

Evidence-based best practice interventions for the treatment of mood disorders:
Annotated Information Package

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The AIP was prepared by Meagan Stephenson (NZHTA Research Fellow). It should be read in conjunction with the appended Information Package prepared by Susan Bidwell (NZHTA Information Specialist Manager).

WHAT IS AN ANNOTATED INFORMATION PACKAGE?

Annotated Information Packages (AIPs), prepared by a NZHTA Reviewer, are overviews of an appended Information Package (IP). The IP provides a folder of printed material relating to a specific topic area identified from a systematic search strategy of electronic databases and website resources. The materials include lists of abstracts, key full text papers (where readily available from local resources), and website resources.

The AIP is aimed at giving the client an informed “guided tour” of their IP to increase its usefulness. The AIP report outlines the contents of the IP, highlights information of particular interest and relevance, summarises key articles, and comments on the stage and extent of the research base. It also makes suggestions for publications that the client may wish to have retrieved, and comments on the potential of the topic for evidence-based reviews, such as NZHTA Technical Brief or Systematic Review outputs. AIPs do not involve systematic processes for the critical appraisal of identified research. Another significant limitation is that full text articles of key interest are not retrieved unless freely obtainable from local resources. As a consequence of this, comments and summaries in the AIP may be based on abstracts rather than full text papers.

DISCLAIMER

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Evidence-based best practice interventions for the treatment of mood disorders

RESEARCH QUESTION

What are the best practice evidence-based interventions for mood disorders across different age groups?

BACKGROUND AND SCOPE OF TOPIC

This AIP is one of a series of five reports presenting the best practice recommendations for the treatment of common mental health disorders. The other reports present recommendations for interventions treating substance-related disorders, schizophrenia/psychotic disorders, anxiety disorders and adjustment disorders. Comorbid disorders were not specifically examined but were discussed in some of the included guidelines.

Interventions

Interventions for the treatment of mood disorders fall into two main categories: pharmacological or drug therapies and psychological therapies, such as cognitive behavioural therapy (CBT), interpersonal therapy (IPT), and problem-solving therapy. A third category of alternative or recently-developed therapies includes interventions such as light therapy, electroconvulsive therapy (ECT), St John's Wort, exercise, befriending, family therapy, acupuncture, transcranial magnetic stimulation, and vagus nerve stimulation.

People with mental health conditions may be identified and offered treatment in a variety of health settings and so interventions through primary, community and secondary or specialist care services are included in the AIP.

Client/population group and condition

The population group of interest are people who present for treatment of a mood disorder within primary or secondary health settings. Best practice guidelines for interventions across different age groups, including adults over 18 years of age, older adults (over 60 years) and children and adolescents are presented. Where available, information has been included regarding special populations, for example, pregnant or breastfeeding women.

According to DSM IV diagnostic criteria, mood disorders include major depression, dysthymia, bipolar disorder, cyclothymia, mood disorder due to a general medical condition, substance-induced mood disorder, seasonal affective disorder, postpartum depression and premenstrual dysphoria. The primary mood disorders included in the guidelines and reviews examined for this report were depression and bipolar disorder, however within these major topic areas, separate best practice advice was available for particular conditions or special populations. Pharmacological, psychological and alternative therapies (e.g. light therapy) were included in this review.

METHODOLOGY

Search strategy

The search covered systematic reviews from 2000 onwards in English. Sources included the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects (DARE), BMJ Clinical Evidence reviews, and the Health Technology Assessment database. Guidelines websites were also searched.

The bibliographic databases Medline, PubMed (added in last 60 days), Embase and PsychInfo were searched for systematic reviews on treatment for mood disorders and linked with validated filters for

systematic reviews or relevant keywords where no filters were available. Full details of the sources searched and the strategies used are given in the attached Information Package. The searches were completed in the first week of July 2007. After the completion of the search process, it came to our attention that the August update of BMJ Clinical Evidence included relevant new reviews and updates on mood disorders. Because of the importance of these documents they have been included even though they were published after the official search cut-off date.

Methods

The author (MS) carefully considered the contents, including identified article abstracts, of the appended IP. An overview of its contents was provided, highlighting information of particular interest and relevance. Clinical guidelines of key interest, where freely obtainable from local resources, were retrieved and summarised. Those not retrieved were summarised based on their abstract, and suggested for retrieval in the AIP. Based on the research identified in the IP, a description of the stage and extent of the research base was prepared. Finally, a recommendation was made on whether there was potential for appraisal and evidence-based review of the topic (i.e., as a NZHTA Technical Brief or Systematic Review).

OVERVIEW OF FINDINGS – INTERVENTIONS FOR DEPRESSION

A number of recent, high quality guidelines were available which presented best practice recommendations for the treatment of depressive disorders. Those that are particularly relevant or thorough are summarised in detail below. Where recommendations were presented in a fairly concise fashion, they have been included in full in the body of the AIP. For some guidelines, either the number of recommendations or the number of interventions evaluated exceeded what was practical to include in full text. For these guidelines a list of the interventions has been included and the recommendations can be found in the appended IP. Additional relevant systematic reviews which were not included in the guidelines or were published subsequent to them are also summarised in brief. The final section is comprised of a list of other less relevant reviews or randomised controlled trials which were not summarised in this report but are provided in the appended IP.

SUMMARY OF KEY RESEARCH

Clinical Guidelines and Standards

NICE CLINICAL GUIDELINES: MANAGEMENT OF DEPRESSION IN PRIMARY AND SECONDARY CARE

Published: December 2004

Amended: April 2006 but only with regards to the prescription of venlafaxine

Next expected update: December 2008

Target population:

The guideline offers best practice advice on the care of people over 18 years of age who meet the standard diagnostic criteria for depression or related disorders. There is no upper age limit. It is relevant for patients with mild, moderate and severe depression.

Health care settings:

It covers the care provided by primary, community and secondary health care professionals who have direct contact with and make decisions concerning the care of patients with depression.

Included/excluded diagnoses:

The guideline does not specifically look at:

Depression in children

Dysthymia

Postnatal depression

Seasonal affective disorder

People with depression who have a separate physical or mental illness

Versions of the guidelines available:

The guideline is available in different formats. The main guideline is referred to most in the current report as it contains definitive summaries of best practice recommendations based on the best available evidence. This guideline was in turn created following the completion of a detailed report (358pp) which provides further information about the quality and strength of evidence obtained for each of the recommendations, including appraisals of contributing studies and the results obtained. The full report is not included in this AIP as it contains very detailed information about the generation of each recommendation. It does however demonstrate that the guidelines themselves were developed using the best available evidence and can be regarded as a reliable source of information. It is available in full text from the NICE clinical guidelines website (<http://guidance.nice.org.uk/topic/behavioural>). The guideline contains the same recommendations and includes a grading level for each but does not include the actual studies on which these were based. In terms of best practice, it is probably sufficient to rely on the guideline and refer to the complete report only if detailed information about particular studies or sources of evidence is required. There is also a summary of the guideline included in this AIP, which contains the general and stepped care recommendations and the grade of evidence upon which each was based.

Main priority recommendations for implementation:

- Screening should be undertaken in primary care and general hospital settings for depression in high risk groups – for example, those with a past history of depression, significant physical illnesses causing disability, or other mental health problems, such as dementia.
- For patients with mild depression who do not want an intervention or who, in the opinion of the healthcare professional, may recover with no intervention, a further assessment should be arranged, normally within 2 weeks ('watchful waiting').
- Antidepressants are not recommended for the initial treatment of mild depression, because the risk-benefit ratio is poor.
- For patients with mild depression, healthcare professionals should consider recommending a guided self-help programme based on cognitive behavioural therapy (CBT).
- In both mild and moderate depression, psychological treatment specifically focussed on depression (such as problem-solving therapy, brief CBT and counselling) of 6-8 sessions over 10-12 weeks should be considered.
- When an antidepressant is to be prescribed in routine care it should be a selective serotonin reuptake inhibitor (SSRI), because SSRIs are as effective as tricyclic antidepressants and are less likely to be discontinued because of side effects.
- All patients prescribed antidepressants should be informed that, although the drugs are not associated with tolerance and craving, discontinuation/withdrawal symptoms may occur on stopping, missing doses or, occasionally, on reducing the dose of the drug. These symptoms are usually mild and self-limiting but can occasionally be severe, particularly if the drug is stopped abruptly.
- When patients present initially with severe depression, a combination of antidepressants and individual CBT should be considered as the combination is more cost-effective than either treatment on its own.
- Patients who have had two or more depressive episodes in the recent past, and who have experienced significant functional impairment during the episodes, should be advised to continue antidepressants for 2 years.
- For patients whose depression is treatment resistant, the combination of antidepressant medication with CBT should be considered.
- CBT should be considered for patients with recurrent depression who have relapsed despite antidepressant treatment, or who express a preference for psychological interventions.

Other points:

In subsequent sections of the guideline, recommendations are divided on the basis of general good practice points for the treatment of patients with depression:

Good practice points are offered in the following areas:

- Depression and anxiety
- Providing good information, informed consent and mutual support
- Language
- Advance directives
- Patient preference
- Assessment and coordination of care

Stepped Care Model:

Recommendations are also provided for the treatment of depression based on levels of severity or the stage at which the depression is recognised. This is referred to as the 'stepped care model' and is presented on page 15 of the guideline. While this guideline was developed for use within the UK National Health Service (NHS), the stepped care model does not specifically refer to the NHS and is described briefly below:

Step 1: recognition of depression in primary care and general hospital settings

Step 2: managing recognised depression in primary care – mild depression

Step 3: managing recognised depression in primary care – moderate to severe depression

Step 4: involvement of specialist mental health services including crisis teams – treatment-resistant, recurrent, atypical and psychotic depression, and those at significant risk

Step 5: depression needing inpatient care

Each step introduces higher interventions and the guidelines provide specific and detailed recommendations for best practice interventions at each stage.

Final sections of the report provide:

- Research recommendations to address areas where the evidence base is incomplete or lacking
- Information regarding other versions of this guideline and other related guidelines
- A framework for the implementation of guideline recommendations
- Audit criteria for primary and secondary care settings who are implementing the recommendations – this is divided into possible objectives for an audit, people who could be included in an audit, and measures that could be used as a basis for an audit (criterion, measures, exceptions and definition of terms).

CLINICAL EVIDENCE GUIDELINES**DEPRESSION IN ADULTS (2006), DEPRESSION IN ADULTS: DRUG AND OTHER PHYSICAL TREATMENTS (2007), DEPRESSION IN ADULTS: PSYCHOLOGICAL TREATMENTS AND CARE PATHWAYS (2007)**

Butler et al. (2006)

Search date: September 2004 and updated in April 2006

Published: 2006 and updated in August 2007

This guideline is used as the basis for the BMJ Best Treatments for depression guidance, which is provided as a link from the New Zealand Ministry of Health's national depression initiative website.

Versions of the clinical evidence guidelines included in this AIP

The initial literature and database search, conducted in July 2007, identified the 2006 clinical evidence guidelines titled 'Depression in adults'. After the completion of the search process, it came to our attention that the August update of BMJ Clinical Evidence included relevant new reviews and updates on depression in adults, separated into pharmacological and psychological interventions. Checks of the updated recommendations revealed that the conclusions and categorisation of treatments as beneficial, likely to be beneficial, and of unknown effectiveness had not changed from the earlier version. Consequently, the updated versions of the guidelines have been included in the appended IP along with the earlier version but the recommendations below are taken from the guidelines published in 2006. A list of substantive changes to the earlier guidelines appears on page 25 of the pharmacological and physical treatments guidelines and on page 14 of the psychological and care pathways guidelines.

The guidelines address the following questions and summarise and present the best evidence for the following interventions:

1) What are the effects of treatments in mild to moderate or severe depression?

Prescription AD drugs versus placebo
 TCAs versus other prescription AD drugs
 SSRIs versus other prescription AD drugs
 MAOIs versus other prescription AD drugs
 Venlafaxine versus other prescription AD drugs
 Reboxetine versus other prescription AD drugs
 St John's Wort (*Hypericum Perforatum*)
 ECT
 Cognitive Therapy
 Interpersonal Psychotherapy
 Nondirective Counselling
 Problem Solving Therapy
 Combining Psychological Treatments and AD drugs
 Befriending
 Exercise

2) What are the effects of interventions in treatment resistant depression?

Augmenting prescription AD drug treatment with Lithium
 Augmenting prescription AD drug treatment with Pindolol

3) Which interventions reduce relapse rates?

Continuing prescription AD drug treatment
 Cognitive Therapy
 Relapse prevention programme

4) What are the effects of interventions to improve delivery of treatments?

Care pathways

For each treatment or intervention they discussed evidence based on systematic reviews and RCTs and provided an indication of the strength of the effect and confidence intervals. Information regarding benefits and harms, any additional comments, and a summary of the evidence was provided for each of the different types or combinations of treatment.

Main recommendations:

- In mild to moderate depression, there is no reliable evidence that any one treatment is superior in improving symptoms of depression, but the strength of the evidence supporting different treatments varies.
- In severe depression, only prescription antidepressants and electroconvulsive therapy are known to improve symptoms.
- Tricyclic antidepressants, SSRIs, MAOIs, Reboxetine and Venlafaxine improve symptoms in the short term. However, long-term studies are lacking.
- No one class of individual antidepressant has been shown to be superior to the others in the short term, but adverse effects vary between classes.
- St John's Wort may have similar efficacy compared with antidepressants, but preparations vary and drug interactions can occur.
- CAUTION: TCAs and SSRIs may induce or worsen suicidal ideation and behaviour and agitation after initiation of treatment. Since the last update of this topic, a drug safety alert has been issued on major congenital malformations with Paroxetine (www.fda.gov/medwatch).
- Cognitive therapy and interpersonal psychotherapy reduce symptoms of mild to moderate depression although studies have been small.
- Combining psychological treatment with antidepressant drugs may be more effective than either treatment alone.

- Non-directive counselling may also be effective, but we don't know whether problem-solving therapy, befriending, or exercise are beneficial.
- Care pathways may improve the effectiveness of treatment for depression.
- We don't know whether adding lithium or Pindolol reduces symptoms in people with treatment resistant depression.
- Continuing prescription antidepressant drugs reduces the risk of relapse after recovery, but we don't know whether cognitive therapy or relapse prevention programmes are also beneficial.

More detailed recommendations are provided at the beginning of each treatment or intervention section and are bolded. An excerpt from the section on AD drugs compared with placebo is provided below as an example of the summary recommendations:

Option: Prescription antidepressant drugs versus placebo

Systematic reviews and subsequent RCTs in people aged 18 years or over in primary and secondary care found that prescription antidepressant drugs were effective for treatment of all grades of depressive disorders compared with placebo. However, the most robust available evidence of efficacy of treatment with antidepressant drugs is in the pharmacological management of moderate and severe depression. One systematic review and two subsequent RCTs in people aged 55 years or over with all grades of depressive disorder found that TCAs, SSRIs, or MAOIs reduced the proportion of people who failed to recover over 26 – 49 days compared with placebo. The reviews gave little information on severe adverse effects of AD drugs compared with placebo...Current evidence indicates no clear relationship between SSRIs and increased risk for suicide in adults, but SSRIs and TCAs may induce or worsen suicidal ideation or behaviour during the early phases of treatment. This may be because of increased agitation and activation. In children and adolescents SSRIs generally increase adverse events compared with placebo, and the safety of these drugs is currently under review by regulatory authorities in several countries.

Unlike the NICE guidelines, the Clinical Evidence guidelines do not provide specific recommendations for the implementation of the evidence in practice. They do however provide detailed information regarding the quality, direction and strength of the evidence for each of the different treatment options. They also provide information regarding the evidence for benefits and harms of each intervention in older adults, who are defined as people aged 55 years and over in some studies and age 65 years and over in others. The authors specify the age groups included in studies of older adults responses to interventions.

Not included in this evidence summary were the following treatments:

- Acupuncture
- Behavioural therapy
- Bupropion
- Massage
- Primary physician education
- Transcranial magnetic stimulation
- Treatments for depression in people with a physical illness
- Vagal nerve stimulation

Postnatal depression is covered by a separate clinical evidence update.

Level of evidence considered – high quality systematic reviews wherever possible followed by RCTs. For some interventions there was less evidence available and of a diminished quality, especially for treatments for older adults, but the authors provide details of the source and conclusions of the evidence for each section.

Measures and outcomes considered in the review of the literature:

Depressive symptoms rated by patient or clinician, social functioning, occupational functioning, quality of life, admission to hospital, rates of self harm, relapse of depressive symptoms, rates of adverse events. RCTs often use continuous scales to measure depression (such as HAM-D or CGI scale). A

reduction in score of 50% or more on the HAM-D or a CGI score of 1 (very much improved) or 2 (much improved) is generally considered a clinically important response to treatment. Many RCTs express results in terms of effect size. Older adults: The HAM-D is not ideal for older people because it includes several somatic items that may be positive in older people who are not depressed. It has been the most widely used scale, although specific scales for elderly people (such as the Geriatric Depression scale) avoid somatic items.

ROYAL AUSTRALIAN AND NEW ZEALAND COLLEGE OF PSYCHIATRISTS: CLINICAL PRACTICE GUIDELINES

Ellis (2004)

Search date: 1996 – July 2002 augmented by manual searches

Published: 2004

Scope:

While there are no New Zealand guidelines available for the management of depression in primary care, the RANZCP clinical practice guidelines were developed to provide information for clinicians in specialist mental health services based on an evidence-based review of the literature (Medline and PsychLit). Meta-analyses of RCTs of antidepressant and augmentation strategies for the treatment of depression are reported with the 'numbers needed to treat' (NNT) for significant therapeutic benefit and 'absolute risk reduction' (ARR) provided for each AD medication compared with placebo and each other.

For areas where there was sparse evidence, expert groups were consulted. One advantage of this report is that it was developed for use within NZ and Australian health care settings and that a cultural advisor from the guidelines working group consulted with Maori and the Victorian Transcultural Psychiatry Unit (Australia) at every stage of development of the guidelines.

Target population:

Adults over the age of 18 years.

People affected by moderate to severe depression.

People who do not recover from a first episode or have a partial remission.

Focus on longer term follow-up and relapse prevention.

Main Recommendations:

- Establish an effective therapeutic relationship.
- Provide the patient with information about the conditions, the rationale for treatment, the likelihood of a positive response and the expected timeframe
- Consider the patients strengths, life stresses and supports.
- Treatment choice depends on the clinicians skills and the patients circumstances and should be guided but not determined by these guidelines
- In moderately severe depression, all recognised antidepressants, CBT and IPT are equally effective
- Clinicians should consider treatment burdens as well as benefits, including side effects and toxicity
- In severe depression AD treatment should precede psychological therapy
- For depression with psychosis, ECT or a TCA combined with an antipsychotic are equally helpful
- Treatments for other subtypes are discussed (atypical depression, treatment of recurrence, treatment-resistant, pregnant and breastfeeding women, frail elderly, physical illness, drug-induced alteration in mood)
- Caution is necessary in people on other medication or with medical conditions
- If response to an adequate trial of a first-line treatment is poor, another evidence-based treatment should be used
- Second opinions are useful
- Depression has a high rate of recurrence and efforts to reduce this are crucial

Algorithms for the treatment of depression, evidence-based treatments for uncomplicated, melancholic or atypical depression of mild to high severity, and EBT for psychotic depression are also presented.

ICSI GUIDELINES: MAJOR DEPRESSION IN ADULTS IN PRIMARY CARE

Published May 2006

Target population:

Adults greater than 18 years of age

A substantial part of this guideline provides recommendations regarding screening and diagnosis of depression in adults, including information about the diagnosis and evaluation of depression, substance abuse, bipolar disorder and other comorbidities. As the focus of this AIP is on intervention, that part of the report is not discussed in any detail in this report. Useful information is provided regarding depression in geriatric populations and issues pertinent to treating depression in pregnant or lactating women. There are also recommendations regarding the consideration of cultural differences in the recognition and treatment of depression. While these are general recommendations and not specific to New Zealand culture, there may be some useful general guidance.

Psychological and Pharmacological treatment guidelines:

Psychotherapy

Medications:

Selection of medication

Elderly patients

Pregnancy

Lactation

Herbals and Dietary Supplements

Follow-up plans and referral

Treatment Considerations

Pharmacotherapy vs. Psychotherapy

Pharmacologic Therapy

Light therapy

ECT

Vagus Nerve Stimulation

Transcranial Magnetic Stimulation

Acupuncture

Continuation and Maintenance Treatment

Main Recommendations:

- Antidepressant medications and/or referral for psychotherapy are recommended as treatment for major depression without coexisting medical conditions, substance abuse or other specific psychiatric comorbidities. Physical activity and tailored patient education are also useful tools in easing symptoms of major depression.

When antidepressant therapy is prescribed, medication adherence and completion is critical. The patient should be advised of the following:

- Most people need to be on medication at least 6 months.
- It may take from 2 to 6 weeks before the patient sees improvement.
- Take the medication as prescribed, even after the patient starts feeling better.
- Do not stop taking the medication without calling your provider. Side effects can be managed by changes in the dosage or dosage schedule.

NICE CLINICAL GUIDELINES: DEPRESSION IN CHILDREN AND YOUNG PEOPLE

Identification and management in primary, community and secondary care.

Published: September 2005

Next expected update: September 2009

Target population:

The guideline offers best practice advice on the care of children and young people (from 5 to their 18th birthday) with depression.

Health care settings:

It covers the care provided by primary, community and secondary health care professionals who have direct contact with and make decisions concerning the care of patients with depression.

Versions of the guidelines available:

The guideline is available in different formats. The main guideline is referred to most in the current report as it contains definitive summaries of best practice recommendations based on the best available evidence. This guideline was in turn created following the completion of a detailed report (233pp) which provides further information about the screening and assessment of depression, as well as a discussion of risk factors for depression in children and young people. The quality and strength of evidence obtained for different treatments, including appraisals of contributing studies and the results obtained are also provided. The full report is not included in this AIP but is available in full text from the NICE clinical guidelines website (<http://guidance.nice.org.uk/topic/behavioural>). The guideline contains the same recommendations and includes a grading level for each but does not include the actual studies on which these were based. In terms of best practice, it is probably sufficient to rely on the guideline and refer to the complete report only if detailed information about particular studies or sources of evidence is required. There is also a quick reference guide available on the NICE website.

Main priority recommendations for implementation:

- When assessing a child or young person with depression, healthcare professionals should routinely consider, and record in the patient's notes, potential comorbidities, and the social, educational and family context for the patient and family members, including the quality of interpersonal relationships, both between the patient and other family members and with their friends and peers.
- Psychological therapies used in the treatment of children and young people should be provided by therapists who are also trained child and adolescent mental healthcare professionals.
- Comorbid diagnoses and developmental, social and educational problems should be assessed and managed, either in sequence or in parallel, with the treatment for depression. Where appropriate this should be done through consultation and alliance with a wider network of education and social care.
- Attention should be paid to the possible need for parents' own psychiatric problems (particularly depression) to be treated in parallel, if the child or young person's mental health is to improve. If such a need is identified, then a plan for obtaining such treatment should be made, bearing in mind the availability of adult mental health provision and other services.

Mild depression

- Antidepressant medication should not be used for the initial treatment of children and young people with mild depression.

Moderate to severe depression

- Children and young people with moderate to severe depression should be offered, as a first-line treatment, a specific psychological therapy (individual cognitive behavioural therapy [CBT], interpersonal therapy or shorter-term family therapy; it is suggested that this should be of at least 3 months' duration).
- Antidepressant medication should not be offered to a child or young person with moderate to severe depression except in combination with a concurrent psychological therapy. Specific arrangements must be made for careful monitoring of adverse drug reactions, as well as for reviewing mental state and general progress; for example, weekly contact with the child or young person and their parent(s) or carer(s) for the first 4 weeks of treatment. The precise frequency will need to be decided on an individual basis, and recorded in the notes. In the event that psychological therapies are declined, medication may still be given, but as the young person will not be reviewed at psychological therapy sessions, the prescribing doctor should closely monitor the child or young person's progress on a regular basis and focus particularly on emergent adverse drug reactions.

Other points:

In subsequent sections of the guideline, recommendations are divided on the basis of general good practice points for the treatment of patients with depression based on a stepped care model. In this model, the different needs that depressed children and young people have and the responses that are

required from services are identified. Each step introduces higher interventions and the guidelines provide specific and detailed recommendations for best practice interventions at each stage.

Good practice points based on the best available evidence are offered in the following areas:

- Good information, informed consent and support
- Language and ethnic minorities
- Assessment and coordination of care
- The organisation and planning of services
- Treatment considerations in all settings
- Detection, risk profiling and referral
- Recognition
- Interventions for mild depression
- Interventions for moderate to severe depression
- Use of antidepressants in children and young people
- Treatment of psychotic depression
- Inpatient care
- Electroconvulsive therapy
- Discharge after a first episode
- Recurrent depression and relapse prevention
- Transfer to adult services

Final sections of the report provide:

- Implementation advice (within the framework of the NHS)
- Research recommendations to address areas where the evidence base is incomplete or lacking
- Information regarding other versions of this guideline and other related guidelines
- Audit criteria for primary and secondary care settings who are implementing the recommendations – this is divided into possible objectives for an audit, people who could be included in an audit, and measures that could be used as a basis for an audit (standards, criteria and audit methods).

CLINICAL EVIDENCE GUIDELINES: DEPRESSION IN CHILDREN AND ADOLESCENTS Hazell (2007)

Search date: April 2006

Published: August 2007

The guidelines address the following questions and summarised and presented the best evidence for the following interventions:

1) What are the effects of treatments for depression in children and adolescents?

Fluoxetine plus cognitive behavioural therapy in adolescents

Fluoxetine in children and adolescents

Paroxetine in adolescents

Paroxetine in children

Fluvoxamine in children and adolescents

Sertraline in children and adolescents

Citalopram in children and adolescents

Fluoxetine plus cognitive therapy in children

Specific psychological treatments in children and adolescents

Cognitive behavioural therapy (for relapse prevention) in children and adolescents

CBT (Individual) in children and adolescents

Interpersonal therapy in adolescents

Interpersonal therapy in children

Family therapy in children and adolescents

Group therapeutic support (other than CBT) in children and adolescents

Guided self help in children and adolescents

Individual psychodynamic psychotherapy in children and adolescents

Mirtazapine in children and adolescents

Monoamine oxidase inhibitors in children and adolescents

St John's Wort (*Hypericum Perforatum*) in children and adolescents

Tricyclic antidepressants in children and adolescents
 Venlafaxine in children and adolescents

2) *What are the effects of treatments for refractory depression in children and adolescents?*

Electroconvulsive therapy in children and adolescents with depression
 Lithium in children and adolescents

Main recommendations:

- Depression in children and adolescents may have a more insidious onset than in adults, with irritability a more prominent feature than sadness.
- Depression may affect 2-6% of children and adolescents, with a peak incidence around puberty.
- It may be self-limiting, but about 40% of children experience a recurrent attack, a third will make a suicide attempt, and 3-4% will die from suicide.
- Fluoxetine improves symptoms and may delay relapse compared with placebo over 7-12 weeks in children and adolescents.
- Fluoxetine may be more effective at improving symptoms compared with CBT, and combined fluoxetine plus CBT treatment may be more effective than either treatment alone.
- Paroxetine, fluvoxamine, sertraline, citalopram, and venlafaxine have not been shown to be beneficial in adolescents and children with depression.
- Tricyclic antidepressants have not been shown to reduce symptoms of depression and can be toxic in overdose, so their use is not recommended.
- We do not know whether moclobemide or St John's Wort are beneficial.
- CAUTION: Selective serotonin reuptake inhibitors (other than fluoxetine) and venlafaxine have been associated with serious suicide related events in people under the age of 18 years.
- Group CBT and interpersonal therapy may improve symptoms in children and adolescents with mild to moderate depression, but may not prevent relapse.
- We do not know whether other psychological treatments, guided self help, or individual psychodynamic psychotherapy improve symptoms.
- We do not know whether electroconvulsive therapy or lithium are beneficial in children or adolescents with refractory depression.

Special Populations

NICE CLINICAL GUIDELINES: ANTENATAL AND POSTNATAL MENTAL HEALTH
Clinical management and service guidance

Published: February 2007

Next expected update: September 2009

Target population:

The guideline makes recommendations for the prediction, detection and treatment of mental health disorders in women during pregnancy and the postnatal period (up to 1 year after delivery). It includes advice on the care of women with an existing mental disorder who are planning a pregnancy, and on the organisation of mental health services.

Healthcare settings:

The guideline also makes recommendations about the services required to support the delivery of effective detection and treatment of most mental disorders in the antenatal and postnatal periods in primary and secondary care.

Versions of the guidelines available:

The guideline is available in different formats. The main guideline is referred to most in the current report as it contains definitive summaries of best practice recommendations based on the best available evidence. This guideline was in turn created following the completion of a detailed report (310pp)

which provides further information about the quality and strength of evidence obtained for each of the recommendations, including appraisals of contributing studies and the results obtained. The full report is not included in this AIP but is available in full text from the NICE clinical guidelines website (<http://guidance.nice.org.uk/topic/behavioural>). It does however demonstrate that the guidelines themselves were developed using the best available evidence and can be regarded as a reliable source of information. The guideline contains the same recommendations and includes a grading level for each but does not include the actual studies on which these were based. In terms of best practice, it is probably sufficient to rely on the guideline and refer to the complete report only if detailed information about particular studies or sources of evidence is required. There is also a summary of the guideline which contains the general and stepped care recommendations and the grade of evidence upon which each was based.

Main priority recommendations for implementation:

Psychological treatments

- Women requiring psychological treatment should be seen for treatment normally within 1 month of initial assessment, and no longer than 3 months afterwards. This is because of the lower threshold for access to psychological therapies during pregnancy and the postnatal period arising from the changing risk–benefit ratio for psychotropic medication at this time.

Explaining risks

Before treatment decisions are made, healthcare professionals should discuss with the woman the absolute and relative risks associated with treating and not treating the mental disorder during pregnancy and the postnatal period. They should:

- acknowledge the uncertainty surrounding the risks
- explain the background risk of fetal malformations for pregnant women without a mental disorder
- describe risks using natural frequencies rather than percentages (for example, 1 in 10 rather than 10%) and common denominators (for example, 1 in 100 and 25 in 100, rather than 1 in 100 and 1 in 4)
- if possible use decision aids in a variety of verbal and visual formats that focus on an individualised view of the risks
- provide written material to explain the risks (preferably individualised) and, if possible, audio-taped records of the consultation.

Management of depression

When choosing an antidepressant for pregnant or breastfeeding women, prescribers should, while bearing in mind that the safety of these drugs is not well understood, take into account that:

- tricyclic antidepressants, such as amitriptyline, imipramine and nortriptyline, have lower known risks during pregnancy than other antidepressants
- most tricyclic antidepressants have a higher fatal toxicity index than selective serotonin reuptake inhibitors (SSRIs)
- fluoxetine is the SSRI with the lowest known risk during pregnancy
- imipramine, nortriptyline and sertraline are present in breast milk at relatively low levels
- citalopram and fluoxetine are present in breast milk at relatively high levels
- SSRIs taken after 20 weeks' gestation may be associated with an increased risk of persistent pulmonary hypertension in the neonate
- paroxetine taken in the first trimester may be associated with fetal heart defects
- venlafaxine may be associated with increased risk of high blood pressure at high doses, higher toxicity in overdose than SSRIs and some tricyclic antidepressants, and increased difficulty in withdrawal
- all antidepressants carry the risk of withdrawal or toxicity in neonates; in most cases the effects are mild and self-limiting.

For a woman who develops mild or moderate depression during pregnancy or the postnatal period, the following should be considered:

- self-help strategies (guided self-help, computerised cognitive behavioural therapy or exercise)
- non-directive counselling delivered at home (listening visits)
- brief cognitive behavioural therapy or interpersonal psychotherapy.

There are also guidelines provided for the prediction and detection of mental health problems, and the organisation of care, but as the focus of this AIP is interventions, these have not been described in this report.

Further specific guidance based on the best available evidence is offered in the following areas:

- Principles of care for all women with mental disorders during pregnancy and the postnatal period.
- Prediction, detection and initial management of mental disorders
- Prevention of mental disorders
- Care of women with a mental disorder during pregnancy and the postnatal period (including discussions of the risks and benefits of specific drug treatments and other therapies)
- The organisation of services

Final sections of the report provide:

- Implementation advice (within the framework of the NHS)
- Research recommendations to address areas where the evidence base is incomplete or lacking
- Information regarding other versions of this guideline and other related guidelines

CLINICAL EVIDENCE GUIDELINES: POSTNATAL DEPRESSION

Howard (2007)

Search date: September 2006

Published: August 2007

The guidelines address the following questions and summarised and presented the best evidence for the following interventions:

1) What are the effects of drug treatments for postnatal depression?

SSRI antidepressants (fluoxetine, paroxetine, and sertraline)

Antidepressants other than SSRIs

Hormones

St John's Wort (*Hypericum perforatum*)

2) What are the effects of non-drug treatments for postnatal depression?

Cognitive behavioural therapy (individual)

Interpersonal therapy

Non-directive counselling

Cognitive behavioural therapy (group)

Infant massage by mother

Light therapy

Mother-infant interaction coaching

Physical exercise

Psychodynamic therapy

Psychoeducation with partner

Telephone based peer support (mother to mother)

Main recommendations:

- The differentiation between postnatal depression and other types of depression is often unclear, but there are treatment issues in nursing mothers that do not apply in other situations
- Overall the prevalence of depression in postpartum women is the same as the prevalence in women generally, at about 12-13%
- Suicide is a major cause of maternal mortality in developed countries, but rates are lower in women postpartum than in women who have not had a baby
- Most episodes resolve spontaneously within 3-6 months, but a quarter of depressed mothers still have symptoms at 1 year. Depression can interfere with the mother-infant relationship
- SSRIs may improve symptoms of postnatal depression but few studies have been found that evaluate their effect specifically in postpartum women
- We don't know whether other types of antidepressant are effective compared with placebo or psychological treatments

- We don't know whether oestrogen treatment or St John's Wort improve symptoms compared with placebo
- Psychological treatments such as individual cognitive behavioural therapy, non-directive counselling, interpersonal psychotherapy, and psychodynamic therapy are likely to improve symptoms compared with routine care, but long term benefits are unclear
- We don't know whether light therapy, group cognitive behavioural therapy, psychoeducation with the partner, mother-infant interaction coaching, telephone-based peer support, infant massage, or physical exercise improve symptoms of postnatal depression as few studies have been found

SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK: POSTNATAL DEPRESSION AND PUERPERAL PSYCHOSIS (A National Clinical Guideline)

Search date: Search range 1991 - 2000

Publication: June 2002

Status on SIGN website: Due for review, findings not significantly affected by new evidence

Scope:

Best practice in the management of postnatal depression and puerperal psychosis, including screening, diagnosis, prevention and primary and secondary care treatments.

Methodology:

Literature search of Medline, Embase, Cinahl, PsychInfo and the Cochrane Library (year range 1991 – 2000)

Search of key websites e.g. National Guidelines Clearinghouse and the Marce Society

Searches supplemented by reference lists of relevant papers and group members' files

Consultation and specialist review

Main recommendations:

This guideline was included because it contains recommendations regarding diagnosis, screening and prevention of postnatal depression and puerperal psychosis, as well as treatment recommendations. The more recent guidelines produced by NICE (2007) and Clinical Evidence (2007) should be referred to for the most up-to-date treatment recommendations.

Summary of treatment recommendations appear from page 7 onwards and include psychological and pharmacological interventions.

Additional reviews not included in the NICE or Clinical Evidence Guidelines but relevant for special populations or alternative treatments

Pharmacological Treatments

Mottram et al. (2006) Antidepressants for depressed elderly (Cochrane Review)

Publication date: January 2006

Included studies: Randomised controlled trials, n=32. Antidepressants grouped by class of drug according to the British National Formulary. A list of classes and drugs appears on p.3.

Main findings: No differences in efficacy between classes of antidepressants, although some of the comparisons (e.g. related TCAs versus SSRIs) were based on a small number of trials. Some differences in withdrawal rates due to side effects or irrespective of cause between antidepressant classes. TCAs were associated with higher rates of withdrawal compared with SSRIs. There was a small increase in gastro-intestinal and neuropsychiatric (drowsiness, dizziness) side effects with classical TCAs.

Clinical implications: Some difficulties generalising findings from trials to the general population but findings suggest that TCAs and SSRIs have the same efficacy. All TCAs and classical TCAs showed significantly higher withdrawal rates compared with SSRIs. However, when TCA-related drugs were

compared SSRIs, those differences were not apparent. A cautious interpretation is that TCA-related antidepressants might offer a relatively low side effect profile compared to classical TCAs and may be associated with better tolerability. TCA-related drugs show a similar withdrawal rate to SSRIs and may be a suitable alternative when SSRIs are not acceptable.

Psychological Therapies:

Computerised cognitive behaviour therapy for depression and anxiety (NICE Technology Appraisal 97, 2006).

Publication date: 2006. A review of NICE Technology Appraisal 51.

Examined CCBT for depression and anxiety

Concerns 5 specific CCBT packages accessed by referral from a GP: 3 for depression (Beating the Blues, Cope, Overcoming Depression); 1 for phobia (Fear Fighter) and one for OCD (OC Fighter).

Main findings:

- Beating the Blues recommended as an option for delivering CBT for mild-moderate depression
- Insufficient evidence for Cope or Overcoming Depression as a clinically or cost-effective alternative.
- Fear Fighter recommended for panic and phobia
- OC Fighter (previously known as BT Steps) not recommended
- CCBT recommended as part of the stepped care model (see previously described NICE Clinical Guidelines for the treatment of depression) at step 2.
- Descriptions of the different CCBT packages are provided from pages 9 – 11.
- The contributing studies and effect sizes for each of the CCBT packages for the treatment of depression are detailed from pages 12 – 14. Subsequent sections also provide information regarding the packages for other disorders.
- The cost-effectiveness of each of the packages is also examined in this report, with costing provided in British pounds.

Kaltenthaler et al. (2006). Computerised cognitive behaviour therapy for depression and anxiety update: a systematic review and economic evaluation (UK HTA)

Search: 1966 – 2004

Publication date: 2006

Inclusion criteria: All studies describing trials of CCBT delivered alone or as part of a package and via computer interface or telephone with computer-led response. Total = 20 studies, depression only = 10 studies

Main findings: Six trials were of CCBT packages (Beating the Blues, Cope, Overcoming Depression). There is some evidence that CCBT is more effective than treatment as usual in the treatment of depression/anxiety. In studies reporting accurate estimates of therapist time, CCBT appears to reduce therapist time compared with TCBT and is of use where access to TCBT is limited. There is RCT evidence to support the effectiveness of Beating the Blues. There is no RCT evidence for COPE and Overcoming Depression.

Based on a limited number of RCTs but shows the potential usefulness of CCBT. The authors provide recommendations for future research, highlighting that the position of CCBT in models of best practice and its relationship to other treatments has not been examined.

Tuunainen et al. (2004). Light therapy for non-seasonal depression (Cochrane Review)

Inclusion criteria: RCTs comparing bright light therapy with inactive placebo. N=20 studies (49 reports)

Main findings: Most studies applied bright light as an adjunctive treatment to drug therapy, sleep deprivation or both. Results were based mainly on studies of less than 8 days of treatment. Treatment response to bright light was better than control treatment but not significant. For patients suffering from non-seasonal depression, light therapy offers modest though promising antidepressant efficacy. Hypomania as a potential adverse effect needs to be considered. Due to limited data and heterogeneity of studies, these results need to be interpreted with caution.

Linde et al. (2005). St. John's Wort for depression (Cochrane Review)

Update of previous review which was included in NICE and Clinical Evidence

Inclusion criteria: Randomised and double-blind trials comparing hypericum perforatum with placebo or standard antidepressants in patients with depressive disorders. A total of 37 trials were included: 26 comparisons with placebo and 14 with antidepressants.

Main findings: Current evidence is inconsistent and confusing. Results of several recent placebo-controlled trials suggest minimal beneficial effects of hypericum extracts while other trials suggest hypericum and antidepressants have a similar beneficial effect. Preparations available on the market vary in pharmaceutical quality and this is important. Clinical implications are discussed on page 9, and the authors conclude that 'current best evidence from placebo comparisons shows only minor benefits of hypericum in patients with major depression and perhaps no benefit in patients with prolonged duration of depression'.

Additional reviews included in the appended IP but not summarised in this report:

The summary pages for these reviews, including objectives, main findings, and clinical implications, as well as instructions for their retrieval from the Cochrane Collaboration website are included in the appended IP.

Included in NICE or Clinical Evidence Guidelines:

Pharmacotherapy

Cipriani et al. (2005). Fluoxetine versus other types of pharmacotherapy for depression (Cochrane Review)

Furukawa et al. (2001). Antidepressants plus benzodiazepines for major depression (Cochrane Review)

Furukawa et al. (2003). Low dosage tricyclic antidepressants for depression (Cochrane Review)

Hazell et al. (2002). Tricyclic drugs for depression in children and adolescents (Cochrane Review)

Lima et al. (2005). Drugs versus placebo for dysthymia (Cochrane Review) - previous version in CE, latest version includes 2 further RCTs, not in NICE

Moncrieff et al. (2004). Active placebos versus antidepressants for depression (Cochrane Review)

Van der Wurff (2003). Electroconvulsive therapy for the depressed elderly (Cochrane Review)

Wijkstra et al. (2005). Pharmacological treatment for psychotic depression (Cochrane Review)

Wilson et al. (2001). Antidepressants versus placebo for the depressed elderly (Cochrane Review)

Psychological Treatment

Churchill et al. (2001). A systematic review of controlled trials of the effectiveness and cost-effectiveness of brief psychological treatments for depression (UK HTA) – included in NICE and CE

Kendrick et al. (2005). A trial of problem-solving by community mental health nurses for anxiety, depression and life difficulties among general practice patients. The CPN-GP study (UK HTA)

King et al. (2000). Randomised controlled trial of non-directive counselling, cognitive behaviour therapy and usual general practitioner care in the management of depression as well as mixed anxiety and depression in primary care (UK HTA) – in NICE, not in CE

Simpson et al. (2000). A randomised controlled trial to evaluate the effectiveness and cost-effectiveness of counselling patients with chronic depression (UK HTA) – in NICE, not in CE

Not included in NICE or Clinical Evidence Guidelines:

Pharmacotherapy

American Medical Doctors Association (2005). Pharmacotherapy companion to the depression.

Bains et al. (2002). Antidepressants for treating depression in dementia (Cochrane Review) 7 trials, weak evidence of AD effect, paucity of research

Canadian Coordinating Office for Health Technology Assessment (2004). Duloxetine for major depressive disorder and stress urinary incontinence. HTA Emerging Drug List

Cipriani et al. (2006). Lithium versus antidepressants in the long-term treatment of unipolar affective disorder (Cochrane Review)

Gartlehner et al. (2007). Agency for Healthcare Research and Quality. Comparative effectiveness of second generation antidepressants in the pharmacologic treatment of adult depression.

Greenhalgh et al. (2005). Clinical and cost-effectiveness of electro-convulsive therapy for depressive illness, schizophrenia, catatonia and mania: systematic reviews and economic modelling studies (UK HTA)

Guaiana et al. (2003). Amitriptyline versus other types of pharmacotherapy for depression (Cochrane Review)

Lima et al. (2003). Pharmacotherapy for dysthymia (Cochrane Review)

Peveler et al. (2005). A randomised controlled trial to compare the cost-effectiveness of TCAs, SSRIs and lofepramine (UK HTA)

Shaw et al. (2002). Tryptophan and 5-Hydroxytryptophan for depression (Cochrane Review)

Whitehead et al. (2002). Antidepressants for people with both schizophrenia and depression (Cochrane Review)

Other supplements or nutritional treatments

Taylor et al. (2003). Folate for depressive disorders (Cochrane Review) – not covered by NICE or CE

Taylor et al. (2004). Inositol for depressive disorders (Cochrane Review) – not covered by NICE or CE

Psychological Treatment

Barbato et al (2006). Marital therapy for depression (Cochrane Review) – not in NICE or in CE

Den Boer et al. (2005). Paraprofessionals for anxiety and depressive disorders (Cochrane Review)

Kaltenthaler et al. (2002) A systematic review and economic evaluation of computerised cognitive behaviour therapy for depression and anxiety (UK HTA) – in NICE Guidance on the use of computerised cognitive behavioural therapy for anxiety and depression but updated in 2006

Other therapies:

Martin et al. (2001). Transcranial magnetic stimulation for treating depression (Cochrane Review) – not in NICE, TMS not covered by CE

Ontario Ministry of Health (2004). Repetitive transcranial magnetic stimulation for the treatment of major depressive disorder. Health Technology Literature Review

Parrella et al (2005) Australian Department of Health and Aging. VNS therapy system for the treatment of chronic or recurrent treatment-resistant depression in adults. National Horizon Scanning Unit.

Smith et al (2004). Acupuncture for depression (Cochrane Review) – not in NICE, acupuncture not covered by CE

Treatment of depression during pregnancy

Dennis et al. (1999). Oestrogens and progestins for preventing and treating postpartum depression (Cochrane Review).

Dennis et al. (2004). Psychosocial and psychological interventions for preventing postpartum depression. (Cochrane Review)

Hoffbrand et al. (2001) Antidepressant treatment for postnatal depression (Cochrane Review)

Howard et al. (2005) Antidepressant prevention of postnatal depression (Cochrane Review)

Children and Adolescents

Larun et al. (2006). Exercise in prevention and treatment of anxiety and depression among children and young people (Cochrane Review).

Merry et al 2004). Psychological and/or educational interventions for the prevention of depression in children and adolescents (Cochrane Review).

Treatment of depression in people with physical illnesses

Anderson et al. (2004). Intervention for preventing depression after stroke (Cochrane Review).

Bush et al. (2005). Post-myocardial infarction depression. Agency for Healthcare Research and Quality.

Ghazi-Noori et al. (2003). Therapies for depression in Parkinson's disease (Cochrane Review).

Hackett et al. (2004). Interventions for treating depression after stroke (Cochrane Review).

Lane et al. (2005). Psychological interventions for depression in heart failure (Cochrane Review).

Lip et al. (2003). Psychological interventions for depression in adolescent and adult congenital heart disease (Cochrane Review).

Rabindranath et al. (2005). Psychosocial interventions for depression in dialysis patients (Cochrane Review).

Rabindranath et al. (2005). Physical measures for treating depression in dialysis patients (Cochrane Review).

Rodin et al. (2006). The management of depression in cancer patients: A clinical practice guideline. Cancer Care Ontario.

OVERVIEW OF FINDINGS - INTERVENTIONS FOR BIPOLAR DISORDER

NICE CLINICAL GUIDELINES: BIPOLAR DISORDER

The management of bipolar disorder in adults, children and adolescents, in primary and secondary care

Published: July 2006

Next expected update: July 2010

Target population:

The guideline offers best practice advice on the care of people with bipolar disorder. It draws a distinction between bipolar I disorder (in which episodes of both depression and mania are required for diagnosis) and bipolar II disorder (in which episodes of depression and hypomania, but no evidence of mania, are required for diagnosis).

Healthcare settings:

The guideline makes recommendations for the identification, treatment and management of bipolar disorder for children, adolescents, and adults in primary and secondary care, including those covered by prison medical services.

Versions of the guidelines available:

The guideline is available in different formats. The main guideline is referred to most in the current report as it contains definitive summaries of best practice recommendations based on the best available evidence. This guideline was in turn created following the completion of a detailed report (592pp) which provides further information about the quality and strength of evidence obtained for each of the recommendations, including appraisals of contributing studies and the results obtained. The full report is not included in this AIP but is available in full text from the NICE clinical guidelines website (<http://guidance.nice.org.uk/topic/behavioural>). It does however demonstrate that the guidelines themselves were developed using the best available evidence and can be regarded as a reliable source of information. The guideline contains the same recommendations and includes a grading level for each but does not include the actual studies on which these were based. In terms of best practice, it is probably sufficient to rely on the guideline and refer to the complete report only if detailed information about particular studies or sources of evidence is required. There is also a summary of the guideline which contains the general and stepped care recommendations and the grade of evidence upon which each was based.

Main priority recommendations for implementation:

Treating bipolar disorder with drugs

- Valproate should not be prescribed routinely for women of child-bearing potential. If no effective alternative to valproate can be identified, adequate contraception should be used, and the risks of taking valproate during pregnancy should be explained.
- Lithium, olanzapine or valproate should be considered for long-term treatment of bipolar disorder. The choice should depend on:
 - response to previous treatments
 - the relative risk, and known precipitants, of manic versus depressive relapse
 - physical risk factors, particularly renal disease, obesity and diabetes
 - the patient's preference and history of adherence
 - gender (valproate should not be prescribed for women of child-bearing potential)
 - a brief assessment of cognitive state (such as the Mini-Mental State Examination) if appropriate, for example, for older people.

- If the patient has frequent relapses, or symptoms continue to cause functional impairment, switching to an alternative monotherapy or adding a second prophylactic agent (lithium, olanzapine, valproate) should be considered. Clinical state, side effects and, where relevant, blood levels should be monitored closely. Possible combinations are lithium with valproate*, lithium with olanzapine, and valproate with olanzapine. The reasons for the choice and the discussion with the patient of the potential benefits and risks should be documented.
- If a trial of a combination of prophylactic agents proves ineffective, the following should be considered:
 - consulting with, or referring the patient to, a clinician with expertise in the drug treatment of bipolar disorder
 - prescribing lamotrigine (especially if the patient has bipolar II disorder) or carbamazepine.
- If a patient is taking an antidepressant at the onset of an acute manic episode, the antidepressant should be stopped. This may be done abruptly or gradually, depending on the patient's current clinical need and previous experience of discontinuation/withdrawal symptoms, and the risk of discontinuation/withdrawal symptoms of the antidepressant in question.
- After successful treatment for an acute depressive episode, patients should not routinely continue on antidepressant treatment long-term, because there is no evidence that this reduces relapse rates, and it may be associated with increased risk of switching to mania.

Monitoring physical health

- People with bipolar disorder should have an annual physical health review, normally in primary care, to ensure that the following are assessed each year:
 - lipid levels, including cholesterol in all patients over 40 even if there is no other indication of risk
 - plasma glucose levels
 - weight
 - smoking status and alcohol use
 - blood pressure.

Diagnosing bipolar disorder in adolescents

When diagnosing bipolar I disorder in adolescents the same criteria should be used as for adults except that:

- mania must be present
- euphoria must be present most days, most of the time (for at least 7 days)
- irritability can be helpful in making a diagnosis if it is episodic, severe, results in impaired function and is out of keeping or not in character; however, it should not be a core diagnostic criterion.

The authors note that there is a smaller evidence base for the treatment of bipolar II disorder, as well as significant limitations to the evidence base for both under 18s and older adults (over 65 years)

Subsequent recommendations are made for the following areas:

- General recommendations for the care of people with bipolar disorder
- The assessment, recognition and diagnosis of bipolar disorder in adults (including primary, secondary and crisis and risk management plans)
- Treatment settings and pathways to care
- Treatment and management of bipolar disorder (including management of acute episodes – mania, depression, mixed episodes)
- Long-term management of bipolar disorder (pharmacological, psychological and prevention of relapse)
- Physical care of people with bipolar disorder
- Women with bipolar disorder who are planning a pregnancy, pregnant or breastfeeding
- Children and adolescents with bipolar disorder

Final sections of the report provide:

- Implementation advice (within the framework of the NHS)
- Research recommendations to address areas where the evidence base is incomplete or lacking
- Information regarding other versions of this guideline and other related guidelines

CLINICAL EVIDENCE GUIDELINES: BIPOLAR DISORDER (2006), BIPOLAR DISORDER (2007)

Geddes and Briess (2007)

Search date: November 2004 and updated in July 2006

Published: 2006 and updated in August 2007

Versions of the clinical evidence guidelines included in this AIP

The initial literature and database search, conducted in July 2007, identified the 2006 clinical evidence guidelines. After the completion of the search process, it came to our attention that the August update of BMJ Clinical Evidence included relevant new reviews and updates on depression in adults, separated into pharmacological and psychological interventions. Consequently, the updated versions of the guidelines have been included in the appended IP along with the earlier version and the recommendations below are taken from most recent version (2007). A list of substantive changes to the earlier guidelines appears on page 26 of 2007 guidelines. Any changes have been marked as 'New' in 2007 guidelines and in the list of interventions below.

The clinical evidence guidelines addressed the following questions and summarised and presented the best evidence for the following interventions:

1) What are the effects of treatments in mania?

Lithium
 Valproate
 Chlorpromazine
 Haloperidol
 Risperidone
 Olanzapine
 Ziprasidone
 Quetiapine
 Carbamazepine
 Clonazepam
 Gabapentin
 Lamotrigine
 Topiramate

2) What are the effects of treatments in bipolar depression?

Psychological treatments (no systematic reviews or RCTs found)

Antidepressants
 Lithium
 Carbamazepine
 Valproate
 Lamotrigine
 Topiramate
 Quetiapine - New

3) What are the effects of interventions to prevent relapse of mania or bipolar depression?

Cognitive therapy
 Education to recognise symptoms of relapse
 Family focused psychoeducation
 Lithium
 Valproate
 Carbamazepine
 Lamotrigine
 Antidepressants
 Olanzapine - New

For each treatment or intervention the authors discussed evidence based on systematic reviews and RCTs and provided an indication of the strength of the effect and confidence intervals. Information regarding benefits and harms, any additional comments, and a summary of the evidence was provided for each of the different types or combinations of treatment.

Main recommendations:

- Lithium reduces symptoms of mania compared with placebo, and seems to be as effective as haloperidol, carbamazepine and clonazepam, but can cause adverse effects including hypothyroidism.
- Older antipsychotic drugs such as chlorpromazine and haloperidol are widely used to treat mania, but few studies have been performed to confirm their efficacy.
- Olanzapine, valproate, carbamazepine and risperidone increase the likelihood of response in people with mania compared with placebo and seem to be of similar efficacy to each other, with different adverse-effect profiles.
- Ziprasidone, quetiapine, and clonazepam may also be beneficial, but few studies have been done to assess the effects of lamotrigine or gabapentin in mania.
- Topiramate is unlikely to be beneficial in mania.
- Antidepressants increase treatment response compared with placebo in people with bipolar depression. It is possible that SSRIs are more effective, and less likely to induce mania, compared with TCAs.
- Lamotrigine may increase response rates in people with depression compared with placebo, but can cause headache.
- Quetiapine may also improve depression compared with placebo.
- We don't know whether lithium, carbamazepine, valproate or topiramate improve depression in people with bipolar disorder.
- We don't know whether psychological treatments are effective for people with bipolar depression, as we found no studies.
- Lithium reduces relapse in bipolar disorder compared with placebo.
- Valproate, carbamazepine and lamotrigine seem to be as effective as lithium in reducing relapse.
- Cognitive therapy and patient or family education may reduce the risk of relapse, but studies have given conflicting results.
- We don't know whether antidepressants can prevent relapse, and they may induce mood instability or manic episodes.
- Olanzapine may reduce relapse, but long-term use may be associated with weight gain.

More detailed recommendations are provided at the beginning of each treatment or intervention section and are bolded.

Unlike the NICE guidelines, the Clinical Evidence guidelines do not provide specific recommendations for the implementation of the evidence in practice. They do however provide detailed information regarding the quality, direction and strength of the evidence for each of the different treatment options. The level of evidence considered are high quality systematic reviews wherever possible followed by RCTs.

Measures and outcomes considered in the review of the literature:

Level of symptoms on clinician, patient or joint rating scales; proportion of people with clinically important response to treatment; time to remission; quality of life scores; social and occupational functioning scores; relapse; hospital admission; rates of suicide; frequency of adverse effects; and clinical withdrawal rates.

**CANADIAN NETWORK FOR MOOD AND ANXIETY TREATMENTS (CANMAT)
GUIDELINES FOR THE MANAGEMENT OF PATIENTS WITH BIPOLAR DISORDER:
CONSENSUS AND CONTROVERSIES**

Publication: 2005 and updated 2007 (both included in the appended IP)

Scope:

This guideline aims to review evidence-based treatments for bipolar disorder since 1997 and use criteria to rate strength of evidence and incorporate effectiveness, safety, and tolerability data to determine global clinical recommendations for treatment of various phases of bipolar disorder. One of the primary aims was to provide internationally relevant guidelines, so international experts from North America, Europe, Australasia, South America and Africa provided supplementary written commentaries.

Target Population:

Most of the focus is on adult populations, however there are separate sections providing guidelines for women who are pregnant or breastfeeding, and for the treatment of children and adolescents with bipolar disorder.

Main recommendations:

- Although pharmacology forms the cornerstone of management, utilisation of adjunctive psychological treatments and incorporation of chronic disease management model involving a healthcare team are required in providing optimal management.
- Lithium, valproate, and several atypical antipsychotics are first-line treatments for acute mania
- Bipolar depression and mixed states are frequently associated with suicidal acts, therefore assessment for suicide should always be an integral part of managing any bipolar patient.
- Lithium, lamotrigine or various combinations of antidepressant and mood-stabilising agents are first-line treatments for bipolar depression.
- Quetiapine is now also recommended as a first-line option for bipolar depression (2007)
- First-line options in the maintenance of bipolar disorder are lithium, lamotrigine, valproate and olanzepine.
- There is recent evidence to recommend the combination of olanzepine and fluoxetine as a second-line maintenance therapy for bipolar depression.

Structure of the report:

For each section:

- tables describing the evidence strength for pharmacological treatment are provided
- a treatment algorithm is provided and first, second and third-line options for treatment are discussed
- concerns and controversial issues are discussed
- a clinical case is used to illustrate how treatment evidence can be incorporated into the management of a patient with BD.

Separated into the following sections:

- basic principles of management
 - Chronic disease management model (table p.11)
- acute mania
 - Strength of pharmacological evidence table p.14
 - Treatment algorithm p.15
- acute bipolar depression
 - Psychological and pharmacological options discussed
 - Strength of pharmacological evidence table p.20
 - Treatment algorithm p.21
- maintenance treatment
 - General principles
 - Psychological and pharmacological interventions
 - Strength of pharmacological evidence table p.27
 - Treatment algorithm p.21
- pregnancy, breastfeeding
 - Table of pharmacological treatment options in pregnancy and adverse effects evidence p.34
 - Pharmacological treatments and breastfeeding p.35
- children and adolescents
 - Pharmacological treatments
- bipolar II evidence
 - Strength of pharmacological evidence table p.42
- safety and monitoring
- Appendix 1: key resources for the treatment of bipolar disorder

ROYAL AUSTRALIAN AND NEW ZEALAND COLLEGE OF PSYCHIATRISTS CLINICAL PRACTICE GUIDELINES TEAM FOR BIPOLAR DISORDER
Australian and New Zealand clinical practice guidelines for the treatment of bipolar disorder

Published: February 2004

Scope:

This guideline provides evidence-based recommendations for the management of bipolar disorder by phase of illness: acute mania, mixed episodes and bipolar depression

Methodology:

Review of Medline/EMBASE/Index Medicus plus hand searching of journals.

Consultation with an expert committee

Representatives of patients and carers were included.

Structure:

Reviews the evidence for each treatment within each phase of illness

Treatment guidelines for each phase of illness from pages 291 - 299

Main recommendations:

General issues in treatment

- Treatment should aim to restore the person to full health and a meaningful life
- Prevention of suicide must be a central goal
- Integration of a range of health professionals, as well as family and friends, is required

Acute treatment of mania and mixed episodes

- initial assessment

- comprehensive clinical assessment

- pharmacological treatment:

- Lithium
- Carbamazepine
- Valproate
- Lamotrigine - no RCTS
- Gabapentin
- Topiramate - no RCTs
- Clozapine - no RCTs but open case series reported
- Olanzapine -
- Respiradone - no placebo-controlled studies
- ECT
- Adverse effects of pharmacological treatment - detailed adverse effects for each drug treatment divided by system
- Therapeutic drug monitoring

Acute treatment of bipolar disorder

- assessment

- pharmacological treatment

- Lithium
- Carbamazepine
- Valproate
- Lamotrigine
- Antidepressants - SSRIs, TCAs, MAOIs, others
- Antipsychotics -
- ECT

Prophylaxis

- assessment

- pharmacological treatments

- Lithium
 - Carbamazepine
 - Valproate
 - Lamotrigine
 - Combination drug therapies
 - Suicide prevention
- psychological treatments
- Psychoanalysis - no controlled trials
 - Psycho-education
 - Cognitive Therapy
 - Interpersonal and social rhythm therapy
 - Group therapy
 - Family-focused treatment

Treatment Guidelines by phase of illness

- acute treatment of mania and mixed episodes:
- use of a mood stabiliser (lithium, carbamazepine, valproate, or olanzapine)
 - concurrent use of an antipsychotic or benzodiazepine to calm or sedate until mood stabiliser takes effect
 - algorithm for treatment of manic episode page 292
 - best evidence for mixed episodes is from valproate
 - failure to respond options
 - continuing treatment
- acute treatment of bipolar depression
- de novo depression
mood stabiliser alone
mood stabiliser and antidepressant combined
 - breakthrough depression
adding an antidepressant
adding a second mood stabiliser
choosing an antidepressant
choosing a mood stabiliser
failure to respond
continuing treatment
- prophylaxis of bipolar disorder
- non-rapid cycling
 - rapid cycling
 - psychological interventions
 - failure to respond
- special groups
- pregnancy - lithium, anticonvulsants, recommendations for treatment in first trimester, recommendations for treatment in second and third trimester
 - breastfeeding - lithium, carbamazepine, valproate

SCOTTISH INTERCOLLEGIATE GUIDELINES NETWORK. BIPOLAR AFFECTIVE DISORDER: A NATIONAL CLINICAL GUIDELINE.

Search date: April 2004

Published: May 2005 (will be considered for review in 2008)

Scope:

This guideline provides diagnostic, treatment and suicide prevention recommendations for adults (aged 18 years and over) with bipolar affective disorders. A discussion of diagnostic issues in adolescence is included because of the often early onset of the condition.

Methodology:

Literature search of Medline, Embase, Cinahl, PsychInfo and the Cochrane Library (year range 1990 – 2003)

Search of key websites e.g. National Guidelines Clearinghouse

Searches supplemented by reference lists of relevant papers and group members' files

Consultation and specialist review

Main recommendations:

Treatment options are presented from page 10 onwards with the quality of evidence for each recommendation provided. A quick reference summary appears on page 42.

Acute treatment for mania:

- Acute manic episodes should be treated with oral administration of an antipsychotic drug or semi-sodium valproate.
- Lithium can be used if immediate control of overactive or dangerous behaviour is not needed or otherwise should be used in combination with an antipsychotic.

Acute treatment for depression:

- An antidepressant in combination with an anti-manic drug (lithium, valproate or an antipsychotic drug), or lamotrigine is recommended for the treatment of acute bipolar depression in patients with a history of mania

Pharmacological relapse prevention:

- Lithium is the treatment of choice for relapse prevention in bipolar affective illness.
- Lithium should be prescribed at an appropriate dose with a daily dosing regimen
- The withdrawal of lithium should be gradual to minimise the risk of relapse

Psychosocial interventions:

- Evidence based psychosocial interventions should be available to patients in addition to pharmacological maintenance treatment, especially if complete or continued remission cannot be achieved

Reproductive health issues:

- The dose of the combined oral contraceptive should be adjusted accordingly when given with an enzyme-inducing drug
- Women should be warned that the efficacy of the COC is reduced
- Barrier methods of contraception should also be used for maximum contraceptive effect.

Suicide prevention:

- Acute and maintenance lithium treatment of patients with bipolar affective disorders should be optimised to make every effort to minimise the risk of suicide.

Additional reviews included in the appended IP but not summarised in this report:

Bridle et al. (2004). A rapid and systematic review and economic evaluation of the clinical and cost-effectiveness of newer drugs for treatment of mania associated with bipolar affective disorder (UKHTA)

Burgess et al. (2001). Lithium for maintenance treatment of mood disorders (Cochrane Review)

McLellan et al. (2007). Work group on quality issues. Practice parameter for the assessment and treatment of children and adolescents with bipolar disorder.

Macritchie et al. (2001). Valproic acid, valproate and divalproex in the maintenance and treatment of bipolar disorder (Cochrane Review)

Macritchie et al. (2003). Valproate for acute mood episodes in bipolar disorder (Cochrane Review)

Morriss et al. (2007). Interventions for helping people recognise early signs of recurrence in bipolar disorder (Cochrane Review)

Rendell et al. (2006). Risperidone in long-term treatment for bipolar disorder (Cochrane Review) – no RCTs

Rendell et al. (2006) Risperidone alone or in combination for acute mania (Cochrane Review)

- Rendell et al. (2003). Olanzapine alone or in combination for acute mania (Cochrane Review)
- Vasudev et al. (2006). Tiagabine in the maintenance treatment of bipolar disorders (Cochrane Review) – no RCTs
- Vasudev et al. (2006). Topiramate for acute affective episodes in bipolar disorder (Cochrane Review) – 1 RCT
- Vasudev et al. (2006). Tiagabine in the treatment of acute affective episodes in bipolar disorder: efficacy and acceptability (Cochrane Review) – no RCTs

CONCLUDING COMMENTS

Research base and stage

The research base was in general of very high quality and several guidelines as well as Cochrane Collaboration reviews were identified and retrieved. There are, however, some shortcomings in the literature. All the guidelines point out the lack of long-term outcomes for most interventions and note that this significantly limits the evidence base and therefore the recommendations of the guidelines in many cases. Many guidelines emphasise the importance of cultural considerations in the implementation of recommendations and in the consideration of different interventions for depression. There is however, a paucity of research in culturally-based conceptions of mental health and how these conceptions might affect response or adherence to treatment for mood disorders. Even where reference is made to cultural considerations for treatment, this is not specifically relevant to the ethnic variation in New Zealand. Generally, more robust evidence is available for pharmacological interventions than for psychological or the combination of psychological and pharmacological interventions.

Potential for Technical Brief or Systematic Review

From what has been identified in the AIP, there appears to be sufficient evidence of reasonable quality on this topic to benefit from more extensive review and critical appraisal as an evidence-based review. Due to the nature and size of this topic, which covers a variety of interventions and includes a range of study designs, a systematic review (SR) on this topic is recommended.

Within this topic there is the potential for several reviews so in order to keep this topic manageable within the timeframe it is important to refine the scope of this project. Key parameters of interest and inclusions and exclusions will be determined in consultation with the client and outlined in the Protocol.

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