLUSIONS: Augmentation therapy with atypical antipsychotics was superior to antidepressant monotherapy in patients with treatment-resistant MDD, and had a greater effect in patients with a higher degree of treatment resistance. Atypical antipsychotic augmentation therapy was not superior to antidepressant monotherapy in patients with non-resistant MDD.

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Framingham on depression
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