**Premenstrual Dysphoric Disorder (PMDD)**

**PMDD & Women Casablanca**

- Assessment of premenstrual dysphoric disorder symptoms: population of women in casablanca

**Authors**: McHichi alami Kh, Tahiri SM, Moussaoui D, Kadri N. Centre Psychiatrique Universitaire Ibn Rochd, Casablanca, Maroc.

**Summary**: Menstruation is a biological phenomenon that has been subject of myths and taboos within and among various cultures. These myths distort the reality surrounding menstruation and create ambivalent feelings about the value and usefulness of this function outside of its necessity as mean of reproduction. Thus studies concerning menstruation need to take into account cultural and psychosocial factors that define the meaning, values and behavior associated with this biological phenomenon. According to several studies, 70% of women experience psychological faintness during this menstrual phase, 40% of them have these symptoms at each menstruation and between 3 to 8% of them suffer severely reacquiring medical support. This entity called premenstrual dysphoric disorder is defined by the presence of several symptoms (distress, tension, irritability, moodiness.) with a significant impairment in work or social functioning beginning during the week before and ending within a few days after the onset of menses. Several studies conducted over the past few years suggested that selective serotonin reuptake inhibitors (SSRIs) and serotonergic tricyclic drugs may be more effective than other types of antidepressants in treating PMS symptoms. Two protocols are proposed; a continuous treatment or intermittent use during few days during premenstrual and menstrual phase for several cycles. The objective of the current study was to evaluate the prevalence of a potential premenstrual dysphoric disorder (PMDD) during one menstrual cycle, in a representative sample of general population of Casablanca, according the DSM IV criteria. On the other hand, a questionnaire, available from the authors, was used to explore socio-demographic data. Among 618 women interviewed, 310 met the criteria of a potential PMDD (50.2%). The mean age of the population with PMDD was 32.2 years suggested that half-cycle dosing (luteal phase) was effective for DSM-IV-defined premenstrual dysphoric disorder (PMDD), a severe form of PMS. This study examined the effectiveness of half-cycle dosing of citalopram in PMS patients who did not respond to previous SSRI treatment. **Methods**: Seventeen women with no improvement in symptoms after two menstrual cycles on an SSRI were given open-label citalopram (20-40 mg/day). Eleven subjects received half-cycle dosing, and 6 subjects received full-cycle dosing. Scores on the 17-item daily symptom report (DSR) and on each of five DSR symptom clusters were used to measure citalopram efficacy. **Results**: Total premenstrual DSR scores were significantly improved (p<0.001) in both half-cycle and full-cycle dosing groups. The half-cycle group reported lower DSR scores throughout treatment compared with the full-cycle group, but the difference did not reach statistical significance in this small sample. All DSR factor scores (mood, behavioral, pain, physical symptoms, and appetite) significantly improved. Clinical improvement (>or=50% decrease from baseline DSR) was reported by 76% of the subjects overall. Forty-one percent of the subjects has a bad impact on mental health and on quality of life of the women suffering from PMDD.

**PMDD & Paroxetine**

- Paroxetine controlled release

**Authors**: Bang LM, Keating GM. Adis International Limited, Auckland, New Zealand.

**Summary**: A controlled-release (CR) formulation of the SSRI paroxetine has been developed. This CR formulation delays the release of paroxetine until the tablet has passed through the stomach; the drug is then released over 4–5 hours. In well designed placebo-controlled trials in patients with major depressive disorder (including a study in the elderly), social anxiety disorder or premenstrual dysphoric disorder (PMDD), paroxetine CR was consistently superior to placebo with regards to primary endpoints (i.e., mean Hamilton Rating Scale for Depression total score [major depressive disorder], Liebowitz social anxiety scale total score and Clinical Global Impressions-Global Improvement score [social anxiety disorder] and Visual Analog Scale-Mood score [PMDD]). The duration of treatment was 12 weeks or, in PMDD, over three menstrual cycles (intermittent or continuous administration). Paroxetine CR also demonstrated efficacy in three well designed studies in patients with panic disorder with or without agoraphobia. Paroxetine CR was generally well tolerated in clinical trials, with an adverse-event profile typical of SSRIs, although recipients of paroxetine CR experienced significantly less nausea than recipients of immediate-release paroxetine in the first week of treatment.

**PMDD (Severe PMS) & Citalopram**

- Citalopram in PMS patients with prior SSRI treatment failure: a preliminary study

**Authors**: Freeman EW, Jabara S, Sondheimer SJ, Auletto R. Departments of Obstetrics/Gynecology, University of Pennsylvania Medical Center, Philadelphia, Pennsylvania, USA.

**Summary**: OBJECTIVES: Evidence shows that the selective serotonin reuptake inhibitors (SSRIs) effectively reduce the symptoms of severe premenstrual syndrome (PMS). A placebo-controlled study of citalopram, the most selective SSRI, demonstrated that half-cycle dosing (luteal phase) was effective for DSM-IV-defined premenstrual dysphoric disorder (PMDD), a severe form of PMS. This study examined the effectiveness of half-cycle dosing of citalopram in PMS patients who did not respond to previous SSRI treatment. **Methods**: Seventeen women with no improvement in symptoms after two menstrual cycles on an SSRI were given open-label citalopram (20-40 mg/day). Eleven subjects received half-cycle dosing, and 6 subjects received full-cycle dosing. Scores on the 17-item daily symptom report (DSR) and on each of five DSR symptom clusters were used to measure citalopram efficacy. **Results**: Total premenstrual DSR scores were significantly improved (p <0.001) in both half-cycle and full-cycle dosing groups. The half-cycle group reported lower DSR scores throughout treatment compared with the full-cycle group, but the difference did not reach statistical significance in this small sample. All DSR factor scores (mood, behavioral, pain, physical symptoms, and appetite) significantly improved. Clinical improvement (>or=50% decrease from baseline DSR) was reported by 76% of the subjects overall. Forty-one percent of the subjects

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experienced symptom remission, defined as a decrease in symptoms to postmenstrual levels. **CONCLUSIONS:** These results from a small number of subjects with open-label treatment must be viewed as preliminary but suggest that citalopram treatment is effective for PMS patients who failed previous SSRI treatment.

**PMDD & Venlafaxine**

* Effective open-label treatment of premenstrual dysphoric disorder with

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**Summary:** Various studies have demonstrated the efficacy of selective serotonergic re-uptake inhibitors in the treatment of premenstrual dysphoric disorder (PMDD). But the effectiveness of novel antidepressant, venlafaxine, in PMDD has been reported in only one Western study. The purpose of the present open-label study was to provide preliminary data on the effectiveness of venlafaxine for Asian women with PMDD. Thirty women with PMDD were enrolled and treated with a flexible dosage of venlafaxine for two menstrual cycles. Responses were assessed every 2 weeks. Outcome measures included the scores of the Prospective Record of the Impact and Severity of Menstrual Symptomatology (PRISM) calendar, self-rating Zung Depressive Scale (Zung), State and Trait Anxiety Inventory (STAI), Hamilton Rating Scale for Depression/Anxiety (HAM-D/HAM-A), and the Clinical Global Impression scale (CGI). Twenty patients completed the trial. All patients had significant improvement of the mood and behavior components in the PRISM calendar. The effects of active treatment were marked by the first active cycle of menstruation. Venlafaxine at a mean dose of 60.1 +/- 29.1 mg per day was effective in reducing PMDD symptoms. The results of the present open trial indicated that venlafaxine is effective in the treatment of ethnic Taiwanese women with PMDD.

**PMDD, PMS & SSRI**

* Selective serotonin reuptake inhibitors for premenstrual syndrome

**Authors:** Wyatt KM, Dimmock PW, O'Brien PMS

**Summary:** An substantial amendment to this systematic review was last made on 08 October 2001. Cochrane reviews are regularly checked and updated if necessary. Background: Severe premenstrual syndrome affects between three to five per cent of women of reproductive age. Such severe PMS is classified under the Diagnostic and Statistical Manual of Mental Disorders as premenstrual dysphoric disorder, PMDD. Selective serotonin reuptake inhibitors (SSRIs) are increasingly being used as a front-line therapy for premenstrual syndrome (PMS). A systematic review was undertaken on the efficacy of SSRIs in the management of severe PMS/PMDD, to assess the evidence for this treatment option.

Objectives: The objective of this review was to evaluate the effectiveness of SSRIs in reducing premenstrual syndrome symptoms in women diagnosed with severe premenstrual syndrome. Search strategy: Electronic searches for relevant randomised controlled trials of the Cochrane Menstrual Disorders and Subfertility Group specialised register of controlled trials, Cochrane Controlled Trials Register, MEDLINE, EMBASE and PsyCIL were undertaken. References were searched interactively to identify missed trials. Where insufficient data were presented original authors were contacted for further details.

Selection criteria: All trials were considered in which women with a prospective diagnosis of PMS/PMDD were randomised to receive SSRIs or placebo in a double blind trial for the treatment of premenstrual syndrome. Data collection and analysis: 31 randomised controlled trials were identified which reported the use of SSRIs in the management of PMS. 16 trials were excluded, 15 trials were included in the systematic review, and ten trials were included in the main analyses. The reviewers extracted the data independently and standardised mean differences for continuous outcomes were estimated from the data. Main results: The primary analysis of reduction in overall symptomatology included data on 844 women with premenstrual syndrome. SSRIs were found to be highly effective in treating premenstrual symptoms. Secondary analysis showed that they were as effective in treating physical as well as behavioural symptoms. There was no significant difference between trials funded by pharmaceutical companies and those independently funded. Withdrawals due to side effects were 2.5 times more likely to occur in the treatment group, particularly at higher doses.

Reviewers’ conclusions: There is now very good evidence to support the use of selective serotonin reuptake inhibitors in the management of severe premenstrual syndrome.
**MDD & Clinician-Rated Measures**

* Comparison of self-rated and clinician-rated measures of depressive symptoms: A naturalistic study

**Authors:** Dorz S, Borgerini G, Conforti D, Scarso C, Magni G. Affective Disorders Unit, Casa di Cura Parco dei Tigli, Padova, Italy.

**Source:** Psychol Psychother. 2004 Sep;77(Pt 3):353-61.

**Summary:** In order to assess the concordance between self-rating and clinician’s assessment tools of depression, as well as factors involved in the differences between auto and hetero evaluation, 198 depressed in-patients were assessed at admission and at discharge using the Montgomery Asberg Depression Rating Scale (10-item version, MADRS) and the self-rating scale Symptoms CheckList (90-item version, SCL-90). We found that about 18% of patients overestimated and about 15% underestimated their depressive symptomatology (SCL-90 depression subscale) relative to the psychiatrist’s assessment. Logistic regression analysis showed that the presence of personality disorders and previous history of psychiatric disorders predicted the overestimating group. Discriminant analysis showed that approximately 75% of participants were correctly classified when previous history of psychiatric disorders, presence of personality disorders and age were entered separately into the equation.

**MDD & Reasons for Depression**

* The Reasons for Depression Questionnaire (RFD): UK Standardization for clinical and non-clinical populations

**Authors:** Thwaites R, Dagnan D, Huey D, Addis ME. North Cumbria Mental Health and Learning Disabilities NHS Trust, UK.

**Source:** Psychol Psychother. 2004 Sep;77(Pt 3):363-74

**Summary:** Recent research into reason giving for depression has illustrated the importance of client beliefs about the cause of their depression. Reasons given have been found to be associated with level of depression, perceived credibility of treatments and therapy outcome. It has been suggested that giving reasons for depression is a form of rule-governed behaviour and as such can cause the depression to be harder to treat (i.e. the reasons become functionally true for the individual). This study investigates the reliability and validity of the Reasons for Depression Questionnaire (RFD; Addis, Truax, & Jacobson, 1995), a 48-item self-report measure developed to measure explanations for the causes of depression. The study provides preliminary normative data for both clinical (n = 123) and non-clinical (n = 105) UK samples. The data indicate high reliability for all subscales including a further subscale (biological) added since the measure was initially developed. Certain subscales correlate significantly with level of depression and specific aspects of self-esteem. This supports the validity of the measure and suggests that it is measuring a distinct concept rather than significantly overlapping with individuals’ general beliefs about themselves.

**MDD & High Dose L-Thyroxine**

* High dose L-thyroxine in treatment refractory depression. Case analysis and catamnesis as quality control

**Authors:** Pfieffer H, Scherer J, Albus M. Bezirkskrankenhaus Haar, Haar. pfeiffer@krankenhaus-haar.de

**Source:** Nervenarzt. 2004 Mar;75(3):242-8.

**Summary:** In a depression unit in a state hospital, 28 patients who had failed in six antidepressant strategies were treated with L-thyroxine at an average dose of 350 micro g/die. Outcomes were moderate in 39.3% and very good in 21.5%, corresponding to 21-item HAMD scores of < or = 8 and < or = 8 and clinical judgement. Of all patients, 39.3% had to stop treatment due to nonresponse or side effects. Follow-up of all responders to treatment was conducted 45.2 weeks after discharge. Those 28.6% patients who had stopped treatment had significantly more readmissions, i.e., 62.5%, vs none in those who continued, whereas subjective clinical ratings did not differ between the two groups. In contrast to the literature not finding serious side effects in 70 mainly bipolar patients, we found cardiac arrhythmia in 10.7% of inpatients and 7.1% of follow-up patients that was serious enough to discontinue treatment. In conclusion, systematic investigation of high-dose L-thyroxine treatment in treatment-resistant depression seems promising and necessary.

**MDD & Review of Studies**

* A Review of Studies of the Hamilton Depression Rating Scale in Healthy Controls: Implications for the Definition of Remission in Treatment Studies of Depression.

**Authors:** Zimmerman M, Chelminske I, Posternak M. Department of Psychiatry and Human Behavior, Brown University School of Medicine, Rhode Island Hospital, Providence, RI.

**Source:** J Nerv Ment Dis. 2004 Sep;192(9):595-601.

**Summary:** The Hamilton Rating Scale for Depression (HRSD) is the most commonly used symptom severity scale to evaluate the efficacy of antidepressant treatment. On the basis of an expert consensus panel, an HRSD score of ≤7 was recommended as a cutoff to define remission. Since that recommendation, little empirical work has been conducted to confirm the validity of this threshold. One approach toward determining a cutoff score for defining remission is to establish the range of values for healthy controls. We therefore conducted a literature review of studies of the HRSD in healthy controls to determine the normal range of values. Studies of the HRSD in healthy control groups were identified in two ways. First, a MEDLINE search for the years 1966 to 2002 was conducted using the key words Hamilton, depression, and controls, and articles were reviewed. Second, the 69 studies included in two review articles written by the authors were examined. We identified 27 studies that included data on the HRSD for 1014 healthy controls. Across all studies, the weighted mean (SD) HRSD score, adjusting for sample size, was 3.2 (3.2; 95% CI, 3.0 to 3.4). HRSD scores were similar in geriatric and nongeriatric samples, and in men and women. Because HRSD scores in healthy controls are more likely to follow a skewed than a normal distribution, based on a mean of 3.2 and a SD of 3.2, at least 84% of healthy controls scored 7 or less on the HRSD, and 97.5% scored 10 or less. Thus, these results can be taken as support for the recommended cutoff of 7 on the HRSD to define remission.
MDD, Antidepressant & Benzodiazepine

**Antidepressant and Benzodiazepine for Major Depression**

Authors: Furukawa TA, Streiner DL, Young LT

**Summary:** A substantive amendment to this systematic review was last made on 04 April 2001. Cochrane reviews are regularly checked and updated if necessary.

**Background:** Anxiety frequently coexists with depression. Adding benzodiazepines to antidepressants is commonly used to treat people with depression, although there has been no convincing evidence to show that such a combination is more effective than antidepressants alone and that there are suggestions that benzodiazepines may lose their efficacy with long-term administration and that their chronic use carries risks of dependence.

**Objectives:** To determine whether, among adult patients with major depression, adding benzodiazepines to antidepressants brings about any benefit in terms of symptomatic recovery or side-effects in the short term (less than 8 weeks) and long term (more than 2 months), in comparison with treatment by antidepressants alone.


**Selection criteria:** All randomised controlled trials that compared combined antidepressant-benzodiazepine treatment with antidepressant alone for adult patients with major depression. Exclusion criteria are: antidepressant dosage with antidepressant alone for adult patients with major depression, adding benzodiazepines to antidepressants brings about any benefit in terms of symptomatic recovery or side-effects in the short term (less than 8 weeks) and long term (more than 2 months), in comparison with treatment by antidepressants alone.

**Data collection and analysis:** Two reviewers independently assessed the eligibility and quality of the studies. Two reviewers independently extracted the data. Standardized weighted mean differences and relative risks were estimated with random effects model. The dropouts were assigned the least favourable outcome. Two sensitivity analyses examined the effect of this assumption as well as the effect of including medium quality studies. Three a priori subgroup analyses were performed with regard to the patients with or without comorbid anxiety and with regard to the type.

**Main results:** Aggregating nine studies with a total of 679 patients, the combination therapy group was less likely to drop out than the antidepressant alone group (relative risk 0.63, 95% confidence interval 0.49 to 0.81). The intention-to-treat analysis (with people dropping out assigned the least favourable outcome) showed that the combination group was more likely to show improvement in their depression (defined as 50% or greater reduction in the depression scale from baseline) (relative risk 1.63, 95% confidence interval 1.18 to 2.27 at one week and relative risk 1.38, 95% confidence interval 1.15 to 1.66 at four weeks). The difference was no longer significant at six to eight weeks. None of the included RCTs lasted longer than eight weeks. The patients allocated to the combination therapy were less likely to drop out from the treatment due to side effects than those receiving antidepressants alone (relative risk 0.53, 95% confidence interval 0.32 to 0.86). However, these two groups of patients were equally likely to report at least one side effect (relative risk 0.99, 95% confidence interval 0.92 to 1.07).

**Reviewers’ conclusions:** The potential benefits of adding a benzodiazepine to an antidepressant must be balanced judiciously against possible harms including development of dependence and accident proneness, on the one hand, and against continued suffering following no response and drop-out, on the other.

**MDD, SSRIs & Tricyclics**

**Selective serotonin reuptake inhibitors (SSRIs) versus other antidepressants for depression**

Authors: Geddes JR, Freemantle N, Mason J, Eccles MP, Boynton J

**Summary:** A substantive amendment to this systematic review was last made on 15 July 1999. Cochrane reviews are regularly checked and updated if necessary.

**Background:** The relatively new class of antidepressant, the selective serotonin reuptake inhibitors (SSRIs), may be better tolerated than the older tricyclic antidepressants. This review compares the efficacy of SSRIs with other antidepressants.

**Objectives:** To examine the relative efficacy of selective serotonin reuptake inhibitors (SSRIs) compared to other antidepressants.

**Search strategy:** The search strategy included a search of (a) Electronic bibliographic databases (MEDLINE, EMBASE); (b) reference lists of related reviews (c) reference lists of all located studies (d) contact with the manufacturer and (e) the Cochrane Group register of controlled trials.

**Selection criteria:** Randomised controlled trials comparing selective serotonin reuptake inhibitors with other kinds of antidepressants in the treatment of patients with depressive disorders. The outcome measures assessed included measures of the severity of depression.

**Data collection and analysis:** Data were collected from each study the main outcome measure from each study. These included: mean Hamilton depression rating scale, mean Montgomery & Asberg depression rating scale, Clinical Global Impression rating scale. An analysis of standardised mean difference of these scales was performed using Review Manager 3.1 software. The presence of heterogeneity of treatment effect was assessed.

**Main results:** Ninety-eight trials contributed data to the analysis of the relative efficacy of SSRIs and related drugs with comparator antidepressants (Figure 3 & Appendix 3). Analysis of efficacy was based upon 5044 patients treated with an SSRI or related drug, and 4510 treated with an alternative antidepressant. The standardised effect size for SSRIs and related drugs together versus alternative antidepressants using a fixed effects model was 0.035 (95% CI -0.006 to 0.076; Q = 149.25, df = 97, p < 0.001).

**Reviewers’ conclusions:** There are no clinically significant differences in effectiveness between selective serotonin reuptake inhibitors and tricyclic antidepressants. Treatment decisions need to be based on considerations of relative patient acceptability, toxicity and cost.
MDD & TMS

* Transcranial magnetic stimulation for treating depression

Authors: Martin JLR, Barbanoj MJ, Schlaepfer TE, Clos S, Perez V, Kulisevsky J, Gironell, A

Summary: A substantive amendment to this systematic review was last made on 12 July 2001. Cochrane reviews are regularly checked and updated if necessary.

Background: Transcranial magnetic stimulation can either excite or inhibit cortical areas of the brain, depending on whether the speed of the repetitive stimulation is applied at high or low frequencies. It has been used for physiological studies and it has also been proposed as a treatment for depression.

Objectives: To assess the clinical efficacy and safety of transcranial magnetic stimulation for treating depression.

Search strategy: An electronic search was performed including the Cochrane Collaboration Depression, Neurosis and Anxiety Review Group trials register (last searched June, 2001), the Cochrane Controlled Trials Register (Issue 2, 2001), MEDLINE (1966-2001), EMBASE (1974-2001), PsycLIT (1980-2001), and bibliographies from reviewed articles. Unpublished data and grey literature were searched through personal communications with researchers.

Selection criteria: Randomised controlled trials assessing the therapeutic efficacy and safety of transcranial magnetic stimulation for depression.

Data collection and analysis: All reviewers independently extracted the information and verified it by cross-checking. Disagreements were resolved through discussion. Continuous data: When similar studies were grouped, the overall standardised mean difference was calculated under a fixed effect model weighted by the inverse variance method with 95% confidence intervals. (In the presence of statistical heterogeneity, a random effects model was to be used.)

Main results: Sixteen trials were included in the review and fourteen contained data in a suitable form for quantitative analysis. Most comparisons did not show differences between rTMS and other interventions. No difference was seen between rTMS and sham TMS using the Beck Depression Inventory or the Hamilton Depression Rating Scale, except for one time period (after two weeks of treatment) for left dorsolateral prefrontal cortex and high frequency; and also for right dorsolateral prefrontal cortex and low frequency, both in favour of rTMS and both using the Hamilton scale.

Comparison of rTMS (left dorsolateral prefrontal cortex and high frequency) with electroconvulsive therapy showed no difference except for psychotic patients after two weeks treatment, using the Hamilton scale, which indicated that electroconvulsive therapy was more effective than rTMS.

Reviewers’ conclusions: The information in this review suggests that there is no strong evidence for benefit from using transcranial magnetic stimulation to treat depression, although the small sample sizes do not exclude the possibility of benefit.

MDD & Stroke

* Interventions for preventing depression after stroke

Authors: Anderson CS, Hackett ML, House AO

Summary: A substantive amendment to this systematic review was last made on 17 November 2003. Cochrane reviews are regularly checked and updated if necessary.

Background: Abnormal mood is an important consequence of stroke and may affect recovery and outcome. However, depression and anxiety are often not detected or inadequately treated. This may in part be due to doubts about whether antidepressant treatments commenced early after the onset of stroke will prevent depression and improve outcome.

Objectives: To determine if pharmacological or psychological interventions can prevent the onset of depression, including depressive illness and abnormal mood, and improve physical and psychological outcomes, in patients with stroke.

Search strategy: We searched the Cochrane Stroke Group trials register (June 2003). In addition we searched the following electronic databases: Cochrane Central Register of Controlled Trials (The Cochrane Library, Issue 3, 2002), MEDLINE (1966 to September 2002), EMBASE (1980 to September 2002), CINAHL (1982 to September 2002), PsychINFO (1967 to September 2002), Applied Science and Technology Plus (1986 to September 2002), Arts and Humanities Index (1991 to September 2002), Biological Abstracts (1969 to September 2002), General Science Plus (1994 to September 2002), Social Sciences Citation Index (1992 to September 2002), Social Sciences Citation Index (1991 to September 2002), and Sociofile (1974 to September 2002). Reference lists from relevant articles and textbooks were searched, and authors of known studies and pharmaceutical companies who manufacture psychotropic medications were contacted.

Selection criteria: Randomised and quasi-randomised controlled trials comparing different types of pharmaceutical agents (eg selective serotonin reuptake inhibitors) with placebo, or various forms of psychotherapy against standard care (or attention control), in patients with a recent clinical diagnosis of stroke, where the treatment was undertaken with the explicit intention of preventing depression.

Data collection and analysis: The primary analyses focussed on the proportion of patients who met the standard diagnostic criteria for depression applied in the trials at the end of follow-up. Secondary outcomes included depression or mood scores on standard scales, disability or physical function, death, recurrent stroke, and adverse effects.

Main results: Twelve trials involving 1245 participants were included in the review. Data were available for nine trials (11 comparisons) involving different pharmaceutical agents, and three trials of psychotherapy. The time from stroke onset to entry ranged from a few hours to six months, but most patients were recruited within one month of acute stroke. The duration of treatments ranged from two weeks to one year. There was no clear effect of pharmacological therapy on the prevention of depression or on other measures. A significant improvement in mood was evident for psychotherapy, but this treatment effect was small and from a single trial. There was no effect on diagnosed depression.

Reviewers’ conclusions: This review identified a small but significant effect of psychotherapy on improving mood, but no effect of either pharmacotherapy or psychotherapy on the prevention of depressive illness, disability, or other outcomes. More evidence is therefore required before any recommendations can be made about the routine use of such treatments to improve recovery after stroke.
**MDD, Escitalopram & Venlafaxine**

A double-blind comparison of escitalopram and venlafaxine extended release in the treatment of major depressive disorder.

**Authors**: Bielski RJ, Ventura D, Chang CC. - Summit Research Network, Okemos, Mich. (Dr. Bielski); and Forest Laboratories, Inc., New York, N.Y. (Drs. Ventura and Chang).

**Source**: J Clin Psychiatry. 2004 Sep;65(9):1190-6

**Summary**: Escitalopram is the most selective serotonin reuptake inhibitor (SRI) antidepressant available. Venlafaxine is a non-selective SRI that also inhibits noradrenergic reuptake. This study compared escitalopram and venlafaxine extended release (XR) in depressed outpatients at the highest doses recommended in the United States. METHOD: In this randomized study, patients (diagnosis of DSM-IV-defined major depressive disorder; baseline Hamilton Rating Scale for Depression score of ≥ 20) received a 1-week period of single-blind placebo treatment, followed by 8 weeks of double-blind, fixed-dose treatment with either escitalopram or venlafaxine XR (rapidly titrated to 20 mg/day and 225 mg/day, respectively, in accordance with prescribing information). The primary efficacy variable was change from baseline to week 8 in Montgomery-Asberg Depression Rating Scale (MADRS) total score. Data were collected from May to December 2002. RESULTS: Mean baseline MADRS scores for the escitalopram (N = 97) and venlafaxine XR (N = 98) groups were 30.7 and 30.0, respectively. There were no significant differences in measures of efficacy between the 2 antidepressants. Mean changes from baseline to endpoint in MADRS total score for escitalopram and venlafaxine XR were -15.9 and -13.6, respectively. Remission (MADRS score of < 10) rates at endpoint were 41.2% for escitalopram and 36.7% for venlafaxine XR. Response (≥ 50% reduction from baseline MADRS score) rates for the escitalopram and venlafaxine XR groups were 58.8% and 48.0%, respectively. Tolerability measures favored escitalopram over venlafaxine XR treatment. The venlafaxine XR group had a higher incidence than the escitalopram group of treatment-emergent adverse events (85.0% vs. 68.4%) and discontinuation due to adverse events (16.0% vs. 4.1%; P < .01). CONCLUSION: Results of this study indicate that, when titrated rapidly to their maximum recommended doses, escitalopram is at least as effective as venlafaxine XR and significantly better tolerated. These results do not support the hypothesis that nonselective SRIs have greater efficacy than selective SRIs.

**MDD & Emotional Information**

Emotional information processing in first and recurrent major depressive episodes.

**Authors**: Nandino JL, Dodin V, Martin P, Henniaux M - Department of Psychology, UPRES 2453, Domaine Universitaire du pont de Bois, University of Lille 3, F-59653 Villeneuve d’Ascq cedex, France

**Source**: J Psychiatr Res. 2004 Sep-Oct;38(5):475-84

**Summary**: Depressive states are classically associated to increased sensitivity to negative events. However, this hypersensitivity may not be stable in time, being absent in remission periods or further reinforced with recurrent depressive episodes, or may concern positive stimuli instead, e.g. in young depressive patients. To study the evolution of the processing of emotional information in depression we recorded late components of evoked potentials in first-episode and recurrent depressed patients before and after recovery. We used a visual attentional paradigm manipulating the processing of emotional information. Subjects first counted words with positive valence, and then words with negative valence from lists of usual words. The results showed that recurrent patients had increased P300 amplitudes for negative words selection only in negative words counting situation, while first-episode patients had decreased P300 amplitudes for positive words selection. After clinical improvement, the negative biases in recurrent patients group disappeared but P300 amplitudes of first-episode patients remained significantly low for positive words. First-episode depressed patients show a selective impairment for positive stimuli, with decreased response to pleasant stimuli, while recurrent depressive subjects show signs of hyperesthesia for negative stimuli. These results suggest that responses to emotional stimuli in word processing are related to the duration of the mood disorders.

**MDD & Electroencephalographic Sleep**

Electroencephalographic sleep profiles in treatment course and long-term outcome of major depression: association with DEX/CRH-test response

**Authors**: Hatzinger M, Hemmeter UM, Brand S, Ising M, Holsboer-Trachsler E. - Psychiatric University Hospital, Depression Research Unit, Wilhelm Klein-Str. 27, CH-4025 Basel, Switzerland


**Summary**: Altered electroencephalographic (EEG) sleep patterns are among the most prominent neurobiological findings in depression. Several of these alterations have been suggested to be associated with an unfavorable long-term outcome. However, the impact of pathological sleep parameters on a more recent course of illness or vice versa still warrants clarification. Underlying mechanisms may involve systems known to be related to both sleep regulation and long-term course of depression such as the hypothalamic-pituitary-adrenocortical (HPA) axis. Thus, EEG sleep profiles of patients with depression were examined to determine whether (1) the retrospective clinical course of depression, and (2) the prospective long-term outcome in follow-up are associated with EEG sleep parameters. To elucidate related mechanisms HPA system functioning was evaluated by using the combined DEX/CRH test. Fifteen patients with affective disorders who participated in an earlier controlled antidepressant treatment study over 6 weeks were consecutively enrolled in an exploratory follow-up study. The retrospective analysis revealed that during the acute state of depression predominantly sleep continuity measures were associated with the number of previously experienced episodes. While this relation disappeared during treatment and did not correlate with the prospective course, decreased slow wave sleep variables especially in the first sleep period and increased rapid eye movement density were predictive for the occurrence of recurrences in follow-up and, hence, probably reflect more trait-like markers. Additionally, EEG sleep variables unfavorable for long-term outcome were related to excessive stress hormone response in the DEX/CRH-test. These disturbances may reflect important mechanisms responsible of causing and maintaining the disease process of...
Depression.

**MDD & Medical Illness**

- Comorbid medical illness and relapse of major depressive disorder in the continuation phase of treatment.

Authors: Iosifescu DV, Nierenberg AA, Alpert JE, Papakostas GI, Perlis RH, Sonawalla S, Fava M. - Depression Clinical and Research Program, Psychiatry Department, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA. diasiosfescu@partners.org

Source: Psychosomatics. 2004 Sep-Oct;45(5):419-25

Summary: The authors examined the impact of comorbid medical illness on the rate of relapse of major depressive disorder during continuation therapy. Subjects (N = 128) with major depressive disorder (according to DSM-III-R criteria) achieved clinical remission (a 17-item Hamilton Depression Rating Scale score < or = 7) after 8 weeks of treatment with fluoxetine and entered the continuation phase of antidepressant treatment. They used the Cumulative Illness Rating Scale to measure the severity of comorbid medical illness. Eight patients (6.3%) relapsed during the 28-week continuation phase. With logistic regression, the total burden and the severity of comorbid medical illness significantly predicted the relapse of major depressive disorder during continuation therapy with fluoxetine. Greater medical comorbidity was also associated with higher increases in self-reported symptoms of depression, anxiety, and anger during the follow-up.

**MDD, Venlafaxine & SSRI**

- Cost and effectiveness of venlafaxine extended-release and selective serotonin reuptake inhibitors in the acute phase of outpatient treatment for major depressive disorder.

Authors: Trivedi MH, Wan GJ, Mallick R, Chen J, Casciano R, Geissler EC, Panish JM. - University of Texas Southwestern Medical Center, Dallas, TX; daggerWyeth Research, Global Health Outcomes Assessment, Collegeville, PA and double daggerThe Analytica Group, New York, NY.


Summary: The purpose of this retrospective analysis was to estimate the cost and effectiveness of venlafaxine extended-release (VXR) compared with selective serotonin reuptake inhibitors in the outpatient treatment of major depressive disorder. METHODS: Pooled data from 8, 8-week, randomized, double-blind studies comparing treatment of major depressive disorder with venlafaxine/venlafaxine XR (n = 851), selective serotonin reuptake inhibitors (fluoxetine, paroxetine, fluvoxamine; n = 748), or placebo (4 studies; n = 448) were retrospectively analyzed to determine the economic implications of symptom remission from the perspective of a US third party payer and that of an employer. A decision modeling approach was used to determine cost and effectiveness ratios. RESULTS: Patients on VXR were associated with 22.8 depression-free days versus 18.6 depression-free days with the studied selective serotonin reuptake inhibitors, based on the decision model. Productive and quality-adjusted days were also expected to increase for VXR patients (22.06 vs. 19.34 and 4.56 to 9.36 vs. 7.63), as was the percentage of patients achieving full activity (25.9% vs. 19.6%). The expected cost per patient achieving remission of symptoms was US$1303.94 and US$1514.96, and the cost per depression-free days was US$25.87 and US$28.25, for the VXR and selective serotonin reuptake inhibitors groups, respectively. CONCLUSIONS: Treatment with VXR is not only expected to increase the rate of remission of symptoms but is also associated with achievement of full activity, higher number of depression-free days, productive days, and quality-adjusted days. VXR is a cost-effective treatment option for major depressive disorder.

**MDD, Fluoxetine & Psychosocial Functioning**

- Psychosocial functioning during the treatment of major depressive disorder with fluoxetine.

Authors: Papakostas GI, Petersen T, Denninger JW, Tossani E, Pava JA, Alpert JE, Nierenberg AA, Fava M. - Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA.


Summary: Major depressive disorder (MDD) is associated with significant disability, having a profound impact on psychosocial functioning. Therefore, studying the impact of treatment on psychosocial functioning in MDD could help further improve the standard of care. METHODS: Two hundred twenty-two MDD outpatients were treated openly with 20 mg fluoxetine for 8 weeks. The self-report version of the Social Adjustment Scale was administered at baseline and during the final visit. We then tested for the relationships between (1) self-report version of the Social Adjustment Scale scores at baseline and clinical response, (2) nonresponse, response and remission status and overall psychosocial adjustment at end point, (3) the number/severity of residual depressive symptoms and overall psychosocial adjustment at end point, and (4) the time to onset of response and overall psychosocial adjustment at end point. RESULTS: An earlier onset of clinical response predicted better overall psychosocial functioning at end point (P = 0.0440). Responders (n = 128) demonstrated better overall psychosocial adjustment at end point than nonresponders (P = 0.0003), while remitters (n = 64) demonstrated better overall psychosocial adjustment at end point than nonremitting responders (P = 0.0031). In fact, a greater number/severity of residual symptoms predicted poorer overall psychosocial adjustment at end point in responders (P = 0.0011). Psychosocial functioning at baseline did not predict response. CONCLUSIONS: While MDD patients appear equally likely to respond to treatment with fluoxetine, regardless of their level of functioning immediately before treatment, the above results stress the importance of achieving early symptom improvement then followed by full remission of depressive symptoms with respect to restoring psychosocial functioning in MDD.

**MDD & Treatment**

- Depressed patients may need treatment for both physical and emotional symptoms.

Source: Blackwell Publishing Ltd

Summary: Physical symptoms (such as headache, back pain, stomach problems, joint or muscle pains, and dizziness) are
nearly as common in depression as emotional symptoms and are the predominant complaint depressed patients present with in the primary care setting.

A study published in the Journal of General Internal Medicine examined the prevalence, impact on quality of life, and outcome of physical symptoms in depressed patients during nine months of antidepressant therapy. While physical symptoms showed, on average, some improvement with antidepressant treatment, the improvement was typically less than for emotional symptoms. The physical symptoms showed the greatest improvement during the initial month of treatment. In contrast, depression continued to show gradual improvements over the 9-month period. Unlike depression, however, improvement in physical symptoms typically plateaued with minimal resolution in subsequent months. Therefore, it is important to recognize the physical symptoms that commonly co-exist with depression and, if they fail to improve during the first month of treatment, to consider additional therapies. Corresponding author, Dr. Kroenke states, "It is important to ask patients with depression about physical symptoms at the start of treatment and when assessing improvement ask about physical as well as emotional symptoms."

**Prediction of antidepressant response to milnacipran by norepinephrine transporter gene polymorphisms.**

**Authors:** Yoshida K, Takahashi H, Higuchi H, Kamata M, Ito K, Sato K, Naito S, Shimizu T, Itoh K, Inoue K, Suzuki T, Nemeroff CB. - Department of Psychiatry, Akita University School of Medicine, 1-1-1 Hondo, Akita 010-8543, Japan.

**Source:** Am J Psychiatry. 2004 Sep;161(9):1575-80

**Summary:** With a multitude of antidepressants available, predictors of response to different classes of antidepressants are of considerable interest. The purpose of the present study was to determine whether norepinephrine transporter gene (NET) and serotonin transporter gene (5-HTT) polymorphisms are associated with the antidepressant response to milnacipran, a dual serotonin/norepinephrine reuptake inhibitor. METHOD: Ninety-six Japanese patients with major depressive disorder were treated with milnacipran, 50-100 mg/day, for 6 weeks. Severity of depression was assessed with the Montgomery-Asberg Depression Rating Scale. Assessments were carried out at baseline and at 1, 2, 4, and 6 weeks of treatment. The method of polymerase chain reaction was used to determine allelic variants. RESULTS: Eighty patients completed the study. The presence of the T allele of the NET T-182C polymorphism was associated with a superior antidepressant response, whereas the A/A genotype of the NET G1287A polymorphism was associated with a slower onset of therapeutic response. In contrast, no influence of 5-HTT polymorphisms on the antidepressant response to milnacipran was detected. CONCLUSIONS: The results suggest that NET but not 5-HTT polymorphisms in part determine the antidepressant response to milnacipran.

**Depression in Men**

**Depression in Men: Factors Associated with Prevalence of Depression in Men**

**Authors:** Shiels C, Gabbay M, Dowrick C, Hulbert C. - Department of Primary Care, Whelan Building, University of Liverpool, Liverpool L69 3GB, UK.

**Source:** Br J Psychiatry. 2004 Sep;185:239-44

**Summary:** BACKGROUND: Doctors are less likely to diagnose depression in men than in women. Little research has been conducted to explore the underlying reasons for this in rural settings, or to compare primary care doctors' and male patients' ratings of perceived depression. AIM: To identify symptomatic and socio-demographic correlates of depression in men attending a rural practice, and to compare and contrast general practitioners' and patients' assessments of depression. METHOD: All male patients of working age attending a rural general practice over a 12-month period were invited to participate. RESULTS: Men reporting recent "chest pain" or "feeling tired/little energy", expressing low job enjoyment or with a previous diagnosis of depression were more likely to be scored above threshold on the Hospital Anxiety and Depression Scale-Depression sub-scale. There was little agreement between the doctors and their male patients about the degree of perceived depression. CONCLUSIONS: Educational interventions aimed at addressing the diagnosis of depression in men should take greater account of factors within a particular social setting.

**Depressive Symptoms and Diagnosis.**

**Authors:** Shiels C, Gabbay M, Dowrick C, Hulbert C. - Department of Primary Care, Whelan Building, University of Liverpool, Liverpool L69 3GB, UK.

**Source:** cs50@liv.ac.uk

**Summary:** It is important to ask patients with depression about additional therapies. Corresponding author, Dr. Kroenke states, "It is important to ask patients with depression about physical symptoms at the start of treatment and when assessing improvement ask about physical as well as emotional symptoms."
Depression has been identified as a hallmark feature of rapid-cycling bipolar disorder, although less attention has been paid to the presence of manic features accompanying depression in rapid cyclers. To provide greater information about the extent to which depression arises with or without salient manic features in rapid cycling, we conducted a preliminary study of rapid cycling in outpatients seeking treatment at an academic specialty center for bipolar disorder. Forty DSM-IV affectively symptomatic bipolar outpatients with past year DSM-IV rapid cycling underwent systematic evaluation of symptoms and illness characteristics. Manic and depressive symptoms, treatments, and clinical features were rated by standardized scales. Major depression was present in most rapid cyclers (85%), but salient manic features were also evident in half of all depressed rapid cyclers. A lifetime history of suicide attempts was significantly more common in rapid cyclers who presented with major depression plus salient manic features than in those who presented with pure depression or pure mania (p = .033). Antidepressants were being prescribed for approximately one third of depressed rapid cycling patients regardless of the presence of concomitant manic features, whereas mood stabilizers tended to be used less often when manic features accompanied depression. Depression in conjunction with manic symptoms, rather than pure depression alone, may be more common among rapid-cycling bipolar patients who seek treatment. Lifetime suicide risk may be greater among rapid cycling patients whose depression occurs in tandem with manic symptoms. Prescribing habits in the community that favor antidepressants over mood stabilizers may promote further mood destabilization in this population. Further studies with larger sample sizes are needed to affirm these provisional findings.

**BD & Affective Disorders**

**Affective disorders specific to ageing**

**Authors:** Pellerin J. Service de psychiatrie du sujet age, groupe hospitalier Charles Foix, 94205 Ivry-sur-Seine Cedex. jerome.pellerin@cxf.ap-hop-paris.fr

**Source:** Rev Prat. 2004 Apr 15;54(7):717-24.

**Summary:** With time, affects evolution can lead old people to a pathological organisation of their own mental universe. A general feeling of ill-being (syndrome of ageing badly) may appear and must be differentiated from an usual depressive syndrome. Post-traumatic disorders indicate a current or an old inability to metabolise painful life events. The "syndrome de glissement" (failure-to-thrive) generate not only bedridden old inability to metabolise painful life events. The "syndrome syndrome. Post-traumatic disord ers indicate a current or an appearance and must be differentiated from an usual depressive syndrome of ageing badly. A pathological organisation of their own mental universe. A dissatisfaction or hostility. in caregivers. Those particular forms of ageing determine the relation with the practitioner and can induce feeling of dissatisfaction or hostility.

**BD, Valproate & Acute Mania**

**Authors:** Macincluding K, Geddes JR, Scott J, Haslam D, de Lima M, Goodwin G.

**Source:** The Cochrane Library, Issue 3, 2004. Chichester, UK: John Wiley & Sons, Ltd

**Summary:** A substantive amendment to this systematic review was last made on 08 September 2002. Cochrane reviews are regularly checked and updated if necessary. Background: Valproate has become a leading adjunctive and alternative treatment to lithium in bipolar disorder. Objectives: To determine the efficacy and acceptability of valproate in acute episodes of bipolar disorder. Search strategy: Registers and databases: Cochrane Collaboration Depression, Anxiety and Neurosis Controlled Trials Register (version 2-2002) Cochrane Controlled Clinical Trials Register (3-2002) Medline (1966-January 1999) PsycLIt (1996-June 1999) Embase (1980-January 1999) Reference lists of relevant papers/books. Trial authors, experts and pharmaceutical companies. Handsearches (specialist journals and conference proceedings, listed below). Selection criteria: Randomised controlled trials comparing valproate with placebo and other medications for any acute episode. Bipolar patients, male and female, of all ages were included. Data collection and analysis: Data extraction and methodological quality assessment were each performed independently by two reviewers. For analysis, relative risk was used for binary efficacy outcomes and the weighted mean difference or standardised mean difference used for continuously distributed outcomes. Main results: Ten trials compared valproate with other interventions in mania. None examined depression or mixed affective episodes. Data were extracted on failure to respond by the end of the study (i.e. less than 50% reduction in Young Mania Rating Scale or SADS-S mania scale). Three trials (316 participants) compared valproate with placebo. Three trials (158 participants) compared valproate with lithium. Two trials (363 participants) compared valproate with olanzapine. One trial (36 participants) compared valproate with haloperidol. Two trials (59 patients) compared valproate with carbamazepine. Treatment acceptability was estimated by the ‘total number withdrawing from the study’. Three trials (321 patients) compared valproate and placebo, two (144 patients) compared valproate with lithium. One study (30 patients) compared valproate and carbamazepine. Pooled relative risks (95% confidence intervals) were calculated using fixed effect. Valproate was more efficacious than placebo (RRR 38%; RR 0.62; 95% CI. 0.51 to 0.77) in the treatment of mania. There was no significant difference between valproate and lithium (RRI 5%; RR 1.05; 95% CI. 0.74-1.50) or between valproate and carbamazepine (RRI 34%; RR 0.66; 95% CI. 0.38 to 1.16). Valproate was less effective than olanzapine (failure to achieve clinical response; RRI 25%; RR 1.25, 95% CI. 1.01 to 1.54; average of 2.8 point less change on the Mania Rating Scale (95% CI 0.83 to 4.79). There were no significant differences in those withdrawing from the study. Reviewers’ conclusions: There is consistent, if limited, evidence that valproate is an efficacious treatment for acute mania. Valproate may be less efficacious than olanzapine. More, rigorously designed, trials over the full range of acute affective episodes are required.
**Bipolar Disorder**

* Impact of family burden and affective response on clinical outcome among patients with bipolar disorder.

**Authors:** Perlick DA, Rosenheck RA, Clarkin JF, Maciejewski PK, Sirey J, Struening E, Link BG. the Yale University School of Medicine in New Haven, Connecticut.

**Source:** Psychiatr Serv. 2004 Sep;55(9):1029-35

**Summary:** This study evaluated the direct and indirect effects of family burden and affective response on medication adherence and outcome among patients with bipolar disorder. METHODS: Data were examined for 126 patients who were consecutively admitted to the psychiatric service at a university-affiliated hospital and who met research diagnostic criteria for bipolar I or II disorder or for schizoaffective disorder, manic type, and their family caregivers. A total of 101 pairs of patients and family caregivers (80 percent) completed 15 months of study and were included in the analyses. Patients and their identified caregivers were assessed within two weeks of either discharge from the index inpatient admission or initiation of outpatient treatment (baseline assessment). Patients and caregivers were also assessed seven and 15 months after the baseline assessment. Structural equation modeling was used to evaluate caregivers’ influences on patients’ medication adherence seven months after baseline and on clinical outcome 15 months after baseline. RESULTS: The indexes of overall fit for the path model confirmed the a priori measurement model. Significant paths were found from the caregiver’s perceived burden at baseline to the caregiver’s emotional overinvolvement at baseline, from the caregiver’s emotional overinvolvement at baseline to the patient’s medication adherence at the seven month follow-up, and from the patient’s medication adherence at the seven-month follow-up to the patient’s outcome at the 15-month follow-up. The paths from the caregiver’s perceived burden at baseline to the patient’s medication adherence seven months after baseline and the patient’s outcome 15 months after baseline were not significant. CONCLUSIONS: When caregivers of patients with bipolar illness experience a high burden, patient outcome is adversely affected. This relationship is mediated through families’ affective response and patients’ medication adherence.

**Bipolar I Disorder & Olanzapine**

* Use of olanzapine in the treatment of bipolar I disorder

**Authors:** DZ Lieberman & FK Goodwin


**Summary:** Olanzapine (Zyprexa®, Eli Lilly & Co.) is an atypical antipsychotic medication with once-daily dosing that was originally developed for the treatment of schizophrenia. It has shown broad efficacy in the treatment of bipolar mixed and manic episodes, but is less effective in the treatment of bipolar depression. Double-blind studies have demonstrated a rapid onset of action in acute bipolar mania, significantly greater rates of response compared with placebo, and a remission rate of 88.3% in a 49-week open-label study. Diverse presentations of the illness responded well to olanzapine including patients with rapid-cycling bipolar disorder, mixed episodes, as well as psychotic and nonpsychotic manias. Olanzapine monotherapy improved symptoms of depression related to its sedating and appetite-enhancing profile, but core symptoms such as depressed mood did not improve significantly. However, in combination with fluoxetine, bipolar depressed patients responded without an increased risk of mania. Weight gain and sedation are prominent adverse effects, and it has been associated with atherogenic dyslipidemia and glucose intolerance.

**BD & Antidepressants**

* Antidepressants for bipolar depression: a systematic review of randomized, controlled trials.

**Authors:** Gijsman HJ, Geddes JR, Rendell JM, Nolen WA, Goodwin GM. - Scutari Clinic, St. Thomas’ Hospital, Lambeth Palace Rd., London, U.K. harm.gijsman@doctors.net.uk

**Source:** Am J Psychiatry. 2004 Sep;161(9):1537-47

**Summary:** OBJECTIVE: This study reviewed the evidence from randomized, controlled trials on the efficacy and safety of antidepressants in the short-term treatment of bipolar depression. METHOD: The authors performed a systematic review and meta-analysis of randomized, controlled trials. They searched the Cochrane Collaboration Depression, Anxiety, and Neurosis Controlled Trials Register, incorporating results of searches of MEDLINE, EMBASE, CINAHL, PsycLIT, PSYINDEX, and Lilacs. The main outcome measures were the proportion of patients who clinically responded to treatment and the rate of switching to mania. RESULTS: Twelve randomized trials were included, with a total of 1,088 randomly assigned patients. Five trials compared one or more antidepressants with placebo: 75% of these patients were receiving a concurrent mood stabilizer or an atypical antipsychotic. Antidepressants were more effective than placebo. Antidepressants did not induce more switching to mania (the event rate for antidepressants was 3.8% and for placebo, it was 4.7%). Six trials allowed comparison between two antidepressants. The rate of switching for tricyclic antidepressants was 10%, and for all other antidepressants combined, it was 3.2%. CONCLUSIONS: Antidepressants are effective in the short-term treatment of bipolar depression. The trial data do not suggest that switching is a common early complication of treatment with antidepressants. It may be prudent to use a selective serotonin reuptake inhibitor or a monoamine oxidase inhibitor rather than a tricyclic antidepressant as first-line treatment. Given the limited evidence, there is a compelling need for further studies with longer follow-up periods and careful definition and follow-up of emerging mania and partial remission.

**B D & Sted**

* Strategies for improving treatment of bipolar disorder: integration of measurement and management.

**Authors:** Sachs GS.

**Source:** Acta Psychiatr Scand Suppl. 2004 Sep;(422):7-17

**Summary:** Bipolar disorder is a common and complex condition associated with high rates of disability and high health care costs. The aim of this article is to provide an
overview of the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). Method: The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) was conceived in response to an NIMH request for proposals to study the effectiveness of treatments for Bipolar Disorder. Aspects of this program have been adapted and enriched for presentation in this paper. Result: Designed for implementation in routine practice across a variety of settings, STEP-BD offers a disease management program in which standardized assessments are linked to critical decision points in clinical management pathways. Conclusion: This paper describes strategies used in STEP-BD to improve the treatment of Bipolar disorder: a simple conceptual model, which integrates assessments and management, and several specialized elements, used in the STEP-BD assessment package.

**BD & New Medication**

* New medication treatment options for bipolar disorders.

**Authors**: Ketter TA, Wang PW, Nowakowska C, Marsh WK. - Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, California, USA

**Source**: Acta Psychiatr Scand Suppl. 2004 Sep;(422):18-33

**Summary**: Objective: To assess new treatment options for bipolar disorders. Method: Controlled studies of new treatments for bipolar disorders were identified by computerized searches and reviews of scientific meeting proceedings, and were compiled by drug category. Results: Two main categories of medications, newer anticonvulsants and newer antipsychotics, are yielding emerging new treatment options for bipolar disorders. Newer anticonvulsants have diverse psychotropic profiles, and although not generally effective for acute mania, may have utility for other aspects of bipolar disorders (e.g. lamotrigine for maintenance or acute bipolar depression), or for comorbid conditions (e.g. gabapentin for anxiety or pain, topiramate for obesity, bulimia, alcohol dependence, or migraine, and zonisamide for obesity). In contrast, newer antipsychotics generally appear effective for acute mania, and some may ultimately prove effective in acute depression (e.g. olanzapine combined with fluoxetine, quetiapine) and maintenance (e.g. olanzapine). Conclusion: Emerging research is yielding new treatment options for bipolar disorders and comorbid conditions.

**BD & Psychological Interventions**

* Psychological interventions in bipolar disorder: From wishful thinking to an evidence-based approach.

**Authors**: Vieta E, Colom F. - Bipolar Disorders Program, Hospital Clinic, University of Barcelona, IDIBAPS, Stanley Medical Research Center, Barcelona, Spain.

**Source**: Acta Psychiatr Scand Suppl. 2004 Sep;(422):34-8

**Summary**: Objective: We aimed to examine the historical and current relevance of psychosocial approaches to bipolar illness by conducting a systematic review of prospective studies assessing the effectiveness of psychological interventions for bipolar disorder. Method: A systematic literature search was conducted using EMBASE, MedLine and PsychLIT and reference sections of papers were scrutinized for further relevant reports. Only four trials met the criteria of a prospective study and achieved the necessary methodological standards. Results: The studies showed benefits for patients in terms of relapse prevention and the reduction of hospitalization rates. Psychoeducation (delivered in groups or as part of a family intervention) and cognitive behavioural therapy were also found to be effective prophylactic treatments for bipolar disorder in medicated patients. Other interventions do not appear to be supported by sufficient evidence. Conclusion: Psychological approaches, and particularly psychoeducation and cognitive-behavioural therapies, are evidence-based prophylactic therapies for bipolar patients receiving pharmacotherapy. They should be used as adjuncts to medication where possible in the prevention of bipolar disorder.

**BD & Scale Matters**

* Scale matters: the need for a Bipolar Depression Rating Scale (BDRS).

**Authors**: Berk M, Malhi GS, Mitchell PB, Cahill CM, Carman AC, Hadzi-Pavlovic D, Hawkins MT, Tohen M. - Barwon Health and The Geelong Clinic, Geelong, Australia.


**Summary**: Objective: To briefly review the clinical and biological distinctions between unipolar and bipolar depression critiquing in particular currently available depression rating scales and discuss the need for a new observer-rated scale tailored to bipolar depression. Method: Relevant literature pertaining to the symptomatic differences between bipolar disorder and unipolar disorder as well as their measurement using existing assessment scales was identified by computerized searches and reviews of scientific journals known to the authors. Results: Bipolar depression is distinct from unipolar depression in terms of phenomenology and clinical characteristics. These distinguishing features can be used to identify bipolarity in patients that present with recurrent depressive episodes. This is important because current self-report and observer-rated scales are optimized for unipolar depression, and hence limited in their ability to accurately assess bipolar depression. Conclusion: The development of a specific bipolar depression rating scale will improve the assessment of bipolar depression in both research and clinical settings and assist the development of better treatments and interventions.

**Bipolaroids**

* Bipolaroids: functional imaging in bipolar disorder.

**Authors**: Malhi GS, Lagopoulos J, Owen AM, Yatham LN. - School of Psychiatry, The University of New South Wales, Australia

**Source**: Acta Psychiatr Scand Suppl. 2004 Sep;(422):46-54

**Summary**: Objective: To evaluate the literature pertaining to the use of functional magnetic resonance imaging (fMRI) in bipolar disorder research. Method: A search for papers published in English in journals from 1984 onwards was conducted using MedLine and EMBASE with the following terms: functional neuroimaging or fMRI and depression or bipolar disorder. In addition, retrieved papers and literature known to the authors was also scrutinized for further relevant reports. Results: The research findings from 26 articles are tabulated and the results from 10 articles dealing specifically with bipolar disorder are discussed in detail. Conclusion: fMRI
is a useful tool for investigating bipolar disorder. Preliminary studies point to trait and state abnormalities involving structures known to be associated with the generation and modulation of emotion. The patterns of FMRI activation are different to those found in healthy subjects and patients with major depression. FMRI studies are likely to provide valuable insights into the pathophysiology of bipolar disorder.

**Post Natal Depression (PND & PPD)**

**Oestrogens and Progestogens for Preventing and Treating Postnatal Depression**

*Authors*: Lawrie TA, Henxheimer A, Dalton K


*Summary*: A substantive amendment to this systematic review was last made on 13 January 1999. Cochrane reviews are regularly checked and updated if necessary. Background: Postnatal depression, with a prevalence of at least 10%, is probably the most common complication of the puerperium. A deficiency or imbalance of sex hormones has repeatedly been suggested as a cause. Objectives: The objective of this review was to evaluate the role of oestrogens and progestogens in the prevention and treatment of postnatal depression. Search strategy: The register of clinical trials maintained and updated by the Cochrane Pregnancy and Childbirth Group and the Cochrane Pregnancy and Childbirth Group were searched. Contact was made with pharmaceutical companies and experts in the field. Selection criteria: All trials were considered in which women with depression in the first six months postpartum were randomised to receive antidepressants alone or in combination with another treatment, or to receive any other treatment including placebo. Data collection and analysis: Data was extracted independently from the trial reports by the reviewers. Missing information was requested from investigators wherever possible. Data was sought to allow an "intention to treat" analysis. Main results: Only one trial could be included in this review, leaving most of the objectives of the review unfulfilled. Appleby et al (1997) reported that Fluoxetine was significantly more effective than placebo and, after an initial session of counselling, as effective as a full course of cognitive-behavioural counselling in the treatment of postnatal depression. There was no interaction between medication and counselling. Reviewers’ conclusions: Women with postnatal depression can be effectively treated with fluoxetine, which is as effective as a course of cognitive-behavioural counselling in the short-term. However, more trials with a longer follow-up period are needed to compare different antidepressants in the treatment of postnatal depression, and to compare antidepressant treatment with psychosocial interventions. This is an area that has been neglected despite the large public health impact described above.

**Antidepressant Treatment for Postnatal Depression**

*Authors*: Hoffbrand S, Howard L, Crawley H


*Summary*: A substantive amendment to this systematic review was last made on 12 January 2001. Cochrane reviews are regularly checked and updated if necessary. Background: Postnatal depression is a common disorder, which can have profound short and long term effects on maternal morbidity, the new infant and the family as a whole. Social factors appear to be particularly important in the aetiology and prognosis of postnatal depression, and treatment is often largely social support and psychological interventions. It is not known whether antidepressants are an effective and safe choice for treatment of this disorder. Objectives: To evaluate the effectiveness of different antidepressant drugs and compare their effectiveness with other forms of treatment. To assess any adverse effects of antidepressants in the mother or the nursing baby. Search strategy: The registers of clinical trials maintained and updated by the Cochrane Depression, Anxiety and Neurosis Group and the Cochrane Pregnancy and Childbirth Group were searched. Data collection and analysis: Data was extracted independently from the trial reports by the reviewers. Missing information was requested from investigators wherever possible. Main results: Only one trial could be included in this review, leaving most of the objectives of the review unfulfilled. Appleby et al (1997) reported that Fluoxetine was significantly more effective than placebo and, after an initial session of counselling, as effective as a full course of cognitive-behavioural counselling in the treatment of postnatal depression. There was no interaction between medication and counselling. Reviewers’ conclusions: Women with postnatal depression can be effectively treated with fluoxetine, which is as effective as a course of cognitive-behavioural counselling in the short-term. However, more trials with a longer follow-up period are needed to compare different antidepressants in the treatment of postnatal depression, and to compare antidepressant treatment with psychosocial interventions. This is an area that has been neglected despite the large public health impact described above.
from 1966 to 2003. The search terms used were postpartum/postnatal depression and randomized controlled/clinical trials. Published peer-reviewed articles in English from 1990 to 2003 were included in the review, although select earlier studies were also included based on good methodological quality and/or the absence of more recent work. METHOD: The criteria used to evaluate the interventions were based on the standardized methodology developed by the U.S. Preventive Services Task Force and the Canadian Task Force on Preventive Health Care. RESULTS: Twenty-one studies that met inclusion criteria were examined. These studies included interpersonal psychotherapy, cognitive-behavioral therapy, peer and partner support, nondirective counseling, relaxation/massage therapy, infant sleep interventions, infant-mother relationship therapy, and maternal exercise. Although some of these interventions have been better studied for depression unrelated to childbirth, methodological limitations render their efficacy equivocal for postpartum depression. CONCLUSIONS: Definite conclusions cannot be reached about the relative effectiveness of most of the nonbiological treatment approaches due to the lack of well-designed investigations. Randomized controlled trials are needed to compare different treatment modalities, examine the effectiveness of individual treatment components, and determine which treatments are most useful for women with different risk factors or clinical presentations of postpartum depression.

**PPD & Treatment**

**Postpartum Depression Recurrence Versus Discontinuation Syndrome: Observations From A Randomized Controlled Trial.**

**Authors:** Sunder KR, Wisner KL, Hanusa BH, Perel JM. Departments of Psychiatry (Drs. Sunder and Wisner), Obstetrics and Gynecology and Reproductive Sciences, and Epidemiology (Dr. Wisner), and Women’s Behavioral HealthCARE, Western Psychiatric Institute and Clinic, University of Pittsburgh Medical Center (Drs. Sunder, Wisner, and Perel); and the Center for Research on Health Care, Division of General Medicine, Department of Medicine, University of Pittsburgh (Dr. Hanusa), Pittsburgh, Pa.

**Source:** J Clin Psychiatry. 2004 Sep;65(9):1266-1268.

**Summary:** To differentiate characteristics of a discontinuation syndrome from a recurrence of major depressive disorder in the context of a randomized trial. METHOD: We performed a randomized clinical trial to compare the efficacy of sertraline versus placebo for the prevention of recurrent postpartum DSM-IV major depressive disorder, when first depressive episode did not recur in the initial 17-week active treatment trial were followed through the taper phase (weeks 18-20). At week 17, 3 women assigned to placebo and 8 assigned to sertraline remained in the trial. Nine symptoms that characterize discontinuation syndrome were extracted from the 25-item Asberg Rating Scale for Side Effects (ASE) and assessed weekly during the taper phase. The 21-item Hamilton Rating Scale for Depression was used to evaluate depressive symptoms. RESULTS: In the taper phase, there were no significant differences between the sertraline- and placebo-treated women on the sum of the ASE-derived symptoms. Both groups had low levels of symptoms on the ASE during the weeks of taper. None of the 3 women assigned to placebo and 2 of the 8 women assigned to sertraline suffered a depressive recurrence within 6 weeks of the end of the study.

**CONCLUSIONS:** A gradual taper of sertraline (75 mg) over 3 weeks did not lead to discontinuation syndrome; however, the systematic dissection of symptoms resulted in our conclusion that the duration of preventive therapy should be extended to 26 weeks (about 6 months) in subsequent randomized trials, consistent with the treatment guidelines for a single episode of depression.

**PPD, PAROXETINE & CBT**

**The Use of Paroxetine and Cognitive-Behavioral Therapy in Postpartum Depression and Anxiety: A Randomized Controlled Trial.**

**Authors:** Misri S, Reebye P, Corral M, Mills L. - Department of Psychiatry (Drs. Misri, Reebye, and Corral) and the Department of Obstetrics and Gynecology (Dr. Misri), Faculty of Medicine, University of British Columbia and Reproductive Mental Health Programs, St. Paul’s Hospital and BC Women’s Hospital and Health Centre (Drs. Misri and Corral and Ms. Mills), Vancouver, British Columbia, Canada.

**Summary:** While postpartum depression is a major health issue for many women from diverse cultures, this affective condition often remains undiagnosed and untreated. The objective of this article is to critically review the literature to determine the current state of scientific knowledge related to the treatment of postpartum depression from a biological perspective. METHOD: Databases searched for this review included MEDLINE, PubMed, CINAH, PsycINFO, EMBASE, ProQuest, the Cochrane Library, and the WHO Reproductive Health Library from 1966 to 2003. The search terms used were postpartum/postnatal depression and randomized controlled/c clinical trials in various combinations. Published peer-reviewed articles in English from 1990 to 2003 were chosen for review, although select earlier studies were also included based on good methodological quality and/or the absence of more recent work. The criteria used to evaluate the interventions were based on the standardized methodology developed by the U.S. Preventive Services Task Force and the Canadian Task Force on Preventive Health Care. RESULTS: Nine studies that met study criteria were examined. The interventions studied included antidepressant medication, estrogen therapy, critically timed sleep deprivation, and bright light therapy. Although some of these interventions have been better studied for depression unrelated to childbirth, methodological limitations render their efficacy equivocal for postpartum depression with limited strong evidence available to guide practice or policy recommendations. CONCLUSIONS: Despite the recent upsurge of interest in this area, many questions remain unanswered, resulting in diverse research implications. In view of the lack of randomized controlled trials, psychiatrists who are experts in the treatment of postpartum mood disorders have developed consensus guidelines. These guidelines will require regular updating as better and stronger evidence emerges.
These data suggest that PPD may be associated with unique alterations in serotonergic function that are specific to the puerperium.

**PPD & Serotonergic Function**

* Alterations in platelet serotonin transporter binding in women with postpartum onset major depression.

**Source:** J Clin Psychiatry. 2004 Sep;65(9):1236-1241

**Summary:** Approximately 10% to 16% of women experience a major depressive episode after childbirth. A significant proportion of these women also suffer from comorbid anxiety disorders. The purpose of this study was to evaluate whether the addition of cognitive-behavioral therapy (CBT) to standard antidepressant therapy offers additional benefits in the treatment of postpartum depression with comorbid anxiety disorders. METHOD: Thirty-five women referred to a tertiary care hospital outpatient program with a DSM-IV diagnosis of postpartum depression with comorbid anxiety disorder were randomly assigned to 1 of 2 treatment groups-paroxetine-only monotherapy group (N = 16) or paroxetine plus 12 sessions of CBT combination therapy group (N = 19)-for a 12-week trial. Progress was monitored by a psychiatrist blinded to treatment group, using the Hamilton Rating Scale for Depression, Hamilton Rating Scale for Anxiety, Yale-Brown Obsessive Compulsive Scale, Clinical Global Impressions scale, and Edinburgh Postnatal Depression Scale. Data were analyzed using 2-tailed statistical tests at an alpha level of .05. The study was conducted from April 1, 2002, to June 30, 2003.

**RESULTS:** Both treatment groups showed a highly significant improvement (p < .01) in mood and anxiety symptoms. Groups did not differ significantly in week of recovery, dose of paroxetine at remission, or measures of depression, anxiety, and obsessive-compulsive symptoms at outcome.

**CONCLUSION:** Antidepressant monotherapy and combination therapy with antidepressants and CBT were both efficacious in reducing depression and anxiety symptoms. However, in this sample of acutely depressed/ anxious postpartum women, there were no additional benefits from combining the 2 treatment modalities. Further research into the efficacy of combination therapy in the treatment of moderate-to-severe depression with comorbid disorders in postpartum women is recommended.

**Women Mental Health (WMH)**

* Breastfeeding During Maternal Antidepressant Treatment With Serotonin Reuptake Inhibitors: Infant Exposure, Clinical Symptoms, and Cytochrome P450 Genotypes.

**Authors:** Berle Jy J, Steen VM, Aamo TO, Breilid H, Zahlisen K, Spigset O. - Centre for Child and Adolescent Mental Health (Dr. Berle) and the Dr. Einar Martens Research Group for Biological Psychiatry and Locus on Neuroscience, Center for Medical Genetics and Molecular Medicine (Drs. Steen and Breilid), University of Bergen, Bergen; the Center for Medical Genetics and Molecular Medicine, Haukeland University Hospital, Bergen (Drs. Steen and Breilid); and the Department of Clinical Pharmacology, St. Olav’s University Hospital, Trondheim (Drs. Aamo, Zahlisen, and Spigset), Norway.

**Source:** J Clin Psychiatry. 2004 Sep;65(9):1228-1234

**Summary:** The aims of the study were to quantify the drug exposure in breastfed infants of antidepressant-treated mothers, to identify possible adverse events, and to correlate these variables to maternal and infant drug metabolism-relevant genotypes and milk triglyceride content. METHOD: The study included 25 lactating women treated with citalopram (N = 9), sertraline (N = 6), paroxetine (N = 6), fluoxetine (N = 1), or venlafaxine (N = 3) and their 26 breastfed infants. Drug concentrations in maternal and infant serum and milk were analyzed using liquid chromatography mass spectrometry methods; milk triglyceride levels were measured with a commercial kit. Cytochrome P450 (CYP) 2D6 and CYP2C19 activity was determined by polymerase chain reaction-based genotyping of the mothers and infants. An infant adverse event questionnaire was completed by the medication-treated mothers as well as by a control group of medication-free breastfeeding mothers of 68 infants. RESULTS: Sertraline and paroxetine were not detected in any of the drug-exposed infants. The infant serum level of citalopram was either undetectable (N = 4) or low (N = 6). All venlafaxine-exposed infants had measurable drug concentrations. We identified a paroxetine-treated mother and her infant who were both CYP2D6 poor metabolizers, as well as a citalopram-treated mother with CYP2C19 poor metabolizer status, but the serum drug levels of their infants were still either undetectable (paroxetine) or low (citalopram). There was no evidence of adverse events in the drug-exposed infants. CONCLUSION: Serum drug levels in breastfed infants of antidepressant-treated mothers were undetectable or low. This study adds further evidence to previously published data indicating that breastfeeding should not be generally discouraged in women using serotonin reuptake inhibitor anti-depressants.
Department of Woman and Child Health, Karolinska Institutet, Stockholm, Sweden. Louise.Seimyr@kbh.ki.se

Summary: To study the period and point prevalence of maternal depressive mood at three occasions before and after childbirth, and the relationship to the parents’ psychosocial conditions and experiences of parenthood during the first year after childbirth. In a longitudinal community-based study, 434 pregnant women were invited to complete the Edinburgh Postnatal Depression Scale (EPDS) (cut-off score 9/10) at three time points. The parents’ psychosocial conditions and experiences of parenthood were enquired at two months and at one year after childbirth, when the form Experience of Motherhood/Fatherhood Questionnaire (EMQ/EFQ) was applied. Three times measurement responses from both men and women were analyzed using non-parametric statistical methods and path-analysis. About 75% of the parents responded to the questionnaires. The period prevalence was 28%, and the point prevalence found on the three time points was EPDS I 21%, EPDS II 17% and EPDS III 12%. Correlations between antenatal and postnatal depressive symptoms were found, r = 0.61 and r = 0.45, respectively. Women, who experienced financial worries, lack of social support and losses and strains after childbirth showed more symptoms of depressed mood. The maternal depressive mood influenced negatively on breastfeeding and experiences of motherhood, but not on experiences of fatherhood. The partners of depressed women were neither more involved in childcare nor did they utilize paternal leave more than the other men. Both men and women reported the sexual life as negatively influenced by the women’s depressed mood.

Depression & Sex Hormones In Elderly Women

* Depression and sex hormones in elderly women.

Authors: Erdincler D, Bugay G, Ertan T, Eker E. - Geriatric Unit of the Internal Medicine Department, Cerrahpas? a Medical School, Istanbul University, Istanbul, Turkey.

Source: Arch Gerontol Geriatr. 2004 Nov-Dec;39(3):239-44

Summary: We aimed to study the relation between sex hormones and depression among elderly women. The study was carried out on 74 volunteered female subjects above 60 years of age. Each subject was asked to fulfill the geriatric depression scale (GDS) questionnaire and further evaluated for clinical depression by a psychiatrist using the DSM IV diagnostic criteria. For statistical analysis, subjects were later divided in two groups, according to the presence of clinical depression. Cognitive functions were assessed with the standardized mini mental test (SMMT). Disability in the activities of daily living was assessed with instrumental activities of daily living (IADL) scale. Plasma levels of estrogen, testosterone, progesterone, and dehydroepiandrosterone sulfate (DHEA-S) were measured with chemiluminescent methods, and plasma levels of androstenediolone were measured with radioimmunosassay. Among 74 subjects, 34 (39%) had clinical depression. Age, number of years spent in education, SMMT scores, and IADL scores did not differ between the depressive and non-depressive groups. Plasma sex hormone levels were not found to be different between the two groups.

Emotional Problems & Low Gestational Age

* Behavioral and emotional adjustment of teenagers in mainstream school who were born before 29 weeks' gestation.

Authors: Gardner F, Johnson A, Yudkin P, Bowler U, Hockley C, Mutch L, Wariyar U. Extremely Low Gestational Age Steering Group. - University of Oxford, Department of Social Policy and Social Work, 32 Wellington Square, Oxford, OX1 2ER, United Kingdom. francies.gardner@socres.ox.ac.uk

Source: Pediatrics. 2004 Sep;114(3):676-82

Summary: To investigate behavioral and emotional problems and positive adjustment of 15-to 16-year-olds who were born at extremely low gestational age (ELGA), from the perspective of parents, teachers, and teenagers. METHODS: Prospective follow-up was conducted of birth cohorts, with classroom control subjects. All infants who were born before 29 weeks in 1983-1984 (mean gestational age: 27 weeks) to mothers who resided in 3 regions of the United Kingdom were studied. A total of 82% (179 of 218) of survivors were traced at age 15 to 16. The 150 in mainstream school were compared with age- and gender-matched classroom control subjects (n = 108). Behavioral and emotional problems, delinquency, peer relations, self-esteem, and hobbies, were assessed by standardized, well-validated instruments, including the Strengths and Difficulties Questionnaire, administered by mail to parents, teenagers, and teachers. RESULTS: Parents were more likely to rate ELGA teenagers than control subjects as in the “abnormal” range for hyperactivity (8% vs 1%; difference: 7%; 95% confidence interval [CI]: 2-12), peer relationship problems (19% vs 5%; difference: 14%; 95% CI: 6-21), and emotional problems (18% vs 7%; difference: 11%; 95% CI: 3-19), but not conduct problems (10% vs 5%; difference: 5%; 95% CI: -1 to 12). Teachers reported a similar pattern. In contrast, compared with control subjects, ELGA teenagers did not rate themselves as having more problems with peers, hyperactivity, conduct, depression, or low self-esteem. They reported more emotional problems but less delinquency, alcohol, cannabis, and other drug use. CONCLUSIONS: Compared with mainstream classmates, children who are born extremely early continue to have higher levels of parent- and teacher-reported emotional, attentional, and peer problems well into their teens. However, despite these problems, they do not show signs of more serious conduct disorders, delinquency, drug use, or depression.

Post-Miscarriage Psychiatric Morbidity

* Screening for post-miscarriage psychiatric morbidity.

Authors: Lok IH, Lee DT, Yip SK, Shek D, Tam WH, Chung TK. - Department of Obstetrics and Gynecology, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong SAR, China. ingridlok@cuhk.edu.hk


Summary: The purpose of this study was to evaluate 12-item General Health Questionnaire (GHQ-12) in screening for psychiatric morbidity after miscarriage. STUDY DESIGN: A prospective cohort study was carried out involving 222 patients. Six weeks after miscarriage, the GHQ-12 was applied. Psychiatric “case” or “non-case” was diagnosed by the psychiatrist with use of the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders-III-R.
The patients were computer randomized into Groups A or B. A receiver operating characteristic (ROC) curve was constructed for Group A. The optimal cutoff value of GHQ-12 was determined, and this value was applied to Group B. The test characteristics were assessed. RESULTS: Twenty-seven patients were found to be psychiatric cases. An ROC with area under curve of 0.93 (95% CI 0.87-0.99, P<.001) was constructed. The best GHQ-12 cutoff score was > or =4 in detecting psychiatric caseness. A sensitivity of 83%, specificity of 90%, positive predictive value of 50%, and negative predictive value of 98% were obtained. CONCLUSION: GHQ-12 is an effective screening tool in detecting psychiatric morbidity after miscarriage.

**Maternal Depression & Offspring Dysfunction**

* Psychiatric disorders among offspring of depressed mothers: associations with paternal psychopathology.

**Authors:** Marmorstein NR, Malone SM, Iacono WG. Department of Psychology, Rutgers University, 311 N. 5th St., Camden, NJ 08102. marmorst@camden.rutgers.edu

**Source:** Am J Psychiatry. 2004 Sep;161(9):1588-94

**Summary:** OBJECTIVE: The association between maternal depression and offspring dysfunction is well documented; however, little attention has been paid to psychopathology in the partners of these depressed mothers or to how paternal psychopathology might influence the relationship between maternal depression and offspring dysfunction. The purpose of this study was to explore whether major depression and/or antisocial behavior tended to occur more frequently among partners of depressed mothers (compared to partners of nondepressed mothers) and to examine how these paternal disorders related to offspring psychopathology. METHOD: Participants were drawn from the Minnesota Twin Family Study, a community-based study of twins and their parents. Depressed and nondepressed mothers, their partners (the biological fathers of the twins), and their 17-year-old offspring were included. Structured interviews were used to assess participants for the presence of major depression, conduct disorder, and adult antisocial behavior. RESULTS: Depressed mothers tended to partner with antisocial fathers. Depression in mothers and antisocial behavior in fathers were both significantly and independently associated with offspring depression and conduct disorder. No interactions of the parental diagnoses with each other or with the gender of the offspring were found. CONCLUSIONS: Many offspring of depressed mothers experience the additional risk of having an antisocial father. The implications of these findings for risk among the offspring of depressed mothers are discussed.

**Children & Adolescent Mental Health (CAMH)**

**Tricyclic Drugs, Depression, Children & Adolescents**

* Tricyclic drugs for depression in children and adolescents

**Authors:** Hazell P, O’Connell D, Heathcote D, Henry D


**Summary:** A substantive amendment to this systematic review was last made on 26 February 2002. Cochrane reviews are regularly checked and updated if necessary. Background: There is a need to identify effective and safe treatments for depression in children and adolescents. While tricyclic drugs are effective in treating depression in adults, individual studies involving children and adolescents have been equivocal. Objectives: To assess the effects of oral tricyclic antidepressants compared to placebo in the treatment of child and adolescent depression.

**Tricyclic Drugs, Depression, Children & Adolescents**

* Treatment retention among


**Summary:** A substantive amendment to this systematic review was last made on 26 February 2002. Cochrane reviews are regularly checked and updated if necessary. Background: There is a need to identify effective and safe treatments for depression in children and adolescents. While tricyclic drugs are effective in treating depression in adults, individual studies involving children and adolescents have been equivocal. Objectives: To assess the effects of oral tricyclic antidepressants compared to placebo in the treatment of child and adolescent depression.

Search strategy: We searched MEDLINE (1966-1997), EMBASE, Excerpta Medica (June 1974-1997), the Cochrane Collaboration Depression, Anxiety and Neurosis Group trials register (most recent search 25/11/2000) and bibliographies of previously published reviews and papers describing original research were cross-checked. Current Contents was screened for recent publications. We contacted authors of relevant abstracts in conference proceedings of the American Academy of Child and Adolescent Psychiatry, and we hand searched the Journal of the American Academy of Child and Adolescent Psychiatry (1978-1999). Selection criteria: Randomised controlled trials comparing the efficacy of orally administered tricyclic medication with placebo in depressed people aged 6-18 years.

Data collection and analysis: Most studies reported multiple outcome measures including depression scales and clinical global impression scales. For each study the best available depression measure was taken as the index measure of depression outcome. Predetermined criteria were established to assist in the ranking of measures. Where authors reported categorical outcomes we calculated individual and pooled odds ratios for the odds of improvement in treated compared with control subjects. For continuous outcomes pooled effect sizes were calculated as the number of standard deviations by which the change in depression scores for the treatment group exceeded those for the control groups.

Main results: Thirteen trials (involving 506 participants) were included. No overall improvement with treatment compared to placebo was seen for children or adolescents (odds ratio = 0.84, 95% confidence interval 0.56 to 1.25). A statistically significant but small benefit of treatment over placebo was seen in reducing symptoms (effect size (standardised mean difference) = -0.31, 95% confidence interval -0.62 to -0.01).

Subgroup analyses suggest a larger benefit among adolescents (effect size = -0.47, 95% confidence interval -0.92 to -0.02), and no benefit among children (effect size = 0.15, 95% confidence interval -0.34 to 0.64). Treatment with a tricyclic antidepressant caused more vertigo (odds ratio = 4.38, 95% confidence interval 2.33 to 6.25), orthostatic hypotension (odds ratio = 6.78, 95% confidence interval 2.06 to 22.26), tremor (odds ratio 6.29, 95% confidence interval 1.78 to 22.17) and dry mouth (odds ratio = 5.17, 95% confidence interval 2.68 to 29.99) than did placebo, but no statistically significant difference was found for other possible adverse effects.

Reviewers’ conclusions: Data suggest tricyclic antidepressants are not useful in treating depression in prepubertal children. There is marginal evidence to support the use of tricyclic antidepressants in the treatment of depression in adolescents, although the magnitude of effect is likely to be moderate at best.
Children entering a new episode of mental health care.

**Authors:** Harpaz-Rotem I, Leslie D, Rosenheck RA. - Department of Psychiatry of Yale University School of Medicine, 25 Park Street, Suite 617, New Haven, Connecticut 06519. Ilan. harpaz-rotem@yale.edu

**Source:** Psychiatr Serv. 2004 Sep;55(9):1022-8

**Summary:** This study examined use of mental health services among children and adolescents with private insurance who were entering treatment. Variations in service use were examined by age, gender, diagnosis, recent psychiatric hospitalization, and type of insurance. Differences between children who received treatment from mental health professionals and those who were treated by primary care physicians were also examined. METHODS: Drawn from a large database, the sample comprised 11,659 new users of mental health services. Service use was defined as the total number of days children were retained in treatment and the total number of mental health contacts recorded. RESULTS: The overall mean number of visits within a six-month period was 3.9. The average duration of treatment was 75.36 days. Children who were treated by a mental health specialist were less likely to drop out of treatment and had a larger number of visits. Severity of illness, psychiatric hospitalization, and managed care insurance coverage were also associated with lower risk of dropout and greater intensity of care. CONCLUSIONS: Children's access to services does not guarantee sustained involvement in treatment. To more fully address the nature of service use among children, a closer look at specific barriers to continued involvement in services is needed.

Behavioral Health Disorders

*Diagnosis and treatment of behavioral health disorders in pediatric practice.*

**Authors:** Williams J, Klinepeter K, Palmes G, Pulley A, Foy JM. - Department of Pediatrics, Wake Forest University Health Sciences, Winston-Salem, North Carolina 27157-1060, USA. janewill@wfubmc.edu

**Source:** Pediatrics. 2004 Sep;114(3):601-6

**Summary:** There has been a strong push toward the recognition and treatment of children with behavioral health problems by primary care pediatricians. This study was designed to assess the extent to which a sample of primary care pediatricians diagnose and treat behavioral health problems and to identify factors that may contribute to their behavioral health practice. METHODS: A standard interview was conducted with 47 pediatricians who work in primary care settings in a predominantly urban setting in North Carolina. Pediatricians' responses to questions about the estimated percentage of children in their practice with a behavioral health disorder, tools used to make diagnoses, frequent and infrequent diagnoses made, comfort level with making a diagnosis, reasons for not making a diagnosis, use of psychotropic medications, types of nonmedication interventions provided, educational background, and needs involving behavioral health issues were evaluated. RESULTS: Pediatricians estimated that the average percentage of children in their practices with a behavioral health disorder was 15%. The study did not find significant differences in perceptions related to time in practice or gender of the pediatric provider. The most frequent behavioral health diagnosis was attention-deficit/hyperactivity disorder (ADHD), and the majority incorporated behavioral questionnaires, expressed a high level of comfort with the diagnosis, and frequently or occasionally prescribed stimulants. Variability was noted in both practice and comfort for other behavioral health disorders. Slightly fewer than half of the pediatricians frequently diagnosed anxiety and depression. Those who make these diagnoses commonly incorporated questionnaires and reported frequent or occasional use of selective serotonin reuptake inhibitors. Comfort in making the diagnosis of anxiety was highly associated with use of selective serotonin reuptake inhibitors. The vast majority (96%) of pediatricians provided nonmedication interventions, including supportive counseling, education for coping with ADHD, behavior modification, and/or stress management. Diagnosis and treatment of severe behavioral health disorders were infrequent throughout the pediatric practices. Areas of greatest educational interest included psychopharmacology, diagnosis and treatment of depression and anxiety, and updates on ADHD. The majority of pediatric providers did not identify a need for education about several high-prevalence disorders that they do not frequently diagnose or treat, including conduct disorder and substance abuse. CONCLUSIONS: Pediatricians in this sample frequently diagnosed and treated ADHD. For all other behavioral health disorders, pediatricians reported variability in both comfort and practice. They frequently provided both pharmacologic and nonpharmacologic treatments for children and adolescents with mild to moderate behavioral health disorders but not for severe disorders. Although they identified needs for additional education for anxiety and depression, the majority did not identify educational needs for several high-prevalence behavioral health disorders, including conduct disorder and substance abuse.

Methylin & ADHD

*Methylin Chewable Tablets and Methylin Oral Solution for Treatment of Attention Deficit Hyperactivity Disorder Launched in US ATLANTA, GA --September 7, 2004

**Authors:** Alliant Pharmaceuticals, Inc., a leading pediatric specialty pharmaceutical company

**Source:** InView Communications

**Summary:** Alliant Pharmaceuticals, Inc., a leading pediatric specialty pharmaceutical company, today announced FDA approval of Methylin Chewable Tablets and Methylin Oral Solution for the treatment of ADHD. The two products are the first, and only, chewable tablet and oral solution for ADHD to gain FDA acceptance. Compliance with any medical therapy is important. With children, the issue is pronounced, as swallowing pills can be a significant problem. Says Dr. Lyndon Waugh, M.D., Clinical Assistant Professor of Child and Adolescent Psychiatry at Emory University, "The release of this effective, well established medication for ADHD in liquid and chewable tablet form will allow physicians another alternative to carefully fine-tune a dosing strategy for each individual patient. And, it will help diminish family conflict and the child's anxiety when they have difficulty swallowing capsules or tablets." Currently 26% of the total population has difficulty in swallowing tablets and capsules. This percentage is considered to be higher in the pediatric patient population.
ADHD is a disorder of the brain in which the individual repeatedly exhibits inappropriate impulsivity and/or inattention. According to the Attention Deficit Disorder Association, an estimated 3 to 7 percent of school-age children, and an estimated 4 percent of adults suffer from ADHD. The Attention Deficit Disorder Association was instrumental in convincing the U.S. Senate to sign a resolution designating September 7, 2004, "National Attention Deficit Disorder Awareness Day" in hopes of better educating the public about ADHD.

"As with any medication, compliance is critical," adds Mark Pugh, President and CEO of Alliant Pharmaceuticals. "Methylphenidate Chewable Tablet and Methylphenidate Oral Solution were designed specifically to help improve efficacy in treatment." Mr. Pugh adds that Alliant plans to release additional products to help treat ADHD in the hopes of better educating the public about ADHD.

Pugh, President and CEO of Alliant Pharmaceuticals, said that Alliant plans to release additional products designed specifically to help improve efficacy in treatment. Mr. Pugh adds that Alliant plans to release additional information on these products at the upcoming American Academy of Child and Adult Psychiatry meeting October 20 - 23rd in Washington, D.C.

Methylphenidate Chewable Tablets are available in a 2.5 mg, 5 mg and 10 mg dose. The Methylphenidate Oral Solution is available in a 5 mg / 5 mL and 10 mg / 5 mL dose.

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**Children & Behavioral Health Disorders**

*Pediatricians Treating More Children With Behavioral Health Disorders*

**Authors:** WINSTON-SALEM, NC -- September 7, 2004

**Source:** Wake Forest University Baptist Medical Center

**Summary:** Pediatricians are diagnosing and treating a growing number of children with behavioral health problems. However, they do not always feel comfortable or sufficiently trained to fill this new role, according to a study from Wake Forest University Baptist Medical Center. The study involved interviews with community pediatricians who estimated that an average of about 15 percent of the children they see have behavioral health problems, said Jane Williams, Ph.D., lead author of the study. The report was published in the September issue of Pediatrics.

Attention Deficit Hyperactivity Disorder (ADHD) is the most common behavioral health disorder seen by pediatricians, she said. The pediatricians "expressed a high level of comfort with the diagnosis and frequently or occasionally prescribed stimulants" to treat it. But when a child is suffering from anxiety or depression, the pediatricians felt they were on shakier grounds. Fewer than half the pediatricians said they diagnosed anxiety and depression frequently. Those that did typically used questionnaires in making the diagnosis and prescribed drugs from a class that includes Prozac, Zoloft and Paxil. The study found a "strong interest in diagnosing and treating behavioral health disorders within their perceived limits and level of comfort." Williams and her Wake Forest Baptist colleagues reported. "They were very concerned about the correctness of these diagnoses and consider the impact on both the child and family." The researchers said pediatricians are treating more children with psychiatric problems in part because of chronic underfunding of the public mental health system. Only about 2 percent of the children who need treatment are seen by mental health specialists. In fact, the diagnosis and treatment of ADHD has shifted primarily to pediatricians, the results showed. "The diagnosis of anxiety and depression appeared to be shifting more gradually to pediatric providers," Williams said. But many pediatricians felt they were not prepared in medical school and their residency training programs to treat these children, leading to a scramble to find continuing medical education courses to fill that gap. They often felt unprepared to treat depression and anxiety and to choose appropriate drugs for these diagnoses.

"Perhaps the most important and most generalizable findings of this study involve the need for increased training and for continuing medical education in behavioral health," Williams said.

That's of special concern because depression often leads to both suicide and substance abuse. "As primary care settings may be the only environment in which adolescents are seen, their high mortality rate from accidents, homicide and suicide would suggest the critical need for pediatricians to recognize and inquire about these symptoms," she said.

Along with Williams, other researchers included Jane M. Foy, M.D. and Kurt Klinkeper, M.D., both of Brenner Children's Hospital, Guy Palmes, M.D., of the Department of Psychiatry at Wake Forest Baptist and Anita Pulley of Northwest Area Health Education Center. The study was sponsored by a grant from the Duke Endowment as part of its Primary Care-Children's Mental Health Initiative.

**Adolescents & ADHD**

*Response inhibition in adolescents diagnosed with attention deficit hyperactivity disorder during childhood: an event-related FMRI study.*

**Authors:** Schulz KP, Fan J, Tang CY, Newcorn JH, Buchsbaum MS, Cheung AM, Halperin JM. - Department of Psychiatry, Box 1230, Mount Sinai School of Medicine, One Gustave Levy Place, New York, NY 10029.

**Source:** Am J Psychiatry. 2004 Sep;161(9):1650-7

**Summary:** OBJECTIVE: Frontostratial neural abnormalities have been implicated in the response inhibition impairments that are characteristic of attention deficit hyperactivity disorder (ADHD). However, reports of such abnormalities in adolescents are inconsistent. The present study used behavioral and functional neuroimaging techniques to examine inhibitory control processes in adolescents who had been diagnosed with ADHD during childhood.

METHOD: The authors used functional magnetic resonance imaging (fMRI) during performance of a Go/No-Go task to scan 10 male adolescents who were diagnosed with DSM-III-R ADHD when they were 7 to 11 years old and nine age-, sex-, and IQ-matched comparison subjects with no history of ADHD. Response inhibition was tested by contrasting neural activation during No-Go trials with that during Go trials.

RESULTS: The inhibition of a prepotent tendency to respond produced markedly greater activation of the left anterior cingulate gyrus, bilateral frontopolar regions, bilateral ventrolateral prefrontal cortex, and left medial frontal gyrus in the adolescents with childhood ADHD than in the adolescents with no history of ADHD. Activity in the first two regions was inversely related to task performance across the study group.

CONCLUSIONS: Compared with adolescents who had no history of ADHD, adolescents who were diagnosed with ADHD during childhood exhibited enhanced responses during inhibition in ventrolateral prefrontal cortical areas that subserved response inhibition, as well as in anterior cingulate and frontopolar regions implicated in other executive functions.
implications for a greater understanding of the ability of the young brain to reorganize after childhood stroke.

**Bimanual Coordination & Alcohol-Exposed Children**

**Bimanual coordination in alcohol-exposed children: role of the corpus callosum.**

**Authors:** Roebuck-Spencer TM, Mattson SN, Marion SD, Brown WS, Riley EP. - National Rehabilitation Hospital, Washington, DC 20010, USA

**Source:** J Int Neuropsychol Soc. 2004 Jul;10(4):536-48

**Summary:** The corpus callosum (CC) is one of several brain structures affected in children prenatally exposed to alcohol. This structure plays a major role in coordinating motor activity from opposite sides of the body, and deficits in bimanual coordination have been documented in individuals with agensis of or damage to the CC, particularly when the task is performed without visual feedback. The Bimanual Coordination Test was used to assess speed and accuracy on a task where both hands must coordinate to guide a cursor through angled pathways providing measures of interhemispheric interaction or the ability of the two hemispheres to coordinate activity via the corpus callosum. Twenty-one children with fetal alcohol spectrum disorders (FASD) and 17 non-exposed control children (CON), matched closely in age, sex, and ethnicity were tested. For trials with visual feedback (WV), children with FASD were slower than CON children but were equally accurate. Although statistically significant group differences were not observed on most trials completed without visual feedback (WOV), accuracy of the FASD group on WOV trials was highly variable. Group differences in accuracy on WOV angles approached significance after accounting for performance on the WV angles, and children with FASD were significantly less accurate on an individual angle believed to be particularly sensitive to interhemispheric interaction. These results indicate that children with FASD are slower than CON children but equally accurate on basic visuomotor tasks. However, as task complexity and reliance on interhemispheric interaction increases, children with FASD demonstrate variable and inaccurate performance.

**Psychotic Disorder (PD)**

**PD & Hallucinatory Experiences**

**Hallucinatory experiences and onset of psychotic disorders: evidence that the risk is mediated by delusion formation.**

**Authors:** Krabbendam L, Myin-Germeyns I, Hanssen M, Bijl RV, De Graaf R, Vollebergh W, Bak M, Van Os J. Department of Psychiatry and Neuroepidemiology, South Limburg Mental Health Research and Teaching Network, EURON, Maastricht University, Maastricht, The Netherlands.

**Source:** Acta Psychiatr Scand. 2004 Oct;110(4):264-72

**Summary:** Objective: To examine the hypothesis that the risk for onset of psychotic disorder in individuals with self-reported hallucinatory experiences (HE) would be higher in those who developed delusional ideation (DE) than in those who did not. Method: A population sample of 4673 individuals were interviewed with the Composite International Diagnostic...
Interview at baseline and 1 and 3 years later. At year 3, clinical re-interview took place to identify onset of psychotic disorder. Results: Given the presence of HEs at baseline, the increase in risk of having the psychosis outcome at year 3 was much higher in those with DE at year 1 than in those without DE (risk difference between individuals with and without DE: 18.72%, 95% CI: 2.22-35.23, chi(2) = 4.94, df = 1, P = 0.026). Conclusion: The results are in line with current psychological theories stating that clinical outcome of psychosis-like experiences is related to the development of secondary beliefs and appraisals.

PD & Pleasurable Auditory Hallucinations

* Pleasurable auditory hallucinations

Authors: Sanjuan J, Gonzalez JC, Aguilar EJ, Leal C, van Os J. Department of Medicine, Psychiatric Unit, Valencia University, Valencia, Spain


Summary: Pleasurable auditory hallucinations are a phenomenological feature of hallucinations. It is usually on the negative impact of the experience itself. The focus of auditory hallucination (AH) research is usually on the positive impact of the experience itself. There are actually no studies on whether voices can be perceived as pleasurable. The aim of the present study was to assess the frequency of voices as a pleasurable experience in a psychotic patient population. Method: A total of 160 patients with AHs (89 schizophrenia and 17 other psychoses) were assessed with the psychotic symptom rating scale (PSYRATS) for AHs, including an added item on whether the experience was pleasurable. Results: Twenty-eight patients (26%) reported the voices as a pleasurable experience and 10 of them did so frequently. Pleasurable hallucinations showed negative associations with amount and intensity of distress, degree of negative content and loudness. Positive associations were apparent with chronicity and perceived control over the voices. Conclusion: Pleasurable hallucinations can be detected in a substantial proportion of patients, and cross validated with existing instruments.

PD & Serum Lipids in Schizophrenia

* Serum lipids in schizophrenia and other functional psychoses: A general population northern Finland 1966 birth cohort survey

Authors: Saari K, Jokelainen J, Veijola J, Koponen H, Jones PB, Savolainen M, Jarvelin MR, Lauren L, Isohanni M, Lindeman S. Department of Psychiatry, University of Oulu, Finland


Summary: Objective: To compare fasting serum lipid concentrations of subjects with schizophrenia with a comparison group. Method: The study sample consists of 5654 members of the northern Finland 1966 birth cohort who participated in the field study with blood samples after overnight fasting and clinical examination in 1997-98. Total cholesterol (TC), high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides (TG) and glucose were analyzed. Analysis of variance were used for comparing differences in lipids means between diagnostic categories. Results: Mean fasting TC in subjects with schizophrenia was 20 mg/dl higher than in the comparison group. TC and TG levels in the group of other psychoses resembled the schizophrenia group. Conclusion: Blood lipid levels in subjects with schizophrenia and other functional psychoses were high. As these persons are at special risk for hyperlipidemia their lipid levels should be regularly monitored, and cholesterol lowering diet, as well as medication, should be considered.

PD & Neuropsychological Functioning

* Neuropsychological Functioning in First-Break, Never-Medicated Adolescents With Psychosis.

Authors: Brickman AM, Buchsbaum MS, Bloom R, Bokhoven P, Paul-Oduor R, Haznedar MM, Dahlman KL, Hazlett EA, Aronowitz J, Heath D, Shihabuddin L. *Department of Psychiatry, Mount Sinai School of Medicine, New York, NY; daggerTaub Institute for Research on Alzheimer Disease and the Aging Brain, Columbia University, College of Physicians and Surgeons, New York, NY; double daggerDepartment of Psychiatry and Behavioral Medicine, Brown Medical School, Providence, RI; and section signDepartment of Veterans Affairs, Bronx VA Medical Center, Bronx, NY.

Source: J Nerv Ment Dis. 2004 Sep;192(9):615-622.

Summary: The purpose of the current study was to examine neuropsychological functioning in a group of never-medicated first-break adolescents with psychosis. It was the first report of cognition in a sample of adolescents with psychosis in which all patients were drug-naive. Twenty-nine adolescent patients (mean age = 16.07; SD = 2.00; 15 male and 14 female patients) experiencing their first psychotic episode and 17 age-matched and sex-matched normal volunteers (mean age = 16.88; SD = 2.39; 9 male and 8 female subjects) were recruited and assessed with a neuropsychological battery. Measures of attention, memory, language, executive functioning, perceptual motor processing, and motor speed were obtained. Psychiatric symptomatology, estimated verbal IQ, and parental socioeconomic status were also determined. Patients with psychosis were significantly more impaired than normal volunteers; effect sizes were greatest in the areas of executive functioning, attention, and memory, and significantly smaller in areas of language, perceptual motor processing, and motor speed. The pattern was not altered when differences in verbal IQ and parental socioeconomic status were controlled. Sex and age interactions indicated that younger male patients were particularly impaired. The findings demonstrate neuropsychological deficits in adolescents with psychosis and suggest that cognitive deficits are core symptoms in psychotic disorders.

New Treatments & Agitation

* New treatments for agitation.

Authors: Citrome L. - S. Kline Institute for Psychiatric Research, Orangeburg, NY 10962, USA. citrome@nki.rfmh.org

Source: Psychiatr Q. 2004 Fall;75(3):197-213

Summary: Acute agitation is a frequent reason for emergency psychiatric intervention. It is important to intervene early to avoid escalation of agitation to aggression. Reducing risk by using effective treatments will result in fewer instances of seclusion and restraint, and fewer injuries to staff and patients. This paper will first review the epidemiology of aggressive behavior and mental disorders, followed by a discussion of assessment and diagnostic considerations. The pathophysiology of safety risk is discussed within the context of psychosis.
of the model of the "triune brain." Pharmacological treatment strategies for acute episodes of agitated behavior will be discussed in detail. This includes newer formulations of novel antipsychotics such as liquids and rapidly disintegrating tablets, as well as intramuscular preparations.

Entorhinal Cortex & First-Episode Psychotic ---

* The entorhinal cortex in first-episode psychotic disorders: a structural magnetic resonance imaging study.

Authors: Prasad KM, Patel AR, Muddasani S, Sweeney J, Keshavan MS. - University of Pittsburgh Medical Center, Western Psychiatric Institute and Clinic, 3811 O'Hara St., Pittsburgh, PA 15213. keshavanms@upmc.edu

Source: Am J Psychiatry. 2004 Sep;161(9):1612-9

Summary: OBJECTIVE: Neuropathological findings regarding the entorhinal cortex in schizophrenia are conflicting. The authors used structural magnetic resonance imaging to examine the entorhinal cortex volumes of healthy subjects and medication-naive patients experiencing their first episode of psychotic illness. METHOD: The study included 33 patients with schizophrenia and related disorders, 11 patients with nonschizophrenic disorders, and 43 matched healthy subjects. All subjects were rated on the Scale for the Assessment of Positive Symptoms and the Scale for the Assessment of Negative Symptoms, and volumetric measurements of the entorhinal cortex were obtained for all subjects. The authors examined differences across the groups as well as clinical correlations of entorhinal cortex volumes adjusted for intracranial volume. RESULTS: A significant diagnosis effect was seen in the left entorhinal cortex: patients with schizophrenia and related disorders and patients with nonschizophrenic psychotic disorders had smaller left entorhinal cortex volumes than healthy subjects. The mean entorhinal cortex volume of patients with schizophrenic disorders did not differ from that of patients with nonschizophrenic psychotic disorders. In patients with schizophrenic disorders, the entorhinal cortex volume positively correlated with severity of delusions. The mean entorhinal cortex volume of patients with nondelusional psychotic disorders was significantly smaller than that of patients with delusional psychotic disorders and healthy subjects. CONCLUSIONS: Smaller entorhinal cortex volume in first-episode, neuroleptic-naive psychotic disorders may not be a confound of the effects of illness chronicity or antipsychotic treatment. Entorhinal cortex pathology appears to have a significant association with positive symptoms, specifically delusions. The impairment of functions in which the entorhinal cortex participates-such as novelty detection, associative learning, and processing episodic, recognition, and autobiographical memory-could be responsible for its association with psychotic disorders and delusions.

Psychotic disorders & Early victimisation experiences


Authors: Bebbington PE, Bhugra D, Brugha T, Singleton N, Farrell M, Jenkins R, Lewis G, Meltzer H. - Department of Mental Health Sciences, 48 Riding House Street, London W1N 8EY, UK. p.bebbington@ucl.ac.uk

Source: Br J Psychiatry. 2004 Sep;185:220-6

Summary: BACKGROUND: Adverse early circumstances may be more common in people who later develop psychotic disorders. AIMS: To use data from the second British National Survey of Psychiatric Morbidity to examine associations between psychotic disorders and a number of early victimisation experiences. METHOD: Psychiatric disorders were identified through structured assessment of adults resident in private households in Britain (n=8580). Respondents were asked whether they had experienced selected events displayed on cards. RESULTS: Compared with respondents with other psychiatric disorders or with none, the prevalence of every experience bar one was significantly elevated in those with definite or probable psychosis. The largest odds ratio was for sexual abuse. Controlling for depressed mood somewhat reduced the odds ratios for the individual experiences. CONCLUSIONS: In people with psychosis, there is a marked excess of victimising experiences, many of which will have occurred during childhood. This is suggestive of a social contribution to aetiology.

Schizophrenia

Schizophrenia & Aripiprazole

* Aripiprazole: a new atypical antipsychotic drug

Authors: Fischer B, Davids E, Gastpar M. - Rheinische Kliniken Essen, Klinik fur Psychiatrie und Psychotherapie der Universitat Duisburg-Essen (Direktor: Prof. Dr. M. Gastpar).

Summary: Aripiprazole is an atypical antipsychotic agent with an intrinsic dopamine agonist activity of 30%. Aripiprazole exerts additional partial agonist action on 5-HT (1A) receptors and has antagonist properties at 5-HT (2A) receptors. Controlled studies demonstrated an effectiveness in acute relapse of schizophrenic psychosis, chronic schizophrenic and schizoaffective disorders. Aripiprazole was effective in the treatment of productive psychotic and negative symptoms. Compared to other antipsychotics aripiprazole demonstrated a favourable profile of side effects: only slight changes of body weight, mild extrapyramidal symptoms, no prolactin elevation and no significant changes in QTc interval. The efficacy in the long term treatment of schizophrenia seems to be similar to other antipsychotics (e.g. olanzapine). The first evaluations of studies with patients with bipolar disorders showed a significant efficacy in the treatment of mania.

Schizophrenia, clozapine & olanzapine

* The effects of clozapine and high-dose olanzapine on brain function in treatment-resistant schizophrenia

Authors: Robert R. Conley, Deanna L. Kelly, Lori L. Beason-Held, Henry H. Holcomb and Charles M. Richardson, - Maryland Psychiatric Research Center, University of Maryland, Baltimore, MD, USA;Maryland Psychiatric Research Center, University of Maryland, Baltimore, MD, USA;Maryland Psychiatric Research Center, University of Maryland, Baltimore, MD, USA;Maryland Psychiatric Research Center, University of Maryland, Baltimore, MD, USA.

Source: Volume 18 Issue 03 - Publication Date: 09/2004
Schizophrenia, Amisulpride & Clozapine

* Amisulpride augmentation of clozapine: an open non-randomized study in patients with schizophrenia partially responsive to clozapine.

**Authors**: Munro J, Matthiasson P, Osborne S, Travis M, Purcell S, Cobb AM, Launer M, Beer MD, Kerwin R. Section of Clinical Neuropsychopharmacology, Division of Psychological Medicine, Institute of Psychiatry, London, UK.


**Summary**: Objective: Treatment options are very limited for individuals with schizophrenia resistant to clozapine. We tested the hypothesis that amisulpride augmentation would lead to an improvement in these patients. Method: This was an open non-randomized study. Thirty-three patients with suboptimal response to clozapine were commenced on amisulpride in addition to clozapine. Clinical status was evaluated at baseline, 3 and 6 months using the Positive And Negative Syndrome Scale (PANSS), Scale for the Assessment of Negative Symptoms (SANS), Global Assessment Scale (GAS), Calgary Depression Scale, Calgary Anxiety Scale and various side effect rating scales. Results: Twenty-eight subjects completed 6 months treatment on clozapine and amisulpride. There was a statistically significant improvement in the mean scores for PANSS, SANS and GAS at follow-up and no significant changes in side effect ratings. Conclusion: Co-administration of amisulpride, in a group of patients partially or non-responsive to clozapine, may lead to a substantial improvement in positive and negative symptoms, without worsening the side effect burden.

Schizophrenia & Cytokine

* Cytokine network in patients with schizophrenia and its significance for the pathophysiology of the illness.

**Authors**: Schuld A, Hinze-Selch D, Pollmacher T. Max-Planck-Institut fur Psychiatrie Munich, Germany.


**Summary**: Experimental findings from psychoneuroimmunologic research in humans and epidemiological data suggest that alterations in cytokine networks may induce acute psychopathologic symptoms and may be involved in the pathogenesis and pathophysiology of schizophrenia by influencing brain development. However, there is insufficient evidence from genetic, post-mortem, and cerebrospinal fluid studies to demonstrate this in the CNS of schizophrenic patients. In contrast, there are quite robust findings from peripheral blood that interleukin (IL)-2, IL-6, tumor necrosis factor-alpha, and interferon cytokine systems in patients are regulated differently than in controls. However, these findings are not specific to schizophrenia, they are confounded by numerous intervening variables such as stress, smoking, and medication, and their pathophysiologic relevance for processes in the CNS is undetermined. Therefore, future research on the involvement of cytokines in the pathogenesis, pathophysiology, and treatment of schizophrenia is needed.

Schizophrenia & Heart Disease

* Hypofrontality in schizophrenia: a meta-analysis of functional imaging studies.

**Authors**: Hill K, Mann L, Laws KR, Stephenson CM, Nimmo-Smith I, McKenna PJ. Fulbourn Hospital, Cambridge, UK.


**Summary**: Objective: Hypofrontality is not a well-replicated finding in schizophrenia either at rest or under conditions of task activation. Method: Studies comparing whole brain and frontal blood flow/metabolism in schizophrenic patients and normal controls were pooled. Voxel-based studies were also combined to examine the pattern of prefrontal activation in schizophrenia. Results: Whole brain flow/metabolism was reduced in schizophrenia to only a small extent. Resting and activation frontal flow/metabolism were both reduced with a medium effect size. Duration of illness significantly moderated resting hypofrontality, but the moderating effects of neuroleptic treatment were consistent with an influence on global flow/metabolism only. Pooling of voxel-based studies did not suggest an abnormal pattern of activation in schizophrenia. Conclusion: Meta-analysis supports resting hypofrontality in schizophrenia. Task-activated hypofrontality is also supported.
but there is little from voxel-based studies to suggest that this is associated with an altered pattern of regional functional architecture.

**Schizophrenia & Maternal Care**

- Poor maternal care and high maternal body mass index in pregnancy as a risk factor for schizophrenia in offspring.

Authors: Kawai M, Minabe Y, Takagai S, Ogai M, Matsumoto H, Mori N, Takei N. Department of Psychiatry and Neurology, Hamamatsu University School of Medicine, Hamamatsu, Japan.


Summary: Objective: We investigated whether antenatal factors in mothers would increase the risk of schizophrenia in the offspring, and also examined any relationship between these factors and histories of obstetric complications (OCs). Method: Using the Mother and Child Health Handbooks of 52 patients with schizophrenia and 284 healthy subjects, we evaluated the risk-increasing effects of the frequency of antenatal care visits and mothers' body mass index (BMI) at both early and late pregnancy. Results: In logistic regression analysis, there was a significant association between the number of antenatal care visits and the risk of the disorder; an increase in a unit of visits corresponds to a reduction of the risk by 12%. We also found a 24% increase in the risk with a one-unit increase of BMI at the early pregnancy, and a 19% increase at the late pregnancy. These antenatal factors were found to contribute, in part, to an excess of OCs in individuals with schizophrenia. Conclusion: Poor maternal care during pregnancy and comparatively high maternal BMI especially at early pregnancy may cause a predisposition to schizophrenia in the offspring.

**Schizophrenia & Cognitive Enhancement**

- Cognitive enhancement therapy for schizophrenia: effects of a 2-year randomized trial on cognition and behavior.

Authors: Hogarty GE, Fleisher S, Ulrich R, Carter M, Greenwald D, Pogue-Geile M, Kechavan M, Cooley S, DiBarry AL, Garrett A, Parepally H, Zoretich R. University of Pittsburgh Medical Center, Western Psychiatric Institute and Clinic, Pittsburgh, PA 15213, USA. hogartyje@upmc.edu

Source: Arch Gen Psychiatry. 2004 Sep;61(9):866-76.

Summary: BACKGROUND: Deficits in social cognition and neurocognition are believed to underlie schizophrenia disability. Attempts at rehabilitation have had circumscribed effects on cognition, without concurrent improvement in broad aspects of behavior and adjustment. OBJECTIVE: To determine the differential effects of cognitive enhancement therapy (a recovery-phase intervention) on cognition and behavior compared with state-of-the-art enriched supportive therapy. DESIGN: A 2-year, randomized controlled trial with neuropsychological and behavioral assessments completed at baseline and at 12 and 24 months. SETTING: An outpatient research clinic housed in a medical center's comprehensive care service for patients with severe mental illness. PATIENTS: A total of 121 symptomatically stable, non-substance-abusing but cognitively disabled and chronically ill patients with schizophrenia or schizoaffective disorder. INTERVENTIONS: Cognitive enhancement therapy is a multidimensional, developmental approach that integrates computer-assisted training in neurocognition with social cognitive group exercises. Enriched supportive therapy fosters illness management through applied coping strategies and education. MAIN OUTCOME MEASURES: Six highly reliable summary measures—Processing Speed, Neurocognition, Cognitive Style, Social Cognition, Social Adjustment and Symptoms—were tested using analysis of covariance and linear trend analysis. RESULTS: At 12 months, robust cognitive enhancement therapy effects were observed on the Neurocognition and Processing Speed composites (P<.003), with marginal effects observed on the behavioral composites. By 24 months, differential cognitive enhancement therapy effects were again observed for the 2 neuropsychological composites and for Cognitive Style (P=.001), Social Cognition (P=.001), and Social Adjustment (P=.01). As expected, no differences were observed on the residual Symptoms composite. Effects were unrelated to the type of antipsychotic medication received. Enriched supportive therapy also demonstrated statistically significant within-group effect sizes, suggesting that supportive psychotherapy can also have positive, although more modest, effects on cognitive deficits. CONCLUSION: Many cognitive deficits and related behaviors of patients with stable schizophrenia are improved when sufficient exposure to relevant rehabilitation is provided.

**Schizophrenia & Disability Reduction**

- Disability Reduction in Elderly Patients with Schizophrenia.

Authors: SCHIMMING, CORBETT MD; HARVEY, PHILIP D. PhD


Summary: This article reviews a frequently overlooked subject, the topic of schizophrenia in late life. By examining the available literature on schizophrenia in this particular population, we hope to provide clinicians with a better understanding of the distinguishing characteristics, course, and optimal treatments of this disease in elderly patients. The validity of the concept of symptom "burn out" is discussed and the cognitive changes seen in schizophrenia as patients age are examined. Similarities and differences between late-onset schizophrenia and early-onset schizophrenia in aging patients are compared. The similarities and differences between schizophrenia and dementia in the elderly are also discussed. Finally, treatments for the illness, including both typical and atypical antipsychotic treatments, as well as nonpharmacological intervention strategies, along with their advantages and disadvantages, are reviewed.

**Schizophrenia & Sulpiride**

- Sulpiride for schizophrenia.

Authors: Soares BGO, Fenton M, Chue P


Summary: A substantive amendment to this systematic review was last made on 24 November 1998. Cochrane reviews are regularly checked and updated if necessary. Background: The antipsychotic drug sulpiride was formulated over 20 years ago and was marked as having a low incidence of adverse effects and an effect on the negative symptoms of schizophrenia. This relatively inexpensive antipsychotic drug has a similar neuropharmacological profile to several novel
atypical drugs.

Objectives: To estimate the clinical efficacy and tolerability of sulpiride.


Selection criteria: All randomised or quasi-randomised clinical trials focusing on the use of different doses of sulpiride or comparing sulpiride to (i) placebo; (ii) typical antipsychotic drugs; or (iii) atypical antipsychotic drugs, for those with schizophrenia or serious mental illness were selected.

Data collection and analysis: Trials were reliably selected and quality rated. Data were independently extracted, by two reviewers (BGOS, MF), and analysed on an intention-to-treat basis. It was assumed that people who did not complete the follow up had no improvement. Authors of trials were contacted for additional and missing data. Relative risk (RR) and 95% confidence intervals (CI) of dichotomous data were calculated with the random effects model and weighted mean differences (WMD) was calculated for continuous data. It was assumed that people who did not complete the follow up had no improvement. Authors of trials were contacted for additional and missing data. Relative risk (RR) and 95% confidence intervals (CI) of dichotomous data were calculated with the random effects model and weighted mean difference (WMD) was calculated for continuous data.

Main results: The review currently includes 18 studies (30 citations). Studies are generally small and of poor quality. Limited evidence suggests that there is little difference between sulpiride and other drugs although the incidence of side effects may be less for sulpiride. There are no clear findings relating to negative symptoms.

Reviewers’ conclusions: Sulpiride may be an effective antipsychotic drug but evidence is limited and data relating to claims for its value against negative symptoms is not trial-based.

Schizophrenia & Quetiapine

* Quetiapine for Schizophrenia

Authors: Srisurapanont M, Maneeton B, Maneeton N

Summary: A substantive amendment to this systematic review was last made on 21 January 2004. Cochrane reviews are regularly checked and updated if necessary. Background: Quetiapine is an atypical antipsychotic with, theoretically, a low propensity for movement disorder adverse effects. It is used for the treatment of schizophrenia and other psychoses.

Objectives: To determine the effects of quetiapine for schizophrenia in comparison to placebo, and other antipsychotics.


Selection criteria: All randomised controlled trials where adults with schizophrenia or similar illnesses were assigned to quetiapine, placebo or other neuroleptic drugs and where clinically relevant outcomes were reported.

Data collection and analysis: Citations and, where possible, abstracts were inspected independently by reviewers, papers ordered, re-inspected and quality assessed. We independently extracted data. We analysed data using fixed effects relative risk (RR) and estimated the 95% confidence interval (CI). Only homogeneous data were interpreted as favouring treatment or control. Where possible we calculated the number needed to treat (NNT) or number needed to harm statistics (NNH). We calculated relative risk (RR) for dichotomous data, and weighted mean differences (WMD) for continuous data.

Main results: Despite the fact that 3443 people were randomised in 12 quetiapine studies, there are almost no data on service utilisation, economic outcomes, social functioning and quality of life. Over half of those within the quetiapine versus placebo comparison were lost to follow up (53% quetiapine vs 61% placebo, n=716, 4 RCTs, RR 0.84 CI 0.7 to 0.9, NNT 11 CI 7 to 55) so it is impossible to interpret any ratings of global or mental state within this comparison with confidence. People allocated quetiapine, however, did not have more movement disorders than those given placebo (n=395, 2 RCTs, RR needing medication for EPS 0.62 CI 0.3 to 1.2). The same applies to the comparison of >/= 250 mg/day quetiapine with < 250 mg/day quetiapine (49% dropout >/= 250 mg/day vs 58% < 250 mg/day, n=1066, 3 RCTs, RR 0.84 CI 0.8 to 0.9, NNT 11 CI 7 to 29). It should be noted that two deaths occurred in the higher dose group (n=618, 1 RCT, RR 0.1 CI 0.0 to 2.1). When quetiapine was compared with typical antipsychotics, about 36% of both groups failed to complete the short-term studies (n=1624, 6 RCTs, RR 0.87 CI 0.8 to 1.0). Average change in global state was heterogeneous and equivocal (n=762, 3 RCTs, WMD in short term 0.19 CI 0.00 to 0.38, 1 squared 76%). Mental state measures were also equivocal (n=1247, RR not improved 0.97 CI 0.9 to 1.1) including specific measures of negative symptoms (n=305, 1 RCT, MD change in SANS short term 0.94 CI -0.2 to 2.0). Movement disorders were less prevalent for those allocated quetiapine (n=1117, 4 RCTs, RR needing medication for extrapyramidal adverse effects 0.47 CI 0.4 to 0.6, NNT 4 CI 4 to 5, 1 squared 88%). Dry mouth (n=649, 2 RCTs, RR short term 2.85 CI 1.5 to 5.6, NNH 17 CI 7 to 65) and sleepiness (n=959, 3 RCTs, RR 1.51 CI 1.1 to 2.2, NNH 18 CI 8 to 181) may also be more prevalent for people given quetiapine compared with the older drugs. In the quetiapine versus risperidone comparison, over 30% of people left the study before completion (n=728, 1 RCT, RR 0.94 CI 0.7 to 1.2). Four people, all treated with quetiapine, died during the study (n=728, 1 RCT, RR 0.86 CI 0.2 to 52.8). Continuous mental state measures did not show clear differences between the two drugs (n=637, 1 RCT, MD PANSS 1.2 CI -2.0 to 4.4). However, considerably fewer people given quetiapine needed medication for extrapyramidal side effects compared with those allocated to risperidone (n=712, 1 RCT, RR 0.27 CI 0.2 to 0.5, NNH 11 CI 10 to 16). Quetiapine caused more dizziness (n=728, 1 RCT, RR 1.85 CI 1.0 to 3.3, NNH 18 CI 7 to 487), more dry mouth (n=728, 1 RCT, RR 2.11 CI 1.2 to 3.8, NNH 14 CI 6 to 82) and more sleepiness than risperidone (n=728, 1 RCT, RR 2.03 CI 1.4 to 2.9, NNH 7 CI 4 to 17).

Reviewers’ conclusions: Quetiapine is effective for the treatment of schizophrenia, but it is not much different from first-generation antipsychotics and risperidone with respect to treatment withdrawal and efficacy. In comparison to first-generation antipsychotics and risperidone, quetiapine has a lower risk of movement disorders but higher risks of dizziness, dry mouth and sleepiness. More clearly reported pragmatic randomised controlled trials should be carried out to determine
its position in everyday clinical practice. Studies of medium and long-term effects, including cost-effectiveness, quality of life, social functioning and service utilisation, in comparison with the effects of typical and atypical antipsychotics should be priority areas.

Schizophrenia & Olanzapine

* Olanzapine for schizophrenia

**Authors:** Duggan L, Fenton M, Dardennes RM, El-Dosoky A, Indran S


**Summary:** A substantive amendment to this systematic review was last made on 27 October 1999. Cochrane reviews are regularly checked and updated if necessary. Olanzapine is an atypical antipsychotic that is reported to be effective without producing the disabling extrapyramidal side effects associated with the older, typical antipsychotic drugs.

**Objectives:** To determine the clinical effects and safety of olanzapine as compared with placebo, typical and other atypical antipsychotic drugs for schizophrenia and schizophreniform psychoses.

**Search strategy:** The reviewers undertook electronic searches of Biological Abstracts (1980-1999), The Cochrane Library (Issue 2, 1999), The Cochrane Schizophrenia Group’s Register (September 1999), EMBASE (1980-1999), MEDLINE (1966-1999), and PsycLIT (1974-1999). References of all identified studies were searched for further trials, and the reviewers contacted relevant pharmaceutical companies and authors of trials.

**Selection criteria:** All randomised clinical trials comparing olanzapine to placebo or any antipsychotic treatment for those with schizophrenia or schizophreniform psychoses. Data collection and analysis: Data were independently extracted. For homogeneous dichotomous data the random effects relative risk (RR), the 95% confidence intervals (CI) and, where appropriate, the number needed to treat (NNT) were calculated on an intention-to-treat basis. For continuous outcomes data the reviewers calculated weighted mean differences.

**Main results:** Twenty trials are included. Attrition from olanzapine versus placebo studies was so great (olanzapine - 61%, placebo - 73% by 6 weeks, RR 0.85 CI 0.7-0.98, NNT 8 CI 5-27) that interpretation of results is problematic. Olanzapine appeared superior to placebo at six weeks for the outcome of ‘no important clinical response’ (RR 0.88 CI 0.8-0.98, NNT 8 CI 5-27), but trial data regarding negative symptoms are equivocal for this comparison. Dizziness and dry mouth were more common in the olanzapine-treated group, and, although not statistically significant, the olanzapine group gained more weight. Data from several small trials are incomplete; but, for the short term outcome of ‘no important clinical response’, olanzapine seems as effective as typical antipsychotics (n=2778, RR 0.9 CI 0.76-1.06). Brief Psychiatric Rating Scale (BPRS) data tended to be equivocal but Positive and Negative Syndrome Scale (PANSS) rating of total score and negative and positive symptom sub-scores favoured olanzapine. With high attrition in both groups (olanzapine - 36%, typical drug - 49% by 6 weeks, n=2738, RR 0.85 CI 0.66-1.1; olanzapine - 83%, typical drug - 90% by 1 year, n=2738, RR 0.9 CI 0.86-1.02), the assumptions included in all continuous data are considerable. Participants allocated olanzapine experienced less extrapyramidal side effects than people given haloperidol. Weight change data for the short term are not conclusive (n=2455, WMD 0.8kg CI -0.6-2.2) but the three to 12 month results suggest an average gain of four kilograms (n=233, WMD 4 CI 0.3-7.8). It is difficult to distinguish between olanzapine and other atypical drugs, although it may cause less extrapyramidal side effects than risperidone (n=339, RR 0.6 CI 0.4-0.9, NNH 8 CI 4-29). Olanzapine did cause more weight gain than its comparators but current data are not statistically significant (3-12 months, n=535, WMD 2.2kg CI -0.6-5.0). One study (n=180) found no clear differences between olanzapine and clozapine for people with treatment resistant illness.

Reviewers’ conclusions: For people with schizophrenia olanzapine may offer antipsychotic efficacy with less extrapyramidal side effects than typical drugs but more weight gain. The large proportions of participants leaving the studies early, in the large multi-centre trials makes it difficult to draw firm conclusions on clinical effects. Large, long-term randomised trials with participants, interventions and primary outcomes that are familiar to those wishing to help those with schizophrenia are long overdue.

Schizophrenia & Haloperidol

* Haloperidol dose for the acute phase of schizophrenia

**Authors:** Waraich PS, Adams CE, Roque M, Hamill KM, Marti J


**Summary:** A substantive amendment to this systematic review was last made on 06 February 2002. Cochrane reviews are regularly checked and updated if necessary. Haloperidol is a benchmark, accessible antipsychotic against which the effects of newer treatments are gauged.

**Objectives:** The primary goal of this review is to determine the best range of doses for haloperidol for the treatment of people acutely ill with schizophrenia.

**Search strategy:** The reviewers searched Biological Abstracts (1980-1999), CINAHL (1982-1999), The Cochrane Library (1999, Issue 2), The Cochrane Schizophrenia Group’s Register (December 1999), EMBASE (1980-1999), MEDLINE (1966-1999) and PsycLIT (1887-1999). They also inspected all references of all identified trials and included studies sought as a citation on SCISEARCH database (1980-1999). Authors of identified studies and pharmaceutical companies were also contacted.

**Selection criteria:** Studies were selected if they involved people being treated for acute schizophrenia, randomised to two or more dose ranges of non-depot haloperidol, and if they reported clinically meaningful outcomes.

**Data collection and analysis:** The reviewers independently and blindly inspected citations (10% reliability check), they ordered papers, and reliably re-inspected and quality assessed the full reports. The reviewers, again working independently, also extracted data. For homogeneous dichotomous data the relative risk (RR), 95% confidence intervals (CI) were calculated on an intention-to-treat basis. Reviewers assumed that people who left the study early or were lost to follow-up had a negative outcome. Weighted mean differences (WMD) were calculated for continuous outcomes that reported intention to treat (ITT), last observation carried forward (LOCF) data. Data was excluded if loss to follow-up was greater than 50%. Main results: Sixteen trials with nineteen different randomised dose comparisons were included. No studies...
reported data on relapse rates, quality of life and none compared >1.5-3.0 mg/day haloperidol to higher dose ranges. Using low doses (≥3-7.5mg/day) did not clearly result in loss of efficacy (no clinically important improvement in global state, versus >7.5-15mg/day n=48, 1 RCT, RR 1.09 CI 0.7 to 1.8; versus >15-35mg/day n=81, 2 RCTs, 0.95 CI 0.8 to 1.2). Doses of haloperidol in the range of >7.5 mg/day had a lower rate of development of clinically significant extrapyramidal adverse effects than higher doses (clinically significant extrapyramidal adverse effects, versus >7.5-15mg/day n=64, 2 RCTs, RR 0.12 CI 0.01 to 2.1; versus >15-35mg/day n=144, 3 RCTs RR 0.59 CI 0.5 to 0.8, NNH 3 CI 2 to 6; versus >35mg/day n=86, 2 RCTs, RR 0.70 CI 0.5 to 1.1). All other comparisons between dose ranges did not yield statistically significant differences, but several, particularly with lower dose ranges, were underpowered to detect clinically meaningful differences.

Reviewers’ conclusions: No results are conclusive and all are based on small, short, studies. It would be understandable, however, if clinicians were cautious in prescribing doses in excess of 7.5 mg/day of haloperidol to a person with uncomplicated acute schizophrenia, and if people with schizophrenia were equally reticent to take greater doses. Further research is needed regarding the efficacy and tolerability of the >1.5-3.0 mg/day dose range.

Schizophrenia, Schizoaffective & Carbamazepine ——

* Carbamazepine for Schizophrenia and Schizoaffective Psychoses

Authors : Leucht S, McGrath J, White P, Kissling W
Summary: A substantive amendment to this systematic review was last made on 09 April 2002. Cochrane reviews are regularly checked and updated if necessary.
Background: Many people with schizophrenia do not achieve a satisfactory treatment response with ordinary antipsychotic drug treatment and various additional medications are used to promote additional response. The antiepileptic carbamazepine is one such drug.
Objectives: To review the effects of carbamazepine and its derivatives for the treatment of schizophrenia and schizoaffective psychoses.
Search strategy: We searched Biological Abstracts (1980-2001), The Cochrane Library (Issue 3, 2001), The Cochrane Schizophrenia Group's Register of Trials (December 2001), EMBASE (1980-2001), MEDLINE (1966-2001), PsycLIT (1886-2001) and PSYNDEx (1974-2001). Citations from included trials were also inspected and relevant companies and authors contacted for additional data.
Selection criteria: All randomised controlled trials comparing carbamazepine or compounds of the carbamazepine family to placebo or no intervention, whether as sole treatment or as an adjunct to antipsychotic medication for the treatment of schizophrenia and/or schizoaffective psychoses.
Data collection and analysis: Citations and, where possible, abstracts were independently inspected by reviewers, papers ordered, re-inspected and quality assessed. Data were extracted independently by at least two reviewers. Dichotomous data were analysed using relative risks (RR) and the 95% confidence interval (CI) estimated. Where possible the number needed to treat (NNT) or number needed to harm statistics were calculated.
Main results: Ten studies with a total of 258 participants were included. One study comparing carbamazepine with placebo (RR) with 95% confidence intervals (CI) and number needed to treat (NNT) were estimated. The reviewers assume that people who died or dropped out had no improvement and tested the sensitivity of the final results to this assumption.
Main results: Family intervention may decrease the frequency of relapse (n=721, 14 RCTs, RR 0.72 CI 0.6 to 0.9, NNT 7 CI 5 to 16). These data are statistically heterogeneous, the trend over time of this finding is towards the null and some small but negative studies may not have been identified by the search. Family intervention may also encourage compliance with medication (n=369, 7 RCTs, RR 0.74 CI 0.6 to 0.9, NNT 7 CI 4 to 19) but does not obviously affect the tendency of individuals/families to drop out of care (n=327, 4 RCTs, RR attrition at 3 months 0.86 CI 0.3 to 2.1). It may improve general social impairment and the levels of expressed emotion within the family. This review provides no data to suggest that family intervention either prevents or promotes suicide.
Reviewers’ conclusions: Clinicians, researchers, policy makers and recipients of care cannot be confident of the effects of family intervention from the findings of this review. Further data from already completed trials could greatly inform practice and more trials are justified as long as their participants, interventions and outcomes are applicable to routine care.
as the sole treatment for schizophrenia (n=31) was stopped early due to high relapse rate. No effect of carbamazepine was evident (RR relapse 4.1 CI 0.8 to 1.5). Another study (n=38) compared carbamazepine with antipsychotics as the sole treatment for schizophrenia. No differences in terms of mental state were found (RR 50% BPRS reduction 1.2 CI 0.8 to 1.9). More people who received the antipsychotic (perphenazine) had parkinsonism (RR 0.03 CI 0.00 to 0.04, NNH 1 CI 0.9 to 1.4). Eight studies compared adjunctive carbamazepine plus antipsychotics versus placebo plus antipsychotics. Adding carbamazepine was as acceptable as adding placebo (n=182, RR leaving the study early 0.5 CI 0.2 to 1.4). Carbamazepine augmentation of antipsychotics was superior compared with antipsychotics alone in terms of overall improvement, but participant numbers were low (2 RCTs, n=38, RR 0.6 CI 0.4 to 0.9, NNT 2 CI 1 to 5). There were no differences for mental state outcomes (6 RCTs n=147, RR 50% BPRS reduction 0.9 CI 0.7 to 1.1). Less people in the carbamazepine augmentation group had movement disorders than those taking haloperidol alone (1 RCT, n=20, RR 0.4 CI 0.1 to 1.0). The effects of carbamazepine on subgroups of people with schizophrenia and aggressive behaviour, negative symptoms or EEG abnormalities or with schizoaffective disorder are unknown.

Reviewers' conclusions: Based on currently available randomised trial-derived evidence, carbamazepine cannot be recommended for routine clinical use for treatment or augmentation of antipsychotic treatment of schizophrenia. At present large, simple well-designed and reported trials are justified especially if focusing on those with violent episodes and people with schizoaffective disorders or on those with both schizophrenia and EEG abnormalities.

Schizophrenia & Long-Acting Risperidone

* Practical application of pharmacotherapy with long-acting risperidone for patients with schizophrenia.


** Source:** Psychiatr Serv. 2004 Sep;55(9):997-1005

** Summary:** It is now generally accepted that the use of second-generation, or atypical, antipsychotics for schizophrenia represents an advance over conventional antipsychotic agents. However, adherence continues to be a problem, as with other medications for chronic disorders. Long-acting formulations of conventional antipsychotics partly address adherence problems, but their use is limited by tolerability issues. This article provides practical advice to physicians on the characteristics of patients who would benefit from treatment with long-acting atypical antipsychotic agents and offers suggestions on how to initiate treatment. METHODS: A literature search for studies published between 1980 and 2003 that evaluated the treatment of patients with schizophrenia with long-acting atypical agents was conducted by using MEDLINE and EMBASE. The primary search parameters were “schizophrenia,” “atypical,” “antipsychotic,” and “long-acting.” As expected, long-acting risperidone was the only long-acting atypical agent identified; thus this article focuses on practical advice and suggestions on how to initiate therapy with long-acting risperidone. RESULTS AND DISCUSSION: From the results of the literature search and the discussion of a panel of experts at a meeting held in Dublin in 2003 and supported by Johnson & Johnson, it is possible to conclude that long-acting risperidone has demonstrated efficacy and tolerability, even among patients who are considered clinically stable on other antipsychotics. Most patients can switch safely and effectively to long-acting risperidone if appropriate strategies are applied. Long-acting risperidone provides a new and promising therapeutic option for the treatment of schizophrenia.

Schizophrenia & The Independent Living Scales

* The independent living scales as a measure of functional outcome for schizophrenia.

** Authors:** Revheim N, Medalia A. - Bronx, New York

** Source:** Psychiatr Serv. 2004 Sep;55(9):1052-4
Summary: The Independent Living Scales (ILS) measures cognitive skills required for independent living and is intended to provide guidelines for appropriate supervision requirements for persons in residential placement. To assess the validity of the ILS among persons with schizophrenia, the instrument was administered to 162 individuals with schizophrenia who were living in three gradations of care: maximum supervision, moderate supervision, and minimal supervision. Scores on the ILS differed significantly across the three levels of care, whereas scores on the Global Assessment of Functioning (GAF) that were provided by clinicians discriminated only two levels of care. The ILS can be used among patients with schizophrenia to measure cognition as it affects functional outcome.

Schizophrenia & Tobacoo Dependence

* A CASE SERIES OF NICOTINE NASAL SPRAY IN THE TREATMENT OF TOBACCO DEPENDENCE AMONG PATIENTS WITH SCHIZOPHRENIA.

Authors: Williams JM, Ziedonis DM, Foulds J. - the University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, 671 Hoes Lane, D339, Piscataway, New Jersey 08855. jill.williams@umdnj.edu

Source: Psychiatr Serv. 2004 Sep;55(9):1064-6

Summary: A retrospective case series of 12 smokers with schizophrenia or schizoaffective disorder who had not successfully quit smoking with previous treatments for tobacco dependence were treated with nicotine nasal spray. All but one patient (92 percent) tolerated the nasal spray well, and nine (75 percent) used it at maximal doses for prolonged periods. After treatment five patients (42 percent) were abstinent from smoking for more than 90 days, and four patients (33 percent) substantially reduced the amount that they smoked. Ten patients (83 percent) used the spray in combination with other medications, and all received psychosocial support. Nicotine nasal spray was found to be well tolerated.

Schizoaffective Disorder

* IS SCHIZOAFFECTIVE DISORDER A STABLE DIAGNOSTIC CATEGORY: A RETROSPECTIVE EXAMINATION.

Authors: Averill PM, Reas DL, Shack A, Shah NN, Cowan K, Krajewski K, Kopecky C, Guynn RW. - University of Texas Health Science Center at Houston, Department of Psychiatry and Behavioral Sciences and the Harris County Psychiatric Center, Houston, Texas, USA. patricia.averill@uth.tmc.edu

Source: Psychiatr Q. 2004 Fall;75(3):215-27

Summary: Debate continues about whether clear nosologic boundaries can be drawn between schizoaffective disorder (SA), schizophrenia (SP), and bipolar disorder (BPD). This study attempted to clarify these boundaries. A retrospective review of the records of adult psychiatric inpatients with DSM-IV diagnoses of SA (n = 96), SP (n = 245), and BPD (n = 203) was conducted. Patients were assessed at admission and discharge using standardized rating scales (completed by physicians and nurses) and self-report inventories. Differential improvement over time also was examined. Significant differences were found for gender, legal status at admission, age, LOS, episode number, and ethnicity. Overall, SA was rated by clinicians as intermediate between SP and BPD, although SA rated themselves as the most severe. SA was similar to SP on positive symptoms, intermediate on negative symptoms, and similar to BPD on mood- and distress-related symptoms. Independent of diagnosis, differences in change scores from admission to discharge were related to severity level at admission. Although several differences were found in symptom severity across domains, no syndrome was identifiable associated with the diagnosis of SA and the diagnosis was unstable over time, thereby bringing into question the validity of SA as a diagnostic entity.

Schizophrenia & CBT

* COGNITIVE BEHAVIORAL THERAPY IN THE TREATMENT OF SCHIZOPHRENIA

Authors: D Turkington & R Dudley


Summary: This review outlines the role that cognitive behavioral therapy can play in specifically addressing the distress associated with the symptoms of schizophrenia, such as hallucinations and delusions. Some of the features that are given greater emphasis (or are a feature of working with people with psychotic illness), engagement, understanding the onset of the illness and work with hallucinations and delusional beliefs are outlined. The evidence base for the utility of cognitive behavioral therapy is considered, and the development and further application of cognitive behavioral therapy for schizophrenia and related disorders are outlined. Cognitive behavioral therapy, psychosis, schizophrenia.

Schizophrenia Refractory & Clozapine

* EQUIVALENT OCCUPANCY OF DOPAMINE D1 AND D2 RECEPTORS WITH CLOZAPINE: DIFFERENTIATION FROM OTHER ATYPICAL ANTI精神病.

Authors: Tauscher J, Hussain T, Agid O, Verhoef NP, Wilson AA, Houle S, Remington G, Zipursky RB, Kapur S. - Department of General Psychiatry, Medical University of Vienna, Austria, Wahringer Gurtel 18-20, A-1090 Vienna, Austria. johannes.tauscher@meduniwien.ac.at

Source: Am J Psychiatry. 2004 Sep;161(9):1620-5

Summary: OBJECTIVE: Clozapine, the prototype of atypical antipsychotics, remains unique in its efficacy in the treatment of refractory schizophrenia. Its affinity for dopamine D(4) receptors, serotonin 5-HT(2A) receptor antagonism, effects on the noradrenergic system, and its relatively moderate occupancy of D(2) receptors are unlikely to be the critical mechanism underlying its efficacy. In an attempt to elucidate the molecular/synaptic mechanism underlying clozapine’s distinctiveness in refractory schizophrenia, the authors studied the in vivo D(1) and D(2) receptor profile of clozapine compared with other atypical antipsychotics. METHOD: Positron emission tomography with the radioligands [(11)C]SCH23390 and [(11)C]raclopride was used to investigate D(1) and D(2) receptor occupancy in vivo in 25 schizophrenia patients receiving atypical antipsychotic treatment with clozapine, olanzapine, quetiapine, or risperidone. RESULTS: Mean striatal D(1) occupancies ranged from 55% with clozapine to 12% with quetiapine (rank order: clozapine > olanzapine > risperidone > quetiapine). The striatal D(2) occupancy ranged from 81% with risperidone to 30% with quetiapine (rank order: risperidone > olanzapine > quetiapine).
clozapine > quetiapine). The ratio of striatal D(1)/D(2) occupancy was significantly higher for clozapine (0.88) relative to olanzapine (0.54), quetiapine (0.41), or risperidone (0.31). CONCLUSIONS: Among the atypical antipsychotics, clozapine appears to have a simultaneous and equivalent occupancy of dopamine D(1) and D(2) receptors. Whether its effect on D(1) receptors represents agonism or antagonism is not yet clear, as this issue is still unresolved in the preclinical arena. This distinctive effect on D(1)/D(2) receptors may be responsible for clozapine’s unique effectiveness in patients with schizophrenia refractory to other typical and atypical antipsychotics.

Schizophrenia & Stress in Adult Students

* Stress in adult students with schizophrenia in a supported education program.
Authors: Ponizovsky A, Grinshpoon A, Sasson R, Levav I.
Source: Compr Psychiatry. 2004 Sep-Oct;45(5):401-7
Summary: The successful integration of former psychiatric inpatients into the community requires innovative programs of psychosocial rehabilitation, including supported education. This article examines psychological distress as an outcome variable, and social support and coping strategies as mediating variables among 70 service-user students (SUS) with schizophrenia and a comparison group of 55 adult students (AS) with no psychiatric diagnosis. Both groups were participants in a supported education program. The study variables were assessed by standardized research instruments: the Talbieh Brief Distress Inventory (TBDI), the Multidimensional Scale of Perceived Social Support (MSPSS), and the Coping Inventory for Stressful Situations (CISS).
Univariate and multivariate analyses were used. Compared with the control subjects, SUS reported higher emotional distress and the utilization of emotion-oriented coping strategies, and a lesser availability of social support from family and friends. These variables explained 46.3%, 24.5%, and 22.5%, respectively, of the total variance in psychological distress scores. The findings provide the basis for interventions geared to reduce distress and, as a result, to enable students with severe mental illness to fully utilize the supported education program.

Schizophrenia & Diabetes

* Understanding schizophrenia and diabetes.
Authors: Dinan T, Peverel R, Holt R. - University College Cork, National University of Ireland.
Summary: Alongside other risk factors for the development of type 2 diabetes, the presence of severe mental illness is often overlooked. A person with schizophrenia has a two to four times greater risk of developing diabetes than the general population and the prevalence of type 2 diabetes is between 15 and 18% in the schizophrenia population. A full understanding of this issue is vital.

Schizophrenia & Neural Circuity Function

* Changes in distributed neural circuity function in patients with first-episode schizophrenia.

Arabpsynet Journal N°3 - July-August - September 2004

Authors: Mendrek A, Laurens KR, Kiehl KA, Ngan ET, Stip E, Liddle PF. - Department of Psychiatry, University of Montreal, Centre de recherche Fernand-Seguin, 7331 Hochelaga, Montreal, Quebec H1N 3V2, Canada. amendrek@crfs.umontreal.ca
Source: Br J Psychiatry. 2004 Sep;185:205-14
Summary: BACKGROUND: A number of functional brain abnormalities have been reported in schizophrenia, but it remains to be determined which of them represent trait and state markers of the illness. AIMS: To delineate regional brain dysfunctions that remain stable and those that fluctuate during the course of schizophrenia. METHOD: A cohort of patients with first-episode schizophrenia and a matched group of control participants underwent functional magnetic resonance imaging on two occasions 6-8 weeks apart during performance of a working memory task. The patients’ disease was in partial remission at the second scan. RESULTS: Relative to control participants, the function of the left dorsolateral prefrontal cortex, left thalamus and right cerebellum remained disturbed in the people with schizophrenia, whereas the dysfunction of the right dorsolateral prefrontal cortex, right thalamus, left cerebellum and cingulate gyrus normalised, with significant reduction in symptoms. CONCLUSIONS: These results suggest that dysfunction of the left fronto-thalamo-cerebellar circuitry is a relatively stable characteristic of schizophrenia, whereas disturbance of the right circuitry and cingulate gyrus predominantly a state-related phenomenon.

Psychotropic Drugs (PD)

Benzodiazepines & Akathisia

* Benzodiazepines for neuroleptic-induced acute akathisia.
Authors: Lima AR, Soares-Weiser K, Bacaltchuk J, Barnes TRE
Summary: A substantive amendment to this systematic review was last made on 11 August 1999. Cochrane reviews are regularly checked and updated if necessary.
Background: Neuroleptic-induced akathisia is one of the most common and distressing early-onset adverse effects of antipsychotic drugs, being associated with poor compliance with treatment, and thus, ultimately, to an increase risk of relapse. This review assesses the role of benzodiazepines in the pharmacological treatment of this problem.
Objectives: To determine the effects of benzodiazepines versus placebo for people with neuroleptic-induced acute akathisia.
Search strategy: Biological Abstracts (January 1982-March 1999), The Cochrane Library (Issue 3 1999), The Cochrane Schizophrenia Group’s Register (May 2001), EMBASE (January 1980-March 1999), LILACS (January 1982-March 1999), MEDLINE (January 1964-March 1999), PsyCIT (January 1974-March 1999), and SCISEARCH were searched. Further references were sought from published trials and their authors.
Selection criteria: All randomised clinical trials comparing benzodiazepines with placebo for people with antipsychotic-induced acute akathisia.
Data collection and analysis: Two reviewers, working independently, selected, quality assessed and extracted data.
Antidepressants & Smoking Cessation

**Antidepressants for smoking cessation**

**Authors:** Hughes JR, Stead LF, Lancaster T


**Summary:** A substantive amendment to this systematic review was last made on 21 May 2004. Cochrane reviews are regularly checked and updated if necessary.

**Background:** There are at least two reasons to believe antidepressants might help in smoking cessation. Depression may be a symptom of nicotine withdrawal, and smoking cessation sometimes precipitates depression. In some individuals, nicotine may have antidepressant effects that maintain smoking. Antidepressants may substitute for this effect.

**Objectives:** The aim of this review is to assess the effect of antidepressant medications in aiding long-term smoking cessation. The drugs include bupropion; doxepin; fluoxetine; imipramine; moclobemide; nortriptyline; paroxetine; sertraline; tryptophan and venlafaxine.

**Search strategy:** We searched the Cochrane Tobacco Addiction Group trials register which includes trials indexed in MEDLINE, EMBASE, SciSearch and PsycINFO, and other reviews and meeting abstracts, in December 2002. Selection criteria: Studies were required to be prospective, controlled trials of self-administered drug treatments taken regularly to prevent the occurrence of migraine attacks and/or to reduce the intensity of those attacks.

**Main results:** Fifteen papers were included in the review. Of these, 14 reported trials comparing antidepressants with placebo, as follows: four trials of divalproex sodium, three trials of topiramate, two trials of sodium valproate, two trials of gabapentin, and one trial each of carbamazepine, clonazepam, and lamotrigine. One paper reported a trial of sodium valproate versus an active comparator, lamotrigine, and one trial of divalproex sodium versus placebo included a comparison against propranolol, also an active comparator. Data from 2024 patients were considered. Analysis of data

**Main results:** Two small (total N=27) randomised controlled trials were included. By seven to 14 days, there was a reduction in symptoms for those patients receiving clonazepam compared with placebo (2 RCTs, N=26, RR 0.09 CI 0.01 to 0.6, NNT 1.2 CI 0.9 to 1.5). No significant difference was found for adverse events (2 RCTs, N=26, RR 3.00 CI 0.2 to 62) or the need for anticholinergic medication (2 RCTs, N=26, RR 1.56 CI 0.9 to 2.7). No one left the two studies early.

Data on mental, social and family outcomes could not be pooled and there was little or no data on user satisfaction, deaths, violence, criminal behaviour and costs.

**Reviewers’ conclusions:** The antidepressants bupropion and nortriptyline can aid smoking cessation but selective serotonin reuptake inhibitors (e.g. fluoxetine) do not.

**Anticonvulsant Drugs & Migraine**

**Anticonvulsant drugs for migraine prophylaxis**

**Authors:** Chronicle E, Mulleners W


**Summary:** Anticonvulsant drugs seem to be useful in clinical practice for the prophylaxis of migraine. This might be explained by a variety of actions of these drugs in the central nervous system that are probably relevant to the pathophysiology of migraine.

**Objectives:** To describe and assess the evidence from controlled trials on the efficacy and tolerability of anticonvulsants for preventing migraine attacks in adult patients with migraine.

**Search strategy:** We searched MEDLINE (from 1966 on) and the Cochrane Central Register of Controlled Trials (CENTRAL). Date of most recent search: April 2003. Additional information was gained from hand-searching specialist headache journals; correspondence with pharmaceutical companies, authors of reports, and experts in the field; and a wide variety of review articles and book chapters.

**Selection criteria:** Studies were required to be prospective, controlled trials of self-administered drug treatments taken regularly to prevent the occurrence of migraine attacks and/or to reduce the intensity of those attacks.

**Data collection and analysis:** Studies were selected and data extracted by two independent reviewers. For dichotomous data, standardized mean differences (SMDs) were calculated for individual studies and pooled across studies. For dichotomous data on significant reduction in migraine frequency, odds ratios (ORs) and numbers-needed-to-treat (NNTs) were similarly calculated. Adverse events were analyzed by calculating numbers-needed-to-harm (NNHs) for studies using similar agents.

**Main results:** Nine of the bupropion trials have been published in full. Nortriptyline (five trials, OR 2.80, 95% CI 1.81 - 4.32) and bupropion (16 trials, OR 1.97, 95% CI 1.67 - 2.34) both increased the odds of cessation. In one trial the combination of bupropion and nicotine patch produced slightly higher quit rates than patch alone, but this was not replicated in a second study. Two trials of extended therapy with bupropion to prevent relapse after initial cessation have failed to detect a long-term benefit.

Reviewers’ conclusions: The antidepressants bupropion and nortriptyline can aid smoking cessation but selective serotonin reuptake inhibitors (e.g. fluoxetine) do not.
Anticonvulsant Drugs & Chronic Pain

* Anticonvulsant drugs for acute and chronic pain

Authors: Wilfen P, Collins S, McQuay H, Carroll D, Jadad A, Moore A


Summary: A substantive amendment to this systematic review was last made on 23 May 2000. Cochrane reviews are regularly checked and updated if necessary.

Background: Anticonvulsant drugs have been used in the management of pain since the 1960s. The clinical impression is that they are useful for chronic neuropathic pain, especially when the pain is lancinating or burning.

Objectives: To evaluate the analgesic effectiveness and adverse effects of anticonvulsant drugs for pain management in clinical practice and to identify a clinical research agenda. Migraine and headache studies are excluded in this revision.

Search strategy: Randomised trials of anticonvulsants in acute, chronic or cancer pain were identified from the reference list of the retrieved papers, and from searching electronic databases. Cochrane reviews are regularly checked and updated if necessary.

Selection criteria: Randomised trials reporting the analgesic effects of anticonvulsant drugs in patients with subjective pain assessment as either the primary or a secondary outcome.

Data collection and analysis: Data were extracted by two independent reviewers, and quality scored.

Main results: Twenty-three trials of six anticonvulsants were considered eligible (1,074 patients). The only placebo-controlled study in acute pain found no analgesic effect of sodium valproate. Three placebo-controlled studies of carbamazepine in trigeminal neuralgia had a combined NNT (95% confidence interval (CI)) for effectiveness of 2.5 (CI 2.0-3.4). A single placebo-controlled trial of gabapentin in post-herpetic neuralgia had an NNT of 3.2 (CI 2.4-5.0). For diabetic neuropathy NNIs for effectiveness were as follows: (one RCT for each drug) carbamazepine 2.3 (CI 1.6-3.8), gabapentin 3.8 (CI 2.4-8.7) and phenytoin 2.1 (CI 1.5-3.6).

Modafinil & SSRI

* An open-label study of adjunctive modafinil in patients with sedation related to serotonergic antidepressant therapy.

Authors: Schwartz TL, Azhar N, Cole K, Hopkins G, Nihalani N, Simonescu M, Husain J, Jones N. - Department of Psychiatry, State University of New York Upstate Medical University, Syracuse, N.Y.

Source: J Clin Psychiatry. 2004 Sep;65(9):1223-7

Summary: In patients with major depressive disorder (MDD), excessive sleepiness and fatigue not only are major components of the disorder, but also may occur as side effects of antidepressant therapy. In addition, sedation may be a consequence of antidepressant regimens. The novel wake-promoting agent modafinil improves wake-fulness and reduces fatigue across a variety of clinical disorders. This study assessed the use of modafinil as an adjunctive treatment in patients with MDD who reported sedation related to serotonergic antidepressant therapy. METHOD: Data were collected between September 2001 and December 2003. Twenty men and women with DSM-IV-defined MDD were enrolled in this 3-week, open-label, single-center study. In addition to ongoing and stable treatment with selective serotonin reuptake inhibitors (SSRIs), clinic patients received modafinil once daily. Efficacy assessments were conducted at 1-week intervals. RESULTS: Sixteen patients (80%) completed the study. Modafinil plus SSRIs significantly improved overall depressive symptoms, as shown by reductions in mean Hamilton Rating Scale for Depression total scores (p <.001 vs. baseline). Adjunctive modafinil significantly improved subjective estimates of wakefulness on the Epworth Sleepiness Scale (p <.001, all weeks) and reduced fatigue on the Fatigue Severity Scale (p <.009). At the final visit, modafinil had improved overall health status and health.
related quality of life, as shown by significant improvements in mean Medical Outcomes Study Short-Form 12-Item Health Survey total scores (p = .007) and in physical health (p = .04) and mental health (p = .006) subscores. CONCLUSION: In patients with MDD who experience sedation as a side effect of antidepressant therapy, adjunctive modafinil improved wakefulness and reduced fatigue. Modafinil plus SSRIs also improved mood and quality of life.

**Thyroid Hormones & SSRI**

* Peripheral thyroid hormones and response to selective serotonin reuptake inhibitors

**Authors:** Michael Gitlin, MD; Lori L. Altshuler, MD; Mark A. Frye, MD; Rita Suri, MD; Emily L. Huynh, BA; Lynn Fairbanks, PhD; Michael Bauer, MD; Stanley Korenman, MD

**Source:** J Psychiatry Neurosci 2004;29(5):383-6

**Summary:** To examine the relation between baseline measurements of thyroid function and response to selective serotonin reuptake inhibitors (SSRIs) and to consider the effect of these antidepressants on thyroid hormone levels. Methods: Nineteen subjects with major depression, but without a history of thyroid treatment or lithium treatment, were treated openly with either sertraline or fluoxetine in a university-affiliated tertiary care hospital. Hamilton Depression Rating Scale (Ham-D) scores were measured before and after treatment. Clinical Global Impressions (CGI) scores were measured at study end. Thyroid data, consisting of values for thyroid-stimulating hormone (TSH), triiodothyronine (T3), measured by radioimmunoassay ([RIA]), thyroxine (T4), measured by RIA and free T4, were collected before and after treatment. Complete thyroid data were available for 17 subjects. Data were collected during 1997-1999. Results: Baseline TSH correlated strongly with response to treatment as measured by change in Ham-D scores (r = 0.64, p = 0.003). Low TSH values correlated with greater improvement in depressive symptoms. Thyroid hormone levels decreased with treatment, but these decreases did not correlate with clinical improvement. Conclusion: Baseline thyroid function, as measured by serum TSH, may predict a patient’s response to antidepressant treatment with SSRIs. Optimal thyroid function, beyond simply being within the normal laboratory values, may be necessary for an optimal response to antidepressants.

**Weight & Antidepressants**

* Early prediction of changes in weight during six weeks of treatment with antidepressants.

**Authors:** Himmerich H, Schuld A, Haack M, Kaufmann C, Pollmacher T. - Max Planck Institute of Psychiatry, Kraepelinstrasse 10, Munich 80804, Germany

**Source:** J Psychiatr Res. 2004 Sep-Oct;38(5):485-9

**Summary:** Weight gain is a frequent and important side effect of psychotropic treatment. We sought to determine weight change predictors during treatment with antidepressant drugs. In 24 patients weight, plasma levels of leptin, tumor necrosis factor-alpha (TNF-α), [Formula: see text] and soluble TNF receptors were determined longitudinally and a multiple linear regression analysis was used to predict weight change from baseline to the sixth week of treatment. Changes of weight during the first week of treatment, but no other parameter, strongly predicted weight change until endpoint (adjusted [Formula: see text], [Formula: see text], [Formula: see text]). Very early changes in weight during treatment with psychotropic drugs might be a simple and clinically useful predictor of future weight development.

**Antipsychotic Medication & Diabetes**

* Relationship between antipsychotic medication treatment and new cases of diabetes among psychiatric inpatients.

**Authors:** Citrome L, Jaffe A, Levine J, Allingham B, Robinson J. - New York University School of Medicine in New York City.

**Source:** Psychiatr Serv. 2004 Sep;55(9):1006-13

**Summary:** This study examined data on patients with serious and persistent mental illness in a large state hospital system to determine whether patients who took second-generation antipsychotics were more likely to develop diabetes mellitus than patients who took first-generation antipsychotics. METHODS: A case-control study design was used. A new prescription of an antidiabetic medication was used to identify new cases of diabetes mellitus. Odds ratios were calculated for exposure to second-generation antipsychotics (clozapine, risperdone, olanzapine, quetiapine, and multiple second-generation antipsychotics) compared with exposure to first-generation antipsychotics. Cases and controls were identified by using a database that contained drug prescription information from the inpatient facilities that were operated by the New York State Office of Mental Health. Data from January 1, 2000, to December 31, 2002, were examined. Among 13,611 unique patients who received antipsychotics, 8,461 met entry criteria of being hospitalized for at least 60 days and not having an antidiabetic medication prescribed in the past. A total of 181 of these inpatients received prescriptions for an antidiabetic medication at least 30 days after their admission. Eight controls (N=1,448) for each case (N=181) were matched by calendar year, length of observation period, race, age group, and diagnosis, giving a total sample of 1,629 patients. RESULTS: Statistically significant elevations in risk were seen among patients who received more than one second-generation antipsychotic or clozapine or quetiapine.
compared with patients who received first-generation antipsychotics alone. Although not statistically significant, odds ratios for olanzapine and risperidone were also elevated. Conditional logistic regression adjusting for gender and age did not change the results. CONCLUSIONS: Exposure to multiple second-generation antipsychotics or clozapine or quetiapine significantly increased the risk of treatment-emergent diabetes mellitus.

**Stimulant Drugs Psychosis**

**Stimulant psychosis: systematic review.**

**Authors:** Curran C, Byrappa N, McBride A. - Pendine Community Mental Health Trust, 124-126 Cowbridge Road West, Ely, Cardiff CF5 5BT, Wales, UK.

**Source:** Br J Psychiatry. 2004 Sep;185:196-204

**Summary:** Background: Psychosis associated with stimulant use is an increasing problem, but there is little research evidence about the nature of the problem and its management. AIMS: To critically review the literature on stimulant psychosis and sensitisation. METHOD: Systematic review of studies that have investigated stimulant use and psychosis in humans. The main outcome measures were increases in psychosis with stimulant use, and differences between stimulant users and non-users. RESULTS: Fifty-four studies met the inclusion criteria. Experimental studies show that a single dose of a stimulant drug can produce a brief increase in psychosis ratings (a "response") in 50-70% of participants with schizophrenia and pre-existing acute psychotic symptoms, unaffected by the presence of antipsychotic medication. Those with schizophrenia who do not have acute psychotic symptoms respond, but less frequently (30%). There has been little research into the longer-term effects of use. CONCLUSIONS: Compliance with antipsychotic medication by someone with schizophrenia will not prevent a relapse or worsening of psychotic symptoms if stimulants are used. Low-dose antipsychotic treatment may be beneficial in stimulant users, to prevent sensitisation.

**ISSR & Cardiovascular Effects**

**Cardiovascular effects of selective serotonin reuptake inhibitors.**

**Authors:** Jean-Sébastien Hulot, Ivan Berlin

**Source:** Sang Thrombose Vaisseaux. Number 16, volume 6, 302-8, Juin 2004, Mini-revue

**Summary:** Unlike other antidepressants such as tricyclic agents, selective serotonin reuptake inhibitors (SSRIs) have shown no evidence of cardiac toxicity even in patients with heart disease. They thus represent first line treatment in individuals with cardiopathies (notably of ischemic origin) with coexisting depression. SSRIs display some cardiovascular effects that may be beneficial in the management of such patients. Because they block reuptake of serotonin in platelets, some SSRIs may inhibit platelet activation even in patients receiving conventional anti-agregant therapy. This effect, considered as an adverse effect in other situations, may be beneficial in some cardiovascular disorders. Furthermore, SSRIs may reduce increased sympathetic activity, a common feature of depression and some cardiac disorders and re-establish the sympathetic-parasympathetic balance. These mechanisms may be involved in the reduction of cardiovascular morbidity and mortality in SSRI-treated patients reported in recent studies.

**Geriatric Psychiatry (GP)**

**GP & Depression in the Elderly Patient**

**Depression in the elderly patient**

**Authors:** Clement JP. Pole de psychiatrie du sujet age, centre hospitalier Esquirol, 87025 Limoges Cedex.

**Source:** Rev Prat. 2004 Apr 15;54(7):725-33.

**Summary:** Depression is the most usual mental disorder in the elderly, but underdiagnosed and undertreated. Its prevalence is variable and depends on type and severity of episode. Nevertheless, even subsyndromic depression needs to be correctly treated. Depressive symptomatology observed in the elderly is often similar to adult presentation, but it can be masked and difficult to recognise. The different clinical features are described with underlining their particularities. Secondary depressions are also evoked with individualization of “vascular” depression and its etiopathogenic hypotheses in relationship with observations given by cerebral neuro-imagery. Risk factors of depression in old age are known, but recent studies have reviewed some of them, particularly by distinguishing late onset depression and early onset depression. According to therapeutic response and prognosis, it appears necessary to better discriminate them. Risk of...
dementia after depression seems to be related with type of depressive episode and with the treatment efficacy. Finally, the problem of detection of depression in old age is discussed with a suggestion to use assessment instruments as the mini-GDS in all medical practices, to optimise diagnosis and management.

**GP & Treatment of Depression in the Elderly**

* Treatment of depression in the elderly

**Authors:** Robert PH. Centre Memoire de ressources & de recherche, CHU, Universite de Nice-Sophia Antipolis–Pavillon M, hospital Pasteur, 06002 Nice.

**Source:** Rev Prat. 2004 Apr 15;54(7):734-8.

**Summary:** Depression is the most common mental health problem of later life. There is effective treatments for depression in primary care. Recommendation based on current evidence are: in primary care treatment there is no evidence that one class of antidepressant is anymore effective than others; although newer antidepressants are not more effective than older ones, they are better tolerated in healthy older people and in patients with medical co-morbidity and are safer especially in overdose. Lower dose antidepressant treatment is not recommended for older depressed patients.

**GP & Antidepressant Efficacy**

* Antidepressant efficacy and cognitive effects of repetitive transcranial magnetic stimulation in vascular depression: an open trial.

**Authors:** Fabre I, Gallinowski A, Oppenheim C, Gallarda T, Meder JF, De Montigny C, Olie JP, Poirier MF. Sainte-Anne Hospital, University Department of Psychiatry, Paris, France.

**Source:** Int J Geriatr Psychiatry. 2004 Sep;19(9):833-42.

**Summary:** BACKGROUND: Beneficial effects of repetitive transcranial magnetic stimulation (rTMS) were demonstrated by many controlled studies in major depression. Moreover, this promising and non invasive therapeutic tool seems to be better tolerated than electroconvulsive therapy. Vascular depression is a subtype of late-life depression, associated with cerebrovascular disease and means a poorer response to antidepressant treatment. We employed rTMS over the left prefrontal cortex in 11 patients with late-onset resistant vascular depression. The primary purpose of this two-week open study was to examine antidepressant efficacy of rTMS in vascular depression. The secondary aim was to evaluate cognitive effects of rTMS in our sample. METHODS: Clinical status, as measured with the Hamilton Depression Rating Scale (HDRS), and cognitive effects, as evaluated by neuropsychological tests, were assessed at baseline and after two weeks of rTMS. Brain measurements to obtain an index of prefrontal atrophy were performed at both the motor cortex and prefrontal cortex. RESULTS: Five out of 11 resistant patients with late-onset vascular depression were responders. They showed a clinically meaningful improvement in HDRS scores, with a decrease of 11, 4 points (p<0.01). Antidepressant response is correlated to the relative degree of prefrontal atrophy (p = 0.05). After two weeks, verbal fluency and visuospatial memory improved. No cognitive performance deteriorated except for verbal memory, as the delayed recall decreased significantly in the responders’ group.

**Conclusions:** Our preliminary observations prompt to perform a subsequent controlled study to examine if rTMS may constitute an alternative to electroconvulsive therapy.

**GP & Risperidone & Elderly Patients**

* Efficacy and safety of long-acting risperidone in elderly patients with schizophrenia and schizoaffective disorder.

**Authors:** Lasser RA, Bossie CA, Zhu Y, Gharabawi G, Eerdekens M, Davidson M. Janssen Medical Affairs, LLC, Titusville, New Jersey, USA.

**Source:** Int J Geriatr Psychiatry. 2004 Sep;19(9):898-905.

**Summary:** BACKGROUND: Elderly patients are often an underserved population in terms of optimizing treatment outcomes. Long-acting risperidone, the first long-acting injectable atypical antipsychotic, can improve outcomes through continuous medication delivery. OBJECTIVE: To assess the efficacy and safety of long-acting injectable risperidone in elderly patients with psychotic disorders. METHODS: This is a subanalysis of 57 patients aged >/=65 years enrolled in an open-label study of long-acting risperidone that included 725 symptomatically stable patients with schizophrenia or schizoaffective disorder. Patients were assigned to receive 25, 50, or 75 mg of long-acting risperidone every 2 weeks for up to 50 weeks. RESULTS: Fifty-seven elderly patients (mean +/- SE age, 70.9 +/- 0.7 years) were enrolled. Mean Positive and Negative Syndrome Scale (PANSS) total scores improved significantly throughout the study and at endpoint (p < 0.001). The PANSS factor scores (positive symptoms, negative symptoms, disorganized thoughts, uncontrolled hostility/excitement, and anxiety/depression) also significantly improved (p < 0.01). Clinical improvement (>/=20% reduction in PANSS total scores) was achieved by 49% of these stable patients, and 55% improved on the Clinical Global Impressions Scale. Severity of movement disorders (Extrapyramidal Symptom Rating Scale scores) was reduced significantly. Adverse events reported in >/=10% of patients were insomnia (14%), constipation (12%), and bronchitis (12%). CONCLUSIONS: Long-acting risperidone was associated with significant symptom improvements in stable elderly patients with schizophrenia or schizoaffective disorder. Treatment was well tolerated.

**Depression & Sex Hormones**

* Depression & Sex Hormones In Elderly Women.

**Authors:** Erdincler D, Bugay G, Ertan T, Eker E.- Geriatric Unit of the Internal Medicine Department, Cerrahpas a Medical School, Istanbul University, Istanbul, Turkey.

**Source:** Arch Gerontol Geriatr. 2004 Nov-Dec;39(3):239-44.

**Summary:** We aimed to study the relation between sex hormones and depression among elderly women. The study was carried out on 74 volunteered female subjects above 60 years of age. Each subject was asked to fill the geriatric depression scale (GDS) questionnaire and further evaluated for clinical depression by a psychiatrist using the DSM IV diagnostic criteria. For statistical analysis, subjects were later divided in two groups, according to the presence of clinical depression. Cognitive functions were assessed with the standardized mini mental test (SMMT). Disability in the...
activities of daily living was assessed with instrumental activities of daily living (IADL) scale. Plasma levels of estrogen, testosterone, progesterone, and dehydroepiandrosterone sulfate (DHEA-S) were measured with chemiluminescent methods, and plasma levels of androstenedione were measured with radioimmunoassay. Among 74 subjects, 34 (39%) had clinical depression. Age, number of years spent in education, SMMT scores, and IADL scores did not differ between the depressive and non-depressive groups. Plasma sex hormone levels were not found to be different between the two groups.

**Venlafaxine & Late-Life Atypical Depression**

* An open trial of venlafaxine for the treatment of late-life atypical depression.

**Authors**: Roose SP, Miyazaki M, Devanand D, Seidman S, Fitzsimmons L, Turret N, Sackeim H. - New York State Psychiatric Institute, and the College of Physicians and Surgeons of Columbia University, New York, USA

**Source**: Int J Geriatr Psychiatry. 2004 Sep 27;19(10):989

**Summary**: The atypical subtype in patients with major depressive disorder is characterized by mood reactivity, significant weight gain or increase in appetite, hypersomnia, leaden paralysis and a long-standing pattern of interpersonal rejection sensitivity. Though atypical depression is well documented in patients with atypical depression patients. This study reports the patient characteristics and treatment results of an eight-week open-label trial of venlafaxine in a sample of older depressed patients with atypical subtype. METHODS: Patients received fixed dosing schedule (up to 300 mg/day) of venlafaxine (Effexor XR) for 8 weeks. RESULTS: In this sample of 17 patients, the mean age was 65.6 years and 77% were female. Most strikingly, 53% of patients presented with late-onset atypical depression defined as first episode after the age of 50. Fifty of the 17 patients (88%) completed the eight-week treatment trial. The mean score on the HRSD 24-item decreased from 22.2 +/- 5.1 at baseline to 11.8 +/- 8.9 (p<0.001), and the mean total atypical item score decreased from 6.2 +/- 1.6 to 2.8 +/- 2.0 (p < 0.001). Remission was defined as a final HRSD 24 item score of < 10 and a 50% reduction in baseline HRSD score. The intent-to-treat remission rate was 65% and the complete remission rate was 73%. CONCLUSIONS: In this sample of late-life patients with atypical depression venlafaxine treatment was reasonably effective and well tolerated. However, the effectiveness of venlafaxine in this study must be considered in the context that this was an open trial of antidepressant medication. Insufficient attention has been given to the atypical subtype in late-life depression. Whether late-onset atypical depression is significantly different from early-onset atypical depression, and whether late-onset patients with atypical depression are significantly different from late-onset patients with other depressive subtypes are questions of compelling interest.

**Dementia**

**Dementia & Diagnosis & Treatment**

* Effectiveness of a clinical pathway for the diagnosis and treatment of dementia and for the treatment of dementia.

**Authors**: Kazui H, Hashimoto M, Nakano Y, Matsumoto K, Yamamura S, Nagaoka K, Mori E, Endo H, Tokunaga H, Ikejiri Y, Takeda M. Psychiatry and Behavioral Science, Osaka University Graduate School of Medicine, Japan.

**Source**: Int J Geriatr Psychiatry. 2004 Sep;19(9):892-7

**Summary**: AIMS: Clinical pathways (CPs) are rarely used in the treatment of dementia. We established a CP for a series of medical practices (diagnosis, treatment, establishment of a care system, and caregiver education) for patients with dementia hospitalized for a three-week period, and evaluated its usefulness. METHODS: The length of hospital stay and hospital costs were compared between 23 consecutive patients with dementia hospitalized and treated using a CP and 20 controls treated by conventional medical practice without using a CP in a special ward for dementia patients. In the CP group, at the time of discharge, primary caregivers, physicians, and nurses were given a questionnaire to obtain their comments about the impression of treatment with the CP. RESULTS: The questionnaire survey indicated that the CP deepened the caregiver’s understanding of the sequence of medical practices for the patient, the disorders of the patient, the treatment methods, and the methods for coping with the disorder. The CP was also useful for facilitating inpatient medical practice and promoting the establishment of a care system after discharge. The use of the CP significantly shortened the length of hospital stay and decreased hospital costs during hospitalization but increased the amount of work per day and made the medical staff feel that their freedom to choose medical procedures had been restricted. CONCLUSIONS: The CP was useful for execution of inpatient medical practices for patients with dementia.

**Dementia & Antidepressants**

* Antidepressants for treating depression in dementia.

**Authors**: Bains J, Birks JS, Dening TR


**Summary**: A substantive amendment to this systematic review was last made on 17 July 2002. Cochrane reviews are regularly checked and updated if necessary. Background: The use of antidepressants for patients with dementia accompanied by depressive symptoms is widespread, but their clinical efficacy is uncertain. This uncertainty is due to the difficulties of interpreting the results of clinical trials. Many of the individual trials of antidepressants have been too small to provide precise estimates of the moderate benefits that might realistically be expected. Combining the information from all appropriate trials may provide a better estimate of the likely effects of treatment. Objectives: This review aims to determine whether antidepressants are clinically effective and acceptable for the treatment of patients diagnosed as having depression and also diagnosed as having dementia. Search strategy: The CDCIG Specialized Register which includes records from all major medical databases and many trial databases was searched on 21 January 2001. The (long) list of search terms can be found in the main body of the review. Medical information departments of pharmaceutical companies were asked to search their databases for any relevant clinical trials. Where necessary authors of trials were approached with requests for additional information.
Selection criteria: All relevant unconfounded, double-blind, randomized trials comparing any antidepressant drug (as defined by the British National Formulary) with placebo, for patients diagnosed as having dementia and diagnosed as having a depression, according to established criteria.

Data collection and analysis: Data were extracted independently by two of the reviewers and any differences settled by agreement. Main results: There were six included studies with a total 1077 subjects, of whom 739 met inclusion criteria. Of these, four studies (including a total of 234 subjects) reported results in sufficient detail to enter into meta-analyses. One study’s results were limited to adverse results data, therefore the meta-analysis concerning efficacy was limited to three studies (Lyketsos 2000, Petracca 1996, Reifler 1989), with a total of 107 subjects. Of these three studies, two (Petracca 1996, Reifler 1989) investigated the properties of tricyclic antidepressants, drugs not commonly used in this population, and only one study investigated the properties of the more commonly used selective serotonin reuptake inhibitors (Lyketsos 2000). One of these studies (Lyketsos 2000) produced two significant differences in favour of treatment, the Cornell Scale for Depression in Dementia at 6-9 weeks (WMD -7.1, 95% CI -13.05, -1.15) and the psychiatrists’ global rating (Peto OR (95% Fixed) 8.17 (1.58, 42.09)). However, the Cornell Scale for Depression in Dementia was not used in any of the other studies and no statistical differences were found with the other measures used in the meta-analysis. The meta-analysis of the number of patients suffering at least one adverse event at 6-9 weeks, using the Peto-ods ratio, showed a significant difference in favour of placebo. There were no other significant results.

Reviewers’ conclusions: Available evidence offers weak support to the contention that antidepressants are effective for patients with depression and dementia. However, only three studies are included in the meta-analysis relating to efficacy, and sample sizes are small. Moreover, only one of the studies included in the analysis of efficacy data investigated the properties of the more commonly used selective serotonin reuptake inhibitors and no studies investigated the properties of newer classes of antidepressants (e.g. selective noradrenergic reuptake inhibitors). This review draws attention to the paucity of research and evidence in this area. It is not that antidepressants are necessarily ineffective but there is not much evidence to support their efficacy either. Given that they may produce serious side-effects clinicians should prescribe with due caution.

**Musical Therapy for People with Dementia**

**Authors:** Vink AC, Birks JS, Bruinsma MS, Scholten RJJS


**Summary:** A substantive amendment to this systematic review was last made on 27 February 2002. Cochrane reviews are regularly checked and updated if necessary.

**Background:** Dementia is a clinical syndrome with a number of different causes which is characterised by deterioration in cognitive functions. Research is pursuing a variety of promising findings for the treatment of dementia. Pharmacological interventions are available but have limited ability to treat many of the syndrome’s features. Little research has been directed towards non-pharmacological treatments. In this review the evidence for music therapy as a treatment is examined.

**Objectives:** To assess the effects of music therapy in the treatment of behavioural, social, cognitive and emotional problems of older people with dementia.

**Search strategy:** The Cochrane Dementia and Cognitive Improvement Group (CDCIG) Specialised Register was searched on 30 June 2003 using the term "music*". This Register contains records from all major health care databases and many ongoing trial databases and is updated regularly. The principal reviewer conducted additional searches to retrieve randomised controlled trials (RCTs) concerning the effect of music therapy on older people with dementia.

**Selection criteria:** Randomised controlled trials that reported clinically relevant outcomes associated with music therapy in treatment of behavioural, social, cognitive and emotional problems of older people with dementia.

**Data collection and analysis:** Two reviewers screened retrieved studies independently for methodological quality using a checklist. Data from accepted studies were independently extracted by the reviewers.

**Main results:** Five studies were included. The methodological quality of the studies was generally poor and the study results could not be validated or pooled for further analyses.

**Reviewers’ conclusions:** The methodological quality and the reporting of the included studies were too poor to draw any useful conclusions.

**Haloperidol for Agitation in Dementia**

**Authors:** Lonergan E, Luxenberg J, Colford J


**Summary:** A substantive amendment to this systematic review was last made on 27 February 2002. Cochrane reviews are regularly checked and updated if necessary.

**Background:** Agitation occurs in up to 70% of demented patients. Haloperidol has been used for decades to control agitation in dementia, but its effectiveness remains unclear. Previous meta-analyses examined only English language publications or compared haloperidol with other drugs rather than with placebo. To study the effectiveness of haloperidol a more widely based review was performed.

**Objectives:** To determine whether evidence supported the use of haloperidol in agitated dementia.

**Search strategy:** The trials were identified from a last updated search of the Specialized Register of the Cochrane Dementia and Cognitive Improvement Group on 10 July 2003 using the terms halop*, aloperid*, haldol, galoperidol. This register is updated regularly and contains records from all major health care databases and many ongoing trial databases.

**Selection criteria:** Randomized, placebo-controlled trials, with concealed allocation, where subjects’ dementia and agitation were assessed.

**Data collection and analysis:** 1. Two reviewers extracted data from included trials. Data were pooled where possible, and analysed using appropriate statistical methods. Only ‘intention to treat’ data were included. Analysis included haloperidol treated patients, compared with placebo.
Women Dementia, Hormone & Cognitive function

Hormone Replacement Therapy to Maintain Cognitive Function in Women with Dementia

Authors: Hogervorst E, Yaffe K, Richards M, Huppert F

Summary: A substantive amendment to this systematic review was last made on 27 May 2002. Cochrane reviews are regularly checked and updated if necessary.

Background: As estrogens have been shown to have several potentially beneficial effects on the central nervous system, it is biologically plausible that maintaining high levels of estrogens in postmenopausal women by means of estrogen replacement therapy (ERT) could be protective against cognitive decline and the development of Alzheimer's disease (AD) or other dementia syndromes.

Objectives: To investigate the effects of ERT (estrogens only) or HRT (estrogens combined with a progestagen) compared with placebo in randomized controlled trials (RCTs) on cognitive function of postmenopausal women with dementia. Search strategy: The CDCG Specialized Register, which contains up-to-date records from many medical databases was searched using the terms ORT, PORT, ERT, HRT, estrogen*, oestrogen*, progesteron* and Alzheimer* on 16th of May 2002. In addition, MEDLINE (1966-2002/01); EMBASE (1985-2002/01) and PsycINFO (1967-2002/01) were searched. Selection criteria: All double-blind randomized controlled trials (RCTs) into the effect of ERT or HRT for cognitive function with a treatment period of at least two weeks in postmenopausal women with AD or other types of dementia. Data collection and analysis: Abstracts of the references retrieved by the searches were read by two reviewers (EH and KY) independently in order to discard those that were clearly not eligible for inclusion. The two reviewers studied the full text of the remaining references and independently selected studies for inclusion. Any disparity in the ensuing lists was resolved by discussion with all reviewers in order to arrive at the final list of included studies. The selection criteria ensured that the blinding and randomization of the included studies was adequate. The two reviewers also assessed the quality of other aspects of the included trials. One reviewer (EH) extracted the data from the studies, but was aided and checked by JB from Cochrane.

Main results: The five included trials led to the following results:
1. There was no significant improvement in agitation among haloperidol treated patients, compared with controls.
2. Aggression decreased among patients with agitated dementia; other aspects of agitation were not affected significantly in treated patients compared with controls. Although two studies showed increased drop-outs due to adverse effects among haloperidol patients, there was no significant difference in drop-out rates, comparing all haloperidol treated patients with controls.
3. The data were insufficient to examine response to treatment in relation to length of treatment, degree of dementia, age or sex of patients, and cause of dementia.
4. The present study confirmed that haloperidol should not be used routinely to treat agitation in dementia.

Reviewers' conclusions: 1. Evidence suggests that haloperidol was useful in reducing aggression, but was associated with adverse effects; there was no evidence to support the routine use of this drug for other manifestations of agitation in dementia.
2. Similar drop-out rates among haloperidol and placebo treated patients suggested that poorly controlled symptoms, or other factors, may be important in causing treatment discontinuation.
3. Variations in degree of dementia, dosage and length of haloperidol treatment, and in ways of assessing response to treatment suggested caution in the interpretation of reported effects of haloperidol in the management of agitation in dementia.
4. The present study confirmed that haloperidol should not be used routinely to treat patients with agitated dementia. Treatment of agitated dementia with haloperidol should be individualized and patients should be monitored for adverse effects of therapy.
**Summary:** A substantive amendment to this systematic review was last made on 27 May 2003. Cochrane reviews are regularly checked and updated if necessary. Background: Alzheimer's disease is the most common cause of dementia in older people. One of the aims of therapy is to inhibit the breakdown of a chemical neurotransmitter, acetylcholine, by blocking the relevant enzyme. This can be done by a group of chemicals known as cholinesterase inhibitors. However, some (like tacrine) are associated with adverse effects such as hepatotoxicity, but donepezil (E2020, Aricept) is safer.

Objectives: The objective of this review is to assess whether donepezil improves the well-being of patients with dementia due to Alzheimer's disease.

Search strategy: The Cochrane Dementia and Cognitive Improvement Group's Specialized Register was searched using the terms 'donepezil', 'E2020' and 'Aricept' on 9 October 2002. This Register contains up-to-date records of all major health care databases and many ongoing trial databases. Members of the Donepezil Study Group and Eisai Inc were contacted.

Selection criteria: All unconfounded, double-blind, randomized controlled trials in which treatment with donepezil was compared with placebo for patients with mild, moderate or severe dementia due to Alzheimer's disease.

Data collection and analysis: Data were extracted by one reviewer (JSB), pooled where appropriate and possible, and the weighted mean differences or Peto odds ratios (95% CI) estimated.

Main results: Sixteen trials are included, involving 4365 participants. The trials were of 12, 24 or 52 weeks duration in selected patients. Available outcome data cover domains including cognitive function and global clinical state, but data on several important dimensions of outcome are unavailable. For cognition there is a statistically significant improvement for both 5 and 10 mg/day of donepezil at 24 weeks compared with placebo (-2.02 points on the ADAS-Cog scale WMD, 95% CI -2.77 to -1.26, p<0.0001; -2.92 points on the ADAS-Cog scale WMD 95% CI -3.74 to -2.10, p<0.0001) and for 10 mg/day donepezil compared with placebo at 52 weeks (1.84MMSE points, 95% CI, 0.53 to 3.15, p=0.008). The results show some improvement in global clinical state (assessed by an independent clinician) in people treated with 5 and 10 mg/day of donepezil compared with placebo at 12 and 24 weeks. Benefits of treatment were also seen on measures of activities of daily living and behaviour. There were significantly more withdrawals before the end of treatment from the 10 mg/day (but not the 5 mg/day) donepezil group compared with placebo which may have resulted in some overestimation of beneficial changes at 10 mg/day. A variety of adverse effects were recorded, with more incidents of nausea, vomiting, diarrhoea and anorexia in the 10 mg/day group compared with placebo and the 5 mg/day group, but very few patients left a trial as a direct result of the intervention.

Reviewers’ conclusions: People with mild, moderate or severe dementia due to Alzheimer's disease treated for periods of 12, 24 or 52 weeks with donepezil experienced benefits in cognitive function, activities of daily living and behaviour. Study clinicians rated global clinical state more positively in treated patients, and measured less decline in measures of global disease severity. Although no significant changes were measured on a patient-rated quality of life scales, the instrument used was crude and possibly unsuited to the task. The additional data now available confirm the findings of the previous issue of this review and extend the evidence for the effectiveness of treatment to at least 52 weeks and to those with severe dementia. More evidence is still needed for the economic efficacy of donepezil, but clinical efficacy is confirmed.

**Eating Disorders**

**Eating Disorders & Personality Disorders**

- **Eating disorders and personality disorders: awareness of possible interactions & their therapeutic implications.**

**Authors:** Kristine Godt

**Summary:** Personality disorders are defined by a characteristic and enduring pattern of behaviour and inner experience that deviates distinctly from culturally defined norms. Examples include social insecurity or even distrust leading to withdrawal, or patterns of impulsiveness, affective instability or, possibly, self-harm. Personality disorders are distinct from other psychiatric disorders primarily by their enduring character. The prevalence of personality disorders among patients with eating disorders depends on population characteristics. In a specialised outpatient clinic that serves a defined catchment area, nearly one third of patients will fulfill the diagnostic criteria for a personality disorder. Hospitalized patients or patients in more specialised units will surely show a co-occurrence of several modes of interaction between eating disorders and personality disorders could be hypothesized. The treatment of patients with eating disorder should take into account the subgroup with concomitant personality pathology and evaluation and treatment should be planned accordingly, though this requires time and expertise. The issue should also be acknowledged in primary health care and attention be paid to symptoms of eating disorder also in cases in which symptoms of a personality disorder are more pronounced.

**Authors:** Stein Frostad

**Summary:** Eating disorders are associated with several medical complications. Growth retardation and osteoporosis can cause permanent sequelae if treatment is delayed. Severe eating disorders are associated with significant mortality. Cardiac arrhythmias are the most common somatic cause of death. Hypokalaemia is a common complication and is associated with increased risk of cardiac arrhythmias. Occasionally, overzealous refeeding may induce a potentially life-threatening condition, the refeeding syndrome. In any patient with severe eating disorder, a physician should perform diagnostic evaluation including assessment of possible somatic complications. This is necessary in order to determine where and how the patient should be treated. Most of the somatic complications of eating disorders are partly or completely reversible if the patient receives adequate treatment in time.