Depression in Children:

identification and management of depression in children and young people in primary, community and secondary care

National Clinical Practice Guideline Number ___

National Collaborating Centre for Mental Health
Commissioned by the National Institute for Clinical Excellence
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1 Introduction

This guideline has been developed to advise on the identification and management of depression in children and young people in primary, community and secondary care. The guideline recommendations have been developed by a multidisciplinary team of healthcare professionals, carers, and guideline methodologists after careful consideration of the best available evidence. It is intended that the guidelines will be useful to clinicians and service commissioners in providing and planning high quality care for children and young people with depression while also emphasising the importance of the experience of care for patients and their families.

1.1 National guidelines

1.1.1 What are clinical practice guidelines?
Clinical practice guidelines are ‘systematically developed statements that assist clinicians and patients in making decisions about appropriate treatment for specific conditions’ (Department of Health, 1996). They are derived from the best available research evidence, using predetermined and systematic methods to identify and evaluate all the evidence relating to the specific condition in question. Where evidence is lacking, the guidelines will incorporate statements and recommendations based upon the consensus statements developed by the guideline development group (GDG).

Clinical guidelines are intended to improve the process and outcomes of healthcare in a number of different ways. Clinical guidelines can:
provide up-to-date evidence-based recommendations for the management of conditions and disorders by healthcare professionals
be used as the basis to set standards to assess the practice of healthcare professionals
form the basis for education and training of healthcare professionals
assist patients and carers in making informed decisions about their treatment and care
improve communication between healthcare professionals, patients and carers
help identify priority areas for further research.
1.1.2 Uses and limitations of clinical guidelines

Guidelines are not a substitute for professional knowledge and clinical judgment. Guidelines can be limited in their usefulness and applicability by a number of different factors: the availability of high quality research evidence, the quality of the methodology used in the development of the guideline, the generalisability of research findings and the uniqueness of individual patients.

Although the quality of research in depression in children and young people is variable, the methodology used here reflects current international understanding on the appropriate practice for guideline development (AGREE: Appraisal of Guidelines for Research and Evaluation Instrument; www.agreecollaboration.org), ensuring the collection and selection of the best research evidence available, and the systematic generation of treatment recommendations applicable to the majority of patients and situations. However, there will always be some patients for whom clinical guideline recommendations are not appropriate and situations in which the recommendations are not readily applicable. This guideline does not, therefore, override the individual responsibility of healthcare professionals to make appropriate decisions in the circumstances of the individual patient, in consultation with the patient and/or carer.

In addition to the clinical evidence, cost-effectiveness information, where available, is taken into account in the generation of statements and recommendations of the clinical guidelines. While national guidelines are concerned with clinical and cost effectiveness, issues of affordability and implementation costs are to be determined by the NHS.

In using guidelines, it is important to remember that the absence of empirical evidence for the effectiveness of a particular intervention is not the same as evidence for ineffectiveness. In addition, of particular relevance in mental health, evidence-based treatments are often delivered within the context of an overall treatment programme including a range of activities, the purpose of which may be to help engage the patient, and provide an appropriate context for the delivery of specific interventions. It is important to maintain and enhance the service context in which these interventions are delivered, otherwise the specific benefits of effective interventions will be lost. Indeed, the importance of organising care, so as to support and encourage a good therapeutic relationship, is at times more important than the specific treatments offered.

1.1.3 Why develop national guidelines?

The National Institute for Clinical Excellence (NICE) was established as a Special Health Authority for England and Wales in 1999, with a remit to provide a single source of authoritative and reliable guidance for patients, professionals and the public. NICE guidance aims to improve standards of
care, to diminish unacceptable variations in the provision and quality of care across the NHS and to ensure that the health service is patient-centred. All guidance is developed in a transparent and collaborative manner using the best available evidence and involving all relevant stakeholders.

NICE generates guidance in a number of different ways, two of which are relevant here. First, national guidance is produced by the Technology Appraisal Committee to give robust advice about a particular treatment, intervention, procedure or other health technology. Second, NICE commissions the production of national clinical practice guidelines focused upon the overall treatment and management of a specific condition. To enable this latter development, NICE established seven National Collaborating Centres in conjunction with a range of professional organisations involved in healthcare.

1.1.4 The National Collaborating Centre for Mental Health
This guideline has been commissioned by NICE and developed within the National Collaborating Centre for Mental Health (NCCMH). The NCCMH is a collaboration of the professional organisations involved in the field of mental health, national service-user and carer organisations, a number of academic institutions and NICE. The NCCMH is funded by NICE and led by a partnership between the Royal College of Psychiatrists’ research unit (College Research Unit – CRU) and the British Psychological Society’s equivalent unit (Centre for Outcomes Research and Effectiveness – CORE). Members of the NCCMH reference group come from the following organisations:

Royal College of Psychiatrists (RCPsych)

British Psychological Society (BPS)

Royal College of Nursing (RCN)

National Institute for Social Work (NISW)

College of Occupational Therapists (COT), now replaced by the Clinical Effectiveness Forum for the Allied Health Professions (CEFAHP)

Royal College of General Practitioners (RCGP)

Royal Pharmaceutical Society (RPS)

Rethink Severe Mental Illness

Manic Depression Fellowship (MDF)
1.1.5 From national guidelines to local protocols
Once a national guideline has been published and disseminated, local healthcare groups will be expected to produce a plan and identify resources for implementation, along with appropriate timetables. Subsequently, a multidisciplinary group involving commissioners of health care, primary care and specialist mental health professionals, patients and carers should undertake the translation of the implementation plan into local protocols. The nature and pace of the local plan will reflect local health care needs and the nature of existing services; full implementation may take a considerable time, especially where substantial training needs are identified.

1.1.6 Auditing the implementation of guidelines
This guideline identifies key areas of clinical practice and service delivery for local and national audit. Although the generation of audit standards is an important and necessary step in the implementation of this guidance, a more broadly based implementation strategy should be developed. Nevertheless, it should be noted that the Healthcare Commission will monitor the extent to which Primary Care Trusts (PCTs), trusts responsible for mental health and social care and Health Authorities have implemented these guidelines.

1.2 The national Depression in Children guideline

1.2.1 Who has developed this guideline?
The ‘Guideline Development Group’ (GDG) was convened by the NCCMH, and supported by funding from NICE. The GDG consisted of carers, professionals from primary care, psychiatry, clinical psychology, nursing, social work services and the voluntary sector.

Staff from the NCCMH provided leadership and support throughout the process of guideline development, undertaking systematic searches, information retrieval, appraisal and systematic review of the evidence. Members of the GDG received training in the process of guideline development. The National Guidelines Support and Research Unit, also
All members of the Group made formal declarations of interest at the outset, updated at every GDG meeting. GDG members met a total of 20 times throughout the process of guideline development. For ease of evidence identification and analysis, some members of the GDG became topic leads, covering identifiable treatment approaches. The NCCMH technical team supported group members, with additional expert advice from special advisers where necessary. All statements and recommendations in this guideline have been generated and agreed by the whole GDG.

1.2.2 For whom is this guideline intended?
This guideline will be of relevance to children and young people from 5 to 18 years who have experience of depression.

The guideline covers the care provided by primary, community, secondary and other healthcare professionals who have direct contact with, and make decisions concerning the care of, children and young people with depression.

The guideline will also be relevant to the work, but will not cover the practice, of those in:
occupational health services
social services
the independent sector.

The experience of depression can affect the whole family and often the community. The guideline recognises the role of both in the treatment and support of children and young people with depression.

1.2.3 Specific aims of this guideline
The guideline makes recommendations and suggests good practice points for the treatment and management of depression in children and young people. Specifically, it aims to:

- Evaluate the role of specific psychological interventions in the treatment and management of depression in children and young people
- Evaluate the role of specific pharmacological interventions in the treatment and management of depression in children and young people
• Address the issues of diagnosis, detection and the use of screening techniques in high-risk situations.

• Provide key review criteria for audit, which will enable objective measurements to be made of the extent and nature of local implementation of this guidance, particularly its impact upon practice and outcomes for children and young people with depression.

The guideline will not cover treatments that are not normally available in the NHS.

2 Methods used to develop this guideline

2.1 Overview

The development of this guideline drew upon methods outlined by NICE (NICE, 2002; Eccles & Mason, 2001). A team of experts, professionals, service user(s) and carer(s), known as the Guideline Development Group (GDG), with support from the NCCMH staff, undertook the development of a patient centred, evidence-based guideline. There are six basic steps in the process of developing a guideline:

• Define the scope, which sets the parameters of the guideline and provides a focus and steer for the development work.

• Define clinical questions considered important for practitioners and service users.

• Develop criteria for evidence searching and search for evidence.

• Design validated protocols for systematic review and apply to evidence recovered by search.

• Synthesise and (meta-) analyse data retrieved, guided by the clinical questions, and produce evidence statements.

• Answer clinical questions with evidence-based recommendations for clinical practice.
The clinical practice recommendations made by the GDG are therefore derived from the most up-to-date and robust evidence base for the clinical and cost effectiveness of the treatments and services used in the management of depression in children. In addition, to ensure a service user and carer focus, the concerns of service users and carers regarding clinical practice have been highlighted and addressed by good practice points and recommendations agreed by the whole GDG. The evidence-based recommendations and good practice points are the core of this guideline.

2.2 The Guideline Development Group

The GDG consisted of: professionals in psychiatry, clinical psychology, nursing, social work, and general practice; academic experts in psychiatry and psychology; a service user representatives and a carer. The guideline development process was supported by staff from the NCCMH, who undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GDG, managed the process, and contributed to the drafting of the guideline.

2.2.1 Guideline Development Group meetings

Twenty GDG meetings were held between February 2003 and November 2004. During each day-long GDG meeting, in a plenary session, clinical questions and clinical evidence were reviewed and assessed, statements developed and recommendations formulated. At each meeting, all GDG members declared any potential conflict of interests, and service user and carer concerns were routinely discussed as part of a standing agenda.

2.2.2 Topic groups

The GDG divided its workload along clinically relevant lines to simplify the guideline development process, and GDG members formed smaller topic groups to undertake guideline work in that area of clinical practice. Topic group 1 covered questions relating to risk factors, screening, detection, self-help, family support and inpatient treatment. Topic group 2 covered pharmacological interventions and relapse prevention, and topic group 3 covered psychological interventions and relapse prevention. In addition, both topic groups 2 and 3 looked at the issue of combining pharmacological and psychological interventions.

The topic groups were designed to efficiently manage the large volume of evidence appraisal prior to presenting it to the GDG as a whole. Each topic group was chaired by a GDG member with expert knowledge of the topic area (one of the health care professionals). Topic groups refined the clinical definitions of treatment interventions, reviewed and prepared the evidence with the systematic reviewer before presenting it to the GDG as a whole, and helped the GDG to identify further expertise in the topic. Topic group leaders reported the status of the group’s work as part of the standing agenda. They also introduced and led the GDG discussion of the evidence review for that
2.2.3 Service users and carers

In order to obtain the views of children and young people concerning their experience of depression and the care and treatment they received, the Guideline Development Group commissioned a consultation with service users aged 7 to 18. Details about this consultation are given in Chapter 3, section 3.7.

Carers with experience of services also gave an integral carer/service user focus to the GDG and the guideline. The GDG included a service user representative and a representative of a national service user group. They contributed as full GDG members to writing the clinical questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology associated with depression in children, and bringing service-user research to the attention of the GDG. In drafting the guideline, they contributed to the editing of the first draft of the guideline’s introduction and identified good practice points from the service user and carer perspective; their suggestions were incorporated before distributing the draft to the GDG for further review.

2.2.4 Special advisers

Special advisers, who had specific expertise in one or more aspects of treatment and management relevant to the guideline, assisted the GDG, commenting on specific aspects of the developing guideline and making presentations to the GDG (see acknowledgements for the names of special advisers).

2.2.5 National and international experts

National and international experts in the area under review were identified through the literature search and through the experience of the GDG members. These experts were contacted to recommend unpublished or soon-to-be published studies in order to ensure up-to-date evidence was included in the development of the guideline (see Appendix D for a list of names).

2.3 Clinical questions

Clinical questions were used to guide the identification and interrogation of the evidence-base relevant to the topic of the guideline. The questions were developed using a modified nominal group technique. The process began by asking each member of the GDG to submit as many questions as possible. The questions were then collated and refined by the review team. At a subsequent meeting, the guideline chair facilitated a discussion to further refine the questions. At this point, the GDG members were asked to rate each question for importance. The results of this process were then discussed and consensus reached about which questions would be of primary importance and which
would be secondary. The GDG aimed to address all primary questions, while secondary questions would only be covered time permitting. Appendix E lists the clinical questions.

2.4 Systematic clinical literature review
The aim of the clinical literature review was to systematically identify and synthesise relevant evidence from the literature in order to answer the specific clinical questions developed by the GDG. Thus, clinical practice recommendations are evidence-based, where possible, and if evidence was not available, informal consensus methods were used (see section 3.4.6) and the need for future research was specified.

2.4.1 Methodology
A stepwise, hierarchical approach was taken to locating and presenting evidence to the GDG. The NCCMH developed this process based on advice from the National Guidelines Support and Research Unit (NICE) and after considering recommendations from a range of other sources. These included:

- Centre for Clinical Policy and Practice of the New South Wales Health Department (Australia)
- Clinical Evidence Online
- Cochrane Collaboration
- New Zealand Guideline Group
- NHS Centre for Reviews and Dissemination
- Oxford Centre for Evidence-Based Medicine
- Scottish Intercollegiate Guidelines Network (SIGN)
- United States Agency for Health Research and Quality
- Oxford Systematic Review Development Programme.

2.4.2 The review process
A brief search of the major bibliographic databases for recent systematic reviews and existing guidelines was first conducted to help inform the development of the scope. After the scope was finalised, a more extensive search for systematic reviews was undertaken. At this point, the review team, in conjunction with the GDG, developed an evidence map that detailed all comparisons necessary to answer the clinical questions. The initial approach taken to locating primary-level studies depended on the type of clinical question and availability of evidence.

After consulting the GDG, the review team decided which questions were likely to have a good evidence base and which questions were likely to have little or no directly relevant evidence. For questions in the latter category, a
brief descriptive review was initially undertaken by a member of the GDG (see section 3.4.6). For questions with a good evidence base, the review process depended on the type of clinical question.

2.4.2.1 The search process for questions concerning interventions

For questions related to interventions, the initial evidence base was formed from well-conducted randomised controlled trials (RCTs) that addressed at least one of the clinical questions. Although there are a number of difficulties with the use of RCTs in the evaluation of interventions in mental health, the RCT remains the most important method for establishing treatment efficacy. The initial search for RCTs involved searching the standard mental health bibliographic databases (EMBASE, MEDLINE, PsycINFO, Cochrane Library) for all RCTs potentially relevant to the guideline. If the number of citations generated from this search was large (>5000), question-specific search filters were developed to restrict the search while minimising loss of sensitivity.

After the initial search results were scanned liberally to exclude irrelevant papers, the review team used a purpose built ‘study information’ database to manage both the included and the excluded studies (eligibility criteria were developed after consultation with the GDG). For questions without good quality evidence (after the initial search), a decision was made by the GDG about whether to, (a) repeat the search using subject-specific databases (e.g., CINAHL, AMED, SIGLE or PILOTS), (b) conduct a new search for lower levels of evidence, or (c) adopt a consensus process (see Section 3.4.6). Future guidelines will be able to update and extend the usable evidence base starting from the evidence collected, synthesised and analysed for this guideline.

Recent high-quality English-language systematic reviews were used primarily as a source of RCTs (see Appendix H for quality criteria). However, where existing data sets were available from appropriate reviews, they were cross-checked for accuracy before use. New RCTs meeting inclusion criteria set by the GDG were incorporated into the existing reviews and fresh analyses performed. The review process is illustrated in Flowchart 1.

Additional searches were made of the reference lists of all eligible systematic reviews and RCTs, and the list of evidence submitted by stakeholders. Known experts in the field (see Appendix D), based both on the references identified in early steps and on advice from GDG members, were sent letters requesting systematic reviews or RCTs that were in the process of being published. Unpublished full trial reports were also accepted where sufficient information was provided to judge eligibility and quality. Conference abstracts or poster presentations were not generally acceptable. If data had not been published in a peer-reviewed journal, the authors were contacted requesting full trial reports. In addition to the searches described above, the tables of contents of appropriate
Flowchart 1: Guideline Review Process

NCCMH Review team tasks
- Brief search for recent SRs to help inform the development of the scope
- Conduct systematic search for relevant systematic reviews (initial 5 year limit)
- Perform first scan; retrieve all eligible papers for more detailed evaluation
- Apply eligibility/quality criteria to retrieved papers
- Produce evidence map with all comparisons necessary to answer clinical questions
- Consult GDG about appropriate level of evidence to begin searching for
- Conduct systematic search for relevant level(s) of evidence

GDG tasks
- Draft clinical questions with help from GDG chairperson
- No. of citations excluded; No. that could not be located
- No. of citations excluded
- Help produce evidence map
- Consider known RCT evidence
- Finalise clinical questions
- Consider known available evidence for each question
- For questions unlikely to have lower levels of evidence, begin consensus process
- For questions likely to have lower levels of evidence, conduct new question specific search

No. of citations excluded
- Scan titles and abstracts & apply eligibility criteria liberally; cross-check excluded
- Check SRs for additional evidence
- Set up Access database according to evidence map
- Enter study info. into database & apply eligibility/quality criteria
- Update evidence map - highlight areas without evidence
- Consult GDG about likely-hood of lower levels of evidence
- Develop clinical question specific search filters:
  - Update existing high-quality SRs
  - Run new filters only where necessary
- <5000 hits
- For questions unlikely to have lower levels of evidence, begin consensus process
- Consider known available evidence for each question
journals were periodically checked for relevant studies. In addition, the tables of contents of appropriate journals were periodically checked for relevant studies.

2.4.2.2 The search process for questions of diagnosis and prognosis
For questions related to diagnosis and prognosis, the search process was the same as described above, except that the initial evidence base was formed from studies with the most appropriate and reliable design to answer the particular question. That is, for questions about diagnosis, the initial search was for cross-sectional studies; for questions about prognosis, it was for cohort studies of representative patients. In situations where it was not possible to identify a substantial body of appropriately designed studies that directly addressed each clinical question, a consensus process was adopted (see Section 3.4.6).

2.4.2.3 Search filters
Search filters developed by the review team consisted of a combination of subject heading and free-text phrases. Specific filters were developed for the guideline topic, and where necessary, for each clinical question. In addition, the review team used filters developed for systematic reviews, RCTs and other appropriate research designs (Appendix H).

2.4.2.4 Study selection
All primary-level studies included after the first scan of citations were acquired in full and re-evaluated for eligibility at the time they were being entered into the study information database. Appendices P-R list the standard inclusion and exclusion criteria. More specific eligibility criteria were developed for each clinical question. Systematic reviews were assessed for eligibility using a standardised form (see Appendix G). All eligible papers were then critically appraised for methodological quality (see Appendix H). The eligibility of each study was confirmed by at least one member of the appropriate TG.

For some clinical questions, it was necessary to prioritise the evidence with respect to the UK context. To make this process explicit, the TGs took into account the following factors when assessing the evidence:

- Participant factors (e.g., gender, age, ethnicity)
- Provider factors (e.g., model fidelity, the conditions under which the intervention was performed, the availability of experienced staff to undertake the procedure)
- Cultural factors (e.g., differences in standard care, differences in the welfare system).
It was the responsibility of each TG to decide which prioritisation factors were relevant to each clinical question in light of the UK context, and then decide how they should modify their recommendations.

2.4.3 Synthesising the evidence
Where possible, outcome data were extracted directly from all eligible studies, which met the quality criteria, into Review Manager 4.2 (Cochrane Collaboration, 2003). Meta-analysis was then used, where appropriate, to synthesise the evidence using Review Manager. If necessary, reanalyses of the data or sensitivity analyses were used to answer clinical questions not addressed in the original studies or reviews. For continuous outcomes, where more than 50% of the total number randomised in a particular study were not accounted for, the data were excluded from the analysis because of the risk of bias. In the case of dichotomous outcomes (except for the outcome of leaving the study early), the effects of high attrition rates were examined with sensitivity analyses.

Included and excluded studies tables, generated automatically from the study information database, were used to summarise general information about each study (see Appendices P - R). Where meta-analysis was not appropriate and/or possible, the reported results from each primary-level study were presented in the appropriate included studies table.

Consultation was used to overcome difficulties with coding. Data from studies included in existing systematic reviews were extracted independently by one reviewer directly into Review Manager and cross-checked with the existing data set. Two independent reviewers extracted data from new studies, and disagreements were resolved with discussion. Where consensus could not be reached, a third reviewer resolved the disagreement. Masked assessment (i.e., blind to the journal from which the article comes, the authors, the institution, and the magnitude of the effect) was not used since it is unclear that doing so reduces bias (Jadad et al., 1996; Berlin, 2001).

2.4.4 Presenting the data to the GDG
Where possible, the GDG were given a graphical presentation of the results using forest plots generated with the Review Manager software. Each forest plot displayed the effect size and confidence interval (CI) for each study as well as the overall summary statistic. The graphs were organised so that the display of data in the area to the left of the ‘line of no effect’ indicated a ‘favourable’ outcome for the treatment in question. Dichotomous outcomes were presented as relative risks (RR) with the associated 95% CI (For an example, see Figure 1). A relative risk (or risk ratio) is the ratio of the treatment event rate to the control event rate. A RR of 1 indicates no difference between treatment and control. In Figure 1, the overall RR of 0.73 indicates that the event rate (i.e., non-remission rate) associated with intervention A is about ¾ of that with the control intervention, or in other
words, intervention A reduces non-remission rates by 27%. In addition, the CI around the RR does not cross the ‘line of no effect’ indicating that this is a statistically significant effect. The CI shows with 95% certainty the range within which the true treatment effect should lie.

Binary outcomes used to measure efficacy were calculated on an intention-to-treat basis (i.e., a ‘once-randomised-always-analyse’ basis). This assumes that those participants who ceased to engage in the study – from whatever group – had an unfavourable outcome. For adverse events, we extracted the data as reported by the study authors favouring intention-to-treat where possible.

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Intervention A</th>
<th>Control</th>
<th>RR (fixed) 95% CI</th>
<th>Weight %</th>
<th>RR (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Intervention A vs. control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Griffiths1994</td>
<td>13/23</td>
<td>27/28</td>
<td>38.79 0.59 [0.41, 0.84]</td>
<td></td>
<td></td>
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<tr>
<td>Lee1986</td>
<td>11/15</td>
<td>14/15</td>
<td>22.30 0.70 [0.56, 1.10]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treasure1994</td>
<td>21/28</td>
<td>24/27</td>
<td>58.92 0.84 [0.60, 1.10]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>45/66</td>
<td>65/70</td>
<td>100.00 0.73 [0.61, 0.88]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 2.83, df = 2 (P = 0.24), I² = 29.3%
Test for overall effect: Z = 3.37 (P = 0.0007)

Figure 1. Example of a forest plot displaying dichotomous data

Continuous outcomes were analysed as weighted mean differences (WMD), or as standardised mean differences (SMD) when different measures were used in different studies to estimate the same underlying effect (for an example, see Figure 2). If provided, intention-to-treat data, using a method such as ‘last observation carried forward’, were preferred over data from completers.

<table>
<thead>
<tr>
<th>Study or sub-category</th>
<th>Intervention A</th>
<th>Control</th>
<th>SMD (fixed) 95% CI</th>
<th>Weight %</th>
<th>SMD (fixed) 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>01 Intervention A vs. control</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Freeman1988</td>
<td>32 1.30(3.40)</td>
<td>20 3.70(3.60)</td>
<td>25.91 -0.68 [-1.25, -0.10]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Griffiths1994</td>
<td>10 1.25(1.45)</td>
<td>22 4.14(2.21)</td>
<td>17.83 -1.50 [-2.20, -0.81]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lee1986</td>
<td>14 3.70(4.00)</td>
<td>14 10.10(13.10)</td>
<td>15.60 -0.49 [-1.29, 0.34]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treasure1994</td>
<td>29 44.23(27.04)</td>
<td>24 41.45(24.47)</td>
<td>27.94 -0.45 [-1.24, 0.34]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wolf1992</td>
<td>15 5.30(5.10)</td>
<td>11 7.10(4.00)</td>
<td>13.90 -0.36 [-1.14, 0.43]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>109</td>
<td>91</td>
<td>100.00 -0.74 [-1.34, 0.84]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Test for heterogeneity: Chi² = 6.13, df = 4 (P = 0.19), I² = 34.8%
Test for overall effect: Z = 4.98 (P < 0.00001)

Figure 2. Example of a forest plot displaying continuous data

To check for heterogeneity between studies, both the I² test of heterogeneity and the chi-squared test of heterogeneity (p < .10), as well as visual inspection of the forest plots were used. The I² statistic describes the proportion of total
variation in study estimates that is due to heterogeneity (Higgins & Thompson, 2002). An $I^2$ of less than 30% was taken to indicate mild heterogeneity and a fixed effects model was used to synthesise the results. An $I^2$ of more than 50% was taken as notable heterogeneity. In this case, an attempt was made to explain the variation. If studies with heterogeneous results were found to be comparable, a random effects model was used to summarise the results (DerSimonian & Laird, 1986). In the random effects analysis, heterogeneity is accounted for both in the width of CIs and in the estimate of the treatment effect. With decreasing heterogeneity the random effects approach moves asymptotically towards a fixed effects model. An $I^2$ of 30 to 50% was taken to indicate moderate heterogeneity. In this case, both the chi-squared test of heterogeneity and a visual inspection of the forest plot were used to decide between a fixed and random effects model.

To explore the possibility that the results entered into each meta-analysis suffered from publication bias, data from included studies were entered, where there was sufficient data, into a funnel plot. Asymmetry of the plot was taken to indicate possible publication bias and investigated further.

### 2.4.5 Forming and grading the statements and recommendations

The evidence tables, forest plots, and included studies tables formed the basis for developing clinical statements and recommendations.

#### 2.4.5.1 Intervention studies

Each clinical evidence statement was classified according to a hierarchy (see text box 1). Recommendations were then graded A to C based on the level of associated evidence, or noted as coming from a previous NICE guideline or technology appraisal (see text box 1).
Text Box 1: Hierarchy of evidence and recommendations grading scheme

<table>
<thead>
<tr>
<th>Level</th>
<th>Type of evidence</th>
<th>Grade</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Evidence obtained from a single randomised controlled trial or a meta-analysis of randomised controlled trials</td>
<td>A</td>
<td>At least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation (evidence level I) without extrapolation</td>
</tr>
<tr>
<td>IIa</td>
<td>Evidence obtained from at least one well-designed controlled study without randomisation</td>
<td>B</td>
<td>Well-conducted clinical studies but no randomised clinical trials on the topic of recommendation (evidence levels II or III); or extrapolated from level I evidence</td>
</tr>
<tr>
<td>IIb</td>
<td>Evidence obtained from at least one other well-designed quasi-experimental study</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities</td>
<td>C</td>
<td>Expert committee reports or opinions and/or clinical experiences of respected authorities (evidence level IV) or extrapolated from level I or II evidence. This grading indicates that directly applicable clinical studies of good quality are absent or not readily available</td>
</tr>
<tr>
<td>NICE</td>
<td>Evidence from NICE guideline or technology appraisal</td>
<td>NICE</td>
<td>Evidence from NICE guideline or technology appraisal</td>
</tr>
</tbody>
</table>


In order to facilitate consistency in the interpretation of outcomes, the GDG utilised an algorithm (see flowchart 2) and evidence profile tables (Appendix O). The tables summarise information about the quality of each outcome and the findings. Efficacy outcomes were reported as RR/SMD and as the probability of superiority [Area Under the Curve (AUC)]. The AUC represents the probability that a randomly selected participant in the
treatment group has a better result than one in the comparison group. The following values were used to help judge the magnitude of the effect: 56% = a smaller than typical effect; 64% = typical effect; 71% = larger than typical effect; ≥ 76% = much larger than typical effect. Adverse events were reported as SMD or the Number Needed to Treat – Benefit/Harm (NNTB/H). The NNT was interpreted cautiously were baseline risks varied between studies. In addition, NNTs calculated at follow-up were only reported where the length of follow-up was similar across studies. When the length of follow-up or baseline risk varies (especially with low risk), the NNT is a poor summary of the treatment effect (Deeks, 2002).

**Flowchart 2: Algorithm for determining the clinical importance of the effect**

1. **Is there a clinically important difference between x and y after controlling for heterogeneity?**
   - Yes
   - **Does the range of estimates defined by the confidence interval only include clinically important effects?**
     - Yes
     - Evidence of a clinically important effect favouring...
     - No
     - Limited evidence of a clinically important effect favouring...
       - **Does the range of estimates defined by the confidence interval completely exclude clinically important effects?**
         - Yes
         - Unlikely to be a clinically important difference
         - No
         - Inconclusive
As shown in flowchart 2, the GDG classified the results from each outcome as clinically important or not (i.e., whether or not the treatment is likely to benefit service users), taking into account both the comparison group and the type of outcome. The threshold for clinical importance is described in each evidence profile table.

Where heterogeneity between studies was judged problematic, in the first instance an attempt was made to explain the cause of the heterogeneity (e.g., outliers were removed from the analysis or sub-analyses were conducted to examine the possibility of moderators). Where homogeneity could not be achieved, a random effects model was used.

In cases where the point estimate of the effect was judged clinically important, a further consideration was made about the precision of the evidence by examining the range of estimates defined by the CI. Where the effect size was judged clinically important for the full range of plausible estimates, the result was described as evidence of a clinically important effect. In situations where the point estimate was clinically important but the CI included clinically unimportant effects, the result was described as limited evidence of clinically important effect.

Where the point estimate was judged as not clinically important and the CI did not include any clinically important effects, the result was described as evidence that there was unlikely to be a clinically important difference. Alternatively, if the range of estimates defined by the CI included clinically important benefits as well as no effect or harmful effects, the result was described as inconclusive.

Once the evidence profiles were finalised and agreed by the GDG, the associated recommendations were produced and graded. Grading allowed the GDG to distinguish between the level of evidence and the strength of the associated recommendation. In cases where there was methodologically sound (level I) evidence about an area of practice that had little direct clinical relevance to people with depression in England and Wales, the GDG extrapolated from the available evidence based on their combined clinical experience. The resulting recommendations were then graded with a lower grade (e.g., a ‘B’ grade where data were based upon level I evidence).

This allowed the GDG to moderate recommendations based on factors other than the strength of evidence. Such considerations include the applicability of the evidence to the people in question, economic considerations, values of the development group and society, or the group’s awareness of practical issues (Eccles et al., 1998).
2.4.6 Method used to answer a clinical question in the absence of appropriately designed, high-quality research

In the absence of level I evidence (or a level that is appropriate to the question), or where the GDG were of the opinion (on the basis of previous searches or their knowledge of the literature) that there were unlikely to be such evidence, either an informal or formal consensus process was adopted. This process focused on those questions that the GDG considered a priority.

2.4.6.1 Informal consensus

The starting point for this process of informal consensus was that a member of the topic group identified, with help from the systematic reviewer, a narrative review that most directly addressed the clinical question. Where this was not possible, a brief review of the recent literature was initiated.

This existing narrative review or new review was used as a basis for beginning an iterative process to identify lower levels of evidence relevant to the clinical question and to lead to written statements for the guideline. The process involved a number of steps:

- A description of what is known about the issues concerning the clinical question was written by one of the topic group members

- Evidence from the existing review or new review was then presented in narrative form to the GDG and further comments were sought about the evidence and its perceived relevance to the clinical question

- Based on the feedback from the GDG, additional information was sought and added to the information collected. This may include studies that did not directly address the clinical question but were thought to contain relevant data

- If, during the course of preparing the report, a significant body of primary-level studies (of appropriate design to answer the question) were identified, a full systematic review was done

- At this time, subject possibly to further reviews of the evidence, a series of statements that directly addressed the clinical question were developed

- Following this, on occasions and as deemed appropriate by the development group, the report was then sent to appointed experts outside of the GDG for peer review and comment. The information from this process was then fed back to the GDG for further discussion of the statements
• Recommendations were then developed and could also be sent for further external peer review

• After this final stage of comment, the statements and recommendations were again reviewed and agreed upon by the GDG.

2.5 Health economics review

The number of references identified and the number that met the eligibility criteria are provided Appendix M.

2.6 Stakeholder contributions

Professionals, service users, and companies have contributed to and commented on the guideline at key stages in its development. Stakeholders for this guideline include:

• Service user/carer stakeholders: the national service user and carer organisations that represent people whose care is described in this guideline
• Professional stakeholders: the national organisations that represent health care professionals who are providing services to service users
• Commercial stakeholders: the companies that manufacture medicines used in the treatment of depression
• Primary Care Trusts
• Department of Health and Welsh Assembly Government.

Stakeholders have been involved in the guideline’s development at the following points:

• Commenting on the initial scope of the guideline and attended a briefing meeting held by NICE
• Contributing lists of evidence to the GDG
• Commenting on the first and second drafts of the guideline.

2.7 Validation of this guideline

This guideline has been validated through two consultation exercises. The first consultation draft was submitted to the NICE Guidelines Advisory Committee Panel, and circulated to stakeholders and other reviewers nominated by GDG members.

The GDG reviewed comments from stakeholders, the NICE Guidelines Advisory Committee, a number of health authority and trust representatives and a wide range of national and international experts from the first round of consultation. The GDG then responded to all comments and prepared a final consultation draft which was submitted to NICE, circulated to all stakeholders for final comments and posted on the NICE website for public
consultation. The final draft was then submitted to the NICE Guidelines Advisory Committee for review prior to publication.

3 Depression

This guideline is concerned with the identification, treatment and management of depression in children and young people (from 5 to 18 years) in primary, community and secondary care. This guidance only relates to those identified by the tenth edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) (WHO, 1992), namely, depressive episode (F32), recurrent depressive episode (F33), although some recommendations will also apply to dysthymia (F34.1). Much of this guideline is drawn from research that has utilised a similar, but not identical, classificatory system – the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (DSM-IV) (APA, 1994). Other related NICE guidelines in preparation include depression in adults and older adults, and bipolar disorder in children, young people and adults.

3.1 The disorder

3.1.1 Symptoms, presentation and pattern of illness

Depression is a term in common use in the English language and as such has a range of different meanings. The term refers to an overall lowering of normal functions and not specifically to any one component of mind (Thompson, 1995). Descriptive models of depressive states have been consistent for over 2,000 years in noting the same constellation of signs and symptoms in depressed individuals across the lifespan (Jackson, 1985).

Clinically, the term depression refers to a group of symptoms and behaviours clustered around three core alterations in experience: changes in mood, in thinking and in activity, sufficient to cause impairment in personal and/or social functioning. Mood changes typically include sadness and/or irritability accompanied by a loss of pleasure, even in cherished interests. Cognitive changes generally lead to inefficient thinking, usually with a pronounced self-critical focus. Physically, depressed people become less active, although this may be concealed by the presence of anxiety or agitation. Although there are many similarities between adult depression and depression in younger people, there are important developmental differences in each of these three areas (Goodyer & Cooper, 1993).

As with adults, there is a change in mood from pleasant to unpleasant, that is relatively pervasive, persisting over time and place and sufficiently severe to interrupt every day functioning. Some children will deny feeling sad but will
admit to feeling ‘down’, others will admit to feeling ‘grumpy’ or ‘irritable’. In a significant proportion of cases the depressed young person no longer derives as much pleasure from life (anhedonia). This feature occurs in around 15 to 20% of depressed adolescent females (Goodyer & Cooper, 1993).

Typically young depressed patients have poor self-esteem with little to say when asked about their good points. They may indicate that they are ‘no good’, and that life events and difficulties in their social world are their fault. They may see no future for themselves, consider life hopeless and themselves helpless to effect any change for the better. They may complain of a loss of concentration, poor attention and an inability to make decisions. This may be due to a loss of confidence in their abilities or a difficulty in thinking. In severe cases the patient may feel guilty, or even wicked, and state that they deserve to be punished for past misdemeanours. Some such cases will have suicidal ideas, which are particularly serious. It should be noted that it is normal for children and young people to feel guilty about parental separation. Very rarely young patients will describe delusions or hallucinations.

Physical changes include low energy, apathy, tiredness and poor motivation. Failure to complete tasks may make feelings of guilt and lack of confidence worse. Appetite may increase or decrease, sleep rhythms are often disrupted and activity levels are lower overall. Some young people present with a classical ‘endogenous illness’, very similar to adults, with high levels of anhedonia, prominent physical symptoms of early morning wakening, poor appetite, low sexual drive, physical retardation and low emotional responsiveness. At present there is no evidence that in young people this form of presentation has any special significance other than a markedly severe depressive illness (Goodyer, 1996).

In primary care settings around 2 to 10% of children at any one time complain of aches and pains such as headaches and stomach aches, limb pain, and somewhat less frequently tiredness or fatigue (Campo et al, 2004). An unknown proportion of these will have a depressive illness. Females but not males presenting with headache of unknown origin may have a concurrent depressive illness. In contrast, musculo-skeletal presentations of unknown origin may reflect a depressive disorder for either sex (Egger et al, 1998; Egger et al, 1999).

There is no clear-cut consistency in how depressed children and young people present to health care services. Thus, the clinical picture varies in ways that are poorly understood, with levels of severity, personal impairment and developmental age. For example, cognitive features of worthlessness, self-criticism and poor attention increase in adolescence; and somatic features, such as aches and pains, tend to be more prominent in children (Ryan et al, 1987; Goodyer & Cooper, 1993; Kolvin 2001; Luby et al, 2003). However, these
are tendencies: young children are capable of negative cognitions and adolescents report aches and pains. There is little doubt that primary care physicians see individuals of all ages with distressing and dysfunctional mental states that are not well articulated in the psychiatric nosology and are often not a major consideration to mental health specialists (Pincus et al, 1999). Epidemiological findings in childhood and adolescence have also shown that a significant number of young people between the ages of 6 and 18 years have modest symptoms, no diagnosis, but with overt psychosocial impairment that may warrant treatment (Costello et al, 1996). The natural history of these sub-threshold conditions remains a matter for further research ideally in longitudinal designs such that the temporal relationship between impairments and clinical status can be examined as an evolving rather than static process. What little has been done to date suggests that, from the public health perspective, it would be unwise to ignore sub-threshold depressions if they present with psychosocial impairment (Costello et al, 1999). The evidence is that such young people are adding to the general burden of affective morbidity in the community at large, and may continue to do so over time. Whether there are specific and particular continuities and discontinuities in signs and symptoms between sub-threshold conditions and clinical disorders over the life course is not known.

3.1.2 Course and prognosis
Around 10% of children and young people with depression recover spontaneously within 3 months. A further 40% recover within the first year. At 12 months 50% remain clinically depressed. By 24 months this figure is around 20 to 30% (Harrington & Dubicka, 2001; Goodyer et al, 2003). The influence of treatment on the course of the disorder is not fully known; but clinically, treatment appears to shorten the liability for duration longer than 12 months.

The most serious complication is suicide (a risk of about 3% over the next 10 years) (Harrington, 2001). Suicide prevention and treatment intervention programmes may not effectively treat depression in such patients and specific treatments for affective disorder will be required (Harrington et al, 1998). Other complications include declining school performance and chronic difficulties with making and retaining friendships.

Persistent depressions in young people appear to have a permanent effect upon personal function and personality, and some have suggested that persistent depressions in the young may lead to chemical and physiological ‘scars’ indicating persistently altered brain functions, although this has yet to be systematically demonstrated (Post, 1992; Sokolov & Kutcher, 2001). Nevertheless, it is clear that, with each successive depressive episode, the potency of psychosocial factors necessary to trigger a new depressive episode
decreases (Kendler et al, 2000; Kendler et al, 2001) suggesting that repeated depressions do in fact increase a person’s vulnerability to become depressed.

Around 30% of cases recur within 5 years and many of these develop episodes into adult life (Fombonne et al, 2001). In the longer term, those children and young people who develop a recurrent or chronic disorder extending into adulthood are likely to suffer considerable disability and impairment. Depression affects the whole of a person’s life, impairing occupational, social, emotional and physical health, and carrying considerable stigma to make matters worse (see NICE adult depression guideline, section 2.1.3). However, most children and young people who develop a depressive episode and present to clinical services do not go on to suffer a recurrent depressive illness in adult life, although the long-term impact of treatment on prognosis remains unknown.

3.2 Incidence and prevalence
The 12-month period prevalence estimates for major depression are approximately 1% for pre-pubertal children and around 3% for post-pubertal adolescents (Angold & Costello, 2001). In pre-pubertal children, there is no sex difference in prevalence, whereas in post-pubertal adolescents there is a marked increase in females (2%) compared with males (1%), whose prevalence continues to rise but at a much slower rate.

In the national survey of children and adolescents’ mental health (Meltzer et al, 1999), 10% of 5 to 15 year olds had a mental disorder including 4% with emotional disorder (anxiety and depression). Children and young people with emotional disorders, when compared with children without a mental disorder, were nearly twice as likely to be living with a lone parent (28% versus 15%), more than twice as likely to be with both parents being unemployed (27% versus 12%), and more likely to have parents who were on low incomes, had fewer qualifications and living in social sector housing. Moreover, 50% of children with emotional disorder had a parent with a GHQ-12 of 3 or more (twice the proportion of children without a mental disorder) and 34% with a parent scoring 6 or more (more than 3 times the proportion for children/young people without a mental disorder). Importantly, for both conduct disorder and emotional disorder, but not attention deficit hyperactivity disorder (ADHD) or other mental disorders, the higher the parents GHQ-12 score, the greater the prevalence of these disorders in their children.

Depression in children and young people tends to occur in conjunction with other mental health problems; indeed, most fulfil the diagnostic criteria for a second disorder (see below). Moreover, looked-after children and young people, and those in correctional institutions, have a particularly high incidence of all mental disorders, including depression (Meltzer et al, 2003b).
However, depression is more commonly encountered in a number of particular settings, including and especially the following:

- School refusal in adolescent girls
- Adolescent onset behavioural difficulties, following a disciplinary crisis
- Children or adolescents who have been maltreated or experienced very traumatic events
- Children or adolescents who repeatedly harm themselves
- Adolescents engaged in chronic family disputes.

Risk factors for depression and the potential for screening is addressed in Chapter 4.

3.3 Diagnosis

Depression is a particularly heterogeneous diagnostic category with changing boundaries and methods of classification. However, the introduction of operational diagnostic criteria has at least improved the reliability of diagnosis, although there has been no parallel improvement in diagnostic validity (Dohrenwend, 1990). Nevertheless, the distinction between mild, moderate and severe depression, as described and defined in ICD-10 (WHO, 1992), has clinical validity, and comparable systems have been employed for much of the research underlying this guideline. This approach has, therefore, been used to structure this guideline.

The diagnosis of mild depression (ICD-10: Depressive episode - mild) is made when depressed mood (or irritability), with either anhedonia or tiredness, is experienced in conjunction with two further symptoms from a list of nine commonly associated with depression (i.e. a total of four symptoms). The mood change must last throughout the waking hours (although some may improve gradually through the day, only to return to feeling depressed on waking), and both the mood change and concurrent symptoms must persist for at least 2 weeks. For moderate depression the number of symptoms rises to 5 or 6 (including depressed mood), and for severe the number rises to 7 or more.

There are no requirements for a particular pattern of cognitions and/or physical symptoms. Equally, no distinction is made regarding the duration of symptoms, which, providing they have been present for at least 2 weeks, may vary in length for any period of time, even years. In cases with duration greater than 52 weeks the diagnosis of dysthymia must be considered (but see below). In adolescents major depression may occur against a childhood history of dysthymia (Kovacs et al, 1994). It is important to reiterate that for children and young people, the clinical characteristics vary somewhat according to age at presentation. Children have a higher rate of physical complaints than adolescents including headaches and abdominal pains and...
tend not to look depressed. Adolescents are more likely than children to complain of subjective feelings of low mood, and to have a higher rate of suicidal thoughts and self-blame.

3.3.1 Differential diagnosis and comorbidity
Depressive illness should only be diagnosed when the signs and symptoms lead to significant personal suffering and are accompanied by observable social impairment, although in mild depressions social impairment may be less obvious to the observer. The diagnosis requires clinical skills and time to elicit. Depressed young people will not describe their symptoms readily or easily, even to their parents. Although adolescents can be moody and unpredictable these do not constitute clinical characteristics of depression. Similarly tearfulness is of itself not a clinical characteristic of depression particularly in younger children.

In specialist services and community studies major depression seldom occurs as a single psychiatric disorder (Mitchell et al, 1988; Goodyer & Cooper, 1993; Herbert et al, 1996). Concurrent symptoms of anxiety and behavioural disturbances are present in almost all cases, and between 50% and 80% of depressed cases will also meet criteria for another non depressive disorder. Conduct disorder and/or oppositional disorder occur in around 25% of depressed youth, with a similar proportion meeting criteria for separation anxiety disorder. Around 15% will meet criteria for obsessive-compulsive disorder, and a further 5% will be concurrently suffering from an eating disorder, other anxiety states or ADHD.

Although there is, as yet, no systematic evidence for an association between concurrent substance misuse and depression in young people, it is widely believed that many depressed youth turn to drugs in an attempt to alleviate persistent low mood. However, there is evidence to suggest that smoking in teenage boys is associated with an increased risk of comorbid substance misuse and psychopathology (including depression) in general (Boys et al, 2003; Meltzer et al, 2003).

It is clear that depression in children and young people usually occurs in the context of other detectable problems or comorbidity. However, clinically it is important to avoid counting the same symptoms more than once. Thus, a double diagnosis should only be made when the signs and symptoms indicate the presence of two quite clear and separate psychiatric disorders, occurring at the same time. Very few cases have more than two comorbid diagnoses, and when they do occur they usually indicate severe psychiatric disorder.

3.3.1.1 Dysthymia
Dysthymia has been described as a chronic mood disturbance of young people characterised by: long standing gloom and dysphoria, brooding about
feeling unloved and affective dysregulation. The dominant negative cognition is self-deprecation or negative self-esteem. There are high rates of irritability and anger in everyday circumstances, occurring as a hyperemotional response to social problems in the everyday environment (Kovacs 1994). According to DSM-IV, dysthymia is a chronic depressive condition that in childhood or adolescence presents with the same general characteristic of lowered mood (dysphoria or irritability) as major depression, but of insufficient severity to gain the full diagnosis. The symptoms must have been present for at least 1 year or more. ICD-10 requires that symptoms be present for 2 years or more and defines the disorder as likely to begin in late teens or early adult life and makes no reference to a childhood onset form. In addition to depressed mood the subject must have two out of a further six symptoms from the depressive symptoms list for unipolar major depression, except that feelings of guilt and suicidal behaviour are not included. The implication is that the latter two symptoms are not found in dysthymic disorders and if present suggest that the patient is likely to be suffering from an episode of major depression.

The best clinical description of dysthymia comes from the work of Kovacs and colleagues based on children referred to mental health services in Pittsburgh, USA. Compared with major depression, dysthymia is distinguished by the virtual absence and significantly lower prevalence of anhedonia and social withdrawal; and comparatively lower levels of guilt, morbid preoccupation and impaired concentration. Practically none of the dysthymic children had reduced appetite and few had hyposomnia or fatigue (Kovacs, 1994).

In diagnosing dysthymia, it is important to establish that the patient does not fulfil criteria for current major depression. If major depression has preceded the onset of dysthymia then there must have been full remission of all depressive symptoms for at least 2 months before the development of dysthymia. By contrast, episodes of major depression can be superimposed on dysthymia disorder, in which circumstances both diagnoses can be given.

In the absence of a published evidence-base for the treatment of dysthymia at present, in this guideline the treatment of dysthymia, if clinically necessary, should follow that for mild depression.

### 3.4 Aetiology

More than 95% of major depressive episodes in young people arise in children and adolescents with long-standing psychosocial difficulties. A very small number of depressive episodes in children and young people will arise in the absence of prior difficulties, and resulting from an acute, very negative life event, usually involving a severe personal assault. Between 50% and 70% of cases are acute, occurring within a few weeks of a precipitating event, such as a breakdown in a personal confiding relationship. In the other 30% to 50%,
onsets emerge more slowly against a background of family disharmony and/or friendship problems (Rueter et al., 1999; Goodyer et al., 2000).

There are multiple pathways to the onset of depression in adults and there is every reason to believe that the same is true for depressions across the lifespan (Kendler et al., 2002). Moreover, there are numerous aetiological theories to account for depression, including genetic, biochemical and endocrine, psychological, social and socio-economic. None has gained widespread acceptance, although a pragmatic model, integrating the various theories (the ‘Stress-Vulnerability’ model; Nuechterlein & Dawson, 1984) has broad clinical utility and is widely subscribed to. In this approach, young people (or adults) will, to varying degrees, have a vulnerability to depression rooted in genetic, endocrine and early family factors. This vulnerability will interact with current social circumstances, such as poverty, social adversity or family discord, with stressful life events acting as the trigger for an episode of depression (Harris, 2000).

Although this model can be used to understand and research depression in children and young people, what counts as a current social factor in the young child may well count as a vulnerability factor for an adolescent. For example, about 30% of the variation in risk for adolescent depressive symptoms is genetic. Genes appear to act through increasing the liability for other ‘depressogenic’ risks, such as negative temperament, experiencing more negative life events and difficulties, or responding to them with more distress and impairment (Caspi et al., 2003; Kendler et al., 2004). On the other hand, genetic factors overall appear somewhat less important in depressive symptoms arising in pre-pubertal children (Rice et al., 2002). Whether this is precisely the same for depressive syndromes and for a depressive illness in particular is not clear.

Biochemical theories of depression, such as the monoamine hypothesis, sit at least some of the vulnerability to depression within the ‘serotonin systems’ in the brain (Birmaher & Heydl, 2001). Other monoamines have also been invoked. There is also evidence for a steroid vulnerability to depression (Birmaher & Heydl, 2001). This suggests that high cortisol levels precede the onset of depression and impair brain functions, including those of serotonin (Goodyer et al., 2000). Of particular interest here, it appears that, amongst well adolescents, those whose mothers suffered with postnatal depression had higher circulating levels of cortisol (Halligan et al., 2004), raising the possibility that early events have long-term biochemical effects that may increase a young person’s vulnerability to depression.

Psychological processes, such as ingrained patterns of thinking, may also increase a young person’s vulnerability to depression. For example, the tendency to negative thinking about oneself at times of low mood, and the characteristic of ruminating or perseverating on these negative thoughts, in
the presence of psychosocial adversity, are known to increase the risk for a depressive episode (Lyubomirsky & Nolen-Hoeksm, 1995; Kelvin et al, 1999; Park et al, 2004). Individuals who possess both these cognitive characteristics appear to be particularly vulnerable to become depressed (Nolen-Hoeksema, 2000; Spasojevic & Alloy, 2001).

To reiterate, current social difficulties associated with depression in children and young people include marital disharmony, parental depression and other psychiatric disorders, family discord and maltreatment. The most important non-familial factors are breakdown in friendships and substance misuse. Of course, once a child or young person is depressed, these same factors can act to maintain the state of depression. In addition, poor friendships and further negative life events during the course of the disorder are especially associated with longer duration of disorder (Goodyer et al, 2001). Although it is unclear as to why about 30% of first depressive episodes in young people persist beyond 18 months (Goodyer et al, 2003), strong ‘candidate-factors’ include chronic friendship difficulties, ongoing family discord and untreated severe symptoms.

In conclusion, acute life events associated with onset of a depressive episode are personal disappointments derived in the main from friendship difficulties in adolescents and family discord in childhood. However, almost any event that carries a high negative and distressing impact has the potential to trigger the onset of depression in vulnerable young people, with pre-existing chronic family (and/or friendship) difficulties (Goodyer, 2001).

3.5 Use of health service resources and other costs

Morbidity associated with childhood depression continues into adulthood in about 30% of cases. This circumstance, with specialist services often required, can be expensive in terms of both emotional and economic cost. Indeed, this disorder often leads to long-term social maladjustment and a higher risk of suicide, with 37.5% continuing to experience social dysfunction into adulthood, coupled with a high risk of criminality, and 32.3% attempting suicide between childhood and adulthood (Fombonne et al, 2001). Given the fact that in 2003 there were 3.6 million children aged between 0 and 5, 4 million aged between 6 and 11, and 7 million aged between 12 and 18 (UN Population Division), these risks affect a large fraction of the national population.

In terms of pharmaceutical costs, there are currently more than 40,000 children and adolescents using antidepressants in the UK for all mental health disorders (Ramchandani, 2004). These include fluoxetine as well as other SSRIs that were permissible prior to December 2003 (Committee on Safety of Medicines, 16 Dec 2003). These latter medications may be continued or gradually withdrawn or replaced, and it is essential that the alternative costs
of these three possibilities be estimated. Using the lowest price ranges for SSRIs, the total health care cost of these drugs amounts to at least £12,360,000 per year, including initial prescribing and follow-up consultations (PSSRU 2003). The societal cost of failing to treat depression at an early stage, however, far outweighs any health service costs to the NHS.

To demonstrate this trade-off, the Maudsley long-term follow-up study of depression in childhood and adolescence found a high degree of continuity in psychiatric morbidity persisting into adulthood (Fombonne et al., 2001). Knapp and colleagues (2002) compared long-term cost of major depressive disorder (MDD) and comorbid conduct disorder (CD-MDD) among adults, who as children presented with depression in the Child and Adolescent Psychiatric Department of the Maudsley Hospital between 1970 and 1983. They found that in both groups inpatient hospital cost was the largest component of total cost.

In the case of each child diagnosed with MDD or CD-MDD, the total psychiatric inpatient hospital costs per year were estimated at GBP 193 and GBP 422, respectively (Knapp et al., 2002). Members of the CD-MDD group utilised more than double the specialist inpatient resources in comparison with those in the MDD group. The problem is that costs range far beyond the childhood years and present a downstream burden that increases with time.

The total cost accrued as a result of depression in childhood is difficult to measure, as it extends beyond the period of adolescence and can present its largest economic burden in adulthood. However, all estimations show that it is the long-term costs that are ultimately the more important parameters. For instance, depression in adults was estimated to cost the UK to an amount of £9,000 million each year (Thomas and Morris, 2003). Of this amount, £370 million represents direct treatment costs and the remainder is attributable to indirect costs resulting from 109.7 million working days lost and 2615 deaths due to depression in the year 2000 alone (ibid.). Based on these estimates, if 30% of children continue to be depressed in adulthood, they may present costs to an amount of £3,000 million each year once they become an adult. This is in addition to the costs of social and health care accrued during their childhood. Estimates in the US are proportionately the same, given a population about five times larger than the UK (Greenberg et al., 2003). Since depression often starts in and continues beyond childhood with increasing severity in time (Meltzer et al., 2000), the economic consequences of this disorder must be evaluated alongside episodes of treatment and parental work disruptions.

The disability-adjusted life year reflects the total amount of healthy life lost from premature mortality or from disability over time. A study by Haby and colleagues (2004) analysed the costs of treating with CBT the 2.3% of children and adolescents (6-17 years) who presented for MDD in Australia. The study
modelled twelve 1 hour sessions of CBT added to two parent sessions and GP diagnosis with referral time. They found that delivery of CBT by a public psychologist costs $9,000 (equivalent to £3,567) per DALY saved, and CBT proved to be 23% more efficacious than the control group. Additionally, the same study modelled a 9-month course of SSRI treatment (i.e. 20 mg fluoxetine with 14 doctor visits weekly for the first month, fortnightly for 2 months, and then every remaining month) and found that SSRIs were 16% more efficacious than the control group. While both CBT and SSRIs have lower efficacies in children and adolescents than in adults (being less cost-effective in comparison to adults) the cost-effectiveness of less than £5,000 per DALY saved would appear well within the NICE recommended thresholds, particularly in light of the high cost of not treating patients. However, the utilities that underlie the definition of DALYs are not universally accepted, nor does this measure reflect individuals’ differential abilities to cope with their functional limitations.

What is certain is that, due to its high prevalence and treatment costs and its role as probably the most important risk factor for suicide (Knapp & Ilson, 2002), the cost of antidepressant drug overdose and the disease have a great impact on productivity. This circumstance places an enormous economic burden not only on the health care system but also on the broader society.

Recently, the WHO has cited the ‘undefined burden’ of mental problems in children to highlight the economic and social burden for families, communities, and the wider society. This burden has not been measured due to a dearth of quantitative evidence. In addition, there is a ‘hidden burden’ that refers to association of childhood depression with stigma and violations of human rights (WHO, 2001). The overall economic costs affect, not least the NHS, but also the criminal justice system, social welfare, education and the employment sectors (ibid.). Administrative costs also accrue due to form-filling and any other associated tasks that may be related to prescribing and/or delivering treatments for childhood depression.

As debate continues over the efficacy and safety of antidepressants in children and over the usefulness of quality of life estimates in mental health disorders, more research is required into the relationship of age and sex on predispositions to childhood depression, and the economic consequences of alternative treatments. Since major depressive disorder is at least twice as common in adolescent and adult females in comparison to adolescent and adult males (cf. Angold et al, 2002), it stands to reason that recommendations for the treatment and prevention of MDD should be particularly directed at females. This is not to ignore the importance of treating such conditions in males, yet it highlights the fact that a 2-3:1 female to male ratio exists in the case of childhood depression (ibid.). The acknowledgement of this allows for a more synchronised co-ordination between healthcare professionals, their patients, and the policies that guide them.
3.6 Treatment and management in the NHS

As with depression in adults, the provision of treatment for children and young people who get depressed is significantly limited by public stigma, our failure to detect or recognise depression, and the way that services are organised for this group of young people. There is little doubt that children and young people are often unwilling to seek help because of the stigma associated with mental health problems. Moreover, the heterogeneity in the nature, course, comorbidity and outcomes of depression in all age groups is likely to lead to poor recognition, especially amongst healthcare professionals in schools and community and primary care settings. All this is made all the more complicated by the considerable variation in the local organisation of mental health services for children and young people. In any event, studies both in the UK and the USA have estimated that as many as 75% of children and adolescents with a clinically identifiable mood disorder remain undetected in the community. There are many barriers to the availability and delivery of care (Andrews et al., 2002; Coyle et al., 2003).

Considerations regarding the organisation of services for depressed children and young people, including the use of inpatient facilities, are reviewed in Chapter 8.

3.6.1 Assessment, detection and co-ordination of care

Given that the majority of depressed children and young people do not receive assessment, treatment or care, it is essential that all healthcare professionals involved in the care of children and young people should be able to detect and assess children with depression. They should also be able to determine and recognise those who are at risk of depression. Nowhere is this more important than at Tier 1 and Tier 2. However, it is equally important that all services from Tier 1 to 4 should work as an integrated, seamless service, properly co-ordinated, with higher tiers helping to train lower tiers wherever this is possible and appropriate.

3.6.2 Initial management

Treatment is aimed at the whole child and not a particular pattern of signs and symptoms or a single diagnosis when comorbidity is present. Direct treatment of depressive disorders should always be accompanied by support for the family who will be key in assisting focused treatments for their offspring. As yet we do not have a sound evidence-based protocol for the management of different forms of depression in young people (Park & Goodyer, 2000). A treatment programme therefore has multiple aims: to alleviate depressive disorder, to reduce comorbid conditions, to promote normal social and emotional development and school performance, relieve family distress, and to prevent or reduce the risk of relapse.
The place of family support and social/environmental interventions in the general treatment of children and young people with depression is reviewed in Chapter 5.

### 3.6.3 Psychological treatments

A wide range of psychological treatments, including self-help, has been considered for the acute treatment of depression in children and young people, although few have been evaluated for relapse prevention. Psychological interventions include cognitive behavioural therapy (CBT) in individual and group formats, interpersonal psychotherapy (IPT), non-directive supportive therapy, psychoanalytic/psychodynamic child psychotherapy, family therapy, relaxation, self-modelling, guided self-help and control enhancement training. However, the evidence base for the majority of these treatments is extremely limited.

The evidence for the use of psychological treatments in the acutely depressed individual, and to prevent relapse is reviewed in Chapter 6. We also consider the possible impact of patient and therapist characteristics upon outcome.

### 3.6.4 Pharmacological and physical treatments

The use of pharmaceutical agents in the treatment of depression in children and young people has generally followed their use in adults, although far fewer trials exist. Thus, tricyclic antidepressants, selective serotonin re-uptake inhibitors (SSRIs) and some other atypical antidepressants have been tried as an acute treatment. Antidepressants have also been used to prevent relapse in susceptible young people. Other drug treatments used include lithium. SSRIs have also been combined and compared with psychological treatment.

However, the recent review of the efficacy and safety of antidepressant drugs for depression in children and young people by the Expert Working Group of the Committee on Safety of Medicines (CSM), has led the Medicines and Healthcare products Regulatory Agency (MHRA) to contraindicate the use of all the SSRIs except fluoxetine in this context.

The evidence base for these interventions and the advice given by the MHRA are reviewed in Chapter 7. The use of ECT in depressed children and young people is also considered.

### 3.7 Consultation with children and young people

The Guideline Development Group commissioned a consultation with children and young people with depression in order to obtain their views on their experience of depression and the care and treatment they received. Twenty-five children and young people aged between 7 and 18 years were invited to take part in the consultation through the involvement of CAMHS teams, consultant psychiatrists, nursing staff and carer support groups.
Recruitment to the consultation process took place in Liverpool, Hampshire, Lewisham, Richmond, North Wales and South Wales.

Children and young people involved in the consultation comprised those who had recently completed a period of treatment; those who were currently receiving treatment; and some who had yet to be offered any care or treatment. Of the 25 who took part in the interviews, eight had a diagnosis of depression and seven had depression with a comorbid diagnosis (ten were unspecified). Three were inpatients.

The consultation consisted of sentence completion exercises sent out to over 500 children and young people (with over 60 returns), 25 interviews with children and young people, and eight interviews with parents and carers, who were also invited to share their experiences of caring for a child or a young person receiving treatment for depression. The interviews with the children and young people were structured but informal, leaving the interviewee to set the pace and comment on what was important to them. They were not asked for details of their diagnosis or their past history (some interviewees talked freely about their past history but it was made clear by the interviewer that this was not an expectation). Interviewees were invited to comment on their experiences and make suggestions for change where they felt this was needed. All of the children and young people involved were asked the following questions:

- Who do you turn to you when you feel sad/depressed?
- What help is given to you?
- What did you think about the treatment and care that you received?
- How would you like to be cared for and treated?

Over all, the responses from the children and young provided an important context in which the effective treatment and management of depression in children and young people, as described in this guideline, can be understood. The exercise aimed to help inform and illustrate the different experiences and views of services of some children and young people with depression. It was not a formal, scientifically-conducted survey, but rather a consultation exercise. However, combined with the collective experience of the guideline development group, we developed a number of recommendations related to the experience of accessing and receiving services for children and young people with depression.

### 3.8 Black and minority ethnic groups

In the national survey of mental disorder amongst children and adolescents (Meltzer et al, 1999), nearly 10% of white children, 12% of black children, 8% of Pakistani and Bangladeshi children and 4% of Indian children were assessed as having a mental health problem. These prevalence figures vary...
with age and diagnostic category differentially between different ethnic
groups, although differences are not usually large. For example, amongst
boys between 5 and 10 years old, there are relatively small differences in the
prevalence of emotional disorder (anxiety and depression). However, there
are significant differences for one age group and gender: white, black and
Indian 11 to 15 year old boys, all showed very similar prevalence rates
(around 5% in each group), whereas Pakistani and Bangladeshi adolescents
had a prevalence rate of over 12%. Importantly, especially given the extent of
comorbidity amongst depressed youth, Black male adolescent are particularly
likely to have conduct disorders, with a prevalence rate at over twice that for
white adolescent males. However, there is some evidence that there are lower
rates of access to mental health services for children and adolescents from
ethnic minorities.

At least two studies have shown a ‘statistically significant bias in relation to
the referral route to CAMHS and ethnicity of children’ (Malek & Joughin,
2004; Daryani et al, 2001), resulting in lower referral rates for children and
young people from black and minority ethnic groups when compared with
their white peers. This may be the result of cultural attitudes to mental health
problems amongst some ethnic minorities, leading parents to ignore problems
or hide them as a result of shame. Also, it seems likely that CAMHS services,
either through institutional racism or a lack of understanding of other
cultures generally, are less responsive to the needs of minority ethnic children
with any mental health problem including depression.

Language may also present a barrier for some of parents of children of black
and minority ethnic groups. Parents’ inability to express themselves as plainly
in English as in their mother tongue can lead to professionals making a
physical rather than psychological diagnosis. Parents’ anxiety around
navigating the health service and the fear of stigma can lead to them
accepting an inaccurate diagnosis. Trans-cultural considerations are also
particularly important when assessing and diagnosing people from ‘other’
cultures. In some societies, the European concept of ‘depression’ is
meaningless. Overlooking this consideration can result in either missed
diagnosis or misdiagnosis of depression. This factor along with linguistic
considerations is especially relevant when considering the experiences of
children who are refugees and asylum seekers. Often readjusting from
situations of extreme loss and trauma, refugee children and British born
children of refugee parents are likely to present with emotional distress
(Hodes, 2004). Moreover, problems in the delivery of psychological
treatments for all groups are more acute for those whose first language is not
English. This is a complex area that requires sophisticated two-way training
of both interpreters and other staff (Malek, 2004).

Service providers therefore need to take account of diverse cultural, religious
and social mores and how they might affect individual experiences. This
might require taking account of research into the racial identity of mental health practitioners (Carter, 1995), which considers the racial identity status of black (African American) and white adult clients and therapists as a key dynamic factor in psychotherapeutic dyads.

In respect to implementation of the Race Relations (Amendment) Act (2000), it has become a mandatory requirement that all key NHS services put into effect an Equalities Policy. This includes the ethnic monitoring of service users. But recent research shows that only a few CAMHS units have to date introduced ethnic monitoring of their service users. Of those that did, very few have used the information to adapt services and meet the needs of the diverse communities they serve. Thus few existing services are structured to communicate with, to enable access to acceptable pathways to services for, or to meet adequately the particular service provision needs of Britain’s diverse black and minority ethnic populations. Malek and Joughin (2004) make a number of recommendations concerning mental health services for minority ethnic children and adolescents, including that services are developed and evaluated in collaboration with members of minority ethnic groups.

3.9 Clinical practice recommendations

3.9.1.1 Healthcare professionals involved in the detection, assessment or treatment of children or young people with depression should ensure that the patient and their carers are provided with age-appropriate information on the nature, course and treatment of depression, including the likely side effect profile of medication should this be offered. (GPP) (1.1.1.1 NICE)

3.9.1.2 Healthcare professionals involved in the treatment of children/young people with depression should take time to build a supportive and collaborative relationship with both the patient and the family. (GPP) (1.1.1.2 NICE)

3.9.1.3 Healthcare professionals should make all efforts necessary to engage the child/young person and their family in treatment decisions, taking full account of the patient and parental expectations, so that the patient and their carers can give meaningful and properly informed consent before treatment is initiated. (GPP) (1.1.1.3 NICE)

3.9.1.4 Where possible, all services should provide written information or audio taped material in the language of the patient and their family, and independent interpreters should be sought for those whose preferred language is not English. (GPP) (1.1.2.1 NICE)
3.9.1.5 Consideration should be given to providing psychotherapies and information and medication and local services in the language of the patient and their family where the patient’s first language is not English. (GPP) (1.1.2.2 NICE)

3.9.1.6 Healthcare professionals in primary, secondary and relevant community settings should be trained in cultural competence to aid in the diagnosis and treatment for minority ethnic groups. This training should take into consideration the impact of the patient’s and healthcare professional’s racial identity status on the patient’s depression. (GPP) (1.1.2.3 NICE)

3.9.1.7 Depression services in both community and clinic settings should be developed and evaluated in collaboration with stakeholders including service users and their families, and members of minority ethnic groups. (GPP) (1.1.2.4 NICE)

4 Screening and risk factors

4.1 Introduction

This chapter reviews information currently available on the ways of identifying depression in children and young people using self-report and other report and interview assessments. The second part of the chapter identifies factors (social and individual) that are known to be associated with depression in children and young people. We need to be aware of the limitations in the ability to identify depression unequivocally as well as the probabilistic nature of the factors that increase the likelihood of the presence of depression. The judicious combination of knowledge of risk factors and the appropriate use of screening instruments, however, could greatly increase our sensitivity to the presence of this disorder in children and young people.

4.2 Screening instruments

4.2.1 Introduction

Epidemiological studies have shown that many young people and some children in the community who are depressed remain undetected (Angold & Costello, 2001). Even in child mental health clinics depressive signs and symptoms may be missed through cursory inquiry or greater attention being paid to other concurrent difficulties in the child or family. As a consequence
efforts have been made to develop instruments that are capable of detecting clinically depressed children and young people in different community and clinical settings (Dierker et al., 2001; Pavuluri & Birmaher, 2004).

4.2.2 Principles of detection
The purpose of clinical detection is to identify from within a group of individuals those who have the phenomena of interest. To date most instruments developed for the purpose of detecting depression in young people have been focussed on either detecting a given disorder according to operationally defined criteria or characterising a defined set of signs and symptoms according to a given content. **Criterion validity** refers to the ability of the instrument to ‘find’ the cases of interest in the population being examined. **Content validity** refers to the ability of the instrument to characterise the symptoms that occur within the disorder. These key issues are not the same and it cannot be assumed that they will always work together in producing the ‘best instrument’. For example criterion validity for DSM-IV major depression may be best achieved by merely asking a few questions knowing that if these are answered ‘yes’ there is a very good chance the young person is currently clinically depressed. In contrast, content validity requires asking many questions to determine the full form of symptoms, which would include uncommon and common symptoms, many of which might only be weakly associated with disorder. If we want to find individuals with a predefined syndrome of major depression we need instruments that are focussed on criterion validity. If the task is to determine the range of depressive symptoms in the community at large that may contribute with varying degrees of magnitude we need instruments that are focussed on content validity.

4.2.3 Who should be asked?
There is general agreement in child mental health research that both criterion and content validity for common behavioural and emotional problems in children and adolescents are best achieved by asking both a parent and the child about their current symptoms and problems and combining the two sets of answers to achieve a best estimate of detection. For depression it appears that parent reports alone are likely to miss clinically depressed off-spring (Pavuluri & Birmaher, 2004). In contrast, child and adolescent reports are likely to include individuals who are not depressed. Thus parents appear to under report and children over report depressive signs and symptoms. Other potential reporters, teachers, siblings and peers appear somewhat more like parents except in the case of close confidants who may report more like the index child.

4.2.4 What should be asked?
This depends on the prevailing set of definitions for depression. Signs and symptoms based on existing syndrome definitions (DSM-IV and ICD-10) are
generally seen as the most efficient way of detecting people with disorders. Inclusion of items considered i) important by some clinicians but not in the agreed definition or ii) providing more detail of a given construct that is considered key needs to be very carefully considered. Seldom is greater detail or wider coverage likely to improve on the ability of the instrument to detect real cases. Often this is an attempt to deal with worries about content when the focus is really on criterion validity. For example some authorities believe that physical signs and symptoms are too important to cover in just one or two questions. Others with a different perspective may express concerns about the lack of detail about the items asking about current depressive thinking. Invariably the key items in an instrument are already closely associated with the additional items and lengthening the instrument to include more content will not improve the ability to find individuals who meet criterion.

4.2.5 Purpose of detection
The purpose of clinical detection is to identify from within a group of individuals those who have the disorder of interest (depressive symptomatology). Is the screening purpose attempting to detect all forms of clinical depression or just a particular type? Is it trying to find individuals who are currently depressed, recently depressed or depressed at previous points in time? Are there special requirements that must be incorporated such as culture, language and ethnicity or features in the child such as age, educational ability or gender? As yet these factors are seldom taken into account in instrument development.

4.2.6 Pragmatics of screening
The likelihood of instruments being acceptable to the population of interest must be considered. This attention to the ecological validity is important—even crucial. The length of the screen, complexity of instructions, method of completion and presentation (e.g. paper and pencil, handheld computer, via the web) all influence the extent to which a screening instrument will be completed fully, reliably and by as many respondents as possible.

**Psychometrics**: Instruments must show reliability generally through test-retest on the same population at intervals between 1 and 4 weeks apart. If data recorded is not consistent then the instrument is unreliable and cannot be used. The type of statistic used depends on whether the reliability of items, their total scale score or sub-scales, a categorical threshold or specific diagnosis, that is being measured. The internal consistency of the instrument refers to the extent to which different items measure the same overt construct (e.g. negative thoughts or physical changes). Instrument length can be considerably shortened by reducing the number of items required through these methods to ensure that key areas are covered by as few items as is statistically possible. Validity of the instrument refers to the extent that it is
measuring what it purports to measure. There are a number of forms of validity that require different statistical methods. First, items in the instrument should be seen to be measuring the construct of interest (face validity); new instruments can be compared with existing ones known to be valid (concurrent validity); a new instrument can be assessed against a different form of measure already in use as a gold standard e.g. questionnaire for depression against clinical diagnosis by interview (criterion validity); an instrument can be used to determine a given outcome, such as response to treatment or the risk of recurrence (predictive validity); finally a measure can be used to determine change in severity or nature of depression over time (sensitivity to change).

From the public health perspective it is essential to establish how good the instrument is at doing the job it is intended for. The sensitivity of an instrument refers to the proportion of true cases in the population correctly identified by the tests. An instrument that detects a low percentage of depressed cases will not be very helpful in determining the numbers of children who should receive a known effective treatment, as many individuals who should receive the intervention will not do so. This would make for poor planning and underestimating the prevalence of the disorder and the cost of treatments to the community. Sensitivity can also be defined in terms of the false negatives it ‘detects’ (i.e. the number of subjects who the instrument says are well who are in fact depressed).

The specificity of an instrument refers to the proportion of well individuals correctly identified by the test. This is important so that well individuals are not given treatments or other interventions they do not need. This can also be defined in terms of the false negative rate it detects (i.e. the number of depressed cases who are said to be well).

Instruments with low sensitivity and specificity are very unhelpful screening instruments. They will fail to identify the depressed population with sufficient validity.

There are a number of statistical procedures for determining sensitivity and specificity of which the area under the (receiver operating characteristic) curve (AUC) is the most valid as it displays the trade off between sensitivity and specificity at all possible scores available to the instrument. This is displayed as a figure between 0 and 1. An instrument’s diagnostic accuracy is considered as follows: AUC ≤ 0.7, low; 0.7-0.9, moderate, >0.9 high (Henderson, 1993).

4.2.7 Self-rated depression scales as screens
The commonest method used for detecting clinical depression is to ask the child to complete a questionnaire that asks them to record how they have
been feeling and thinking recently—often over the past week or two weeks. To date, most screening instruments have been about current depression. In addition the focus has in the main been on determining the presence or absence of major depressive disorder. There are six available instruments with psychometric data (see Appendix J for further details).

The Beck Depression Inventory (BDI) is a commonly used scale in adult studies, especially when measuring mild/moderate depression (Beck et al, 1961). In adolescents however it is not clear that the BDI is truly measuring depression (LeBlanc et al, 2002). The reading level and response format may present problems for young adolescents and those with low literacy skills. The scale is sensitive to change in depressed young adult patients (Reynolds & Coates, 1986). The sensitivity and specificity of the scale are not particularly good in adolescents (Roberts et al, 1991). Several authors have suggested that rather than clinical depressive disorders the scale measures dissatisfaction and demoralization, non-clinical low mood and anxiety (Brooks & Kutcher 2001).

The Children’s Depression Inventory (CDI) is specifically aimed at children under 12 (Kovacs, 1992). The instrument is a modified version of the original BDI developed originally for children under the age of 8. The reliability and internal consistency data are not particularly satisfactory and no single cut-off score works well in both clinical and community settings (Asarnow & Carlson 1985; Stark et al, 1987; Kovacs, 1992). There is evidence for sensitivity to change but there are serious concerns that the instrument does not discriminate adequately between depressed and non-depressed children (Stark et al, 1987; Meyer et al, 1989; Fine et al, 1991; Stark & Laurent, 2001). The instrument may be better as a continuous measure of current dysphoric mood than as a screen for the presence or absence of major depression.

The Mood and Feelings Questionnaire (MFQ) has a parent and a child form and good diagnostic validity and some predictive validity has been established (Wood et al, 1995; Kent & Vostanis 1997). The scale has been used in both epidemiological and clinical studies (Costello & Angold 1988; Messer & Gross 1995; Messer et al, 1995; Goodyer et al, 1996; Goodyer et al, 2000; Angold et al, 2002). There is normative data showing that the probability of being clinically depressed varies with age and sex (Angold & Rutter 1992; Cooper & Goodyer 1993; Goodyer & Cooper 1993; Angold et al, 2002). A score of 50 or more (scale range 0-66) in a 13-year-old girl indicates a 30% probability of being clinically depressed compared with 68% for the same score in a 16-year-old girl (see figure 1). There is acceptable case detection ability (AUC ranging from 0.75- 0.85) in clinical settings with a cut off score of ≥ 27. The instrument does not assess suicidal ideation. There is adequate diagnostic validity for depressed patients but modest epidemiological data on validity of case detection in the community.
The Reynolds Adolescent Depression Scale (RADS) is specifically for adolescents aged 13 to 18 years (Reynolds 1987). It has well documented reliability and validity and normative data obtained from school settings in the manual but there are few independent studies reported using this measure. What data there are (including unpublished reports cited in the manual) suggest that the scale has a rather high false negative rate (30%) at the suggested cut-off score for clinical depression and is not particularly effective at detecting change (Radloff, 1977; Brooks & Kutcher, 2001).

The Center for Epidemiological Studies—Depression Scale (CES-D) was developed for use in community studies of adults and subsequently used in adolescents (Radloff, 1977). The overall view is that this scale does not have any clear strengths and many weaknesses when used with adolescents (Garrison et al, 1991; Olsson & von-Knorring, 1997; Brooks & Kutcher, 2001). In the younger age group this scale measures general non-clinical emotional turmoil rather than depression.

The Kutcher Adolescent Depression Scale (KADS) shows good reliability and validity and promising sensitivity and specificity (AUC 0.89). There is a very brief 6 item and a longer 16 item version. The brief screen may be effective in ruling out major depression in community samples and appears better than the BDI (LeBlanc et al, 2002).

There are other depression instruments in the literature but the above have the most evidence base on which to form a judgement regarding reliability, validity and clinical utility. However the Birleson Depression Inventory deserves mention (Birleson et al, 1987). This has been used in studies of anxiety, PTSD and depressive conditions (Kashani et al, 1989; Yule et al, 1990; Yule & Udwin, 1991). The psychometric properties of the scale are not well described but clinical use suggests that there are very similar component properties to the BDI and the MFQ.

4.2.8 Interviewer-based instruments

There are four instruments available for assessing the diagnosis of depressive syndromes using direct face-to-face interview procedures (see Appendix J for further details).

The Schedule for Affective Disorders and Schizophrenia for School Age Children (K-SADS) is a well used reliable and valid procedure for diagnostic assessment of depression including severity of current episode (Kaufman et al, 1997). It is interviewer led, very time consuming and designed to be used by trained individuals with some clinical experience. It is designed for use with participants aged 6 through to 17 years. Originally focussed on patients with current psychiatric disorder the most frequently used version has been used in community studies and can assess current and past lifetime episodes according to DSM criteria. Reliability is acceptable but studies are few.
(Kaufman et al, 1997). There is reasonable evidence for validity including the severity scales, predicting clinical depression over time and diagnosing comorbid disorders with major depression (Ambrosini et al, 1987; McCauley et al, 1988; McGee & Williams 1988; Herbert et al, 1996). The instrument is strong in the assessment of the depression and good for detailed psychopathology evaluations. In contrast it is time consuming and inefficient for everyday clinic use and not an efficient means of assessing change in symptom severity. A brief screening version has been used in one community research project which may prelude a more flexible screening tool in future studies, particularly in combination with a self-report instrument (Goodyer et al, 2000).

The Diagnostic Interview Schedule for Children (DISC) is a highly structured interview that is respondent-based (Costello et al, 1985; Edelbrock et al, 1985). The strengths are that it can be given by non-clinical personnel in community settings after a few days training. The psychometric properties are suspect for depression with high estimates of depression obtained with its use in epidemiological and clinical studies. There are however considerable data with this instrument on a range of psychiatric disorders using both a full and acute down screening version (Shaffer, 1988; Fisher et al, 1993; Shaffer et al, 1993; Schwab-Stone et al, 1996; Shaffer et al, 1996; Shaffer et al, 2000; Lucas et al, 2001). The instrument is not particularly suited to assess change in symptoms.

The Diagnostic Interview for Children and Adolescents-Revised (DICA-R) is also a respondent-based interview with somewhat better features than the DISC that result in quite good validity for clinical depression diagnoses in those detected (Herjanic & Reich 1982; Reich et al, 1982). The psychometric properties are acceptable to good with more recent versions to be used with both child and parent (Welner et al, 1987; Reich, 2000a; Reich, 2000b). The instrument can be used in both community and clinical populations but its relationship to DSM-IV diagnosis is unclear. There appears to be, however, a potential tendency to under diagnose depression in adolescents whilst over-diagnosing externalising disorders although there is modest data overall in this regard.

The Child and Adolescent Psychiatric Assessment (CAPA) is a detailed interview led instrument that is good at delineating clinical depression and other diagnoses (Angold & Costello, 2000). Lay interviewers can use it with training. The CAPA incorporates interviewer and respondent-based approaches. There is an extensive glossary for interviewers that details operational definitions for symptoms, distress ratings and symptom frequencies which interviewers make. There is a child and a parent version. The instrument is highly reliable for diagnosing depression (Angold & Costello, 1995). There is as yet no concurrent validity study for the instrument but considerable support for its concurrent validity has accumulated from
other sources, twins, sex differences and family studies (Angold et al, 1996; Costello et al, 1996; Angold et al, 1998). The strengths of the instrument are in the highly reliable diagnosis of major depression in the 9- to 16-year-old population of both sexes; that lay persons can use it after 2-4 weeks training; and the extensive glossary for standard coding within and between interviewers.

4.2.9  Clinical summary

4.2.9.1 Self-report questionnaires

There are a number self-report measures available for screening in community and clinical populations. There is very little comparative data between the available questionnaires. With the exception of the MFQ there is no developmental sensitivity data. The evidence suggests that a self-report questionnaire approach for diagnostic screening of depression in pre-pubertal children is not advised. For adolescents the MFQ is amongst the most studied and the most robust.

4.2.9.2 Interviews

The interview measures available were not designed to act as screens. Their current form makes them unlikely to enhance the screening process. A direct screen interview would be highly desirable for certain settings such as in residential care, with learning disabled patients or others with special needs limiting the use of self-reports. Again, computer-based interview procedures have yet to be made available.

Overall universal screening for depressive disorders in the community at large is not recommended. In addition there is no evidence to screen very high-risk groups (e.g. looked after children, asylum seekers and refugees, and those with exposure to multiple risk). Current available tools, both self-report and interviewer-based instruments are potentially important adjuncts in the detection of depressive diagnoses in symptomatic individuals and those of concern to child professionals.

4.2.9.3 Conclusion

Depressive disorders in children of primary school age are unlikely to be detected using paper and pencil tests. There is insufficient use of computer technology and more child friendly methods of assessing current mood and feelings. Pictorial and interactive methods should be examined for future use. For primary care use, any screening instrument should be very friendly for the health worker. Computer versions could assist by automatically scoring and even recommending action on the basis of resultant scores. This may improve take-up of screening devices in schools, other community settings.
and even busy clinical services looking to improve the time it takes to
determine the needs and assessment pathway of new referrals.

Despite these caveats the evidence is that child mental health policies have
been influenced by the findings using the available instruments. For example
screening programmes have been utilised in schools as part of intervention
programmes for depressed children and young people (Andrews et al, 2002;
Burns et al, 2002). Clinical services can now consider the use of self-reports as
adjuncts to the standard clinical process. Uptake is probably influenced by a
large perceived increase in workload compared with the small clinical gain
over standard clinical procedures.

There is a reason to be optimistic that a second generation of screening
devices could be used in primary care and clinical services. The biggest
obstacles will be delivery by an overworked professional workforce poorly
trained and/or supported in computer aided assessment tools. Computerised
devices that allow item responses to be converted into scale scores and into
written advice options is likely to greatly enhance their use. This technology
could be applied to both questionnaire and interview data.

Figure 1

The legend indicates three levels of mood and feelings (MFQ) self-report scores, 20,
30 and 50, from a possible range of 0 to 66, obtained from 1056 girls aged 11 to 16.
The estimated proportion of cases (y axis) is, as expected, greater for higher scores at each age. Importantly the same level of symptom scores at each age estimates significantly different proportions of cases. This suggests developmentally sensitive differences in adolescent girls for the liability for detecting major depression from self-reports. [Data first published in Cooper & Goodyer (1993), pp. 369-374].
4.3 Risk factors

4.3.1 Introduction

4.3.1.1 What is meant by risk
Risk is the degree to which the likelihood of a given adverse outcome will occur following exposure to a defined toxic agent. The relative importance of exposure is estimated by the probability of the outcome occurring in a given population compared with the level of occurrence in a non-exposed population. Risks for depression occur from a variety of sources both within and external to the child. For example, individuals may be born with genes that render them susceptible to depression, acquire lesions such as head injury that alter their ability to control mood, suffer infections that result in altered brain metabolism, be exposed to chronic family discord or to negative peer group environments that alter the development of emotional processing and self percep (Goodyer, 2001). In addition, neighbourhood risks may occur such as poor housing or living in a violent or dangerous society. Almost all research concurs that the onset of clinical depressions occur as a consequence of multiple rather than single risk effects that are frequently not independent of each other (Kraemer et al, 1997). There is however less agreement about how risks exert their effects over time or what they do to the individual to bring about psychiatric signs and symptoms and functional impairments.

4.3.1.2 Relations between risks over time and the magnitude of their effects
Demonstrating the size of the association between a risk factor and onset of disorder indicates its potency and is the maximal discrepancy achievable between depressed and not depressed groups exposed and unexposed to risk. For example exposure to severely and personally disappointing life events in adolescents occurring in the month prior to onset of depression is estimated to increase the risk for depression about nine times over not being exposed (Goodyer et al, 2000). These estimates regarding one type of risk can be misleading as seldom are all the known adversities measured in one study. When measuring a range of possible risks in the same study we need to know three things: i) if risks that occur at a distance in time (i.e. months and years previously) influence the occurrence and the effects of more recent adversities such as acute personally undesirable life events; ii) if these distal processes themselves increase the liability for depression regardless of proximal risks and; iii) if there is some form of combined effect arising from exposure or possession of risks occurring distally and proximally not explained by one set or the other.

For example 60% of all cases of major depression in adolescents are exposed to acutely disappointing life events in the month prior to the onset of disorder.
but greater than 90% are already exposed to two or more previous ongoing risks either in their social environment or within themselves (Goodyer et al, 2000; Goodyer, 2001). The impact of the recent adversity can only best be appreciated by taking into account the contribution of past risks on both the liability for the recent event and the onset of disorder. Current evidence from adult studies shows that there are very likely to be multiple risk pathways that may lead to the emergence of depressive illnesses (Kraemer et al, 1997). These involve genetic predispositions, different types of adversities occurring during the first two decades of life and acute personally disappointing life events not a consequence solely of past difficulties in the weeks prior to onset (Kendler, 2002). Adolescents at high risk for depression are exposed to, or possess on average, three psychosocial risks in the 12 months before follow-up (Goodyer et al, 2000). Around 1 in 5 of this high psychosocial risk population will get depressed over the ensuing 12 months. Thus even amongst those at very high risk a significant number do not immediately become depressed. The presence of an acute event considerably increases this liability.

4.3.2 Typology of risk

Environmental risks are invariably classified by their:

- personal characteristics (e.g. accident, illness, financial etc.)
- latent psychological process inferred from these (e.g. disappointment, danger)
- personal focus (self, parent, friend, etc.)
- origin (self-induced, independent of self)
- time of onset and (less frequently) offset giving duration of exposure
- locus of control (uncontrollable by self, controllable)
- age and developmental stage of exposure (infancy, childhood adolescence, pre- or post-puberty).

Unfortunately there is no agreed standard definition for classifying risks and most studies use widely different methods and classification processes.

4.3.3 Social risks

Social adversities that are most associated with the onset of depression are those that are outside the child's control, occur as unpredictable happenings in the daily environment and recur over time. They mainly arise within family relationships or within friendships and are largely interpersonal in nature (Rueter et al, 1999; Goodyer, 2001).
4.3.3.1 Family risks
The most common group of adversities to occur within the family, which are relational in origin and produce negative effects on the child, arise from dysfunctions between two or more people. Perhaps the commonest of these are marital discord and emotional difficulties between one parent and the child, although parental psychopathology may underlie a significant proportion of these (Hammen & Brennan 2003; Hammen et al, 2004).

The impact of events within the family on the child, such as physical maltreatment, are also associated with the onset of depression, but the onset appears often to be at a considerable distance in time from such abuse events (Jaffee et al, 2002). However both violence and sexual abuse are associated with depression, as are severe acute family difficulties such as sudden death, serious physical illness in a close relative or sudden separation of parents.

In contrast, unhappy marriages, parents being away from home due to work, low income, poor housing and living in a deprived neighbourhood occurring singly are not strongly associated with clinical depressive onsets in young people. Overall mild ongoing dysfunctions in family life do not appear on their own to be markedly associated with the subsequent onset of clinical depression (Tamplin et al, 1997; Tamplin & Goodyer 2001). However, persistent family disagreement through early adolescence does increase the general level of low mood and depressive symptoms over time (years) and it is this rising level of non-clinical negative mood and thoughts that is associated with the onset of later clinical depression in older adolescents (Rueter et al, 1999).

Those children with higher IQ, better family functioning, closer parental monitoring, more adults in the household, and higher educational aspiration are less likely to show depression in the presence of elevated psychosocial risk (Tiet et al, 1998). In the absence of these protective or buffering factors the risk for both emotional and behavioural difficulties arises when children and young people are exposed to adversities. The more the family environment is chronically emotionally neglectful, involves chronic marital discord and a lack of authoritative parenting (the ability to be firm and clear within a positive emotional environment), the greater the risks for psychiatric disorders in general including personality difficulties in young adult life. Psychiatric disorder in a parent is another high-risk adversity for the child, with parental history of recurrent depression over the lifetime of the child strongly associated with depression in the off-spring (Hammen et al, 1990; Hammen & Brennan, 2003).

4.3.3.2 Friendship risks
Non-family-based adversities are also associated with the onset of depression and other psychopathologies in young people. Children with poor friendships, characterised by low numbers of friends, infrequent contact and
no intimate relations, are more likely to develop depression as well as deviant behaviours and increased social isolation from the desired peer network (Goodyer et al, 1990; Cairns et al, 1995; Bukowski et al, 1996; Hartup, 1996). This appears to be independent of family strengths and weaknesses. The most potent form of acute negative life event is that of a recent (last few weeks) severe personal disappointment (i.e. the failure of a previously held belief in an expected outcome) with a close friend (Goodyer et al, 2000). When recent personal disappointments with a close friend arises its effects as a risk factor is particularly large in those with previous psychosocial risks (Goodyer et al, 2000). Depression is markedly increased in the presence of multiple adverse experiences involving both longstanding family and more recent friendship events and difficulties. Under these social conditions, the child may not perceive an emotionally supportive relationship in their social world.

4.3.4 Individual risks

4.3.4.1 Genetic risks

Current evidence suggests that there are genetic contributions to adolescent but not to child onset depression (Rice et al, 2002). The environmental processes may be similar in nature but the implication is that these are sufficient to cause depression in the pre-pubertal child but insufficient in the post-pubertal adolescent. The studies on which this review is based are twin samples in which depressive symptoms are the outcome rather than clinical disorders. It is not clear if genetic factors are low in pre-pubertal children with clinical depressions, which are rare in this population (Angold & Costello, 2001). The precise genes involved remain unknown. In addition, the genetic risks may not act directly to produce the disorder, but act through increasing the liability for other risks in the environment. There may be a complex patterning of gene-environment interactions combining to cause depressions in the post-pubertal depressed adolescent (Caspi et al, 2003). In contrast, direct associations (and therefore effects) of single genes with depression are uncommon (Henderson et al, 2000; Zill et al, 2002).

4.3.4.2 Temperament

Children and adolescents (as well as adults) with a highly emotional temperamental style (react quickly to everyday events, easily brought to tears, easily soothed) are more likely to be depressed than those low in these behavioural characteristics (Goodyer et al, 1993; Hodgins & Ellenbogen 2003; McWilliams, 2003). Although this is true for both sexes, more girls than boys have this temperament and this may be one component that differentially increases the risk for depression in females over males. The evidence suggests that there are genetic influences on individual variations in temperament (Eley et al, 2003; Sen et al, 2004). The relationships between temperament and personality development over time suggests that there is coherence across
time between the commonest used in both terms although the precise definitions appear to be somewhat different (Caspi et al., 2003; Shiner et al., 2003). The precise relations between personality and later depression remain unclear but neuroticism shows an important but complex relationship with depressive onset (Kendler et al., 2004).

### 4.3.4.3 Cognitions
As well as emotional style there are thinking styles that increase the liability for depression. High levels of particular types of self-critical thoughts known as global self-devaluations (abandoned, a failure, feeble, incapable, a loser, a mess, pathetic, pitiful, rejected, stupid, unlovable, unwanted, useless, worthless), if present at times of low mood are significantly associated with clinical depression (Teasdale & Cox, 2001). A ruminative style, in which young people dwell or even perseverate on a particular thought, also increases the risk for depression. Adults and adolescents with both global self-devaluations and a ruminative style have markedly increased risk for depression (Alloy et al., 1999). Ruminating lowers mood and increases memory difficulties in adolescents (Park et al., 2004).

### 4.3.4.4 Physiological risks
Studies of physiological factors as risk components for depression in young people are relatively new and few have been published. There is some evidence that both the monoamines and glucocorticoids are implicated in the biology of depression in children and adolescents (Birmaher & Heydl, 2001). Children with a positive family history of depression show abnormalities of serotonin function even when well, suggesting serotonin vulnerability for subsequent affective disorders. Increased cortisol and a second adrenal steroid dehydroepiandrosterone (DHEA) are both elevated and predict the onset of depression in a sub-set of adolescents at high psychosocial risk for depression (Goodyer et al., 2000). Elevated cortisol levels may themselves arise in part from interpersonal difficulties in early parenting related to maternal depression (Halligan et al., 2004). High risk children and young people with no history of prior depression but with a positive family history for the disorder have also been shown to have abnormalities in sleep architecture associated with subtle changes in cortisol secretion (Dahl et al., 1996; Feder et al., 2004). Overall the evidence suggests biological vulnerabilities in both the serotonin and the adrenal steroid systems. These are likely to be brought about by a combination of genetic and environmental influences.

### 4.3.5 Very high risk groups
Within the child and adolescent population at large there are known groups at very high risk for mental health difficulties including depression. These are already the focus of policy review and include looked after children, refugees, the homeless and asylum seekers. Children and adolescent offenders,
particularly those in secure institutions, are particularly at risk for mental difficulties. The known incident rates of successful suicides in this later group strongly indicates high levels of depression in this very high-risk group that currently may not be adequately assessed or managed. These groups will require careful consideration for depressive disorders as they are likely to have increased rates of behavioural and emotional behavioural disorders in general. It is unclear if ethnicity exerts a specific risk for depression above and beyond the known increase in social, behavioural and emotional difficulties for selected populations (e.g. Afro-Caribbean).

4.3.6 Summary
1. Risks for depression are multiple in origins and may be correlated with each other. Single risks resulting in the onset of clinically meaningful depression are rare.
2. The majority of first depressive episodes arise in adolescents compared with children and in the presence of at least two and invariably three longstanding psychosocial risks.
3. Acute life events are key destabilising elements in those already at high psychosocial risk evoking relatively sudden onset in about 50% to 70% of cases. The other third to a half appears to arise more slowly through chronic persisting interpersonal difficulties.
4. Genetically mediated factors via the serotonin and adrenal steroid systems may be important features in determining potency of social adversities.
5. The intermediate psychological vulnerabilities for adolescents between physiology and the social environment are a high level of global self-devaluative thinking at times of low mood in combination with a ruminative thinking style.
6. There is increasing evidence that the pattern and potency of risks varies with development, severity and number of episodes of depression. The physiological risks for recurrence appear to be greater with an increasing number of past depressive episodes suggesting an effect of depression on brain function.

4.3.7 Risk classification
It is critical to remember when looking at this list that the specificity of individual risk factors to the onset of depressive disorders is low to moderate, with the exception of those starred * where specificity is high.

4.3.7.1 Probable vulnerability factors
These increase the general liability to but seldom directly provoke disorder:

- Presence of short arm serotonin promoter gene
- Elevated morning cortisol levels
- Acquired fetal infections
• Maltreatment or emotional neglect through infancy
• Maternal postnatal depression
• Parental history of depressive disorder*
• Brain illnesses in childhood including trauma and infection
• Being female*
• Being post-pubertal*
• Divorced parents
• Chronic parental psychiatric illness.

4.3.7.2 Probable activating factors
These are directly implicated in the onset of depressions and in the presence of vulnerability factors their effects can be large:

• Personally undesirable life events resulting in permanent change of interpersonal relationships in friends or family*
• Acute brain illnesses
• Community disasters such as war, famine and infections.

4.3.7.3 Formation factors
These are responsible for the clinical characteristics of the depressive state:

• Past history of depressive symptoms*
• High trait levels of neuroticism (Kendler et al, 2004) or emotionality*
• Ruminative style of thinking*.

4.3.7.4 Known risk factors whose precise role is currently unclear
These may be vulnerability, activating or formation factors but currently available information does not permit the classification of their role:

• Self-devaluative thinking
• Poor school performance
• Bullying
• Co-existing medical illnesses
• Death of close relative.

4.3.7.5 Protective factors
These reduce the likelihood of depression in the presence of vulnerability and activating factors:

• A good sense of humour
• Positive friendship networks
• Close relationship with one or more family member
• Socially valued personal achievements
• High normal intelligence.

4.4 Clinical recommendations

4.4.1 Screening

4.4.1.1 Children and young people of 11 years or older referred to CAMHS without a diagnosis of depression, should be routinely screened with a self-report questionnaire for depression (of which the Mood and Feelings Questionnaire [MFQ] is currently the best) as part of a general assessment procedure. (B) (1.4.1.1 NICE)

4.4.1.2 Training opportunities should be made available to improve the accuracy of CAMHS professionals in diagnosing depressive conditions. The existing interviewer-based instruments (e.g. Kiddie-Sads [K-SADS] and Child and Adolescent Psychiatric Assessment [CAPA]) could be used for this purpose. (C) (1.4.1.2 NICE)

4.4.1.3 Tier 3 CAMHS staff specialising in the treatment of depression should have been trained in interview-based assessment instruments (e.g. K-SADS and CAPA). (GPP) (1.4.1.3 NICE)

4.4.2 Risk Factors

4.4.2.1 Healthcare professionals in primary care, in schools and other relevant community settings, should be trained to detect depressive symptoms, and to assess children and young people who may be at risk of depression. Training should include the evaluation of recent and past psychosocial risk factors, such as age, gender, family discord, bullying, physical, sexual or emotional abuse, comorbid disorders and a history of parental depression; the natural history of single loss events; the importance of multiple risk factors; ethnic and cultural factors; and factors known to be associated with a high risk of depression and other health problems, such as homelessness, refugee status and living in institutional settings. (C) (1.3.1.1 NICE)

4.4.2.2 Healthcare professionals in primary care, in schools and other relevant community settings, should be trained in communications skills such as ‘active listening’ and ‘conversational technique’, so that they can deal confidently with the acute sadness and distress (‘situational dysphoria’) encountered in children and young people following recent adverse events. (GPP) (1.3.1.2 NICE)
4.4.2.3 CAMHS tier 2/3 should work with healthcare professionals in primary care, schools and other relevant community settings, to provide training and develop ethnically and culturally sensitive systems for detecting, assessing, supporting and referring children and young people who are either depressed or at significant risk of becoming depressed. (GPP) (1.3.1.3 NICE)

4.4.2.4 When a child or young person is exposed to a single recent undesirable life event such as bereavement, divorce or a severely disappointing experience, healthcare professionals in primary care, schools or other relevant community settings should undertake an assessment of the risks associated with depression. The risk profile should be recorded in the child/young person’s records. (C) (1.3.1.5 NICE)

4.4.2.5 When a child or young person is exposed to a single recent undesirable life event such as bereavement, divorce or a severely disappointing experience, in the absence of other risk factors for depression, healthcare professionals in primary care, schools or other relevant community settings, should offer support and the opportunity to talk over the event with the child or young person. (GPP) (1.3.1.6 NICE)

4.4.2.6 Following an uncomplicated undesirable event, children and young people should not normally be referred for further assessment or treatment, as single events are unlikely to lead to a depressive illness. (C) (1.3.1.7 NICE)

4.4.2.7 When a child or young person is exposed to a recent undesirable event, such as bereavement, divorce or a severely disappointing experience, and is identified to be at high risk of depression (the presence of two or more other risk factors for depression), they should be offered the opportunity to talk over their recent negative experiences with a professional in Tier 1 and assessed for depression. Early referral should be considered if there is evidence of depression and/or self-harm. (GPP)(1.3.1.8 NICE)

4.4.2.8 When a child or young person is exposed to a recent undesirable event, such as bereavement, divorce or a severely disappointing experience, in the context of multiple-risk histories for depression in one or more family members (parents or children), they should be offered the opportunity to talk-over their recent negative experiences with a professional in Tier 1 and assessed for depression. Early referral should be considered if there is evidence of depression and/or self-harm. (GPP) (1.3.1.9 NICE)
4.4.2.9 When monitoring the clinical progress of children and young people with depression, the self-report questionnaire, the Mood and Feelings Questionnaire (MFQ), should be considered as an adjunct to clinical judgment. (C) (1.1.3.6 NICE)

5 Self-help, family support/parental education and social/environmental interventions

5.1 Self-help

5.1.1 Introduction
Self-help is not well defined and the term is often used interchangeably with ‘self-management’, ‘self-instruction’, ‘self-care’ or ‘psycho-educational’ interventions (Department of Health, 2003). Recent research considered self-help to be characterised by two particular features:

- Either no or only ‘minimal’ practitioner input
- Instruction on how users can improve their skills to cope and manage their difficulties (Lewis et al, 2003).

In its broadest context, ‘self-help’ for depression could include any activity or lifestyle choice that an individual makes in the belief that it will confer therapeutic benefit (e.g. taking more exercise, modifying diet, reducing or increasing alcohol intake).

The majority of self-help approaches are used outside the health service, by individuals and self-help organisations (Lewis et al, 2003). Reference to ‘self-help’ for children includes self-help materials that can be used by parents or with the assistance of parents, as it is acknowledged that children, by virtue of their dependence on adults because of their age or developmental status, may be unable to help themselves. When the intervention is based on a psychological approach this may be formalised as guided self-help (see Chapter 6 for further information about the evidence regarding the effectiveness of guided self-help).

Self-help, in the guise of self-management is the underlying principle of the expert patient programme (Department of Health, 2001), which affirms the government’s intention to empower patients to become more involved in their treatment and care. The programme is one of many initiatives that illustrate the changing ethos of the health service as it moves towards an
emphasis on self-sufficiency and patient choice (Department of Health, 2003a; Farrell, 2004).

5.1.2 Types of self-help

For the purposes of this guideline ‘self-help’ involves a structured approach to the use of informational guidance and does not include any activity that results in self-harm (e.g. excessive consumption of alcohol). Self-help materials can be stand-alone, may be used with limited support from healthcare professionals (guided self-help), or used as an adjunct to more intensive psychotherapy or medication.

It may be useful to consider children and young people utilising self-help strategies and resources in three ways:

- To maintain healthy body and mind throughout development
- When they know something’s wrong but are not sure what, or where to go for help
- Following diagnosis of depression.

Information may encourage positive help-seeking behaviour and concordance with treatment plans. Self-help may include:

- Talking to family and friends
- Educational leaflets
- Helpline/Information line/the Internet
- Self-diagnosis tools
- Peer support groups
- Social networks
- Mentoring/spiritual guidance
- Exercise
- Sleep and relaxation
- Healthy diet
- Complementary/alternative therapies
- Contact with voluntary organisations.

These strategies can be used by anyone who has symptoms of depression, whether or not they have been in contact with statutory services or have received a diagnosis. It must be remembered that the majority of depressed children and young people cope alone. Further information about the most common forms of self-help is provided in Appendix K, with additional self-help resources provided in Appendix L.

5.1.3 Who would benefit from self-help?

Children and young people often find it difficult to talk about their feelings to anyone. Research suggests that only a third of teenagers with mental health
problems who need help will ask for it, usually from informal sources such as families and friends (Offer et al, 1991; Rickwood & Braithwaite, 1994; Boldero & Fallon, 1995).

Possible reasons behind adolescent reluctance to seek help include:

- Feeling that their help-seeking behaviour would not be kept confidential
- Feeling that no person or helping services could help
- Feeling that the problem was too personal to tell anyone
- Feeling that they could handle the problem on their own (Dubow et al, 1990).

Healthcare professionals who come into contact with children/young people must therefore remember that children and young people may have difficulty expressing their feelings and may present with physical manifestations of their depressed mood.

It is likely that different types of self-help will appeal to different types of patient depending on an infinite number of variables including age, literacy, knowledge-base, experience, confidence with computers, type, severity and duration of depressive symptoms. In addition, different types of self-help will be relevant according to the severity of symptoms and availability of support. Self-help may be the only option for some children/young people who may not be able to access services either because of lack of parental support, knowledge or understanding, social unacceptability or geographical inaccessibility.

Whenever healthcare professionals come into contact with children and young people who live in families under-going emotional upheaval, the mental health needs of the children/young people should be considered. Recommended action may include referral to relevant support groups (e.g. Young Carers, substance misuse, bereavement) or other targeted self-help options (e.g. leaflets). Due to the common occurrence of depression in the offspring of depressed parents, special consideration should be given to assessing and supporting children with family members being treated for depression.

5.1.4 Evidence for the effectiveness of self-help strategies
A search of the available literature revealed only one study evaluating a self-help intervention in children/young people (Ackerson et al, 1998; further information on this trial can be found in Chapter 6), although some other materials have been studied in adults (see L for a list of self-help resources).

5.1.5 Clinical summary
Self-help interventions may be the treatment of choice for some children/young people themselves, or their parents. It is therefore necessary for any professional who comes into contact with depressed children and young people to know what self-help resources are available, evidence of their effectiveness or contra-indications if there is any and, if not, which resources children/young people and their parents have found to be helpful.

5.2 Family support/parental education

5.2.1 Introduction

Family risk factors for depression in children and adolescents include parent-child conflict, parental discord, divorce and separation, parental death and parental mental illness (Reynolds & Rob, 1988; Patten et al, 1997; Shochet & Dadds, 1997; Beardslee et al, 2003). The risk is thought not to lie in the variable per se but in its effects on attitudes, behaviour and relationships within the family.

Children who are undiagnosed but deemed to be at high risk of depression can be targeted for preventative intervention in two ways: 1) those in subgroups of the population where life events, demographic factors and other variables have been shown to increase risk; 2) children who display some of the symptoms of depression (Gillham et al, 2000).

5.2.2 Narrative review

A systematic search of the literature identified five RCTs where family support/parental education were part of a treatment program aimed at children and adolescents identified as at risk for depression. Four of the studies focused on at-risk populations and one was for children displaying symptoms of depression (Asarnow et al, 2002). The earliest study (Black & Urbanowicz, 1987), was the only one that did not provide minimal intervention for the control group. It was also the only study not to be based on cognitive behavioural therapy (CBT) principles.

5.2.2.1 Bereavement

Research has highlighted increased levels of mental health problems among bereaved children (Sandler et al, 2003). Two studies have examined whether interventions aimed at family bereavement have a positive impact on mental health outcomes (BLACK1987; Sandler2003).

Sandler2003 randomly assigned 156 families (including 244 children between 8-16 years) to either the Family Bereavement Program (FBP) or to a self-study program. The FBP involved separate groups for carers, children and young people. There were twelve group sessions for each group, four of which involved joint carer and child/young person activity and an additional two sessions for each individual family. Two trained facilitators, who worked...
from a manual and received post-session supervision, facilitated the groups. The carer group focused on teaching techniques to improve carer-child relationships and parenting skills. The same skill domains were used across child and young person groups, with programs geared towards different developmental levels. The groups aimed to improve positive coping, coping efficacy, control-related beliefs, self-esteem and negative appraisals for stressful events through teaching skills for cognitive reframing, distinguishing between controllable and uncontrollable events and problem solving. Opportunities were also provided for the expression and validation of grief-related feelings. The self-study group were sent three books each at monthly intervals related to adult, child or adolescent grief. Books were accompanied by a syllabus briefly outlining the important issues covered in the book (further information about the study can be found in Appendix P).

Outcomes measured at pre-intervention, post-intervention and 11-month follow up included several proximal risk and protective factors and distal mental health outcomes in the child/young person. Evaluation of the FBP showed an improvement in family and individual risk and protective factors post-intervention, but at 11 month follow up the improvement in proximal outcomes were found primarily in girls and in those with poor scores at baseline (see Appendix P for further information about the results). Positive effects on child/adolescent mental health were found at 11-month follow up for girls and for those with more mental health problems at baseline. This study had several important strengths that improve generalisability: provision of a detailed manual and had high level of fidelity of implementation; high level of participant retention in both groups; the sample was heterogeneous in terms of ethnicity, socio-economic status, cause of death and gender of deceased.

BLACK1987 conducted a small-scale intervention study in the UK involving 80 families where a parent had died; 45 families (including 83 children) were randomly assigned to a treatment group and another 34 families were randomly assigned to a control group. The treatment group were seen by experienced psychiatric social workers, who worked in child psychiatry settings and who had received training in bereavement counselling. Each family was offered six family therapy sessions at circa two-weekly intervals, in their home. The aim of the intervention was to promote mourning in the children and parent and to improve communication between them. The therapists received regular supervision. No intervention was provided for the control group (further information about the study can be found in Appendix P). Assessment intervals were yearly and occurred at one and two years after the intervention. Data was collected using a structured interview. The attrition rate was high in both groups. The findings showed a modest difference in favour of the treatment group but failed to reach statistical significance. A consistent factor associated with good outcomes in both groups was the well being of the surviving parent (see Appendix P for further
information about the results). The authors highlighted the importance of further research into the needs of bereaved children, factors associated with good outcomes and the evaluation of different interventions (Black & Urbanowicz, 1987).

5.2.2.2 Parental mental illness (depression)

The children of parents who have affective disorders are at increased risk for a number of mental health problems, including depression (Beardslee et al., 2003).

The Preventive Intervention Project is a large-scale efficacy trial of two manual-based intervention programs conducted in the United States and designed to be used in the public health domain by a variety of professional groups (BEARDSLEE1997). To date, approximately 100 families who have at least one parent diagnosed with an affective disorder and their 8-15 year old, non-depressed children have been randomly assigned to either an intervention or a control/lecture group. Both interventions were specified in manuals, and provided by trained facilitators who received regular supervision. The clinician-facilitated intervention comprised six to eleven sessions, including separate meetings with parents and children and a family meeting led by parents, focusing on strategies for promoting mental health in the children. Additional telephone contacts or refresher meetings were also provided at six to nine monthly intervals. The lecture intervention consisted of two group meetings with parents only. Psychoeducational material about mood disorders, and risk and resilience factors were presented to both groups. Both interventions shared the same aims. Namely, the reduction of individual and family risk factors and the development of protective factors in adolescents through changes in parental attitudes and behaviour; increasing parental knowledge about the aetiology of child and adult depression; removing misunderstanding, guilt and blaming by providing information that enabled parents to respond proactively to the effects of the mood disorder on their children and the family (further information about the study can be found in Appendix P).

Assessment was carried out pre-intervention, post-intervention, and approximately 12 and 30 months after the end of treatment. Findings have consistently shown that both interventions are associated with positive change in both parents and children. Additionally, participants in the intervention group report significantly greater levels of assessor-rated and self-reported change, including an overall reduction in internalising symptomatology in children and adolescents (see Appendix P for further information about the results).
5.2.2.3 Divorce
Marital conflict, parental separation and divorce have consistently been shown to be associated with higher levels of depression in children and adolescents (Wolchik et al, 2000).

In the USA, Wolchik and colleagues have been involved in a longitudinal study of prevention programs for divorced families. Families were randomly assigned to a program for mothers (n = 81), a dual mother-child program (n = 83) or to a self-study program (n = 76). The program for mothers and the mother component of the mother-child program consisted of eleven group and two individual sessions. Two trained facilitators, who received regular supervision, led them. The focus was on improving the quality of the mother-child relationship, providing education about parental conflict, divorce and the father-child relationship and improving parenting skills. The child program group met for eleven weeks and there was a conjoint mother-child session. The children were taught skills such as recognising and labelling feelings, relaxation, problem solving, positive cognitive reframing and challenging common negative appraisals. Mothers and children in the self-study group each received three books and syllabi to guide their reading at three-weekly intervals (further information about the study can be found in Appendix P). The lack of direct involvement with fathers can be viewed as a limitation of the study.

Depressive symptomatology in the children/young people was not focused on specifically, but a reduction in internalising problems was reported for those children and adolescents involved in interventions (see Appendix P for further information about the results).

5.2.2.4 Children displaying symptoms of depression
ARSANOW2002 conducted a preliminary treatment development study in the USA. The intervention had been developed and tested using a clinical sample. In this study 88 children at an urban private school were screened for self-reported symptoms of depression using the CDI. Twenty-three of these pupils were subsequently randomly allocated to either an intervention or a waiting list control group. The intervention group participated in ten sessions of a combined CBT and family education intervention. A detailed manual guided each session. The sessions occurred after school, twice a week for five weeks and included a family education session. The control group received the intervention after the post-test assessment of the intervention group had been completed. The “Stress-Busters” intervention has three distinct components: teaching of generic skills, including problem identification, problem solving, social skills, goal setting and relaxation techniques and depression-specific interventions; family education; the development of videotape by the children for parents (further information about the study can be found in Appendix P).
When compared to children in the control group, children in the intervention group were more likely to show a reduction in depressive symptoms, negative cognitions and maladaptive coping responses to stress (see Appendix P for further information about the results). Consumer satisfaction data was examined for the whole sample and all parents rated the family intervention as helpful. However, a sizeable minority (40%) wanted more family sessions. Further research into this area was recommended. There was no indication of how the school was chosen or of how representative of the population it was (Asarnow et al, 2002).

5.2.3 Clinical summary

Despite the evidence to suggest that family interventions might provide helpful preventative strategies, few controlled prevention studies of depression in children and young people have been undertaken to date (Shochet & Dadds, 1997; Beardslee et al, 2003). Those that do exist have mainly originated from the USA and therefore care needs to be taken when generalising to a different cultural context, despite similarities in the cultures involved.

From the limited evidence available, it would appear that preventative intervention for depression in children and young people that target psychosocial risk factors in children, young people and their families may be beneficial.

5.3 Social/environmental interventions

5.3.1 Introduction

The onset of depression tends to be a consequence of multiple rather than a single predisposing factor. Some of these factors are chronically present in the social and broader environment; others arise less predictably in relationships with family or friends and may recur over time. Children and young people are inherently dependent on their social environment, generally mediated by the family. Most will also spend a large part of their time in the school environment (Rutter, 1979). Difficulties encountered in this environment, like bullying, can predispose an individual to depression. Predisposing factors in the wider environment include poor housing, poverty, unemployment (either of a parent or of the young person), exposure to pervasive neighbourhood violence, and disadvantage and victimisation associated with racism and membership of a minority ethnic group, especially if this is also associated with refugee or asylum-seeker status.

5.3.2 Current practice

Social and environmental interventions seek to influence depression through bringing about or facilitating changes in this environment in order to reduce or eliminate known risk factors. This might be either a preventative intervention, or one with the aim of alleviating existing depressive mood or
symptoms. Though not specifically targeted at preventing or alleviating depression, government-sponsored programmes like ‘Head Start’ in the USA and ‘Sure Start’ in the UK have targeted factors in local communities that prevent or inhibit social inclusion, social and educational development, and the maintenance of emotional and physical good health. Though ‘Sure Start’ programmes are aimed at children under four, who are outside the scope of this Guideline, they are concerned with long-term outcomes and prevention and their targets include risk factors for depression like maternal post-natal depression, parental ill-health, poverty and a lack of employment opportunities. The long-term effectiveness of these interventions has not been studied yet.

Epidemiological studies show that many adolescents and some children in the community who are depressed remain undetected (Angold & Costello, 2001). Depression may not be recognised as such by those working with the child or young person - teachers and school support staff, youth workers, sports coaches, social workers, etc. They may be employed by statutory agencies in primary health care, social care, education and the voluntary sector. Their primary concern may be a behavioural manifestation associated with the depression, like substance misuse, delinquency, bullying or child abuse. Any subsequent intervention may well not be informed by input from CAMHS professionals. It may include attempts to modify or influence the child’s social environment, either preventatively or in an effort to improve the situation for an individual or group.

Many schools have developed anti-bullying policies, and may employ a range of strategies and approaches based on evidence from project-based studies (e.g., DfES, 2002). In schools this may include changes in meal and play-time arrangements to reduce bullying and stress, including peer mentoring and mediation training programmes for students; or the introduction of ‘Circle Time’ (Curry & Bromfield, 1994), or a specific intervention like a ‘Circle of Friends’ (Newton et al, 1996) to improve an individual child’s social integration. In non-clinical contexts, such interventions are likely to continue to be tried regardless of clinical guidelines, as humane and common sense responses to children’s unhappiness and misery. For many children this may be the best help that is available, though at the moment there seems little evidence as to what may be more or less effective. However, universal preventative interventions may have a large potential benefit for the wider population but smaller benefits for individuals (Offord et al, 1998).

5.3.3 Definition and aim of the intervention
Children and young people are particularly dependent on their social environment, generally mediated by the family. There are risk factors for depression in the wider environment, like poor housing, poverty, unemployment (either of a parent or of the young person), exposure to pervasive neighbourhood violence, and disadvantage and victimisation.
associated with racism and membership of a minority ethnic group - especially if this is also associated with refugee or asylum-seeker status. Social and environmental interventions are those that seek to influence this environment in order to reduce or eliminate risk factors for depression. This might be either a preventative intervention, or targeted at alleviating existing depressive mood or symptoms.

5.3.4 Narrative review

Though extensive, the search strategy was inevitably limited within a potentially very large field encompassing literature from the social sciences, psychiatry and psychology. A number of studies were found from the US and Canada indicating that environmental and social factors contribute to depression. No studies were found of specific social or environmental interventions that demonstrated a direct effect on preventing or reducing depression. However, a number of studies from Britain and elsewhere of interventions in educational settings suggest positive outcomes in terms of general improvement in emotional well-being, and in some cases more specifically with internalising disorders.

5.3.4.1 Peer friendship networks

Peer support networks can be valuable in preventing and alleviating depression and its effects. Bao et al (2000) emphasise the importance of maintaining and developing the resources of peer-support networks among homeless adolescents. Outreach workers in six participating youth agencies in US cities, measuring depression using the CES-D interviewed 602 homeless and runaway adolescents with an average age of 16. Supportive contact with family members reduced reported depressive symptoms, and peer support was found to be a buffer against depression, though association with deviant peers increased depression. Cornwell (2003) studied a nationally representative sample of 11,835 US adolescents from the National Longitudinal Study of Adolescent Health, using an index of questions from the CES-D scale to measure depression. The results of the study suggested that preventing a falling off of peer and parental support may help reduce a potential intensification of depressive symptoms. Downs & Rose (1991) studied the relationship between peer-group affiliation and psychosocial problems. The study included 127 adolescents aged 13-17 in a hospital-based treatment program providing acute crisis intervention for alcohol or drug intoxication, with a control sample of 114. From their findings, they advocate programmes to increase the individual’s involvement in school activities through identifying interests and improving skills, and to encourage affiliation to a more positively labelled peer group. Ezzell et al. (2000) found that peer and family support is particularly important for the small sample of children aged 6 -14 who they studied who were depressed after being physically abused. This was related to reduced internalising symptoms. The
children specifically identified as important support from a coach, parents' friends and therapists.

5.3.4.2 Social networks and neighbourhood factors.
Perez-Smith et al (2002) looked at the importance of social networks by interviewing 48 adolescents presenting to a paediatric emergency department following a suicide attempt. Their assessment included using the Hopelessness Scale for Children and CESD. They found that living in a neighbourhood with what they defined as weak social networks (i.e. high male-to-female ratios and adult-to-child ratios) led to higher levels of self-reported hopelessness. Caughy et al. (2001) studied the influence of neighbourhood on children under 4 in a socially and economically representative cross-section of African Americans in an inner city. The study found differences in the association between how well a parent knew her neighbours, and internalised and externalised behaviour problems, according to the relative economic impoverishment of the neighbourhood that they lived in. Those children in wealthier neighbourhoods whose parents reported knowing few neighbours had higher levels of internalising problems such as anxiety and depression. However, in poorer neighbourhoods a parent knowing fewer neighbours seemed to protect against internalising problems. The study did not specifically screen for depression. The study challenges any simple relationship between social capital and well being, with implications for planning social interventions. Caution should be used in any attempt to relate these results to the situation of black and minority ethnic children in the UK.

Takeuchi et al (1991) analyses longitudinal data on a sample of children aged 7-11 from the US National Survey of Children to demonstrate that even the transitory perception of financial stress can have an adverse impact on children’s emotions and behaviour, most markedly for depressive symptoms. Depression was assessed using an adaptation of the Child Behaviour Checklist, on parental report. Simons & Miller (1987) administered a self-report questionnaire to 423 US high school students. They found that two socio-environmental factors predicted depression - low parental support and employment problems. They suggest that clinicians should consider offering employment counselling as well as family support and cognitive therapy when treating adolescent depression.

5.3.4.3 The educational environment
A number of studies have demonstrated the adverse effect on the mental health of children and young people of bullying in its various manifestations, including: direct bullying through physical aggression; verbal bullying and intimidation; and indirect bullying through social isolation, and intentional exclusion from the group (Olweus 1994; Kumpulainen et al. 1998; Salmon et al. 2000). Hawker and Boulton (2000) in a useful meta-analysis found a positive
association between bullying and victimisation and depression. Though not specifically addressing depression, studies have indicated that school-based anti-bullying intervention programmes can reduce bullying by up to a half (Olweus, 1993; Smith & Sharp, 1994). However, Salmon et al. (1998) reported that the impact of the introduction of policies on bullying throughout a school seems to be limited. Their own study of 904 pupils aged 12-17 suggested that “bullying interventions are having more of an impact on the direct bullying characteristics of boys and less on the indirect bullying more common among girls”. Dawkins (1995) provides a helpful summary of research-based programmes for tackling bullying in schools, including development of school policies and classroom materials. Sharp & Smith (1994) and Smith & Sharp (1994) describe a school-based anti-bullying project in Sheffield. The lessons learned from this project formed the basis for an anti-bullying pack produced for schools by the Department for Education and Skills (DfES 2002).

PATHS (Greenberg & Kusche 1998) is a whole-school targeted programme for primary age pupils aiming to improve social and emotional competence. Randomised Control Trials were carried out in a number of schools, and at two-year follow-up there were significant differences on teacher and self-report of depressive and conduct problems. A multi-site replication using a shorter version within the Fast Track (CPPRG 2002) programme suggests that the quality of implementation is a key predictor of how teachers and peers assess outcome.

Though there is little evidence from studies as to whether environmental or social interventions have any direct impact on depression in children and young people, a number of studies consider programmes with a broader remit which may still have relevance to depression. For example the LIFT programme (Linking the Interests of Families and Teachers) aimed to reduce the prevalence of conduct disorders in schools through providing parent training, classroom-based social skills training, playground behavioural interventions and improving school-parent communication. The overall intervention was found to have significant effects on physical aggression in the playground, maternal aversive behaviour and child behaviour in the classroom (Reid et al. 1999). A number of studies (Greenberg et al 2000; Wells et al 2001; and Weissberg et al 2003) make suggestions as to best practice in school-based interventions. Interventions should aim to change the school and family context, not just the individual child, and must be culturally appropriate. They suggest it is crucial to ensure the active involvement of the head teacher, and that programmes should be over several years rather than brief interventions. Locally appropriate delivery programmes need to incorporate whatever evidence-based practice there is, and to be implemented with sustainable training and support.

Pritchard (2001) reported considerable success in resolving child and family problems and improving the ethos of the school in a three-year school-based
social work support service, staffed by an experienced project social worker with a background in education social work, and two project teachers. This was shown to positively affect educational achievement, truancy and exclusion rates, all of which have been associated with depression. The project recorded severe personal and social problems affecting children in the target schools - a primary and a secondary school, with comparison schools selected as controls. It was sponsored by the Home Office and specifically focused on reduction of ant-social behaviour and delinquency. Though there was no screening for depression or other mental health problems and consequently no evaluation of effectiveness of the intervention in this respect, it is likely that these were present in the targeted population. 54% of referred problems were described as behavioural disorders and 29% 'neurotic/anxiety' difficulties. There were many potential risk factors present for depression. For example, 20% of referrals were child protection cases, 10% of parents had mental health problems and 20% medical and chronic health disorders, and a majority of the fathers involved were unemployed. Counselling and group work were provided for children and families using a model drawing on a CBT approach. Using what is described as an integrated psycho-socio-educational approach, consultation and support were provided for teachers, and community and school networks were developed to facilitate mutual family support and inter-agency collaboration.

Galaif et al (2003) found that depression could be predicted from the interaction between perceived stress and methods of coping with anger. They suggest from their study of 646 US continuation high school students that school-based programmes should incorporate anger management techniques and skills into the curriculum to enable adolescents, especially females, to deal with the difficulties without having to self-medicate or act out by utilizing maladaptive behavioural coping strategies, and steering them away from more isolated activities. Dumont & Provost (1999) studied a normative sample of 297 adolescents aged 14 - 16 from the same school in Quebec who were experiencing depression and repetitive stress which they called "daily hassles". Depression was assessed using the Beck Depression Inventory. Their study emphasizes the protective role of social support and social activities in building self-esteem, coping strategies and resilience to stress and depression.

5.3.5 Clinical summary
There is evidence that a range of social and environmental factors can impact on the mental health of children and young people, including peer group networks, parental employment status, financial issues, neighbourhood factors and levels of bullying and other school based problems. There is less good evidence of direct relationships between such factors and childhood depression, as few studies have looked for this. Further, systematic review found no controlled trials that specifically looked at social and environmental interventions to prevent or treat depressive disorder in children and young people.
There is, however, evidence from British and European studies of bullying as a predisposing factor for and cause of depression; and also of effectiveness of some anti-bullying interventions in schools. Aside from anti-bullying interventions in schools, many of the studies that do exist have originated from the USA, and these have not evaluated actual interventions. Care also needs to be taken when generalising to a different cultural context, despite similarities in the cultures involved.

From the limited evidence available, it would appear that social and environmental intervention for depression in children and adolescents, including those that target psychosocial risk factors in children, adolescents and their families may be beneficial. In cases where depression remains undiagnosed, such an intervention may be the only that is used.

5.4 Clinical practice recommendations

5.4.1 Self-help

5.4.1.1 In the assessment of children/young people with depression, healthcare professionals should always ask patients, and be prepared to give advice, about the use of self-help materials or methods used or considered by the patient or their family. This may include educational leaflets, help-lines, self-diagnosis tools, peer/social/family support groups, complimentary therapies or religious/spiritual groups. (GPP) (1.1.3.3 NICE)

5.4.1.2 Health professionals should only recommend self-help materials or strategies as part of a supported and planned package of care. (GPP) (1.1.3.4 NICE)

5.4.1.3 Children and young people with depression should be advised of the benefits of regular exercise, and may consider following a structured and supervised exercise programme of typically up to three sessions per week of moderate duration (45 minutes to 1 hour) for between 10 and 12 weeks. (C) (1.1.5.8 NICE)

5.4.1.4 Children and young people and with depression may benefit from advice on sleep hygiene and anxiety management. (C) (1.1.5.9 NICE)

5.4.1.5 Children and young people with depression may benefit from advice about nutrition and the benefits of a balanced diet. (GPP) (1.1.5.10 NICE)
5.4.2 Family support/parental education

5.4.2.1 When assessing a child/young person with depression, healthcare professionals should routinely consider, and record in the notes, the psychological and comorbid factors, 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. (GPP) (1.1.3.1 NICE)

5.4.2.2 In the assessment of children/young people with depression, healthcare professionals should always ask patients and their family directly about alcohol and drug use, self-harm and ideas about suicide. Young people may prefer to initially discuss these issues in private. (GPP) (1.1.3.2 NICE)

5.4.2.3 When a child or young person has been given the diagnosis of depression, consideration should be given to the possibility of parental depression (or other mental health problem) as this is often associated and, untreated, may have a negative impact on treatment offered to the child or young person. (GPP) (1.1.3.5 NICE)

5.4.3 Social/environmental interventions

5.4.3.1 When bullying is considered to be a factor in a child or young person’s depression, CAMHS and educational professionals should work collaboratively to prevent bullying and to develop effective anti-bullying strategies. (C) (1.1.5.3 NICE)

6 Psychological treatment of depression in children and young people

6.1 Introduction

The psychological treatment of depression in childhood is dissimilar from that provided for depressed adults. Although, as with physical treatments for depression, there has been some extrapolation from approaches used for adults (for example cognitive behaviour therapy and psychodynamic therapy), in routine practice these formal individual therapies are not the most common psychological approaches. Whereas adults with depression are often treated for the disorder specifically, children with depression are often not thought of as ‘having’ depression but are often seen as affected by a set of
emotional, behavioural, learning, relationship and family problems which need to be considered together, and may still need to be addressed together, even if depression in the child is a primary concern.

Thus, psychological treatments for depression in children and young people may not be thought about as distinct from working with children, adolescents and families with a wide range of psychosocial difficulties. This is probably especially true with pre-adolescent children, in whom depression is very likely to be seen as a sign of a more complicated situation, or result of earlier stresses within a system (the family or school for example).

As adolescents move towards adult independence (or fail to do so), it is more likely that treatments designed for adults will be thought to be appropriate and extended to these young people. It may be for this reason, as well as because childhood depression is most prevalent in adolescence, that the studies reviewed here have generally been conducted with young people of secondary school age, and our conclusions should not be assumed to apply to younger children, without further investigation.

Children rarely initiate mental health assessment and treatment although adolescents may seek help for emotional difficulties in a wide variety of ways (see self-help section). While many clinically depressed adults recognise that they are depressed (or at least that they are ill) and seek treatment, both would be rare in children and adolescents. At a mild level, children are highly unlikely to be referred, unless it affects their behaviour in some obvious way (e.g. self-harm, withdrawn or aggressive behaviour at school, or failing academic performance). Childhood depression commonly presents as recurrent and unexplained physical symptoms, which may be difficult to recognise as depression, even for the professionals consulted (e.g. a GP, school nurse, paediatrician). Even when they recognise the underlying problem, parents, child, teachers and others involved may well find it difficult to accept the need for psychological or psychiatric treatment, not uncommonly because of feelings of anxiety, anger and shame, or indeed because of stigma and lack of knowledge about mental health problems generally.

It is important, therefore, to note that the recognition of depression, and the likelihood of children or young people receiving effective treatment and care, is mediated through the differing perceptions and reactions of parents, health and non-health professionals already involved in the child’s life, the children/young people themselves and specialist mental health professionals. It is perhaps no surprise that in this context, many children and young people who are depressed have a tendency to think that they are the problem, rather than thinking that they have a problem with which they may be able to get help.
6.2 Psychological interventions

6.2.1 Introduction
Psychological interventions for childhood depression include a number of approaches, involving different activities, people and amounts of time, and different theoretical assumptions. Treatment may involve talking with the child, and perhaps others in the family, to clarify the reasons for the child’s unhappiness, withdrawal and other symptoms, with the aim of recognising possible factors (e.g. bereavement, parental mental ill health, bullying) which may be linked to the child’s depression. Alternatively it may be focussed on identifying roles and communication patterns within the family, or it may focus on changing the child’s depressed behaviour (e.g. staying in bed all day, dropping out of school, self-neglect, social isolation).

6.2.2 Current practice
The current system of NHS CAMHS provision is described in chapter 2. The wider context of non-NHS services, together with self-help resources, is described in chapter 5.

Within the NHS, depression in a young person may first be noticed by one of a range of primary care and community professionals, including GPs, practice nurses, school nurses, community paediatricians. Sometimes these professionals may offer treatment for the depression, particularly if it is not severe and/or it is in the context of long-term physical illness. Some depressed children and young people will be referred to a CAMHS service. Nevertheless, it is estimated that the majority of children and young people with depression will not be recognised as such and will not, therefore, receive any specific help (Andrews et al, 2002; Coyle et al, 2003).

When a child/young person with depression is referred to a CAMHS service, whether the first line treatment offered will be physical or psychological varies considerably. Where the initial approach is social/psychological, this is likely to begin as a generic approach, involving clarification of the problem with the family and child, and locating the child’s depression within a wider psychosocial context. Only a small proportion of children in most services will be referred for a specific psychological intervention, such as CBT, individual child psychotherapy or family therapy. Most cases will thus be treated with a psychological approach, involving elaboration and formulation of the problem, that has not been systematically evaluated for treatment efficacy.

A very small proportion of depressed young people may be so severely self-harming or incapacitated that they will be admitted to inpatient adolescent units. Here, it is more likely that a young person would receive a formal psychological treatment, such as those evaluated in outcome studies. In addition, they would be more likely to receive a form of group therapy, in
addition to care within a milieu which provides intensive adult supervision and monitoring of physical behaviour and safety.

6.2.3 The evidence base for psychological treatments

There is considerable variation in the evidence base for different specific psychological interventions for childhood depression. This variation is a result of a number of factors, including: the cost, ethics and complexity of undertaking randomised controlled trials of psychological treatments, especially those involving even moderately long treatments, or where the goal of change is more than symptomatic improvement; the willingness of therapists to participate in a research study; the level of skill and experience needed for some psychological treatments; and the paucity of funding available for psychological treatment research, especially when compared with the large amount of funding provided by the pharmaceutical industry for drug treatments. Moreover, the funding that is available for psychological treatment research for depressed children and young people has generally been lower than funding for research into externalising (behavioural) problems. This lack of evidence should not, therefore, be taken as evidence of ineffectiveness; there is clearly a need for more research to create an adequate evidence base.

The evidence base for the psychological treatments for depressed children and young people, such as it is, is largest for CBT (especially group), with rather less evidence concerning family therapy, and less still for or against individual child psychotherapy. It is important to recognise that the level of outcome research does not reflect the prevalence of different psychotherapy approaches in current practice within CAMHS services in the NHS (for example, group CBT for depression is rarely practised, while short-term family work is extremely common).

6.2.4 Research limitations

In the early years of this research, it was rare for referred children to be studied; such outcome research as there was, was confined to community samples of young people with sub-clinical levels of depressed mood, or clinically depressed young people who were recruited through advertising or screening of large non-referred samples. There is evidence that children who are referred to CAMHS services show more complex and entrenched sets of problems, not simply comorbid psychiatric disorders but what may be chronic problems in their social and academic functioning, and psychiatric and social problems in their parents and families (e.g. Hammen, 1999).

There has, however, been a gradual move in recent years to recruit ‘real life’ clinical samples, and to include children and young people with comorbid diagnoses in the studies. These changes introduce new practical problems, such as the need for large sample sizes (e.g. to examine the impact of comorbid diagnoses), as well as difficulties of interpretation. Nevertheless,
there is an obvious necessity to increase the external validity (generalisability) of studies’ findings.

The current review includes studies of both referred and recruited samples. We also include studies with samples defined by depression symptom checklists as opposed to clinical diagnosis. Both factors need to be borne in mind in interpreting the research findings for application to NHS patients presenting with diagnosable levels of depression.

Finally, a significant limitation within the parameters of this guideline is that some important studies have not selected their sample, or reported on outcomes, in terms of depression, but have looked at the effectiveness of a treatment approach across the range of disorders and comorbid conditions which present to the service (Fonagy et al, 2002). For example, a psychotherapy service that treats many depressed young people and collects outcome data on internalising symptomatology cannot be included because the data are not depression-specific (Baruch et al, 1998; Baruch et al, 1999). Evaluations of services currently need to be carried out in ways that make reporting possible in terms of diagnoses or disorder-specific symptom scales, if their outcomes are to be included in diagnosis-based guidelines. Alternatively – and probably more appropriately, given the way that services are provided to children and young people – guidelines could address treatment outcomes across groups of related disorders, in this case across internalising disorders (the range of anxiety and depressive disorders and their combinations) as opposed to depression in isolation. However, that would require a shift in research culture, away from the medical model of seeking the most effective treatment for a DSM illness category, towards the biopsychosocial model in which formulation is expected to be complex, and treatment assumed to be broad-based, to fit the multiple causative and mediating factors which impinge on children’s emotional and social development and current functioning.

Future research needs more closely to address the needs of NHS professionals for guidance on treatment choice. It is positive that the culture of research on psychological treatment for children and young people has moved somewhat closer to clinical reality, in its focus on multimodal/multisystemic therapies and developing treatments that can be successfully applied outside the university clinic. The next step may be to make the research more relevant to CAMHS professionals who do not tend to think of the child in isolation from his or her social context, or use a diagnostic category as the basis for treatment choice.

6.2.5 Databases searched and inclusion/exclusion criteria
Table 1. Databases searched and inclusion/exclusion criteria for clinical effectiveness of psychological interventions.

<table>
<thead>
<tr>
<th>Electronic databases</th>
<th>MEDLINE, EMBASE, PsycINFO, Cochrane Library</th>
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<tbody>
<tr>
<td>Date searched</td>
<td>Database inception to January 2004; table of contents February to September 2004</td>
</tr>
<tr>
<td>Study design</td>
<td>RCT</td>
</tr>
<tr>
<td>Patient population</td>
<td>Participants aged 5-18 years old with recognised symptoms of depression</td>
</tr>
<tr>
<td>Interventions*</td>
<td>Cognitive behaviour therapy (CBT)</td>
</tr>
<tr>
<td></td>
<td>CBT + separate parent sessions</td>
</tr>
<tr>
<td></td>
<td>Interpersonal psychotherapy (IPT)</td>
</tr>
<tr>
<td></td>
<td>Psychoanalytic/psychodynamic child psychotherapy</td>
</tr>
<tr>
<td></td>
<td>Self-modelling</td>
</tr>
<tr>
<td></td>
<td>Relaxation</td>
</tr>
<tr>
<td></td>
<td>Social skills training</td>
</tr>
<tr>
<td></td>
<td>Family therapy</td>
</tr>
<tr>
<td></td>
<td>Guided-self help</td>
</tr>
<tr>
<td></td>
<td>Control enhancement training</td>
</tr>
<tr>
<td></td>
<td>Control group (waitlist, non-directive supportive therapy, therapeutic support group, ‘standard care’, clinical management, behavioural problem solving, life skills training)</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Remission, symptom levels, functional status, discontinuation from treatment for any reason</td>
</tr>
</tbody>
</table>

*These interventions can be grouped into a much smaller number of major approaches, with considerable overlap between the different ‘brands’ of, for example cognitive-behavioural approach. We regard the major approaches in current practice as: individual CBT; group CBT; structural/behavioural family therapy; systemic family therapy; psychoanalytic/psychodynamic child psychotherapy; other non-directive therapy which is primarily supportive. Within this framework both social skills training and IPT would be regarded as ‘brands’ of the CBT family.

6.2.6 Studies considered

The review team conducted a new systematic search for RCTs that assessed the efficacy of psychological interventions for children and young people with depression.

Eighteen trials met the eligibility criteria set by the GDG: 14 from the US, three from the UK/Europe, and one from Puerto Rico. In total, data on 1520 participants were used. The trials were published between 1986 and 2004, and were between 4 and 36 weeks long. In addition, two studies, one comparing social skills training with non-directive supportive therapy (REED1994), and one comparing a combined cognitive-behavioural family education intervention with waitlist (ASARNOW2002) were excluded from the analysis due to a lack of usable data. A further three studies were excluded because there was no or an inappropriate control group (MUFSON1994, NELSON2003, SANTOR2001).

Active intervention versus waitlist/standard care/no treatment control

1 Here and elsewhere in the guideline, each study considered for review is referred to by a study ID in capital letters (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).
From the 18 included trials, there was one comparison involving CBT\(^2\) (ROSSELLO1999), seven of group CBT (CLARKE1999, CLARKE2002, KAHN1990, LEWINSOHN1990, REYNOLDS1986, STARK1987, WEISZ1997), two of IPT (MUFSON1999, ROSSELLO1999), one of family therapy (DIAMOND2002), two of group relaxation (KAHN1990, REYNOLDS1986), and one of self-modelling (KAHN1990) (see Table 2 for further details).

\(^2\) Unless otherwise stated, the intervention was given individually to participants.
Table 2. Study information table for trials of psychological interventions versus waitlist/‘standard care’/no treatment control.

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Total no. of trials (total no. of participants)</th>
<th>CBT vs. waitlist</th>
<th>Group CBT vs. waitlist control/‘standard care’/no treatment</th>
<th>IPT vs. waitlist</th>
<th>Family therapy vs. waitlist</th>
<th>Group relaxation vs. waitlist</th>
<th>Self-modelling vs. waitlist</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>1 RCT (N = 71)</td>
<td>7 RCTs (N = 329)</td>
<td>2 RCTs (N = 84)</td>
<td>1 RCT (N = 32)</td>
<td>2 RCTs (N = 98)</td>
<td>1 RCTs (N = 34)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CLARKE2002</td>
<td>REYNOLDS 1986</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>LEWINSOHN 1990</td>
<td>STARK 1987 WEISZ1997</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>KAHN1990</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>REYNOLDS 1986</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline severity:</td>
<td></td>
<td>CDI: Pooled across groups 20.12 (SD 6.95)</td>
<td>CDI/BDI range: Pooled across groups 18.63 (SD 5.32) to 21.67 (SD 11.34)*</td>
<td>CDI/BDI range: Pooled across groups 18.8 (SD 8.5) to 21.21 (SD 7.53)</td>
<td>CDI: Pooled across groups 23.8 (SD 7.4)</td>
<td>BID: Pooled across groups 17.09 (SD 6.36)†</td>
<td>BID range: Pooled across groups 38.06 (SD 15.26) to 46.27 (SD 20.42)</td>
</tr>
<tr>
<td>mean (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BID: Pooled across groups 52.82 (SD 18.45)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment length</td>
<td></td>
<td>12 weeks</td>
<td>5 to 8 weeks</td>
<td>12 weeks</td>
<td>6 weeks</td>
<td>5 weeks</td>
<td>6 to 8 weeks</td>
</tr>
<tr>
<td>Length of follow-up</td>
<td></td>
<td>3 months</td>
<td>1 to 24 months</td>
<td>–</td>
<td>6 months</td>
<td>1 month</td>
<td>1 month</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td>13 to 17 years</td>
<td>10 to 18 years</td>
<td>12 to 18 years</td>
<td>13 to 18 years</td>
<td>10 to 14 years</td>
<td>10 to 14 years</td>
</tr>
</tbody>
</table>

Note: CBT = Cognitive behaviour therapy; IPT = Interpersonal psychotherapy; MDD = Major depressive disorder; DSM = Diagnostic Statistical Manual; RADS = Reynolds Adolescent Depression scale; CDI = Children’s Depressive Inventory; BDI = Beck Depression Inventory.

*Data not available for CLARKE2002 and KAHN1990; †Data not available for KAHN1990.

**Active intervention versus another active intervention**

There were three trials involving a comparison of CBT with non-directive supportive therapy or clinical management (BRENT1997, TADS2004, VOSTANIS1996), one of CBT versus IPT (ROSELLO1999), and one of CBT versus

---

3 Control group was ‘standard care’.
4 Control group was no treatment.
relaxation (WOOD1996), and one of CBT versus family therapy (BRENT1997) (Table 3).

**Table 3. Study information for trials of CBT versus another psychological intervention.**

<table>
<thead>
<tr>
<th>Total no. of trials</th>
<th>CBT vs. non-directive supportive therapy or clinical management</th>
<th>CBT vs. IPT</th>
<th>CBT vs. relaxation</th>
<th>CBT vs. family therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 RCTs (N = 387)</td>
<td>1 RCT (N = 38)</td>
<td>1 RCT (N = 53)</td>
<td>1 RCT (N = 72)</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Minor depression, dysthymia, or MDD (DSM-III-R or DSM-IV)</td>
<td>Dysthymia or MDD (DSM-III-R)</td>
<td>Minor depression (RDC) or MDD (DSM-III-R)</td>
<td>MDD (DSM-III-R)</td>
</tr>
<tr>
<td>Baseline severity:</td>
<td>BDI: Pooled across groups 24.3 (SD 8.1)* CDRS-R 60.35 (SD 9.86)</td>
<td>CDI: Pooled across groups 20.12 (SD 6.95)</td>
<td>--</td>
<td>BDI: Pooled across groups 24.3 (SD 8.1)</td>
</tr>
<tr>
<td>Treatment length</td>
<td>12 to 16 weeks</td>
<td>12 weeks</td>
<td>5 to 8 weeks</td>
<td>12 to 16 weeks</td>
</tr>
<tr>
<td>Length of follow-up</td>
<td>0 to 24 months</td>
<td>8 months</td>
<td>3 to 6 months</td>
<td>--</td>
</tr>
<tr>
<td>Age</td>
<td>12 to 18 years</td>
<td>13 to 17 years</td>
<td>9 to 17 years</td>
<td>13 to 18 years</td>
</tr>
</tbody>
</table>

Note. CBT = Cognitive behaviour therapy; IPT = Interpersonal psychotherapy; MDD = Major depressive disorder; DSM = Diagnostic Statistical Manual; RADS = Reynolds Adolescent Depression scale; CDI = Children's Depressive Inventory; BDI = Beck Depression Inventory; RDC = Research Diagnostic Criteria.

*Data not available for VOSTANIS1996.

In addition, there were two trials of group CBT versus behavioural problem solving/life skills training (ROHDE2004, STARK1987), two trials involving a comparison of group CBT versus group relaxation (KAHN1990, REYNOLDS1986), one trial involving a comparison of group CBT versus self-modelling (KAHN1990), one trial involving a comparison of group relaxation versus self-modelling (KAHN1990), and one trial of family therapy versus individual psychodynamic psychotherapy (TROWELL) (Table 4).

---

5 Control group received placebo pill in addition to clinical management.
Table 4. Study information for trials of group CBT/relaxation or family therapy versus another psychological intervention.

<table>
<thead>
<tr>
<th></th>
<th>Group CBT vs. behavioural problem-solving/life skills training</th>
<th>Group CBT vs. group relaxation</th>
<th>Group CBT vs. self-modelling</th>
<th>Group relaxation vs. self-modelling</th>
<th>Family therapy vs. individual psychodynamic psychotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of trials (total no. of participants)</td>
<td>2 RCTs (N = 117)</td>
<td>2 RCTs (N = 54)</td>
<td>1 RCT (N = 34)</td>
<td>1 RCT (N = 34)</td>
<td>1 RCT (N = 72)</td>
</tr>
<tr>
<td>Study ID</td>
<td>ROHDE2004</td>
<td>KAHN1990</td>
<td>KAHN1990</td>
<td>TROWELL</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>MDD (DSM-IV)/CDI</td>
<td>Minor depression or MDD (DSM-III-R/RDC)</td>
<td>Depression (RADS/CDI/BDI)</td>
<td>Depression (RADS/CDI/BDI)</td>
<td>MDD and/or Dysthymia (K-SADS)</td>
</tr>
<tr>
<td>Baseline severity: mean (SD)</td>
<td>BDI-II: CBT 16.6 (SD 12.8), Control 15.4 (SD 10.6)</td>
<td>BID: Group CBT range 44.65 (SD 15.56) to 50.33 (SD 19.60), Group relaxation: range 38.06 (SD 15.26) to 46.27 (SD 20.42)</td>
<td>BID: Group CBT 44.65 (SD 15.56), Self-modelling 52.82 (18.45)</td>
<td>BID: Group relaxation 38.06 (SD 15.26), Self-modelling 52.82 (18.45)</td>
<td>CDI: Family therapy 23.83 (SD 7.07), Individual therapy 23.00 (SD 7.56)</td>
</tr>
<tr>
<td>Treatment length</td>
<td>5 to 8 weeks</td>
<td>5 to 8 weeks</td>
<td>6 to 8 weeks</td>
<td>6 to 8 weeks</td>
<td>36 weeks</td>
</tr>
<tr>
<td>Length of follow-up</td>
<td>1 to 12 months</td>
<td>1 month</td>
<td>1 month</td>
<td>1 month</td>
<td>9 months</td>
</tr>
<tr>
<td>Age</td>
<td>9 to 17 years</td>
<td>10 to 16 years</td>
<td>10 to 14 years</td>
<td>10 to 14 years</td>
<td>10 to 14 years</td>
</tr>
</tbody>
</table>

Note. CBT = Cognitive behaviour therapy; IPT = Interpersonal psychotherapy; MDD = Major depressive disorder; DSM = Diagnostic Statistical Manual; RADS = Reynolds Adolescent Depression scale; CDI = Children’s Depressive Inventory; BDI = Beck Depression Inventory; RDC = Research Diagnostic Criteria.

There was one trial of IPT versus ‘standard care’ (MUFSON2004), two trials that examined the impact of adding separate parent sessions to group CBT (CLARKE1999, LEWINSOHN1990) and one trial of family therapy versus non-directive supportive therapy (BRENT1997) (Table 5).

**Guided self-help versus waitlist**
There was one trial comparing guided self-help with waitlist control (ACKERSON1998) (Table 5).
Table 5. Study information for trials of group CBT, group CBT plus separate parent sessions, family therapy, and IPT.

<table>
<thead>
<tr>
<th>Study ID</th>
<th>IPT vs. ‘standard care’</th>
<th>Group CBT (+ parent) vs. waitlist</th>
<th>Group CBT vs. group CBT (+ parent)</th>
<th>Family therapy vs. non-directive supportive therapy</th>
<th>Guided self-help vs. waitlist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of trials</td>
<td>1 RCT (N = 64)</td>
<td>2 RCTs (N = 116)</td>
<td>2 RCTs (N = 116)</td>
<td>1 RCT (N = 70)</td>
<td>1 RCT (N = 30)</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>51% MDD (DSM-IV) + other mood disorders</td>
<td>MDD (DSM-III/DSM-III-R)</td>
<td>MDD (DSM-III/DSM-III-R)</td>
<td>MDD (DSM-III-R)</td>
<td>Depression (HDRS/CDI)</td>
</tr>
<tr>
<td>Baseline severity:</td>
<td>HDRS: IPT 18.9 (SD 5.9), standard care 18.3 (SD 5.0)</td>
<td>BDI: Family therapy 22.6 (SD 6.20), Non-directive 25.7 (SD 7.80)</td>
<td>HDRS: GSH 19.9 (SD 5.5), WL 21.0 (SD 5.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment length</td>
<td>16 weeks</td>
<td>7 to 8 weeks</td>
<td>7 to 8 weeks</td>
<td>12 to 16 weeks</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Length of follow-up</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1 month</td>
</tr>
<tr>
<td>Age</td>
<td>12 to 18 years</td>
<td>14 to 18 years</td>
<td>14 to 18 years</td>
<td>13 to 18 years</td>
<td>~16 years</td>
</tr>
</tbody>
</table>

Note. CBT = Cognitive behaviour therapy; IPT = Interpersonal psychotherapy; MDD = Major depressive disorder; DSM = Diagnostic Statistical Manual; BDI = Beck Depressive Inventory; HDRS = Hamilton Depression Rating Scale.
### 6.2.7 Psychological interventions versus waitlist/control group

**Table 6. Evidence summary table for various psychological interventions versus waitlist/control group.**

<table>
<thead>
<tr>
<th></th>
<th>CBT vs. waitlist</th>
<th>Group CBT vs. waitlist control/standard care/no treatment</th>
<th>IPT vs. waitlist</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total no. of trials (total no. of participants)</strong></td>
<td>1 RCT (N = 71)</td>
<td>7 RCTs (N = 329)</td>
<td>2 RCTs (N = 84)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Remission - endpoint</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinician completed</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSM</td>
<td>–</td>
<td>? (K=3; N=217)</td>
<td></td>
</tr>
<tr>
<td>Self-report</td>
<td>CDI/BDI</td>
<td>K=1; N=48</td>
<td></td>
</tr>
<tr>
<td>RADS</td>
<td>–</td>
<td>K=1; N=34</td>
<td></td>
</tr>
</tbody>
</table>

| Remission - follow-up        |                  |                                                          |                  |
| **Clinician completed**      |                  |                                                          |                  |
| DSM                         | –                | × 12/24 months                                           |                  |
| Depressive symptoms - endpoint |                |                                                          |                  |
| **Clinician completed**      |                  |                                                          |                  |
| CDRS/HDRS                    | –                | ? (K=3; N=197)                                           |                  |
| BID                          | –                | ? (K=1; N=34)                                            |                  |
| Self-report                  | CDI/BDI          | K=1; N=39                                               |                  |
| RADS/CES-D                   | –                | K=3; N=179                                              |                  |

| Depressive symptoms – follow-up | | | |
| **Clinician completed**   | HDRS             | × 12 months                                             |                  |
| HDRS                        | –                | ? 24 months                                             |                  |
| Self-report                 | RADS/CES-D       | ? 12/24 months                                          |                  |

| Functional status - endpoint | | | |
| **Clinician completed**     | GAF              | ? (K=2; N=149)                                          |                  |
| Functional status - follow-up | GAF             | × 12/24 months                                          |                  |

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### Active treatment group attrition

<table>
<thead>
<tr>
<th></th>
<th>16%</th>
<th>7% to 18%</th>
<th>13% to 17%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment length (weeks)</td>
<td>12</td>
<td>5 – 8</td>
<td>12</td>
</tr>
<tr>
<td>Length of follow-up (mths)</td>
<td>3</td>
<td>1 – 24</td>
<td>–</td>
</tr>
<tr>
<td>Age of patients (years)</td>
<td>13 – 17</td>
<td>10 – 18</td>
<td>12 – 18</td>
</tr>
</tbody>
</table>

Note. ● = evidence of a clinically important effect favouring active treatment; ○ = limited evidence of a clinically important effect favouring active treatment; ★ = evidence of clinically important effect favouring control; ○ = limited evidence of clinically important effect favouring control; × = there is unlikely to be a clinically important difference between groups; ? = the evidence is inconclusive; K = number of studies; N = total number of participants; NNTB = number needed to treat (benefit); NNTH = number needed to treat (harm).

*Control group was ‘standard care’.
†Control group was no treatment.
**Sensitivity analysis excluding KAHN1990 to remove heterogeneity.
Table 7. Evidence summary table for various psychological interventions versus waitlist control.

<table>
<thead>
<tr>
<th>Total no. of trials (total no. of participants)</th>
<th>Family therapy vs. waitlist</th>
<th>Group relaxation vs. waitlist</th>
<th>Self-modelling vs. waitlist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study ID</td>
<td>DIAMOND 2002</td>
<td>KAHN1990</td>
<td>KAHN1990</td>
</tr>
<tr>
<td>Remission - endpoint</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinician completed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSM</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>Self-report</td>
<td>○</td>
<td>K=2; N=55</td>
<td>○</td>
</tr>
<tr>
<td>CDI/BDI</td>
<td>K=1; N=32</td>
<td>Z</td>
<td>K=1; N=34</td>
</tr>
<tr>
<td>RADS</td>
<td>Z</td>
<td>K=1; N=34</td>
<td>K=1; N=34</td>
</tr>
<tr>
<td>Remission - follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinician completed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms - endpoint</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinician completed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDRS/HDRS</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>BID</td>
<td>○</td>
<td>K=1; N=34</td>
<td>K=1; N=34</td>
</tr>
<tr>
<td>Self-report</td>
<td>○</td>
<td>K=1; N=34</td>
<td>K=1; N=34</td>
</tr>
<tr>
<td>CDI/BDI</td>
<td>○</td>
<td>○</td>
<td>○</td>
</tr>
<tr>
<td>RADS/CES-D</td>
<td>Z</td>
<td>K=1; N=34</td>
<td>K=1; N=34</td>
</tr>
<tr>
<td>Depressive symptoms – follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinician completed</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>HDRS</td>
<td>Z</td>
<td>x</td>
<td>12 months</td>
</tr>
<tr>
<td>HDRS</td>
<td>Z</td>
<td>?</td>
<td>24 months</td>
</tr>
<tr>
<td>New</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RADS/CES-D</td>
<td>Z</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional status - endpoint</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAF</td>
<td>Z</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional status – follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAF</td>
<td>Z</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active treatment group attrition</td>
<td>Z</td>
<td>0% to 27%</td>
<td>0%</td>
</tr>
<tr>
<td>Treatment length (weeks)</td>
<td>6</td>
<td>5</td>
<td>6 – 8</td>
</tr>
<tr>
<td>Length of follow-up (mths)</td>
<td>6</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Age of patients (years)</td>
<td>13 – 18</td>
<td>10 – 14</td>
<td>10 – 14</td>
</tr>
</tbody>
</table>

Note. ● = evidence of a clinically important effect favouring active treatment; ○ = limited evidence of a clinically important effect favouring active treatment; ■ = evidence of clinically important effect favouring control; ⊙ = limited evidence of clinically important effect favouring control; x = there is unlikely to be a clinically important difference between groups; ? = the evidence is inconclusive; K = number of studies; N = total number of participants; NNTB = number needed to treat (benefit); NNTH = number needed to treat (harm).
6.2.8 Psychological interventions versus other psychological interventions/control

Table 8. Evidence summary table for CBT versus other psychological interventions/control intervention.

<table>
<thead>
<tr>
<th></th>
<th>CBT vs. non-directive supportive therapy/clinical management</th>
<th>CBT vs. IPT</th>
<th>CBT vs. relaxation</th>
<th>CBT vs. family therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of trials (total no. of participants)</td>
<td>3 RCTs (N = 387)</td>
<td>1 RCT (N = 38)</td>
<td>1 RCT (N = 53)</td>
<td>1 RCT (N = 72)</td>
</tr>
</tbody>
</table>

**Remission – endpoint**

**Clinician completed**

<table>
<thead>
<tr>
<th></th>
<th>CBT vs. non-directive supportive therapy/clinical management</th>
<th>CBT vs. IPT</th>
<th>CBT vs. relaxation</th>
<th>CBT vs. family therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSM</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td></td>
</tr>
<tr>
<td></td>
<td>K=2; N=129</td>
<td>K=1; N=48</td>
<td>K=1; N=72</td>
<td></td>
</tr>
<tr>
<td><strong>Self-report</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI/BDI</td>
<td>−</td>
<td>?</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>K=1; N=48</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MFQ</td>
<td>−</td>
<td>−</td>
<td>○</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>K=1; N=48</td>
<td></td>
</tr>
</tbody>
</table>

**Remission – follow-up**

**Clinician completed**

<table>
<thead>
<tr>
<th></th>
<th>CBT vs. non-directive supportive therapy/clinical management</th>
<th>CBT vs. IPT</th>
<th>CBT vs. relaxation</th>
<th>CBT vs. family therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSM</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td></td>
</tr>
<tr>
<td></td>
<td>?/24 mths; K=1; N=56/54</td>
<td>N=43/43</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Self-report</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI</td>
<td>−</td>
<td>?</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 months; K=1; N=40</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>MFQ-C</td>
<td>−</td>
<td>−</td>
<td>○</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>K=1; N=43</td>
<td></td>
</tr>
</tbody>
</table>

**Depressive symptoms - endpoint**

**Clinician completed**

<table>
<thead>
<tr>
<th></th>
<th>CBT vs. non-directive supportive therapy/clinical management</th>
<th>CBT vs. IPT</th>
<th>CBT vs. relaxation</th>
<th>CBT vs. family therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDRS</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td></td>
</tr>
<tr>
<td></td>
<td>K=1; N=223</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Self-report</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI/BDI</td>
<td>○</td>
<td>○</td>
<td>○</td>
<td></td>
</tr>
<tr>
<td></td>
<td>K=1; N=68</td>
<td>K=1; N=40</td>
<td>K=1; N=64</td>
<td></td>
</tr>
<tr>
<td>RADS</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td>MFQ-P</td>
<td>−</td>
<td>−</td>
<td>?</td>
<td>K=1; N=48</td>
</tr>
</tbody>
</table>

**Depressive symptoms – follow-up**

**Self-report**

<table>
<thead>
<tr>
<th></th>
<th>CBT vs. non-directive supportive therapy/clinical management</th>
<th>CBT vs. IPT</th>
<th>CBT vs. relaxation</th>
<th>CBT vs. family therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDI/BDI</td>
<td>−</td>
<td>?</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 mths; K=1; N=23</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RADS</td>
<td>−</td>
<td>−</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td>MFQ-P</td>
<td>−</td>
<td>−</td>
<td>?</td>
<td>3/6 mths; K=1; N=48</td>
</tr>
</tbody>
</table>

**Global improvement - endpoint**

<table>
<thead>
<tr>
<th></th>
<th>CBT vs. non-directive supportive therapy/clinical management</th>
<th>CBT vs. IPT</th>
<th>CBT vs. relaxation</th>
<th>CBT vs. family therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CGI-I</td>
<td>?</td>
<td>−</td>
<td>−</td>
<td></td>
</tr>
<tr>
<td></td>
<td>K=1; N=223</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Functional status – endpoint

<table>
<thead>
<tr>
<th>GAF/C-GAS</th>
<th>—</th>
<th>—</th>
<th>—</th>
<th>—</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discontinuation from treatment</td>
<td>K=1; N=255</td>
<td>K=1; N=48</td>
<td>K=1; N=53</td>
<td>K=1; N=72</td>
</tr>
<tr>
<td>Treatment length (weeks)</td>
<td>12 – 16</td>
<td>12</td>
<td>5 – 8</td>
<td>12 – 16</td>
</tr>
<tr>
<td>Length of follow-up (months)</td>
<td>0 – 24</td>
<td>3</td>
<td>3 – 6</td>
<td>—</td>
</tr>
<tr>
<td>Age of patients (years)</td>
<td>12 – 18</td>
<td>13 – 17</td>
<td>9 – 17</td>
<td>13 – 18</td>
</tr>
</tbody>
</table>

**Note.** ● = evidence of a clinically important effect favouring CBT; ○ = limited evidence of a clinically important effect favouring CBT; ⊙ = evidence of clinically important effect favouring control; ⊙ = limited evidence of clinically important effect favouring control; × = there is unlikely to be a clinically important difference between groups; ? = the evidence is inconclusive; K = number of studies; N = total number of participants; NNTB = number needed to treat (benefit); NNTH = number needed to treat (harm).

* Control group received placebo pill in addition to clinical management.
Table 9. Evidence summary table for CBT versus other psychological interventions/comparator intervention.

<table>
<thead>
<tr>
<th></th>
<th>Group CBT vs. group relaxation</th>
<th>Group CBT vs. behavioural problem solving/life skills training</th>
<th>Group CBT vs. self-modelling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no. of trials (total no. of participants)</td>
<td>2 RCTs (N = 54)</td>
<td>2 RCTs (N = 117)</td>
<td>1 RCT (N = 34)</td>
</tr>
<tr>
<td>Study ID</td>
<td>KAHN1990</td>
<td>ROHDE2004</td>
<td>KAHN1990</td>
</tr>
<tr>
<td></td>
<td>REYNOLDS1986</td>
<td>STARK1987</td>
<td></td>
</tr>
</tbody>
</table>

**Remission - endpoint**

<table>
<thead>
<tr>
<th></th>
<th>Clinician completed</th>
<th>Self-report</th>
<th>K=1; N=93</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI/BDI</td>
<td>? K=1; N=19</td>
<td>? K=1; N=19</td>
<td></td>
</tr>
<tr>
<td>MFQ</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

**Remission – follow-up**

<table>
<thead>
<tr>
<th></th>
<th>Clinician completed</th>
<th>Self-report</th>
<th>K=1; N=34</th>
</tr>
</thead>
<tbody>
<tr>
<td>DSM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MFQ-C</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

**Depressive symptoms - endpoint**

<table>
<thead>
<tr>
<th></th>
<th>Clinician completed</th>
<th>Self-report</th>
<th>K=2; N=110</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDRS</td>
<td>-</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BID</td>
<td>? K=1; N=34</td>
<td>? K=1; N=34</td>
<td></td>
</tr>
<tr>
<td>Self-report</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI/BDI</td>
<td>? K=1; N=34</td>
<td>? K=2; N=110</td>
<td>? K=1; N=34</td>
</tr>
<tr>
<td>RADS</td>
<td>? K=1; N=34</td>
<td>O K=1; N=34</td>
<td></td>
</tr>
<tr>
<td>MFQ-P</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

**Depressive symptoms – follow-up**

<table>
<thead>
<tr>
<th></th>
<th>Self-report</th>
<th>Functional status - endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDI/BDI</td>
<td>-</td>
<td>GAF/C-GAS</td>
</tr>
<tr>
<td>RADS</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>MFQ-P</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

**Global improvement - endpoint**

<table>
<thead>
<tr>
<th></th>
<th>CGI-I</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Discontinuation from treatment**

<table>
<thead>
<tr>
<th></th>
<th>? K=2; N=54</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Treatment length (weeks)**

<table>
<thead>
<tr>
<th></th>
<th>5 to 8 weeks</th>
<th>5 to 8 weeks</th>
<th>6 to 8 weeks</th>
</tr>
</thead>
</table>

**Length of follow-up (months)**

<table>
<thead>
<tr>
<th></th>
<th>1 month</th>
<th>1 to 12 months</th>
<th>1 month</th>
</tr>
</thead>
</table>

**Age of patients (years)**

<table>
<thead>
<tr>
<th></th>
<th>10 to 16 years</th>
<th>9 to 17 years</th>
<th>10 to 14 years</th>
</tr>
</thead>
</table>

Note. ● = evidence of a clinically important effect favouring CBT; ○ = limited evidence of a clinically important effect favouring CBT; ⬜ = evidence of clinically important effect favouring control; ⊕ = limited evidence of clinically important effect favouring control; ⬜ = there is unlikely to be a clinically important difference between groups; ? = the evidence is inconclusive; N = total number of participants; NNTB = number needed to treat (benefit); NNTH = number needed to treat (harm).
### Table 10. Evidence summary table for various psychological interventions versus other psychological interventions/‘standard care’/comparator intervention.

<table>
<thead>
<tr>
<th>Group relaxation vs. self-modelling</th>
<th>Family therapy vs. non-directive supportive therapy</th>
<th>Family therapy vs. individual psychotherapy</th>
<th>IPT vs. ‘standard care’</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total no. of trials (total no. of participants)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 RCT (N = 34)</td>
<td>1 RCT (N = 70)</td>
<td>1 RCT (N = 72)</td>
<td>1 RCT (N = 64)</td>
</tr>
<tr>
<td><strong>Study ID</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>KAHN1990</td>
<td>BRENT1997</td>
<td>TROWELL</td>
<td>MUFSON2004</td>
</tr>
</tbody>
</table>

#### Remission - endpoint

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group relaxation vs. self-modelling</th>
<th>Family therapy vs. non-directive supportive therapy</th>
<th>Family therapy vs. individual psychotherapy</th>
<th>IPT vs. ‘standard care’</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinician completed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSM/K-SADS</td>
<td></td>
<td>K=1; N=70</td>
<td>K=1; N=72</td>
<td></td>
</tr>
<tr>
<td>HDRS</td>
<td></td>
<td></td>
<td></td>
<td>K=1; N=63</td>
</tr>
<tr>
<td><strong>Self-report</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI/BDI</td>
<td></td>
<td></td>
<td></td>
<td>K=1; N=63</td>
</tr>
<tr>
<td>MFQ</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

#### Remission – follow-up

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group relaxation vs. self-modelling</th>
<th>Family therapy vs. non-directive supportive therapy</th>
<th>Family therapy vs. individual psychotherapy</th>
<th>IPT vs. ‘standard care’</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinician completed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSM/K-SADS</td>
<td></td>
<td></td>
<td>?</td>
<td></td>
</tr>
<tr>
<td><strong>Self-report</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MFQ-C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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</table>

#### Depressive symptoms - endpoint

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group relaxation vs. self-modelling</th>
<th>Family therapy vs. non-directive supportive therapy</th>
<th>Family therapy vs. individual psychotherapy</th>
<th>IPT vs. ‘standard care’</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinician completed</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDRS</td>
<td></td>
<td></td>
<td></td>
<td>K=1; N=63</td>
</tr>
<tr>
<td>BID</td>
<td>?</td>
<td>K=1; N=34</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Self-report</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI/BDI</td>
<td>?</td>
<td>K=1; N=34</td>
<td>?</td>
<td>K=1; N=62</td>
</tr>
<tr>
<td>RADS</td>
<td>?</td>
<td>K=1; N=34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MFQ-P</td>
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<td></td>
<td></td>
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</table>

#### Depressive symptoms – follow-up

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group relaxation vs. self-modelling</th>
<th>Family therapy vs. non-directive supportive therapy</th>
<th>Family therapy vs. individual psychotherapy</th>
<th>IPT vs. ‘standard care’</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Self-report</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI/BDI</td>
<td></td>
<td></td>
<td>?</td>
<td>K=1; N=72</td>
</tr>
<tr>
<td>RADS</td>
<td></td>
<td></td>
<td></td>
<td>K=1; N=72</td>
</tr>
<tr>
<td>MFQ-P</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Functional status - endpoint

<table>
<thead>
<tr>
<th>Measure</th>
<th>Group relaxation vs. self-modelling</th>
<th>Family therapy vs. non-directive supportive therapy</th>
<th>Family therapy vs. individual psychotherapy</th>
<th>IPT vs. ‘standard care’</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAF/C-GAS</td>
<td></td>
<td></td>
<td>?</td>
<td>K=1; N=63</td>
</tr>
<tr>
<td><strong>Attrition from the study protocol</strong></td>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Treatment length (weeks)

<table>
<thead>
<tr>
<th>Group relaxation vs. self-modelling</th>
<th>Family therapy vs. non-directive supportive therapy</th>
<th>Family therapy vs. individual psychotherapy</th>
<th>IPT vs. ‘standard care’</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 to 8 weeks</td>
<td>12 to 16 weeks</td>
<td>36 weeks</td>
<td>16 weeks</td>
</tr>
</tbody>
</table>

#### Length of follow-up (months)

<table>
<thead>
<tr>
<th>Group relaxation vs. self-modelling</th>
<th>Family therapy vs. non-directive supportive therapy</th>
<th>Family therapy vs. individual psychotherapy</th>
<th>IPT vs. ‘standard care’</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Age of patients (years)

<table>
<thead>
<tr>
<th>Group relaxation vs. self-modelling</th>
<th>Family therapy vs. non-directive supportive therapy</th>
<th>Family therapy vs. individual psychotherapy</th>
<th>IPT vs. ‘standard care’</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 to 14 years</td>
<td>13 to 18 years</td>
<td>12 to 18 years</td>
<td></td>
</tr>
</tbody>
</table>
Note. ● = evidence of a clinically important effect favouring treatment A; ○ = limited evidence of a clinically important effect favouring treatment A; ◊ = evidence of clinically important effect favouring treatment B; ◊ = limited evidence of clinically important effect favouring treatment B; × = there is unlikely to be a clinically important difference between groups; ? = the evidence is inconclusive; K = number of studies; N = total number of participants; NNTB = number needed to treat (benefit); NNTH = number needed to treat (harm).
Table 11. Evidence summary table for group CBT (+ parent) and guided self-help versus waitlist/group CBT.

<table>
<thead>
<tr>
<th>Total no. of trials (total no. of participants)</th>
<th>Group CBT (+ parent) vs. waitlist</th>
<th>Group CBT vs. group CBT (+ parent)</th>
<th>Guided self-help vs. waitlist</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission - endpoint</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinician completed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSM/K-SADS</td>
<td>○ K=2; N=116</td>
<td>? K=2; N=127</td>
<td></td>
</tr>
<tr>
<td>HDRS</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Self-report</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI/BDI</td>
<td>○ K=1; N=38</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>MFQ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remission – follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinician completed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSM/K-SADS</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Self-report</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>MFQ-C</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms – endpoint</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinician completed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDRS</td>
<td>? K=1; N=59</td>
<td>? K=1; N=69</td>
<td>● K=1; N=22</td>
</tr>
<tr>
<td>BID</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Self-report</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI/BDI</td>
<td>? (random effects) K=2; N=97</td>
<td>? (random effects) K=2; N=109</td>
<td>● K=1; N=22</td>
</tr>
<tr>
<td>RADS</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>MFQ-P</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Depressive symptoms – follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-report</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CDI/BDI</td>
<td>–</td>
<td>? 6/12/24 months; K=1; N=30/29/23</td>
<td>–</td>
</tr>
<tr>
<td>RADS</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>MFQ-P</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Functional status – endpoint</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinician completed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAF/C-GAS</td>
<td>? K=1; N=59</td>
<td>? K=1; N=69</td>
<td>–</td>
</tr>
<tr>
<td>Attrition from the study protocol</td>
<td>10% to 24%</td>
<td>? K=1; N=132</td>
<td>20%</td>
</tr>
<tr>
<td>Treatment length (weeks)</td>
<td>7 to 8 weeks</td>
<td>7 to 8 weeks</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Length of follow-up (months)</td>
<td>–</td>
<td>–</td>
<td>1 month</td>
</tr>
<tr>
<td>Age of patients (years)</td>
<td>14 to 18 years</td>
<td>14 to 18 years</td>
<td>~16 years</td>
</tr>
</tbody>
</table>

Note. ● = evidence of a clinically important effect favouring CBT/guided self-help; ○ = limited evidence of a clinically important effect favouring CBT/guided self-help; • = evidence of clinically important effect favouring control; ⊙ = limited evidence of clinically important effect favouring control; ✗ = there is unlikely to be a clinically important difference between groups; ? = the evidence is inconclusive; N = total number of participants; NNTB = number needed to treat (benefit).
6.2.9 Clinical summary

For individual outcomes, the quality of the evidence was generally moderate to low, reflecting the paucity of data and relatively small sample sizes of those studies included in the review.

6.2.9.1 Psychological treatments in general

The evidence regarding the effectiveness of psychological treatments suggests that most of such treatments share two common features. Firstly, a number of psychological treatments have been shown to be effective at treatment endpoint (see below for details) but no psychological treatments have been shown to maintain a significant difference with non-active control treatments at 1 year (or more) follow-up. The single study which did seem to show maintenance of gains at follow-up (TROWELL) involved a comparison of two active treatments (family therapy and individual psychodynamic therapy) without an inactive control condition. Secondly, even with the more effective psychological treatments, a significant proportion of young people remain depressed at the end of treatment or are highly at risk of later relapse (again, with the exception of one unpublished study, TROWELL). There is some evidence that treatments that specifically have planned booster or follow-up sessions may be effective in maintaining treatment gains.

6.2.9.2 Individual treatments

**Individual CBT**

The overall evidence for the effectiveness of individual CBT is inconclusive. Two studies have failed to show that CBT is more effective than waitlist or general clinical management (ROSSELO1999, TADS2004). However, three studies of clinic-referred samples (WOOD1996, VOSTANIS1996, BRENT1997) have indicated clinically important improvement compared with comparison treatments (relaxation, non-directive supportive therapy and systemic family behavioural therapy). These studies indicate that CBT is likely to reduce the length of the depressive episode compared with these treatments. These differential effects were not sustained at longer-term follow-up although this was mainly due to ongoing improvements of comparison treatments, rather than relapse in those receiving CBT.

**Interpersonal therapy (IPT)**

There is limited evidence from three studies (MUFSON1999, MUFSON2004, ROSSELO1999) indicating the efficacy of IPT compared with waitlist or ‘standard care’ in increasing the chance of remission and reducing depressive symptoms. In direct comparison with individual CBT the evidence was inconclusive.
**Individual psychodynamic psychotherapy**
There are no published studies of the effectiveness of psychoanalytic psychotherapy with an untreated or placebo control group. The results of a multi-centre study comparing psychoanalytic psychotherapy and family therapy are currently being prepared for publication. The study recruited moderate to severe cases and appears to have provided good quality treatment. Preliminary results indicate high rates of remission and excellent maintenance of gains at follow-up, in both treatment arms, with limited evidence that family therapy reduced depressive symptoms more rapidly (TROWELL).

### 6.2.9.3 Group treatments

**Group cognitive behaviour therapy (CBT)**
There is considerable evidence from a number of studies to suggest that group CBT is an effective treatment of adolescents for increasing the chance of remission and reducing depressive symptoms compared with waitlist conditions/no treatment/‘standard care’ (CLARKE1999, CLARKE2002, KAHN1990, LEWINSOHN1990, REYNOLDS1986, WEISZ1997). However, the majority of evidence for this is from recruited samples from the USA and the effects of treatment were not maintained at longer follow-up, although this was mainly due to ongoing improvements of comparison treatments, rather than relapse in those receiving group CBT. Group CBT has been directly compared with other treatments such as group relaxation, problem-solving and self-modelling, with either inconclusive or limited evidence favouring group CBT. It is not possible to determine how it compares with other more frequently used treatments. The evidence is inconclusive as to whether this would be an effective treatment for clinic-referred young people with clinical depression.

### 6.2.9.4 Treatments involving the parents

**Family therapy**
There is limited evidence from one study (DIAMOND2002) about the efficacy of family therapy compared with a waitlist condition. A second study (BRENT1997) comparing family therapy with non-directive supportive therapy was inconclusive, and as described above, suggested poorer outcomes relative to individual CBT. A recent multi-centre comparison study (TROWELL) has indicated similar or better efficacy than individual psychodynamic psychotherapy, with high rates of remission and symptom reduction.

**Parent involvement in psychological treatments**

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There was inconclusive evidence from two studies (CLARKE1999, LEWINSOHN1990) to determine whether the additional involvement of parents in a group CBT treatment increased effectiveness.

6.2.9.5 Guided self-help
There is evidence from one small trial (ACKERSON1998) suggesting that guided self-help may improve depressive symptoms when compared with waitlist.

6.3 Association between primary outcomes and characteristics of therapist/patient

6.3.1 Introduction
There is little evidence relating to the association between outcome and therapist characteristics.

In contrast, there were many aspects of service user characteristics identified in a variety of studies, which correlated with outcome. Many of these are well known in clinical practice, particularly that comorbidity makes it less likely that treatment will achieve a good outcome. Around 70% of patients treated for depression were found to have comorbid disorders particularly anxiety (Emslie, 2003). We found the following statement highly relevant as regards clinical practice:

‘The search for a pure i.e. non comorbid form of very early onset affective illness may be a futile undertaking, as comorbidity may be an intrinsic characteristic of children with affective disorders’ (Emslie, 2003, p. 445, op. cit.).

Many authors also stressed the importance of assessing the network around the child because many factors, for example, parental mental ill health (including both affective and non-affective disorders), socio-economic disadvantage and family/parental dysfunction (particularly the impact of divorce and bereavement) (Beardslee, 1993) were negatively correlated with outcome and are also important in treatment selection.

6.3.2 Descriptive review

6.3.2.1 Therapist characteristics
The only study identified was Wiesz (1995), which showed better outcome in treating depression if qualified professional therapists were used rather than non-professional workers.
The importance of a better treatment alliance with the patient was also mentioned (Diamond A), but the evidence was from a case record study rather than an RCT.

6.3.2.2 Service user characteristics

Comorbidity was the most important factor that negatively correlates with treatment outcome and affects the chances of relapse (Belsher & Brent, 1998; Emslie, 2003). There was some evidence that depression which is comorbid with anxiety may be helped by CBT as this has been shown to be effective in reducing anxiety (Brent, 1998).

Severity of the depression, especially higher levels of chronicity, suicidality and hopelessness, as well as higher levels of cognitive distortion, were all negatively correlated with outcome (Emslie 2003; Brent 1998). This may contribute to the difference in outcomes between clinical and advertised or recruited samples (Brent 1998).

Poor parenting, negative interactions and higher family dysfunction/stress were also correlated with negative outcome (Emslie, 2003; Brent, 1998). Children with parents who have an affective disorder experience a rate of major depressive disorder 2.6 times greater than children who have no disorder and their disorders are longer in duration and have an earlier onset. There were also multiple risk factors involved since non-affective disorder was present in the majority of parents and often there was psychiatric disorder in both parents. Divorce or separation also had occurred in a substantial number of families. In fact the main effects of parental affective disorder was significant only when it was in combination with divorce (Beardslee, 1993).

The presence of abuse in all forms as well as trauma was shown in a multitude of studies to be correlated with higher rates of depression and more difficulty in treating this (Becker et al, 1991; Bergen et al, 2003; Brown & Flisher, 1997; Hill & Horesg, 2003; Meyerson et al, 2002; Sadowski 2002; Ramchandani & Jones, 2003).

One would expect the motivation of the patient to change to be correlated with treatment outcome but there was no directly reported evidence of this, other than the frequent report that hopelessness in the patient was negatively correlated with outcome. Similarly the effect of parental depression has been highlighted and this too may be mediated through hopelessness about any treatment proposed for the child. This may be directly communicated to the child or enacted through poor treatment adherence (Brent, 1998; Emslie, 2003).

Parental involvement, treatment attendance, avoiding premature termination and matching parental/patient expectancies to treatment predicted positive
treatment outcome. The presence of social support was also shown to be important especially for girls (Nock & Ramchandani, 2003; Emslie, 2003; Schraedley, 1999).

6.3.3 Clinical summary
Although little is known about therapist factors that influence outcome, there is some evidence that professionally trained therapists have better results than parapersonnel with this group. As there is some evidence that a positive treatment alliance predicts better outcome, therapists who are better able to create this alliance with depressed young people are likely to be more successful.

Several characteristics of service users and their carers have been found to relate to psychological treatment outcome. Comorbid conditions and more severe or complex symptomatology are associated with less good outcomes. Parental depression/mental ill health, the impact of divorce, separation and bereavement are especially important family factors; feelings of hopelessness and family dysfunction can impact on the child in many different ways. Clinical populations generally present with comorbid conditions and more complex sets of problems within the individual, the family and the network; multi-modal treatments in sequence or parallel are therefore likely to be required.

6.4 Relapse prevention

6.4.1 Introduction
As described in Chapter 3 of this Guideline, around 30% of cases recur within 5 years, many within a year of the earlier episode, and some of these young people develop episodes into adult life. Furthermore, as shown in our systematic review, a proportion of cases in all treatment trials remains diagnosable at the end of treatment, or remain symptomatic at a level below the threshold for diagnosis. A very important question for the care of children and young people with depression is thus whether there are ways to reduce the likelihood of either a relapse of depression following remission, or a long-term state of unhappiness and poor functioning following partial improvement during treatment. Clinically, it is likely that attention needs to be paid to social factors that may maintain a depressed state, or cause further episodes. Such factors would be likely to include relationship difficulties in the family or peer group, including for adolescents difficulty in establishing sexual relationships and achieving greater independence from parents. Difficulties arising from cultural and ethnic differences may be important, as may physical illness or any kind of disability, persistent comorbid disorders, and concern about family members e.g. parental psychiatrist illness.

A systematic search of the literature identified no RCTs concerning the prevention of relapse of depression in children and/or young people that met
the eligibility criteria set by the GDG. None of the other reports identified presented compelling evidence.
6.4.2 Databases searched and inclusion/exclusion criteria

Table 12. Databases searched and inclusion/exclusion criteria for studies of relapse prevention.

<table>
<thead>
<tr>
<th>Electronic databases</th>
<th>MEDLINE, EMBASE, PsycINFO, Cochrane Library</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date searched</td>
<td>Database inception to February 2004; table of contents February to September 2004</td>
</tr>
<tr>
<td>Study design</td>
<td>Controlled trials</td>
</tr>
<tr>
<td>Patient population</td>
<td>Participants aged 5-18 years old with recognised symptoms of depression</td>
</tr>
<tr>
<td>Interventions included</td>
<td>- Cognitive behaviour therapy (CBT)</td>
</tr>
<tr>
<td></td>
<td>- Assessment only</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Relapse</td>
</tr>
</tbody>
</table>

6.4.3 Studies considered

The review team conducted a new systematic search for controlled trials that assessed the efficacy of psychological interventions for children and adolescents with depression for the prevention of relapse.

Two trials met the eligibility criteria: one controlled trial (CLARKE1999) comparing group CBT booster sessions (1-2 meetings) with assessment only using a 24-month follow-up, and one study (KROLL1996) comparing continuation with CBT (after acute phase treatment) with a historical control group using a 6-month follow-up.

Table 13. Study information table for trials of CBT booster/continuation treatment versus assessment only/no treatment.

<table>
<thead>
<tr>
<th>Total no. of trials (total no. of participants)</th>
<th>1 controlled trial (N = 41)</th>
<th>1 trial with historical control (N = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study ID</td>
<td>CLARKE1999</td>
<td>KROLL1996</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>MDD or dysthymia (DSM-III-R)</td>
<td>MDD (DSM-III-R)</td>
</tr>
<tr>
<td>Length of follow-up</td>
<td>12 &amp; 24 months</td>
<td>6 months</td>
</tr>
<tr>
<td>Age</td>
<td>14 to 18 years</td>
<td>10 to 17 years</td>
</tr>
</tbody>
</table>

Note. CBT = Cognitive behaviour therapy; MDD = Major depressive disorder; DSM = Diagnostic Statistical Manual.

6.4.4 Continuation/booster treatment

CLARKE1999 randomly assigned participants who had completed an acute phase treatment of group CBT to 1 of 3 two-year follow-up conditions: (1)

* Here and elsewhere in the guideline, each study considered for review is referred to by a study ID in capital letters (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).
booster sessions (1-2 meetings) and independent assessments every 4 months; (2) assessment only every 4 months; or (3) assessment only every 12 months. For the purpose of this review, relapse (defined as meeting criteria for unipolar depression) was analysed at 12 and 24 months in those participants who had recovered by the end of the acute phase treatment.

At the end of 12 and 24 months, the evidence was inconclusive regarding the risk of relapse, although there is only a small probability that group CBT booster sessions prevented relapse.

KROLL1996 compared the risk of relapse in participants who continued to receive group CBT for 6 months (after a course of five to eight sessions of CBT during the acute episode) with a historical control group drawn from a previous study of CBT (WOOD1995). All participants had remitted from MDD by the end of the acute phase.

By the end of 6-month follow-up, there was limited evidence that continuation of group CBT may reduce the risk of relapse (RR = 0.35; 95% CI, 0.11 to 1.14).

6.4.5 Clinical summary

We found no evidence to properly assess whether psychological interventions can prevent relapse in children and/or young people with depression. The evidence from non-randomised studies suggests that continuation of group CBT, but not booster sessions, may reduce the risk of relapse. Nevertheless, until further research is conducted using adequately designed relapse prevention studies, no conclusion can be reached.

6.5 Clinical practice recommendations

6.5.1 Psychological interventions

Watchful waiting

6.5.1.1 For children and young people with diagnosed 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’). (C) (1.5.1.1 NICE)
6.5.1.2 Healthcare professionals should make contact with children and young people with depression who do not attend follow-up appointments. (C) (1.5.1.2 NICE)

Psychological treatments for mild depression

6.5.1.3 Following a period of up to 4 weeks of watchful waiting, all children and young people with continuing mild depression and without significant comorbid problems or signs of suicidal ideation, should be offered individual non-directive supportive therapy, group cognitive behaviour therapy or guided self-help for a time-limited period (approximately 2 to 3 months). This could be provided by appropriately trained staff in primary care, schools, social services and the voluntary sector as well as in tier 2 CAMHS. (B) (1.5.2.1 NICE)

6.5.1.4 Children and young people with mild depression who do not respond after 2 to 3 months to non-directive supportive therapy, group cognitive behavioural therapy or guided self-help should be referred for review by a tier 2/3 CAMHS team. (GPP) (1.5.2.2 NICE)

Psychological treatments for moderate to severe depression

6.5.1.5 Children and young people presenting with moderate to severe depression should be reviewed by a CAMHS tier 2/3 team. (B) (1.6.1.1 NICE)

6.5.1.6 Children and young people with moderate to severe depression should be offered, as a first line treatment, a specific, brief (up to 15 sessions, over at least 15 weeks) psychological intervention (individual cognitive behaviour therapy, interpersonal therapy or family therapy). (B) (1.6.1.2 NICE)

6.5.2 Association between primary outcomes and characteristics of therapist/patient

6.5.2.1 Before any treatment is commenced, healthcare professionals should describe in writing the social network around the child or young person. This should include identifying factors that may impact both positively and negatively on the efficacy of the treatments offered as well as on their compliance. (B) (1.1.5.2 NICE)
6.5.2.2 Professionally trained therapists should provide the psychological treatment of clinically depressed young people wherever possible. (B) (1.1.5.4 NICE)

6.5.2.3 Therapists should develop a joint treatment alliance with the family. If this proves difficult consideration should be given to providing the family with an alternative therapist. (C) (1.1.5.5 NICE)

6.5.2.4 Comorbid diagnoses and social and educational problems should be assessed and treated, either in sequence or in parallel with the treatment for depression. (B) (1.1.5.6 NICE)

6.5.2.5 Attention should be paid to the possible need for parents’ own psychiatric problems (particularly depression) to be treated in parallel, if the child is to improve. (B) (1.1.5.7 NICE)

7 Pharmacological and physical treatment of depression in children and young people

7.1 Introduction
In the absence, until relatively recently, of good quality controlled trials of pharmacological interventions in child and adolescent populations, treatment practice has relied on extrapolation from the results of studies on adults. The mainstay of pharmacological treatment has been antidepressant drugs, initially tricyclic antidepressants and more recently selective serotonin re-uptake inhibitors (SSRIs) and other atypical antidepressants. Other drugs such as lithium salts and antipsychotics have been tried but their use is rare and usually reserved for young people with severe, psychotic and chronic depression. Lithium has also been used to prevent relapse of depression.

7.2 Prescribing for children and young people
In the UK, drug manufacturers do not recommend these drugs for the treatment of depression in those under the age of 16 years and the drugs themselves are not licensed for this use in this age group. However despite this, considerable clinical experience of their use in young people has been developed, initially from open trials and more recently from controlled evaluations of drug treatments.

In 2000, the Royal College of Paediatrics and Child Health issued a policy statement on the use of unlicensed medicines or the use of licensed medicines
for unlicensed applications, in children and young people. This states clearly that such use is necessary in paediatric practice and that doctors are legally allowed to prescribe unlicensed medicines where there are no suitable alternatives and where the use is justified by a responsible body of professional opinion (Joint Royal College of Paediatrics and Child Health/Neonatal and Paediatric Pharmacists Group Standing Committee on Medicines, 2000).

7.3 The Regulatory Framework

In December 2003, following a review by an Expert Working Group of the Committee on Safety of Medicines (CSM, 2003), the CSM advised that the balance of risks and benefits for the treatment of major depressive disorder in under 18s was unfavourable for sertraline, citalopram and escitalopram, and not assessable for fluvoxamine (Duff, 2003c). It had previously advised that paroxetine and venlafaxine should not be used in the treatment of depressive illness in children (June and September 2003, respectively; Duff, 2003a, 2003b). Despite the lack of a marketing authorisation for fluoxetine in the treatment of major depressive disorder, the CSM advised that the balance of risks and benefits for this drug was favourable.

This judgement means that the use of all SSRIs and other atypical antidepressants (except fluoxetine) in the treatment of depression in under 18s is contraindicated. However, the CSM also made clear that child and adolescent psychiatrists are able to prescribe SSRIs other than fluoxetine in certain circumstances, for example, where drug treatment is indicated but a patient is intolerant of or unresponsive to fluoxetine.

In October 2004, following a review of antidepressant medication for children and young people, the US Food and Drug Administration (FDA) directed manufacturers to add a "black box" warning to the health professional labelling of all antidepressant medications. Currently fluoxetine is the only medication approved for the treatment of major depressive disorder in paediatric patients. The “black box” warning will indicate that:

“Antidepressants increase the risk of suicidal thinking and behavior (suicidality) in children and adolescents with MDD and other psychiatric disorders.

Anyone considering the use of an antidepressant in a child or adolescent for any clinical use must balance the risk of increased suicidality with the clinical need.

Patients who are started on therapy should be observed closely for clinical worsening, suicidality, or unusual changes in behavior.
Families and caregivers should be advised to closely observe the patient and to communicate with the prescriber.

A statement regarding whether the particular drug is approved for any paediatric indication(s) and, if so, which one(s).” (FDA, 2004)

The FDA recommends that “paediatric patients being treated with antidepressants for any indication should be closely observed for clinical worsening, as well as agitation, irritability, suicidality, and unusual changes in behavior, especially during the initial few months of a course of drug therapy, or at times of dose changes, either increases or decreases. This monitoring should include daily observation by families and caregivers and frequent contact with the physician. It is also recommended that prescriptions for antidepressants be written for the smallest quantity of tablets consistent with good patient management, in order to reduce the risk of overdose” (FDA, 2004).

7.4 Antidepressant drugs

7.4.1 Introduction
Tricyclic antidepressants are thought to influence mood via their ability to block the synaptic re-uptake of monoamines including noradrenaline (NA), 5-hydroxytryptamine (5HT or serotonin) and dopamine (DA). However, these drugs also have significant side effects and high toxicity in overdose. As a result, newer types of antidepressants have been developed that retain the ability to elevate mood whilst having fewer side effects and being less toxic in overdose. These drugs are also thought to influence mood via their ability to raise levels of intra-synaptic monoamines.

7.4.2 Databases searched and inclusion/ exclusion criteria
Table 14. Databases searched and inclusion/ exclusion criteria for clinical effectiveness and safety of antidepressant drugs.

<table>
<thead>
<tr>
<th>Electronic databases</th>
<th>MEDLINE, EMBASE, PsycINFO, Cochrane Library</th>
</tr>
</thead>
<tbody>
<tr>
<td>Search dates</td>
<td>Databases: inception to January 2004 (key journals searched using the electronic table of contents service until September 2004)</td>
</tr>
<tr>
<td>Study design</td>
<td>RCT</td>
</tr>
<tr>
<td>Patient population</td>
<td>Participants aged 5-18 years old diagnosed with depression</td>
</tr>
</tbody>
</table>
| Interventions        | - Tricyclic and related antidepressants  
                      | - Selective serotonin re-uptake inhibitors (SSRIs: fluoxetine, paroxetine, sertraline, citalopram)  
                      | - Other atypical antidepressants (venlafaxine, mirtazapine, nefazodone)  
                      | - Placebo |
| Outcomes             | Remission, response to treatment, symptom levels, clinical improvement, severity of illness, functional status, adverse events, suicidality, discontinuation from treatment for any reason |
| Exclusion criteria   | |

7.4.3 Studies considered
The review team conducted a new systematic search for RCTs that assessed the efficacy and/or safety of antidepressant drugs for children and adolescents with depression.

Twenty-six trials met the eligibility criteria set by the GDG, providing data on 3874 participants. Of these, nine were unpublished trials reviewed by the CSM (CSM, 2003) or FDA (Hammad, 2004), and the remainder were published in peer-reviewed journals between 1987 and 2004. In addition, 37 other studies were excluded from the analysis. The most common reason for exclusion was that there was no control group (further information about both included and excluded studies can be found in Appendix R).

Of the 26 included trials, there were eight involving a comparison of a tricyclic antidepressant with placebo, 17 involving a comparison of an SSRI/atypical antidepressant with placebo, two involving a comparison of an SSRI with a tricyclic antidepressant, and one involving a comparison of a reversible MAOI with placebo. Of the trials involving an SSRI, there were four published trials of fluoxetine, one published and two unpublished trials of paroxetine, two trials of sertraline (published in one paper using a combined analysis), and one published and one unpublished trial of citalopram (Table 15). Of the trials involving a comparison of an atypical antidepressant with placebo, there was one published and two unpublished trials of venlafaxine, two unpublished trials of mirtazapine, and two unpublished trials of nefazodone (Table 16). Of the trials involving a comparison of a SSRI with a tricyclic antidepressant, there were two published trials of paroxetine versus clomipramine or imipramine (Table 16).

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7 Here and elsewhere in the guideline, each study considered for review is referred to by a study ID (primary author and date of study publication, except where a study is in press or only submitted for publication, then a date is not used).
Table 15. Study information table for tricyclic antidepressants and individual SSRIs versus placebo.

<table>
<thead>
<tr>
<th>Study ID</th>
<th>illuminated with tricyclic antidepressants</th>
<th>Fluoxetine</th>
<th>Paroxetine</th>
<th>Sertraline</th>
<th>Citalopram</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Published only</td>
<td>Published only</td>
<td>Published + unpublished</td>
<td>Published + unpublished</td>
<td>Unpublished only</td>
</tr>
<tr>
<td><strong>Total no. of trials (total no. of participants)</strong></td>
<td>8 RCTs (567)</td>
<td>4 RCTs (576)</td>
<td>3 RCTs (638)</td>
<td>2 RCTs (1 publication) (376)</td>
<td>2 RCTs (422)</td>
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<tr>
<td><strong>Study ID</strong></td>
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<td>EMLIE 1997</td>
<td>KELLER 2001</td>
<td>WAGNER 2003*</td>
<td>WAGNER 2004**</td>
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<td>KUTCHER 1994</td>
<td>KUTCHER 1994</td>
<td>STUDY 2</td>
<td>STUDY 3</td>
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<tr>
<td><strong>Diagnosis</strong></td>
<td>MDD (DSM-III)</td>
<td>MDD (DSM-IV)</td>
<td>MDD (DSM-IV)</td>
<td>MDD (DSM-IV)</td>
<td>MDD (DSM-IV)</td>
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<tr>
<td><strong>Baseline severity</strong></td>
<td>CDRS-R range: 49.9 (4.2) to 51.3 (4.4)</td>
<td>CDRS range: 57.1 (9.9) to 58.5 (10.15)</td>
<td>HDRS: 18.98 (11)</td>
<td>CDRS-R: 64.3 (11)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Treatment length (range)</strong></td>
<td>9 to 18 weeks</td>
<td>7 to 12 weeks</td>
<td>8 to 12 weeks</td>
<td>10 weeks</td>
<td>8 to 12 weeks</td>
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<tr>
<td><strong>Age (range)</strong></td>
<td>6 to 20 years</td>
<td>7 to 18 years</td>
<td>7 to 18 years</td>
<td>6 to 17 years</td>
<td>7 to 18 years</td>
</tr>
</tbody>
</table>

MDD = Major Depressive Disorder; DSM = Diagnostic and Statistical Manual of Mental Disorders; CDRS = Children's Depression Rating Scale; HDRS = Hamilton Depression Rating Scale.

*Reported as SERTRALINE STUDY 1 and SERTRALINE STUDY 2 by the CSM (2003).

**Reported as CITALOPRAM STUDY 1 by the CSM (2003).
Table 16. Study information table for atypical antidepressants versus placebo and SSRIs versus tricyclic antidepressants.

<table>
<thead>
<tr>
<th></th>
<th>Venlafaxine</th>
<th>Mirtazapine</th>
<th>Nefazodone</th>
<th>SSRIs vs. tricyclic anti-depressants</th>
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<tbody>
<tr>
<td></td>
<td>Published +</td>
<td>Unpublished</td>
<td>Unpublished</td>
<td>Published only</td>
</tr>
<tr>
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<td>MIRTAZAPINE STUDY1</td>
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<td>Baseline severity</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>HDRS range: SSRIs: 18.98 (4.15) to 24.1 (5.4); Tricyclics: 18.11 (4.19) to 22.9 (4.1)</td>
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<td>Treatment length</td>
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<td>Age (range)</td>
<td>6 to 17 years</td>
<td>7 to 17 years</td>
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</tr>
</tbody>
</table>

MDD = Major Depressive Disorder; DSM = Diagnostic and Statistical Manual of Mental Disorders; HDRS = Hamilton Depression Rating Scale.
7.4.4 Tricyclic antidepressants and individual SSRIs versus placebo

Table 17 summarises both benefits and harms of tricyclic antidepressants and individual SSRIs versus placebo (full results can be found in Appendix R).

Table 17. Evidence summary table for tricyclic antidepressants and individual SSRIs versus placebo
### Tricyclic anti-depressants

<table>
<thead>
<tr>
<th>Published only</th>
<th>Published only*</th>
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<th>Published + unpublished</th>
<th>Published + unpublished</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 RCTs (567)</td>
<td>2 RCTs (315)</td>
<td>3 RCTs (658)</td>
<td>2 RCTs (376)</td>
<td>2 RCTs (422)</td>
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### Remission

**Clinician completed**

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<th>CDRS/HDRS or DSM criteria</th>
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</thead>
<tbody>
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<td>-</td>
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### Response

**Clinician completed**

<table>
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<tr>
<th>CDRS/HDRS</th>
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<td>×</td>
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<td>K=2; N=364</td>
<td>K=1; N=174</td>
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</table>

### Depressive symptoms

**Clinician completed**

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<th>K-SADS</th>
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<table>
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<th>Published + unpublished</th>
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### Self-report

**BDI**

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### Clinical Improvement

**Clinician completed**

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### Severity of illness

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### Functional status

**Clinician completed**

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### Harms

**Any serious adverse event**

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### Suicidal behaviour/ideation (FDA)

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### Other adverse event

**Adverse event (Asberg SES)**

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</tr>
<tr>
<td>K=2; N=373</td>
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<td></td>
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<tr>
<td>K=2; N=407</td>
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**harm-related adverse event**

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<td>K=2; N=373</td>
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**suicide ideation (SIQ)**

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**gastro-intestinal problems**

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**treatment-emergent adverse event**

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**early discontinuation because of**

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<th>Remission</th>
<th>Suicide attempt</th>
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<table>
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<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
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<table>
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<th>NNTB/NNTH</th>
<th>Remission</th>
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</tr>
<tr>
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<td>NNTB 6 (4 to 15)</td>
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<td>NNTB 7 (4 to 100)</td>
</tr>
<tr>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>NNTB 34 (NNTB 5 to ∞ to NNTH 8)</td>
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<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>NNTB 9 (NNTB 4 to ∞ to NNTH 100)</td>
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<table>
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<th>Serious adverse events</th>
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<td>0.9% vs. 3.6%:</td>
</tr>
<tr>
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<td>12% vs. 4.4%:</td>
</tr>
<tr>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>3.7% vs. 3.3%:</td>
</tr>
<tr>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>79% vs. 70.1%:</td>
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<table>
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<th>Suicidal behaviour/ideation (FDA)</th>
<th>Remission</th>
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</thead>
<tbody>
<tr>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>5.9% vs. 4.5%:</td>
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<td>3.2% vs. 1.4%:</td>
</tr>
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<td>2.6% vs. 1.1%:</td>
</tr>
<tr>
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<td>4.6% vs. 3.4%:</td>
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<table>
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<th>Remission</th>
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</thead>
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<td>25.3% vs. 5.9%:</td>
</tr>
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<td>5.7% vs. 6.3%:</td>
</tr>
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<td>10.5% vs. 5.2%:</td>
</tr>
<tr>
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<td>9.0% vs. 2.7%:</td>
</tr>
<tr>
<td><img src="https://via.placeholder.com/150" alt="Image" /></td>
<td>8.6% vs. 7.1%:</td>
</tr>
</tbody>
</table>

Note. ● = evidence of a clinically important effect favouring drug; ○ = limited evidence of a clinically important effect favouring drug; ♦ = limited evidence of clinically important effect favouring placebo; ✖ = there is unlikely to be a clinically important difference between drug and placebo; ? = the evidence is inconclusive; K = number of studies; N = total number of participants; NNTB = number needed to treat (benefit); NNTH = number needed to treat (harm).

*Data are published except for suicide behaviour that includes unpublished data from the two trials of MDD and from one trial of obsessive-compulsive disorder.
†Outlier removed from analysis because of heterogeneity (KLEIN1994).
‡Reported as not statistically significant without further data.
§Treatment-emergent adverse events.
For individual SSRIs, treatment-emergent adverse events reported by 5% or more of the patients treated with the active drug are displayed in Figure 1 to Figure 4.

**Figure 1.** Treatment-emergent adverse events in patients taking fluoxetine or placebo: pooled placebo-controlled data.

![Graph showing treatment-emergent adverse events in fluoxetine treated patients](image)

**Figure 2.** Treatment-emergent adverse events in patients taking paroxetine or placebo: pooled placebo-controlled data.

![Graph showing treatment-emergent adverse events in paroxetine treated patients](image)
Figure 3. Treatment-emergent adverse events in patients taking sertraline or placebo: pooled placebo-controlled data.

Adverse events reported by 5% or more of the sertraline treated patients

---

Figure 4. Treatment-emergent adverse events in patients taking citalopram or placebo: pooled placebo-controlled data (sample size varied depending on adverse event).

Adverse events reported by 5% or more of the citalopram treated patients
7.4.5 Selective serotonin reuptake inhibitors versus tricyclic and related antidepressants, and atypical antidepressants versus placebo

Table 18 summarises both benefits and harms of SSRIs versus tricyclic antidepressants and venlafaxine/ mirtazapine versus placebo (full results can be found in Appendix R).

Table 18. Evidence summary table for SSRIs versus tricyclic antidepressants, and atypical antidepressants versus placebo.
### SSRIs vs. tricyclic antidepressants

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<td>3 RCTs (374)</td>
<td>2 RCTs (258)</td>
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</table>

### Remission

**Clinician completed**
- CDRS/HDRS
  - Published
  - K=1; N=188

### Response

**Clinician completed**
- CDRS/HDRS
  - ?
  - K=1; N=188

### Depressive symptoms

**Clinician completed**
- K-SADS
  - Published
  - K=1; N=171
- CDRS/HDRS
  - ?
  - K=1; N=184
  - K=3; N=367
  - K=2; N=249

### Clinical Improvement

**Clinician completed**
- CGI-I
  - Published
  - K=2; N=309

### Harms

- Side effects
  - Published
  - K=2; N=309
- Suicidal behaviour/ideation (FDA)
  - Published
  - K=2; N=361
  - K=1; N=259
- Discontinuation because of adverse events
  - Published
  - K=2; N=309
  - K=2; N=361
  - K=1; N=258
- Discontinuation for any reason
  - Published
  - K=2; N=309

### NNTB/NNTH

- Remission (or alternatively response)
  - Published
  - NNTB=9 (NNTB 4 to ∞ to NNTH 50)
  - K=1; N=188
  - 0.6% vs. 0%: NNTH 170 (NNTH 38 to ∞ to NNTB 68)
- Suicidal behaviour/ideation (FDA)
  - Published
  - 4.4% vs. 0%: NNTH 23 (13 to 96)
- Discontinuation because of adverse events
  - Published
  - 14.7% vs. 28.1%: NNTB=9 (NNTB 4 to ∞ to NNTH 10)
  - 9.9% vs. 2.8%: NNTH 14 (7 to 83)
  - 5.3% vs. 3.4%: NNTH 53 (NNTH 15 to ∞ to NNTH 32)
- Length of treatment
  - Published
  - 8 wks
- Age of patients
  - Published
  - 12 - 20 yrs
  - 6 - 17 yrs
  - 7 - 17 yrs

### Note.
- ● = evidence of a clinically important effect favouring drug;
- ○ = limited evidence of a clinically important effect favouring drug;
- ⚫ = evidence of clinically important effect favouring placebo;
- ⚪ = limited evidence of clinically important effect favouring placebo;
- × = there is unlikely to be a clinically important difference between drug and placebo;
- ? = the evidence is inconclusive;
- K = number of studies;
- N = total number of participants;
- NNTB = number needed to treat (benefit);
- NNTH = number needed to treat (harm).

For venlafaxine and mirtazapine, treatment-emergent adverse events reported by 5% or more of the patients treated with the active drug are displayed in Figure 5 and Figure 6.
7.4.6 Safety of selective serotonin reuptake inhibitors/ atypical antidepressants versus placebo

The safety of SSRIs/ atypical antidepressants was further assessed by pooling the data on suicide behaviour/ ideation (full results can be found in Appendix R). When all available data were combined, there was limited evidence that SSRIs/ atypical antidepressants increase the risk of suicide behaviour/ ideation (3.1% vs. 1.8%; RR = 1.79; 95% CI, 1.15 to 2.79). When data from SSRIs were pooled, there remained limited evidence of an increased risk of suicide behaviour/ ideation (4.1% vs. 2.7%; RR = 1.54; 95% CI, 0.66 to 2.46). When all available data were combined, there was limited evidence that SSRIs/ atypical antidepressants increase the risk of early discontinuation of treatment because of adverse events (8.6% vs. 4.8%; RR = 1.79; 95% CI, 1.30 to 2.46).

7.4.7 Clinical summary

For individual outcomes, the quality of the evidence was generally moderate to low, reflecting the paucity of data and relatively small sample sizes of those studies available. Interpretation of harm related outcomes, especially suicidality, was often difficult due to the short duration of some trials and

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because the trials were not necessarily designed to measure harm related outcomes.

**Tricyclic antidepressants**

In children and young people, it is unlikely that tricyclic antidepressants have clinically important benefits over placebo for remission, response to treatment (50% reduction in symptoms) or reduction in symptoms.

At least in young people, there is limited evidence that tricyclics produce more side effects than placebo and are more likely to lead to discontinuation of treatment.

**Fluoxetine (SSRI)**

Fluoxetine (20 mg/day for 7 to 8 weeks) showed efficacy across a range of outcomes in 7-18 year olds. When compared to placebo, fluoxetine produced clinically important improvement in depressive symptoms (when measured with a clinician completed rating scale) and improved the likelihood of both remission and response to treatment, and had a positive impact regarding general clinical improvement and the severity of depression. Evidence is inconclusive regarding the impact on functional status.

The relative risk of serious adverse events and suicidal behaviour is difficult to interpret because of wide confidence intervals, although the rate of harm-related adverse events and suicidal behaviour/ideation was higher in fluoxetine than placebo treated patients. However, there is evidence that fluoxetine is less likely than placebo to lead to discontinuation of treatment for any reason.

Treatment-emergent adverse events were generally similar between fluoxetine and placebo with the exception of hyperkinesias, headache and skin rash, where there is evidence suggesting increased risk for fluoxetine.

**Paroxetine (SSRI)**

In one study, paroxetine (up to 40 mg/day for 8 to 12 weeks) improved the likelihood of remission in 12-18 year olds. However, further evidence suggested paroxetine had little impact on response to treatment, symptom levels, functional status, or clinical improvement.

There is evidence suggesting that paroxetine is more likely than placebo to bring about serious adverse effects, and limited evidence of increased risk of suicidal behaviour/ideation and early discontinuation from treatment because of adverse events or any reason.

Paroxetine is more likely than placebo to cause the following treatment-emergent adverse events: dizziness, hostility, insomnia, somnolence and tremor.
Sertraline (SSRI)
Sertraline (up to 200 mg/day for 10 weeks) when compared to placebo produced a small improvement in depressive symptoms in 6-17 year olds. However, the evidence regarding remission, response to treatment, and clinical improvement is inconclusive. Evidence suggests no impact on functional status.

There is evidence suggesting that sertraline treated patients are more likely to discontinue treatment because of adverse events and there is limited evidence of increased risk of suicidal behaviour/ideation. Evidence is inconclusive regarding serious adverse events. There is limited evidence for an increased risk of discontinuation of treatment for any reason.

Sertraline is more likely than placebo to cause the following treatment-emergent adverse events: nausea, diarrhoea, insomnia, agitation and anorexia.

Citalopram (SSRI)
There was limited evidence that citalopram (up to 40 mg/day for 8 to 12 weeks), when compared with placebo, improved the chance of remission and response to treatment, and improved depressive symptoms in 7-18 year olds.

There was limited evidence that citalopram increases the risk of treatment-emergent adverse events, suicidal behaviour/ideation, early discontinuation because of suicide attempts, and early discontinuation because of adverse events.

Citalopram is more likely than placebo to cause the following treatment-emergent adverse events: rhinitis, nausea, flu-like symptoms, fatigue, diarrhoea, and pharyngitis.

Venlafaxine (SNRI)
There was limited evidence suggesting that venlafaxine (up to 225 mg/day for 8 weeks) when compared to placebo produced a small improvement in depressive symptoms in 6-17 year olds. There is no evidence to judge whether venlafaxine improves the likelihood of remission, response to treatment, or functional status.

Evidence suggests venlafaxine increases the risk of suicidal behaviour/ideation and leads to early discontinuation because of adverse events.

There is limited evidence to suggest that venlafaxine is more likely than placebo to cause the following treatment-emergent adverse events: nausea, anorexia and dizziness.

Mirtazapine (presynaptic α₂-antagonist)
Evidence is inconclusive regarding the effect of mirtazapine (20 mg/day for 8 weeks) when compared to placebo on depressive symptoms in 7-17 year olds.
There was no evidence regarding remission, response to treatment, or functional status.

Evidence for increased risk of suicidal behaviour/ideation was inconclusive. There was limited evidence that mirtazapine increases the risk of early discontinuation because of adverse events. Mirtazapine was more likely than placebo to cause the following treatment-emergent adverse events: weight gain, somnolence, headache, and increased appetite.

**Pooled safety analysis for the SSRIs and the atypical antidepressants**
There is limited evidence that across all available data for the SSRIs and atypical antidepressants, there is an increased risk of suicidal behaviour/ideation. These drugs also increase the risk of early discontinuation because of adverse events. For the SSRIs alone, there is limited evidence of an increased risk of suicidal behaviour/ideation.

**SSRIs versus tricyclic antidepressants**
Evidence suggests that a SSRI (paroxetine; up to 40 mg/day for 8 weeks) when compared to a tricyclic antidepressant (imipramine; up to 200 mg/day for 8 weeks) may increase the likelihood of remission in 12 to 18 year olds. The evidence is inconclusive regarding response to treatment and depressive symptoms. The evidence is also inconclusive regarding clinical improvement when comparing a SSRI (Paroxetine; up to 40 mg/day for 8 weeks) with tricyclics (imipramine [up to 200 mg/day for 8 weeks] or clomipramine [up to 150 mg/day for 8 weeks]) in 12-20 year olds.

Evidence is inconclusive regarding the risk of suffering adverse events and suggests that paroxetine may have a lower risk of early discontinuation of treatment because of adverse events.

**Conclusion**
There is no evidence for the effectiveness of tricyclic antidepressants when compared with placebo or when compared with SSRI and atypical antidepressants. Fluoxetine is the only SSRI/atypical antidepressant where there is evidence of clinical effectiveness across a range of outcome measures.

There is limited evidence that all SSRIs/atypical antidepressants (including fluoxetine) may increase the risk of suicidal ideation and/or behaviour and increase the risk of discontinuation of treatment because of adverse events.

7.5 Antidepressant drug versus psychological interventions, and the combination

7.5.1 Introduction
Little research has focused on the direct comparison of antidepressants with psychological interventions, or on the combination. The most recent trial,
conducted by the Treatment for Adolescents With Depression Study (TADS) team, is the largest community sampled trial of depression in young people. The first stage of the study assessed the safety and effectiveness of fluoxetine, CBT, and their combination when compared to placebo in 439 young people (12-17 years old) with moderate to severe MDD. It is important to note that while the group receiving fluoxetine alone or placebo were blind to treatment, those in the combined treatment group were informed they were receiving fluoxetine.

There is also at least one ongoing study, the Treatment Of Resistant Depression In Adolescents (TORDIA), which aims to recruit 400 boys and girls aged 12-18 years, who are currently prescribed an SSRI, to a 12-week RCT. There are four conditions: (1) switching to an alternative SSRI, (2) switching to a different non-SSRI antidepressant, (3) switching to an alternative SSRI and receiving CBT, or (4) switching to a different non-SSRI antidepressant and receiving CBT. More information can be found through the clinicaltrials.gov website (http://clinicaltrials.gov/show/NCT00018902).

7.5.2 Treatment included
The following treatments were included:
Fluoxetine
CBT.

7.5.3 Studies considered
The review team conducted a new systematic search for RCTs that assessed the efficacy of an antidepressant versus a psychological intervention and/or the combination.

One trial (TADS2004\textsuperscript{8}) met the eligibility criteria set by the GDG, providing data on 439 participants. TADS2004 randomised participants to fluoxetine alone (n = 109), CBT alone (n = 111), fluoxetine with CBT (n = 107), or placebo (n = 112). The duration of the study was 12 weeks. All participants were diagnosed with major depressive disorder by DSM-IV and were between the ages of 12 and 17 years old. Based on the CDRS-R, participants had moderate to severe depression, with 27% having at least minimal suicidal ideation at baseline. Those randomised to fluoxetine alone or placebo were blind to treatment, whereas those receiving the combination of fluoxetine and CBT were not.

A further study (MANDOKI1997), randomised 40 participants with MDD aged 8 to 18 years to venlafaxine with psychotherapy (n = 20) or

\textsuperscript{8} This study was also included in the analysis of antidepressants versus placebo and the analysis of CBT versus non-directive supportive therapy or clinical management.
psychotherapy alone (n = 20). However, this study was excluded from the analysis because it provided no information about the type of psychotherapy used or whether it was manualised.
### 7.5.4 Fluoxetine alone versus CBT alone

Table 19. Evidence summary table for fluoxetine alone/ fluoxetine combined with CBT versus CBT alone/ placebo/ fluoxetine alone.

<table>
<thead>
<tr>
<th></th>
<th>Fluoxetine alone vs. CBT alone</th>
<th>Fluoxetine with CBT vs. placebo</th>
<th>Fluoxetine with CBT vs. fluoxetine alone</th>
<th>Fluoxetine with CBT vs. CBT alone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total no. of trials (total no. of participants)</strong></td>
<td>1 RCT (220)</td>
<td>1 RCT (219)</td>
<td>1 RCT (216)</td>
<td>1 RCT (218)</td>
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<tr>
<td><strong>Depressive symptoms</strong></td>
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<tr>
<td>Clinician completed</td>
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<tr>
<td>CDRS-R</td>
<td>●</td>
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<tr>
<td>Self-report</td>
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<td>RADS</td>
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<tr>
<td><strong>Clinical Improvement</strong></td>
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<td>Clinician completed</td>
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<td>○</td>
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<tr>
<td>CGI-I</td>
<td>K=1; N=220</td>
<td>K=1; N=219</td>
<td>K=1; N=216</td>
<td>K=1; N=218</td>
</tr>
<tr>
<td><strong>Harms</strong></td>
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<td></td>
</tr>
<tr>
<td>Harm-related adverse event</td>
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<tr>
<td>Suicide-related events</td>
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<tr>
<td>Suicide ideation (SIQ)</td>
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<td>×</td>
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<tr>
<td><strong>NNTB/NNTH</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Clinical improvement</td>
<td>NNTB=6 (4 to 25)</td>
<td>NNTB=3 (2 to 5)</td>
<td>NNTB=10 (5 to 50)</td>
<td>NNTB=4 (3 to 7)</td>
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<tr>
<td>(CGI)</td>
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<td></td>
</tr>
<tr>
<td>Harm-related adverse event</td>
<td>11.9% vs. 4.5%:</td>
<td>8.4% vs. 5.4%:</td>
<td>8.4% vs. 11.9%:</td>
<td>11.9% vs. 4.5%:</td>
</tr>
<tr>
<td></td>
<td>NNTH 14 (7 to 455)</td>
<td>NNTH 33 (NNTH 11 to ∞ to NNTH 28)</td>
<td>NNTH 29 (NNTH 9 to ∞ to NNTH 23)</td>
<td>NNTH 14 (7 to 455)</td>
</tr>
<tr>
<td>Suicide attempts</td>
<td>1.8% vs. 0.9%:</td>
<td>3.7% vs. 0%:</td>
<td>3.7% vs. 1.8%:</td>
<td>1.8% vs. 0.9%:</td>
</tr>
<tr>
<td></td>
<td>NNTH 108 (NNTH 25 to ∞ to NNTH 47)</td>
<td>NNTH 27 (NNTH 13 to ∞ to NNTH 455)</td>
<td>NNTH 53 (NNTH 16 to ∞ to NNTH 42)</td>
<td>NNTH 108 (NNTH 25 to ∞ to NNTH 47)</td>
</tr>
<tr>
<td>Suicide-related events</td>
<td>5.6% vs. 4.5%:</td>
<td>5.6% vs. 3.6%:</td>
<td>5.6% vs. 8.3%:</td>
<td>5.6% vs. 4.5%:</td>
</tr>
<tr>
<td></td>
<td>NNTH 91 (NNTH 15 to ∞ to NNTH 22)</td>
<td>NNTH 50 (NNTH 14 to ∞ to NNTH 29)</td>
<td>NNTH 38 (NNTH 11 to ∞ to NNTH 25)</td>
<td>NNTH 91 (NNTH 15 to ∞ to NNTH 22)</td>
</tr>
</tbody>
</table>

**Note.** ● = evidence of a clinically important effect favouring treatment A; ○ = limited evidence of a clinically important effect favouring treatment A; ⊙ = evidence of clinically important effect favouring treatment B; ○ = limited evidence of clinically important effect favouring treatment B; × = there is unlikely to be a clinically important difference between groups; ? = the evidence is inconclusive; K = number of studies; N = total number of participants; NNTB = number needed to treat (benefit); NNTH = number needed to treat (harm).
7.5.5 Clinical summary

For individual outcomes, the quality of the evidence was moderate, reflecting the fact only one study was included in the review.

**Fluoxetine alone versus CBT**
Fluoxetine alone showed evidence of a reduction in depressive symptoms and limited evidence of global clinical improvement when compared with CBT alone.

There is limited evidence favouring CBT in relation to harm-related adverse events, suicide attempts, suicide-related events and suicidal ideation.

**Fluoxetine plus CBT versus placebo**
There is evidence that fluoxetine in combination with CBT reduces depressive symptoms and produces global clinical improvement when compared with placebo.

There is limited evidence that fluoxetine in combination with CBT is more likely to bring about increases in harm-related adverse events, suicide attempts and suicide-related events than placebo. There is evidence that fluoxetine in combination with CBT produces no difference in suicidal ideation.

**Fluoxetine plus CBT versus Fluoxetine alone**
There is limited evidence that fluoxetine in combination with CBT reduces depressive symptoms and produces global clinical improvement when compared with fluoxetine alone.

There is limited evidence that fluoxetine in combination with CBT is less likely to bring about suicide-related events and suicidal ideation but more likely to bring about suicidal attempts. Evidence regarding harm-related adverse events is inconclusive.

**Fluoxetine plus CBT versus CBT alone**
Fluoxetine in combination with CBT showed evidence of a reduction in depressive symptoms and limited evidence of global clinical improvement when compared with CBT alone.

There is limited evidence that fluoxetine in combination with CBT is more likely to bring about increases in harm related adverse events, suicide attempts and suicide related events than CBT alone. There is evidence that fluoxetine in combination with CBT produces no difference in suicidal ideation when compared with CBT alone.
Conclusion
Fluoxetine in combination with CBT is more effective in reducing depressive symptoms and producing global clinical improvement. The effect is strongest when compared with placebo and weakest when compared with fluoxetine alone.

There is limited evidence suggesting that the fluoxetine may increase suicidal ideation and/or behaviour but that the addition of CBT may reduce this risk.

7.6 Other drug treatment

7.6.1 Introduction
There is a paucity of evidence regarding the use of drugs other than antidepressants to treat depression in children and young people. A search of the literature revealed only one RCT that compared lithium with placebo. Lithium is a drug that was first used to treat mania, but is also used to prevent relapse in patients with bipolar disorders or recurrent depression. Lithium has many pharmacological effects and the exact mechanism(s) by which it reduces mania and prevents relapse are unclear.

7.6.2 Treatment included
The following treatment was included:
Lithium.

7.6.3 Studies considered
The review team conducted a new systematic search for RCTs that assessed the efficacy of drugs other than antidepressants for children and adolescents with depression.

One trial (GELLER1998) met the eligibility criteria set by the GDG, providing data on 30 participants. The duration of the study was 10.5 weeks. All participants were diagnosed with major depressive disorder by DSM-III-R and were between the ages of 6 and 12 years old. All participants had family history predictors of future bi-polar disorder. Forty percent also had dysthymia and a significant proportion had comorbid ADHD or an anxiety disorder.

7.6.4 Lithium versus placebo
Evidence reported by GELLER1998 suggests lithium when compared to placebo is unlikely to improve depressive symptoms (K-SADS treatment x time ANCOVA covarying for baseline K-SADS was $F = 0.01, p = 0.91$), or improve general functioning (C-GAS treatment x time ANCOVA covarying for baseline C-GAS was $F = 3.44, p = 0.07$). With regard to adverse events, more lithium treated participants had vomiting (31.3% versus 0%). There is limited evidence that lithium also increased the risk of early discontinuation.
of treatment because of adverse events (RR = 7.00; 95% CI, 0.41 to 119.46) and early discontinuation for any reason (RR = 10.11; 95% CI, 0.62 to 164.68).

7.6.5 Clinical summary
There is no evidence regarding the effect of lithium on remission or response to treatment. Lithium is unlikely to improve depressive symptoms or general functioning over and above placebo. Evidence suggests lithium may increase vomiting and the risk of early discontinuation from treatment because of adverse events.

7.7 Relapse prevention
A systematic search of the literature identified no RCTs concerning the prevention of relapse of depression in children and/or young people that met the eligibility criteria set by the GDG. A wider search revealed only case series and naturalistic follow up reports (Birmhaer et al, 2002; Garber et al, 1988; Emstlie et al, 1998; Pine 2002). Clinical practice follows adult guidance with recommendations that if young people respond to antidepressant medication they should continue on that treatment for 6 to 12 months, with medication being discontinued at that point if the young person is well. Phased withdrawal over 4 to 6 weeks is often recommended but there is no clear evidence to support this. None of the reports identified, presented compelling evidence on either continuation (how long to continue treatment after a positive response) or maintenance (how to prevent recurrence) treatment strategies.

7.8 ECT

7.8.1 Introduction
Electro-convulsive Therapy (ECT) is a controversial treatment, especially when used with young people. However, its use is rare in the UK and, similarly to adults, largely reserved for young people whose depression is resistant to other treatments or in potentially life-threatening situations.

7.8.2 Current practice
ECT is an electrically induced seizure. An electric current is passed briefly through the brain via electrodes applied to the scalp to induce generalised seizure activity. The individual receiving the treatment is placed under general anaesthetic and muscle relaxants are given to prevent body spasms. The ECT electrodes can be placed on both sides of the head (bilateral placement) or on one side of the head (unilateral placement), usually the non-dominant side of the brain.

ECT is used extremely rarely in the UK. Duffett et al (1999) attempted to survey its use in young people under the age of 18 during one year in 1996. They found 12 young people (aged 12 to 17 years) who had received ECT, 8 of
whom had a diagnosis of depression (6 with uni-polar depression). The total
represents a rate of 0.02 per 100,000 total population per year, similar to a 10
year retrospective study in Scotland (Robertson et al, 1997).

7.8.2.1 Indications for use
In 2002 the American Academy of Child and Adolescent Psychiatry
(AACAP) published a Practice Parameter for the Use of ECT with Adolescents
(AACAP, 2002). The following is a summary of the main points relevant to
this Guideline:

- The adolescent should be diagnosed with severe, persistent major
depression, with or without psychotic features
- The symptoms must be severe, persistent and significantly disabling,
including life-threatening symptoms such as refusal to eat or drink,
severe suicidality, or florid psychosis
- Other treatments should have been tried and failed, including at least 2
or more trials of appropriate psychopharmacology, unless the severity
of symptoms precludes waiting for a response to other treatments
- A psychiatrist experienced in the use of ECT, but not involved in the
case should give a second opinion
- Every adolescent should have a memory assessment before treatment,
at the end of treatment and at 3-6 months after treatment
- The anaesthetist should have experience in the treatment of
adolescents
- Policies should be in place covering consent for the use of ECT with
adolescents.

In the UK, Duffett et al (1999) found that of the 8 young people who had a
diagnosis of depressive disorder, ECT was used in 4 as a life-saving
intervention; and in 6 due to a failure to respond to medication.

7.8.3 Studies considered
The review team conducted a new systematic search for RCTs that assessed
the efficacy and/or safety of ECT for children and adolescents with
depression. However, no controlled trials were found. A wider search for
evidence found several reviews of single case studies or case series using
variable methodology and variable outcome measures (Baldwin & Oxlad,
1996; Rey & Walter, 1997; Walter et al., 1999a).

7.8.4 Clinical evidence
No controlled trials were found on the use of ECT in young people. Most of
the evidence relies on single case studies or case series using variable
methodology and variable outcome measures. There is likely to be a
publication bias in favour of positive outcomes, especially with single case
studies.
Rey and Walter (1997) found 66 reports describing ECT in 396 patients aged 18 years or younger. Baldwin and Oxlad (1996) reviewed 217 cases of “minors” who had received ECT between 1947 and 1996. Search strategies were not reported.

Other reviews and case series considered included much smaller numbers.

**7.8.4.1 Efficacy**

Walter et al (1999a) reviewed the outcomes of 87 patients with depression who had been treated with ECT aged 18 years or younger. They concluded 58 (67%) had remitted, or showed marked improvement of symptoms after treatment.

Baldwin and Oxlad, in their review of 217 “minors” also suggest positive outcomes for many following ECT, although they have not included depressive disorder as a sub-group within their analysis. Despite generally positive findings, they question the interpretation of this data due to the methodology and publication bias in the published literature. However, Walter et al (1999a) found significant differences between diagnostic categories, in particular, showing that ECT was more effective with depressed young people than for other diagnoses such as schizophrenia. This is suggestive of a real effect for the depressed group, over and above any possible publication bias.

Duffett et al (1999), in their UK case series of 12 under 18 year olds who received ECT during 1996, used the Clinical Global Impression of Change and found 5 had much, or very much, improved; 3 had improved; 3 were unchanged and for 1 the data was missing. Although this sample is small, it is UK only and avoids the issues of publication bias.

**7.8.4.2 Adverse events**

The main side-effects for young people receiving ECT for depression appear to be the same as for adults. ECT may cause short or long-term memory impairment for past events (retrograde amnesia) and current events (anterograde amnesia). As this type of cognitive impairment is a feature of many mental health problems, including severe depression, it may sometimes be difficult to differentiate the effects of ECT from those associated with the condition itself.

The risks associated with ECT may be enhanced “…in children and young people, and therefore, clinicians should exercise particular caution when considering ECT treatment in [this] group” (NICE 2003).

One small study has been published (Cohen et al, 2000) assessing cognitive functioning, in particular memory functioning, in 10 under 19 year olds who had received bilateral ECT an average of 3.5 years previously. Cognitive test
scores were similar to those in a comparison group matched for sex, age and diagnosis. Six patients reported subjective memory loss immediately after treatment and one complained of persistent memory loss at follow-up. It is not possible to draw firm conclusions from these findings due to the small numbers and retrospective design.

There are no studies which provide evidence of the impact of ECT on the developing brain.

7.8.4.3 User and parent opinion

The views of the young people who had received ECT were mixed, but a small majority believed that ECT was helpful, and more still believed that the effects of their illness were worse than the effects of the ECT. Few young people felt they had any real understanding of the treatment and many expressed a range of fears associated with ECT. Most experienced memory impairment but this largely resolved over time.

Parents were generally as positive, or more positive, than young people who had received ECT in their views about ECT. Parents were more knowledgeable about what ECT entailed.

7.8.5 Clinical summary
In the UK, ECT is used extremely rarely for the treatment of depression in young people. It is usually reserved for cases where there is a perceived life-threatening situation or where extensive alternative treatments have failed. Without controlled trials, the evidence for efficacy is limited, but case studies and case series suggest it may be of benefit.

The most significant side-effect from ECT is memory impairment. The effects of ECT on the developing brain are unknown.

7.9 Psychotic depression

7.9.1 Introduction
Psychotic depression (a major depressive disorder associated with hallucinations and/or delusions) can occur in children and adolescents but has been subject to little systematic study. Pre-pubertal children are more likely to present mostly with auditory hallucinations whilst adolescents may have both delusions and hallucinations. Psychotic depression has been associated with more severe depression, greater long-term morbidity, and
higher risk of recurrence, bipolar disorder and suicidality. The presence of psychotic symptoms is suggested to be an indication for the early use of antidepressant medication but also an indication of greater resistance to antidepressant monotherapy (AACAP, 1998).

7.9.2 The management of psychotic depression
Systematic research into major depression with psychotic features has been limited by the fact that the disorder is not defined clearly as a distinct diagnostic subtype and because of the difficulties in enrolling such patients in research studies. As a result there are no good quality epidemiological studies and no controlled studies on the acute or longer-term treatment of psychotic depression. A systematic search of electronic databases found only anecdotal reports, case series and best practice guidance from expert bodies. One small study of adolescents has suggested that the combination of antidepressants with antipsychotics may be helpful for patients with psychotic depression (Geller et al, 1985), but this study focused more on plasma drug levels than on outcome measures.

7.10 Clinical practice recommendations

7.10.1 Using antidepressants in children and young people

7.10.1.1 Antidepressant medication should not be used for the initial treatment of children and young people with mild depression. (B) (1.5.2.3 NICE)

7.10.1.2 The further treatment of children and young people with persisting mild depression unresponsive to treatment at Tier1/2 should follow the guidance for moderate to severe depression. (GPP) (1.5.2.4 NICE)

7.10.1.3 Antidepressant medication should not be offered to children and young people with moderate to severe depression except in combination with a concurrent psychological treatment. If psychological treatment is declined, specific arrangements must be made for careful monitoring of adverse events. (B) (1.6.4.1 NICE)

7.10.1.4 If an antidepressant is to be prescribed it should only be following assessment and diagnosis by a child and adolescent psychiatrist. (C) (1.6.4.2 NICE)

7.10.1.5 When an antidepressant is prescribed to children and young people with moderate to severe depression, it should be fluoxetine as this is the only antidepressant where clinical trial evidence shows that benefits outweigh risks. (A) (1.6.4.3 NICE)
7.10.1.6 Children and young people started on antidepressant medication should be informed about the rationale for the drug treatment, the delay in onset of effect, the time course of treatment, the possible side effects, and the need to take the medication as prescribed. Discussion of these issues should be supplemented by written information appropriate to the child/young person’s and family’s needs. This should include a copy of the advice from the Committee on Safety of Medicines. (GPP) (1.6.4.4 NICE)

7.10.1.7 Children and young people prescribed antidepressants should be monitored for agitation, suicidal ideation and self-harm by the prescribing doctor and the professional delivering the psychological intervention. Patients and their families should be informed that if there is any sign of new symptoms of these kinds, urgent contact should be made with the prescribing doctor. (GPP) (1.6.4.5 NICE)

7.10.1.8 When an antidepressant is prescribed in the treatment of children and young people with depression, as an adjunct to clinical judgement a patient’s progress may be monitored using a recognised self-report rating scale for depression such as the Mood and Feelings Questionnaire. (GPP) (1.6.4.6 NICE)

7.10.1.9 Where children/young people respond to treatment with fluoxetine, medication should be continued for at least 6 months post recovery (no symptoms and full functioning for at least 8 weeks). (C) (1.6.4.7 NICE)

7.10.1.10 If treatment with fluoxetine is unsuccessful or is not tolerated because of side effects, consideration should be given to the use of another antidepressant. In this case sertraline or citalopram are the recommended second line treatments. (A) (1.6.4.8 NICE)

7.10.1.11 Sertraline and citalopram should only be used when the following criteria have been met:

- The child/young person and their carers have been fully involved in discussions about the likely benefits and risks of the new treatment and have been provided with appropriate written information including the advice from the Committee on Safety of Medicines

- The child/young person’s depression is sufficiently severe and/or causing sufficiently serious symptoms (e.g. weight loss or suicidal behaviour) to justify a trial of another antidepressant

- There is clear evidence that there has been a fair trial of the combination of fluoxetine and a psychological intervention (i.e. that all
efforts have been made to ensure adherence to the recommended treatment regime

• There has been a reassessment of the likely causes of the depression and of treatment resistance (e.g. other diagnoses such as bipolar disorder, substance abuse etc.)

• There has been a review by a senior child and adolescent psychiatrist – usually a consultant

• The child/young person and/or someone with parental responsibility for the child and young person (or the young person alone, if over 16 or deemed competent) has signed an appropriate and valid consent form. (C)(1.6.4.9 NICE)

7.10.1.12 Where children/young people respond to treatment with citalopram or sertraline, medication should be continued for at least 6 months post recovery (no symptoms and full functioning for at least 8 weeks). (C) (1.6.4.10 NICE)

7.10.1.13 Paroxetine and venlafaxine should not be used for the treatment of depression in children and young people. (A) (1.6.4.11 NICE)

7.10.1.14 Where antidepressant medication is to be discontinued, the drug should be phased out over a period of 6 to 12 weeks with the exact timing being titrated against response. (C) (1.6.4.12 NICE)

7.10.1.15 As with all other medications, consideration should be given to possible drug interactions when prescribing medication for depression in children and young people. This should include possible interactions with complementary and alternative medicines as well as with alcohol and ‘recreational’ drugs. (GPP) (1.6.4.13 NICE)

7.10.2 Antidepressants combined with psychological treatments

7.10.2.1 If a child or young person with moderate to severe depression is unresponsive to psychological treatment after 4 to 6 treatment sessions (of the 15 session treatment), a multidisciplinary review should be carried out. (GPP) (1.6.2.1 NICE)

7.10.2.2 If the patient’s depression is not responding to treatment as a result of other co-existing factors such as the presence of comorbid conditions, persisting psychosocial risk factors such as family discord, or the presence of parental mental ill-health, additional or alternative psychological treatment for the patient, a parent or the family, should be considered. (C) (1.6.2.2 NICE)
7.10.2.3 Following multidisciplinary review, if a young person (12 to 18 years) with moderate to severe depression is unresponsive to a specific psychological treatment after 4 to 6 sessions (of the 15 session treatment), fluoxetine should be offered. (B) (1.6.2.3 NICE)

7.10.2.4 Following multidisciplinary review, if a child (5 to 11 years) with moderate to severe depression is unresponsive to a specific psychological treatment after 4 to 6 sessions (of the 15 session treatment), the addition of fluoxetine may be cautiously considered, although the evidence for its effectiveness in this age group is not established. (C) (1.6.2.4 NICE)

7.10.2.5 If the child or young person with moderate to severe depression is unresponsive to combined treatment with a specific psychological treatment and fluoxetine after a further 6 sessions, or the patient and/or their family have declined the offer of fluoxetine, the multidisciplinary team should make a full needs and risk assessment. This should include a review of the diagnosis, examination of the possibility of comorbid diagnoses, reassessment of the causes of depression, whether there has been a fair trial of treatment and for further more intensive psychological treatment for the patient and/or additional help for the family. (GPP) (1.6.3.1 NICE)

7.10.2.6 Following multidisciplinary review, more intensive psychological treatments such as individual child psychotherapy (30 weekly sessions) or systemic family therapy (15 fortnightly sessions) should be considered where first line psychological treatments with fluoxetine have been tried and failed, or where the child/ young person or their families have expressed a preference not to use fluoxetine. (B) (1.6.3.2 NICE)

7.10.3 Discharge after first episode

7.10.3.1 When a child or young person is in remission (less than two symptoms and full functioning for at least 8 weeks) they should be reviewed regularly for 12 months by an experienced CAMHS professional. The exact frequency of contact should be agreed between the CAMHS professional and service user and/ or carer and recorded in the notes. At the end of this period if recovery is maintained the young person can be discharged to primary care. (C) (1.6.8.1 NICE)

7.10.3.2 Children and young people who have been successfully treated, discharged but re-referred should be seen as soon as possible rather than placed on a routine waiting list. (GPP) (1.6.8.2 NICE)
7.10.4 Recurrent depression and relapse prevention

7.10.4.1 In children and young people who are at a high risk of relapse (e.g. individuals who have already experienced two prior episodes, individuals who have high levels of subsyndromal symptoms, or those who remain exposed to multiple risk circumstances), it may be of benefit to offer specific follow-up psychological treatment sessions to reduce the likelihood of, or at least detect, a relapse of depressed state. (B) (1.6.9.1 NICE)

7.10.4.2 CAMHS specialists should teach recognition of illness signatures and other early warning signs to other professionals, the child/ young person with recurrent depression and their families. Self-management techniques may help individuals to avoid and/ or cope with trigger factors. (GPP) (1.6.9.2 NICE)

7.10.4.3 When a child or young person with recurrent depression is in remission (less than two symptoms and full functioning for at least 8 weeks) they should be reviewed regularly for 24 months by an experienced CAMHS professional. The exact frequency of contact should be agreed between the CAMHS professional and service user and/ or carer and recorded in the notes. At the end of this period if recovery is maintained the young person can be discharged to primary care. (C) (1.6.9.3 NICE)

7.10.4.4 Children and young people with recurrent depression who have been successfully treated, discharged but re-referred should be seen as a matter of urgency. (GPP) (1.6.9.4 NICE)

7.10.5 Electroconvulsive therapy

7.10.5.1 Electroconvulsive therapy (ECT) may be considered for young people with either life-threatening symptoms (e.g. suicidal behaviour) or intractable symptoms unresponsive to other treatments. (C) (1.6.7.1 NICE)

7.10.5.2 Electroconvulsive therapy should be used extremely rarely with young people and only after careful assessment by a practitioner experienced in its use and only in a specialist environment in accordance with NICE recommendations. (C) (1.6.7.2 NICE)

7.10.5.3 ECT should not be used in the treatment of depression in children (5 to 11 years). (C) (1.6.7.3 NICE)
7.10.6 Pharmacological management of psychotic depression

7.10.6.1 For children/young people with psychotic depression, augmenting the current treatment plan with antipsychotic medication should be considered, although the optimum dose and duration of treatment are unknown. (C) (1.6.5.1 NICE)

7.10.6.2 Children/young people prescribed antipsychotic medication should be monitored carefully for side effects. (C) (1.6.5.2 NICE)

8 Service configurations

8.1 Implications for service configuration

8.1.1 Introduction
The recommendations in this guideline have been devised to take account of the four-tier model of service organisation. The recommendations in this guideline are consistent with the National Service Framework (NSF) for Children, and will not require an organisational framework outside of the main structures proposed by the NSF. However, the guidance is likely to have significant implications for service capacity. Depression in children and young people is currently a poorly recognised and under-reported disorder; as the number of children and young people with depression receiving treatment and help increases, so will the workload.

It is important to note that, consistent with current government policy regarding all children’s services, the recommendations will have specific implications for healthcare professionals throughout all four tiers, but will also have relevance for non-healthcare professionals involved in the care of children and young people, including some voluntary organisation. This chapter will describe how services for children and young people are organised, highlight some of the problems in the current organisation of services for depressed youth and outline a ‘stepped care’ model used to structure the care pathway for this guideline. As better functional integration of children’s services is a key to both the NSF and this guideline, this chapter will pull together referral criteria for the movement of depressed children and young people between tiers, and identify methods of monitoring progress for patients and services.

In addition, the second part will review the current role and the evidence underpinning the use of inpatient units in the treatment of children and young people with depression.
8.1.2 Organisation of services
Interventions for children with depression may be provided by specialist child and adolescent mental health services (CAMHS), but many children are significantly helped by non-specialist health, social work or education services. In order to recognise the different levels of interventions for many child mental health problems, CAMHS has increasingly been considered to have four main levels, or tiers, of delivery (NHS Health Advisory Service, 1995). The National Service Framework for Children’s Services (Department of Health, 2004), supported by priorities for the CAMHS grant, has defined the key service components for a comprehensive CAMHS that each Primary Care Trust should ensure is in place in each area by 2006. Such comprehensive services should have, at each Tier, appropriately trained staff and services which can prevent, identify, and either treat or contribute to the treatment of, depression in children and young people.

**Tier 1** services include services that have primary or direct contact with youth, primarily for reasons other than mental health. These services include primary care/general practice, social services, health visitors and schools. Although their primary task is not working with child mental health problems, they are the first point of contact with the child/family with mental health problems.

Tier 1 services should be able to draw on specialist CAMHS personnel who can consult and advise them about working with children and young people in their care who either have, or are at risk of developing, a mental health problem. For some children, additional input from an adult they already know may be more acceptable and effective than referral to specialist services. At this level, an important role is to understand the risks for depression amongst the children in their care, but also to detect those at high risk or those who have succumbed to depression.

**Tier 2** services refer to those specialist CAMHS professionals working in a community based setting alongside Tier 1 workers, and therefore work in primary care, schools and other relevant community settings such as social services. Tier 2 staff usually work as a part of a team, with Tier 1 staff, built around the individual child. In this position, Tier 2 CAMHS professionals can provide fairly rapid assessment and treatment to children within Tier 1 settings, as well as consultation/support to Tier 1 workers. This is an important means by which less severely depressed children with lower levels of complexity can access help and treatment in a less stigmatising community-based setting. They will also be able to help identify those children needing referral to more specialist services. Often Tier 2 professionals are also organised into multidisciplinary teams, with good links to Tier 3 services, thereby facilitating a more seamless transition across Tiers. It should be noted that sometimes, Tier 2 services are provided by the
voluntary sector (for example, adolescent counselling and psychotherapy services).

**Tier 3** services comprise multi-disciplinary teams of specialist CAMHS professionals working in (secondary care) specialist CAMHS facilities (e.g. Child and Family Consultation Services or Hospital Liaison Teams). The National Service Framework for Children’s Services states that all PCT areas should have at least one comprehensive Tier 3 multi-disciplinary CAMHS team. They should provide specialist co-ordinated assessments and treatments, and should be able to offer the full range of appropriate psychological and pharmacological interventions.

Outreach services should also be available to those young people who are too depressed or house bound to access Tier 3 services based in secondary care facilities, or to work in conjunction with outpatient treatment plans (e.g. monitoring of medication). Emergency services, with 24-hour availability should also be in place in all localities.

Importantly, Tier 3 professionals can also provide consultation and training to Tier 1 workers and refer when necessary to Tier 4 services.

**Tier 4** services are highly specialised tertiary CAMHS which provide multidisciplinary services for very severe depression (and other serious mental health problems), or for those who need very intensive treatment or supervision. These services vary in how they are organised. Some are acute adolescent or children’s inpatient units, day hospitals and specialist treatment centres. Referrals to Tier 4 units only come from Tier 3 CAMHS professionals, usually a consultant Child and Adolescent psychiatrist, and patients are discharged back to Tier 3 services or outreach services after admission.

Finally, Protocols with adult mental health services need to be in place to ensure the smooth transition of young people to adult services when they turn 18. Such protocols need to ensure that access criteria to adult services are consistent with young people who have been previously treated by CAMHS.

**8.1.3 Problems in the current organisation of services for depressed youth**

In the developed countries there is a low spend on mental health services in general compared to other medical services, despite the WHO highlighting the high priority for mental illness services world-wide (WHO, 2001). Within the general mental health budget child mental health services often struggle to find new monies for development. Recently, however, there has been a significant increase in funding for CAMHS services, both directly to PCTs and through the CAMHS grant.

Alternative sources of funding in the England and Wales can be identified in other public sector services including social services, education and the home
The emphasis for non-health funds is social care, diminishing the rates of anti-social behaviour in the community and ameliorating the effects of deprivation. Service development for non-health organisations is focussed currently on community based interventions for at risk families, provision of parenting programmes to those with young (generally <7 years) children, and support for schools through enhancement of the child worker system aimed at behaviourally disturbed children. Although there is an increasing interest in trying to increase CAMHS access to schools - indeed the CAMHS grant can now be used to set up services in tier 2 (including schools and primary care) - the focus of developments in these areas is away from the needs of depressed youth. This is made all the more problematic because, currently, there is a moderate to low priority within NHS commissioning groups to increase funding to tier 3 outpatient services focussed on current psychiatric illness in young people.

The structure of CAMHS services is highly variable, at least partly as a result of successive re-structuring exercises. For example, CAMHS services can be found in primary care trust services, as well as mental health trusts, and some CAMHS services have had their services split and inserted into non-NHS organisations. Primary care mental health professionals for children and young people may be employed within PCTs, outside of the tier 3 CAMHS services, although with a strong liaison to these colleagues. These arrangements have led to some confusion: currently, ‘specialist CAMHS’ hospital or clinic based outpatient and inpatient services are seen as ‘mental health’, whereas services involving liaison to other resources, such as schools, child protection, prevention and advisory services, are seen as ‘community’. In addition, locality based priorities have increased the plethora of differentiated service provision, but again with an emphasis on a reduction in antisocial behaviour, improving parenting skills and enhancing child protection. It is perhaps these problems that have, at least in part, led to the development of an NSF for children’s services. Indeed, the NSF for children emphasises a more comprehensive and functionally integrated approach, with a target for all local services to increase access to CAMHS services by 10% year on year (Department of Health, 2004).

8.1.4 A ‘stepped care’ approach to organising services
The current arrangement of CAMHS services into four tiers lends itself to a ‘stepped care’ approach. A ‘stepped care’ model for service delivery starts, rather like a wedding cake, at the base, with service provision being as close to a person’s home and place of work or education. At this level, patients have the more common and usually milder problems amenable to simpler interventions; the professionals at this level will be operating within primary and community sites. At this level assessment skills are needed for detection, and monitoring progress. When more complex problems present that require skills beyond those in the lowest step, referral to the next step up will be
needed, based upon clear and agreed referral criteria. Sometimes treatments will be tried at the lowest step which prove unsuccessful, or the patients condition becomes worse, then referral should follow, again based upon agreed referral criteria. The higher steps involve increasing specialisation and will be required for the more complex and difficult problems, or for those at higher risk, or where treatment has failed at lower levels.

For CAMHS services, the tiered model is, effectively a ‘stepped care’ approach. However, because the lower tiers (1 and 2) vary, in terms of the services provided and the types of professionals and treatments available, geographically, in some areas treatments delivered at tier 2 will be delivered by tier 3, or even tier 1, in another area. This has been accommodated in the care pathway developed for this guideline, and is simply illustrated in the figure below.

<table>
<thead>
<tr>
<th>Focus</th>
<th>Action</th>
<th>Responsibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detection</td>
<td>Risk profiling</td>
<td>Tier 1</td>
</tr>
<tr>
<td>Recognition</td>
<td>Detection in presenting children</td>
<td>All Tiers</td>
</tr>
<tr>
<td>Mild depression (including people with dysthymia)</td>
<td>Watchful Waiting, NDST/Group CBT</td>
<td>Tier 1, Tiers 1/2</td>
</tr>
<tr>
<td>Moderate to severe depression</td>
<td>Brief Psychological Intervention +/- Fluoxetine</td>
<td>Tiers 2/3</td>
</tr>
<tr>
<td>Depression unresponsive to treatment/ recurrent depression/ psychotic depression</td>
<td>Intensive psychological intervention +/- Fluoxetine</td>
<td>Tiers 3/4</td>
</tr>
</tbody>
</table>

**Figure 2** The stepped care model

**8.1.5 Integrated working across tiers**

There are a number of ways that integrated working can be enhanced. In any event, clear protocols for communication between tiers, the provision of training by specialist services for those based in lower tiers and joint planning will be needed. Moreover, it is accepted that, given the different ways in
which services are organised, each locality may need to ensure integration in
different ways. Some important issues are highlighted below.

8.1.5.1 Liaison and direct input to secondary education
CAMHS tier 2/3 staff will be expected to provide training for tier 1 staff. For
childhood depression, as part of a targeted detection approach, it is
recommended that this is particularly focussed on pastoral support staff in
secondary schools and educational services for young people excluded or
non-attending main stream provision i.e. Pupil Referral Units, home
education provision etc. Depending on local protocols, this training may be
inclusive of school nurses, school counsellors, special educational needs co-
ordinators and whoever is involved in the identification of troubled young
people in the school setting. In addition, it may be appropriate for tier 2
CAMHS to deliver individual or group interventions in the school setting and
to provide advice to school staff about young people who may need to be
referred to a tier 3 CAMHS team. In order to deliver this service, we
recommend that each secondary school and secondary PRU should have a
CAMHS link worker as part of tier 2 provision within the locality.

8.1.5.2 Links with other services for high-risk groups.
CAMHS provision to services for Looked After Children should develop
systems for the detection and treatment of depression in this population.
Individuals in young offender’s institutions represent a further high-risk
group. Refugees and other ‘Very High Risk Groups’ detailed under section
5.3.5 require special service provision.

8.1.6 Specialist teams for depression in children and young people?
In order for a tier 3 team to achieve these outputs and to deliver effective and
informed psychological treatments, it is essential for a number of clinicians
within the service to develop a special interest in mood disorders in children
and young people. The exact structure about how a team will organise
themselves with respect to this requirement will vary. In some services it may
be appropriate for a team to develop a specialist mood disorders team,
whereas in other services a more integrated model of service may be more
appropriate. Attention will need to be given to the service interface between
management of self-harm and depression, particularly with respect to the
management of children and young people presenting with self-harm at local
Accident and Emergency units.

8.1.7 Referral advice across tiers
To aid in the functional integration of CAMHS services using this stepped
care model, the following referral advice have been developed by the GDG.
Factors for referral to Tier 1

- Exposure to a single uncomplicated undesirable event in the absence of other risk factors for depression
- Exposure to a recent undesirable life event in the presence of two or more other risk factors with no evidence of depression and/or self-harm
- Exposure to a recent undesirable life event in the context of multiple-risk histories for depression in one or more family members (parents or children) providing that there is no evidence of depression and/or self-harm
- Uncomplicated mild depression

Factors for referral to a CAMHS service

- Depression with 2 or more other risks for depression
- Depression with multiple risk histories in another family member (parent or siblings)
- Mild depression who have not responded to interventions in tier 1 after 2 to 3 months
- Moderate or severe depression (including psychotic depression)
- Signs of a recurrence of depression in those who have recovered from previous moderate or severe depression
- Unexplained self neglect of at least one month’s duration that could be harmful to their physical health of the child/young person
- Actively suicidal ideas or plans in the child/young person

Factors for referral to Tier 4

- High recurrent risk of acts of self harm or suicide
- Significant, ongoing self-neglect (for example, poor personal hygiene, or significant reduction in eating that could be harmful to the physical health of the child/young person)
- Intensity of assessment/treatment and/or level of supervision that is not available in tiers 2/3.

8.1.8 Summary

Specialist Child and Adolescent Mental Health Services have four main levels from services that have primary contact with the child and his family, to those specialist services working in the community to multi-disciplinary teams working in secondary care to highly specialised tertiary services.
Problems in the current organisation of services include service development for non-health organisations (e.g. schools), variability of services across the country with varying locality-based priorities, confusion about the specific definitions of the tiers (particularly tier 2/3).

The tier system lends itself to a stepped care approach with specific foci and actions linked to particular tiers along the care pathway for depression in children and young people.

Integrated working across tiers may be enhanced through direct input into secondary education and links with non-mental health services for high-risk groups.

Specialist teams within Tier 3 for depression in children and young people may enhance the quality of services.
8.2 Inpatient units in the treatment of depression

8.2.1 Introduction

Children and young people with depression are rarely admitted to psychiatric inpatient units, with only approximately 400 admissions per annum in England and Wales (O’Herlihy et al in press). Often, when admission is considered necessary, there will be no alternative due to the level of risk, use of mental health legislation or a lack of alternative intensive treatments or supervision available in the community.

The research evidence for the efficacy of inpatient treatment is extremely limited for most, if not all, psychiatric problems across the age range, including depressed youth. A systematic review of the literature revealed no randomised controlled trials specifically looking at admission as a treatment modality for depression in children and young people. There are a number of studies using less rigorous research design methods looking at outcomes for this group, but many of these were carried out in the United States where services are configured differently. Most studies using inpatient samples of depressed young people are designed to explore the impact of interventions other than the effect of admission.

The provision of inpatient units for children and young people within England and Wales is variable (O’Herlihy et al, 2003). Some inpatient services offer acute admission facilities; some longer-stay therapeutic treatment environments and others attempt to offer both. There are also units that specialise in treating specific disorders, such as anorexia nervosa, but none that specialise solely in the treatment of depression.

Of considerable concern, is the finding in one study in the North West of England, which suggested that for young people with a principle diagnosis of mood disorder, more are admitted to other hospital wards, including adult mental health wards and paediatric wards, than to specialist psychiatric inpatient units for young people (Gowers et al, 2001).

For the purposes of this section, inpatient treatment will refer to specialist child and adolescent psychiatric inpatient provision.

8.2.2 Current practice

8.2.2.1 Indications for admission

Garralda (1986) and Wolkind and Gent (1987) in UK studies, not specific to depression, found criteria for admission included failure of outpatient treatment, difficulties with assessment or diagnosis, family difficulties and the
need for 24 hour observation or care. Wrate et al (1994) in a UK multi-centre prospective study looked at reasons for admission in 276 young people admitted to specialised adolescent psychiatric units. The reasons given were: to provide a detailed psychiatric assessment (51%); to establish better therapeutic control of a case (36%); to provide a therapeutic peer group experience (36%); to obtain improved control over the adolescent’s behaviour (26%); to relieve out-patient colleagues from a treatment failure (20%); to assess or facilitate future placement needs (19%); to provide relief to exhausted parents (18%); to achieve psychological separation between parents and the patient (17%); and to provide an out-patient with schooling otherwise unavailable (9%).

Further surveys of criteria for admission to inpatient units have been carried out in the US (Costello et al, 1991; Pottick et al, 1995). Again, the studies were not specific to depression and generally replicate the UK findings, but also include factors specific to the US, such as the presence of insurance cover (Pottic et al, 1995). Costello et al (1991) developed a checklist of criteria which had good predictive value when determining whether or not a child needed admission. However, admission rates in the US are much higher than the UK, one study suggesting by approximately five times (Maskey, 1998). Clearly, caution is needed in applying such findings to settings in England and Wales.

Admission criteria in the UK continue to vary between individual inpatient units, but generally now fall into three broad categories (see Cotgrove, 2001; Green, 2002).

1. High risk: admission may be indicated when there are high levels of risk to the child/young person, secondary to suicidal thoughts or behaviours or self-neglect, beyond the capacity of the family and community based services to manage.

2. Intensive treatment: when the intensity of treatment needed is not available from other services. This is more commonly the case when depression is associated with other psychosocial difficulties, and/or comorbid disorder resulting in difficulties pervading all aspects of the child/young person’s life.

3. Intensive assessment: an inpatient unit can offer 24 hours-a-day assessment and supervision by a multi-disciplinary team to gather information to guide further management. This may involve observing the child/young person’s behaviour and their interaction with others, observing the effects of a specific intervention, such as the use of medication, or allowing time for a range of investigations to be carried out, such as cognitive assessments or physical investigations. The admission can also allow for the assessment of the child/young person’s difficulties out of the context of their home or school. For example, a young person
may appear severely depressed in the context of a problematic home environment or associated with bullying at school, but their mood may lift significantly when admitted. This information can be helpful in guiding future management whether or not further inpatient treatment is indicated. Inpatient assessment may also aid diagnosis. Young people with features of an emerging personality disorder, for example, may present with variable mood, including depression. Evidence of such comorbid disorder can help guide future management.

8.2.2.2 Contra-indications or risks of admission

It is important when considering an admission, that the potential benefits are balanced against potential harm. There is a range of reasons why inpatient treatment may not be appropriate:

- There may be concerns about admitting a particularly vulnerable depressed child/ young person into an environment where there were high levels of disturbance potentially compounding their distress.

- An impressionable child/ young person admitted to an environment with high levels of deliberate self-harm or acting out behaviours is at risk of acquiring additional dysfunctional behaviours or coping strategies, even where a skilled and experienced staff team openly address such difficulties.

- If protracted, an admission runs the risk of “institutionalisation” for the young person, including loss of support from the child’s local environment, and detrimental effects on family life (Green & Jones, 1998).

- Inpatient treatments are expensive (e.g., Green et al, 2001).

For these reasons inpatient admission is often considered a last resort.

8.2.3 Evidence of the efficacy of inpatient treatment

Most of the evidence of efficacy of inpatient treatment comes from single sample pre-test, post-test studies with no control or comparison groups. In many of these studies, outcome ratings are made by the treating clinician, introducing the possibility of rater-bias. Inpatient populations tend to be a heterogeneous group with relatively small numbers, hence few studies specifically look at treatment effects of inpatient admissions for young people with depressive disorder. Randomised controlled trials would not be an appropriate design in this context as the need for admission is often a direct
consequence of alternatives being either unavailable or involving unacceptable risks. Nevertheless, when competing alternatives are justifiable and available, controlled studies become a possibility.

8.2.3.1 Controlled Trials – United States

A small number of controlled trials comparing inpatient treatment with outpatient treatment have been carried out in the United States. Flomenhaft (1974) and Winsberg et al. (1980) just looked at young people with anti-social behaviour or externalising disorder.

The most recently published randomised controlled trial (Henggeler et al., 1999) conducted in the US compared a home based multi-systemic therapy (MST) with brief (1-2 week) inpatient psychiatric hospitalisation. MST offers a range of therapeutic interventions designed to impact on multiple determinants of the youngster’s key problems arising from the individual, family, peers, school and community. The sample was 113 adolescents, aged between 10 to 17 years, who had been approved for emergency psychiatric hospitalisation. Inclusion criteria included the presence of symptoms of suicidal ideation, homicidal ideation, psychosis, or threat of harm to self or others due to mental illness severe enough to warrant psychiatric hospitalisation. When interpreting the results it is notable that 44% of the “home-based” treatment sample also received hospitalisation. In addition, it appears that the MST group benefited from a far more intensive individualised therapeutic intervention. Only 15 of the sample received a diagnosis of major depression according to the Diagnostic Interview Schedule for Children, so it is not possible to draw significant conclusions about this subgroup. However, hospitalisation was more effective in improving young people’s self-esteem. Multi-systemic therapy was more effective in decreasing the young people’s externalising (behavioural) symptoms.

8.2.3.2 Other Studies – UK

Rothery et al. (1995) reviewed outcomes according to a set of 16 predetermined treatment goals and diagnosis in a multi-centre study of 320 consecutive admissions to 4 specialist adolescent units in the UK. Forty-four did not give consent, leaving 276 in the study. Of the 7% diagnosed (by clinical assessment carried out by the multidisciplinary team) with a “major depressive illness”, 90% were rated as having improved affective symptoms at discharge using a clinician rated 5-point scale.

Sheerin et al. (1999), studied a sample of 29 consecutive admissions (results from 26 reported) to a psychiatric inpatient unit for children aged 3 to 13 years (mean age =8.6 years) in Scotland. At 3 month and 15 month post-
discharge follow-up in a subgroup with depressive symptoms (n = 17), they found a significant reduction in symptoms (p<0.05) as rated by the Birleson Depression Scale between admission and at both 3 and 15 month follow-up.

Green et al (2001), in an English study, looked at 55 consecutive admissions of children and adolescents aged 6-17 years (mean 11.4 years) to two inpatient units from late 1995 to 1997. Referrals came from other child mental health specialists. Health gain was inferred from change scores in a range of measures taken at referral, admission, discharge and 6-month follow-up. Measures were made from multiple perspectives, including family, teacher, clinician and an independent researcher. Measures of CGAS and HoNOSCA showed no significant changes between referral and admission (waiting list control). Median waiting list time was 3 months. Significant health gain was found on most measures by discharge and sustained at follow-up. The sample included 40% with a primary mood disorder, but no separate analysis is reported for children and adolescents with depressive disorder.

Jacobs et al (2004) have repeated the Green et al (2001) study on a larger scale (n = 155). The sample consisted of sequential admissions of children and adolescents aged 3-17 years (mean 13.9 years) to 8 UK inpatient units (4 child, 4 adolescent) between January 2001 and April 2002). Diagnosis at admission was made using the researcher-rated schedule of affective disorders for children (K-SADS). A range of measures was used to monitor symptom change and health gain before admission, during admission and one year following discharge. Significant improvements were found in global functioning, psychopathology and 'cardinal problem' measures at discharge, which were maintained at one year follow-up. This compared with a much smaller (although still significant) improvement whilst on the waiting list. The findings based on the whole sample analysis remain significant for a subgroup with the diagnosis of depressive disorder. This subgroup is 44 on the basis of the clinicians ICD-10 diagnosis or 66 when the K-SADS is used, illustrating a difference in rates of diagnosis depending on whether diagnosis is based on use of a diagnostic instrument of clinical judgement. Clinical outcome ratings in this study rely largely on treating clinician scores for the Child Global Assessment Scale (CGAS) and the Health of the Nation Outcome Scale for Children and Adolescents (HoNOSCA).

Gowers et al (2000) used the Health of the Nation Outcome Scales for Children and Adolescents (HoNOSCA), a crude outcome measure rated by the treating clinician, on 35 consecutive admissions to an adolescent unit in England. This showed significant reductions in HoNOSCA scores between admission and discharge of 18.0 to 9.3 respectively in clinician rated scores (p<0.001) and 18.3 to 12.6 respectively in user rated scores (p<0.001).
8.2.4 Predictors of Outcome

Pfeiffer and Strzelecki (1990) carried out a literature search using the Medical Literature Analysis and Retrieval System, the Psychological Information Data Base and Mental Health Abstracts to look for publications on outcome and follow-up investigations of residential and inpatient psychiatric hospitalisations between 1975 and 1990. Thirty-four studies were identified. When analysing the findings weightings were applied that reflected sample size. These studies were not specific to depression in children and young people. They found a positive relationship between good outcome and the following factors:

Specific characteristics of treatments (e.g., completion of treatment programme, planned discharge and therapeutic alliance)

The use of after care

Level of family functioning and involvement with treatment

Length of stay (longer)

Higher intelligence.

Some symptom areas were found to be associated with poorer outcomes, such as:

Presence of psychotic symptoms

Bizarre symptoms

Anti-social behaviours

Under-socialised aggressive conduct disorder.

Kutash and Rivera (1996) carried out a systematic review of subsequent studies using a similar methodology, finding additional support for Pfeiffer and Strzelecki’s conclusions and in particular under scoring the benefit of family participation.

More recent studies have confirmed and clarified the following factors as predictors of outcome: length of stay (Sheerin et al, 1999; Green et al, 2001; Jacobs et al, 2004); therapeutic alliance between the child and their family with the inpatient team, and family participation in the therapeutic process (Green et al, 2001; Jacobs et al, 2004); pre-admission family functioning (King et al, 1997; Green et al, 2001); and severity of depressive symptoms (King et al, 1997).
8.2.5 Issues of consent for admission

It is desirable to admit young people with both the informed consent of both the patient and their parents, not least because the success of any treatment approach significantly depends upon the development of a positive therapeutic alliance between the child, the family and the inpatient team. However, there may be times when professionals consider admission to be necessary, but either the young person or the family do not consent.

If a young person below 18 years of age refuses treatment, but the parent (or guardian) believe strongly enough that treatment is desirable, then the young person’s wishes may be overruled. On the other hand, a child has the right to consent to treatment after their 16th birthday, or younger, if deemed ‘Gillick competent’, without involving the consent of the parents. Whilst the use of parental consent is legal, it is now considered good practice to only use parental consent for up to 2 weeks. In other contexts, the use the Mental Health Act 1983 should be considered as it includes safeguards such as the involvement of other professionals, a time limit and a straightforward procedure for appeals and regular reviews.

Alternative legislation includes using a Care Order (Section 31) under the Children Act 1989 or a Specific Issue Order (Section 8). Both of these options normally involve Social Services and can be time consuming. Another, more rapid alternative to the Children Act, is to apply for a Wardship Order, which in an emergency can be organised over the phone. It should be noted that at the time of writing, a new Mental Health Bill is under consideration which may alter current practice in this area.

8.2.6 Clinical Summary

For some young people and children with depression, particularly those at high risk of self-harm or neglect, or needing intensive assessment and/or treatment, there is often no alternative to inpatient admission. Although there are no randomised control trials specifically looking at psychiatric inpatient admission as a treatment for children and young people with depressive disorder, there are a number of studies using other methodologies suggesting that young people with depression have good outcomes from a period of admission. Clinical factors which appear to predict outcome, include: specific characteristics of treatments (e.g., completion of treatment programme, planned discharge and therapeutic alliance), the use of after care, the level of family functioning pre-admission, the level of family involvement with treatment, length of stay (longer), and higher intelligence. Little is known about the impact of service and treatment variables within the inpatient setting.
8.3 Clinical practice recommendations

8.3.1 Service configuration

8.3.1.1 CAMHS services and PCTs should consider the introduction of a CAMHS link worker into each secondary school and secondary Pupil Referral Unit as part of tier 2 provision within the locality (GPP) (1.1.4.1 NICE)

8.3.1.2 In the provision of training by CAMHS professionals for healthcare professionals in primary care, schools and relevant community settings, priority should be given to the training of pastoral support staff in secondary schools, community paediatricians, and GPs. (GPP) (1.3.1.4 NICE)

8.3.1.3 CAMHS link workers should establish clear lines of communication between CAMHS and Tier 1/2, with named contact people in each Tier/service, and develop systems for the collaborative planning of services for depressed youth in Tiers 1 and 2 (GPP) (1.1.4.2 NICE)

8.3.1.4 CAMHS Tier 1 professionals in conjunction with CAMHS Tier 2/3 professionals should routinely monitor the rates of detection, referral and treatment of children and young people with depression in local schools and primary care. This information should be used for planning services, and made available for local, regional and national comparison. (GPP) (1.1.4.3 NICE)

8.3.1.5 All healthcare professionals should routinely use, and record in the notes, appropriate outcome measures for the assessment and treatment of depression in children and young people. This information should be used for planning services, and made available for local, regional and national comparison. (GPP) (1.1.4.4 NICE)

8.3.1.6 If children and young people who have previously recovered from moderate or severe depression begin to show signs of a recurrence of depression, healthcare professionals in primary care, schools or other relevant community settings should refer them to CAMHS tier 2/3 services for rapid assessment. (GPP) (1.3.1.10 NICE)

8.3.2 Referral Criteria

8.3.2.1 For children and young people, the following factors should be used by healthcare professionals as referral criteria for tier 1 services:
• Exposure to a single uncomplicated undesirable event in the absence of other risk factors for depression
• Exposure to a recent undesirable life event in the presence of two or more other risk factors with no evidence of depression and/or self-harm
• Exposure to a recent undesirable life event in the context of multiple-risk histories for depression in one or more family members (parents or children) providing that there is no evidence of depression and/or self-harm
• Uncomplicated mild depression. (GPP) (1.3.2.1 NICE)

8.3.2.2 For children and young people, the following factors should be used by healthcare professionals as referral criteria for CAMHS:

• Depression with two or more other risks for depression
• Depression with multiple risk histories in another family member (parent or siblings)
• Mild depression in those who have not responded to interventions in tier 1 after 2 to 3 months
• Moderate or severe depression (including psychotic depression)
• Signs of a recurrence of depression in those who have recovered from previous moderate or severe depression
• Unexplained self-neglect of at least one month’s duration that could be harmful to the physical health of the child/young person.
• Actively suicidal ideas or plans in the child/young person. (GPP) (1.3.2.2 NICE)

8.3.2.3 For children and young people, the following factors should be used by healthcare professionals as referral criteria for tier 4 services:

• High recurrent risk of acts of self-harm or suicide
• Significant ongoing self-neglect (e.g. poor personal hygiene or significant reduction in eating that could be harmful to the physical health of the child/young person)
• Intensity of assessment/treatment and/ or level of supervision that is not available in tiers 2/3. (GPP) (1.3.2.3 NICE)

8.3.3 Inpatient Treatment

8.3.3.1 Most children and young people with depression should be treated on an outpatient or community basis. (C) (1.1.5.1 NICE)
8.3.3.2 Inpatient treatment should be considered for children and young people who present with a high risk of suicide, serious self-harm, self-neglect, and/or when the intensity of treatment (or supervision) needed is not available elsewhere, or when intensive assessment is indicated. (C) (1.6.6.1 NICE)

8.3.3.3 When considering admission for a child or young person with depression, the benefits of inpatient treatment need to be balanced against potential detrimental effects, for example loss of family and community support. (C) (1.6.6.2 NICE)

8.3.3.4 When inpatient treatment is indicated, professionals need to involve the child or young person and their family in the admission and treatment process whenever possible. (B) (1.6.6.3 NICE)

8.3.3.5 Commissioners and strategic health authorities should ensure that inpatient treatment should be available within reasonable travelling distance to enable the involvement of families and maintain social links. (B) (1.6.6.4 NICE)

8.3.3.6 Inpatient services need to have a range of treatments available including medication, individual and group psychological interventions and family support. (C) (1.6.6.5 NICE)

8.3.3.7 Inpatient facilities should be age-appropriate with the capacity to provide appropriate educational and related activities. (C) (1.6.6.6 NICE)

8.3.3.8 Planning for after care arrangements should take place prior to admission or as early as possible during an admission and should be based on the Care Programme Approach. (GPP) (1.6.6.7 NICE)

8.3.3.9 Those professionals (tier 4 CAMHS staff) involved in assessing children or young people for possible inpatient admission should be specifically trained in issues of consent and capacity, the use of current mental health legislation, and the use of Child Care Laws, as they apply to this group of patients. (GPP) (1.6.6.8 NICE)
9 The Human and Financial Cost of Childhood Depression in the UK Population

Productivity foregone due to premature deaths and morbidity arising as a consequence of childhood and adolescent depression (preventing parents and affected individuals from working in adulthood) has not been calculated in any study to date. We therefore constructed a model to compare a) healthcare costs of childhood depression with b) lost employment costs by parents, or by sufferers upon reaching adulthood.

The incidence of major depression tends to present itself in childhood from the age of 6 years onwards, at a rate of 0.5-0.75% in children aged 6-11 years (See Table 1). This means that 1/130 to 1/200 children aged 6-11 will experience major depression. However staggering this may appear, the figure increases up to 8-fold in the case of children aged 12-18 years, with 2-4% developing symptoms of major depression (See Table 1). Stated another way, 1/50 to 1/25 children aged 12-18 years will experience major depression. Including all depression criteria, the incidence rates for the 0-5, 6-11 and 12-18 age ranges are 1, 6 and 9%, respectively. Given that in 2003 there were 3.6m children aged 0-5, 4m children aged 6-11 and 7m children aged 12-18 (UN Population Division), the societal cost per year of depression in all these ages may total up to £149 million in treatment costs. However, the societal cost of depression in children and young persons rises to £14,393 million when 10% of patients who require such care are left untreated and, as a result, incur work-related absences in adulthood.

9.1.1 Counting the Costs
The methods of economic evaluation command a fairly high level of consensus and are reported in papers such as Drummond and Colleagues (1997). However, costing data for depression in children and adolescents are scarce to nonexistent. The few studies that do address this subject fail to meet rigorous criteria for health economic appraisal. To remedy this situation, there is a need for robust efficacy data and reliable cost estimates for alternative treatments that can be administered during childhood.

There is a pressing need for studies that report treatment costs alongside costs that accrue over a lifetime as a result of the condition. A child or young person who suffered childhood depression that prevented them from working in adulthood will on average lose £483.04 for every week they are absent (IDS Report, 2003), as well as opportunities for career advancement.
The same can be said if one or both parents losing work as a result of their child’s condition. From an economic vantage point, therefore, even a single week lost could fund a number of treatments. The challenge is to stratify these costs according to age and treatment modality and to compare these values to the cost of lost employment, which accounts for the major societal cost.

9.1.2 Treatment Costs and Work Absenteeism

The costs of alternative SSRI treatments are now comparable. For example, a one-year course of the SSRI fluoxetine (£13.26 in 2003 for 20mg tablet in generic form) would cost an estimated £216 including initial GP prescribing and follow-up costs.\(^9\) It is believed that patients will require up to 18 months of drug therapy to fully recover and avoid withdrawal symptoms. Therefore, a 1.5-year course of fluoxetine would cost £309.\(^{10}\)

Both the costs and benefits of treatment are known to be higher in the case of CBT. For example, 15 one-hour sessions of CBT delivered by a clinical psychologist costs an estimated £990\(^{11}\), or £681 more than the 1.5-year SSRI therapy. From a societal perspective, this cost needs to be weighed against the reduction of work-related absences, which may be much more costly than additional sessions of either of these psychological or pharmacological interventions.

Based on expert opinion, on average, an adult person with MDD loses fully 5 years of wages over a lifetime. An MDD sufferer will incur losses of £483.04 for every week they are absent (IDS Report, 2003), and this amounts to £25,118 per year, or £125,590 over this 5-year period. This does not include the costs placed on the criminal justices system and lost opportunities for career advancement.

From a societal perspective, prevention of one individual’s work absences in one year alone could fund therapist-led CBT treatments for more than 25 additional depression sufferers who have yet to recover. This same prevention of one patient’s 1-year work absences could fund a full course of fluoxetine treatment for more than 80 sufferers who have yet to recover, or combined fluoxetine and CBT/family therapy treatments for almost 20 individuals. If the maximum treatment costs were doubled (i.e. to a total amount of £2,000 per patient per year, as a result of more intensive treatments or higher patient costs) and the response rate halved (e.g. 5% responders), it will still be cost-efficient to offer to sufferers the full 1-year course of CBT, a

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\(^9\) £13.26 per month for the direct drug costs (West Midlands Medicines Information Service, 2003) plus £31 for first prescribing session (PSSRU 2003), plus an average of 1.5 x £26 for clinical consultations (Ibid), including indirect and qualification costs = £309.

\(^{10}\) Prescribing costs are included in the first-year only; thereafter, an average of 1.5 follow-up sessions are offered over six months.

\(^{11}\) £66 (per hour of client contact, PSSRU 2003) * 16 = £1,056
1.5-year course of fluoxetine, or both of these in combination. Indeed, prevention of one patient’s lost work time could potentially fund more than 12 patients’ intensive, combined CBT-fluoxetine treatments.

Results
Table 1: UK Age-Specific Treatment vs. Societal Costs for 14.6 million children ages 0-18 (2002-2003 estimations)
### Ages for Moderate and Severe Depression (MD) and Mild Depression Cases (D)

| Age Group | Incidence (%) | UK Age-Specific Population Size (Millions) | Affected Individuals (Millions) | \(^1\) Cost of Fluoxetine alone Assuming 1% so Treated (£Millions) | \(^2\) Cost of CBT or Family Therapy alone Assuming 10% so Treated (£Millions) | \(^3\) Cost of Combined Fluoxetine + CBT (£Millions) Assuming 10% so Treated (£Millions) | \(^4\) Societal Cost to UK Population where 10% of children and young persons incur 5-year work losses from MDD into adulthood

| 0-5 MD  | N/A     | 3.6  | 0 | -- | -- | -- | -- |
| 0.5 D  | 1.0     | 3.6  | 0.036 | 0.10 | 3.56 | 4.68 | 452.1 |
| 6-11 MD | 0.6     | 4    | 0.03 | 0.09 | 2.97 | 3.90 | 376.8 |
| 6-11 D  | 6.0     | 4    | 0.24 | 0.74 | 23.76 | 31.18 | 3,014.2 |
| 12-18 MD | 3.0    | 7    | 0.21 | 0.65 | 20.79 | 27.28 | 2,637.4 |
| 12-18 D | 9.0     | 7    | 0.63 | 1.95 | 62.37 | 81.84 | 7,912.2 |
| Total Aggregate Estimates | 7.8 (weighted average all ages) | 14.6 | 1.15 | 3.54 | 113.45 | 148.88 | 14,392.7 |
* MD = Moderate and Severe Depression Cases, D = Mild Depression Cases.

Footnotes for Table 1:

1. Calculated as £239 for the direct drug costs (West Midlands Medicines Information Service, 2003) over 18 months, plus £31 for first prescribing session (PSSRU 2003), plus 1.5 x £26 for clinical consultations (Ibid), including indirect and qualification costs = £309. Indeed, it is believed that patients will require up to 1.5 years of drug therapy to fully recover and avoid withdrawal symptoms. Prescribing costs are included in the first-year only; thereafter, an average of 1.5 follow-up sessions are offered over a course of six months.

2. £66 (per hour of client contact, PSSRU 2003) * 15 = £990; assumes family therapy and CBT are the same in aggregate cost, though the duration and modality of treatment may be different between them—fortnightly in the case of the former, monthly in the case of the latter.

3. This amounts to the sum of numbers 1 and 2, or £1,299. per patient, assuming their combination costs are additive.

4. If a depressed child incurs losses of £483.04 for every week they are absent (IDS Report, 2003) from work in adulthood, or their parents incur equivalent losses, this would amount to a total of £25,118 per year, or £125,590 due to unemployment over this 5-year period, not including costs placed upon the criminal justices system, lost opportunities for career advancement, and/or the intangible cost of suicide.

5. Alternatively, this projection holds true where the child’s parent(s) incur(s) up to 5-years lost employment.
9.1.3 Discussion

Table 1 illustrates the fact that depression in children and young persons may potentially cost the UK health services per annum up to £3.54 million for fluoxetine treatment, £113.45 million for CBT treatment, and £148.88 million for combined CBT and fluoxetine treatments. Even if 100% of the total number (1,150,000 individuals) of depressed children and young persons in the UK receive treatments equivalent to the cost of combined CBT plus a full course of fluoxetine, the health system would incur losses of an estimated £1,494 million. From a societal perspective, this cost must be weighed against the estimated £14,393 million cost of failing to treat the population of 10% of depressed children who may later incur work losses of their own or of their parents.

Initial results indicate a national cost due to childhood depression of £2,879 million per year, which is comparable to the total cost calculated by Kind and Sorensen (1993) a decade ago as referenced in the 2003 (Adult) Depression Guideline. Projecting this calculation over the 40 year working life of individuals yields £115,144 million in future societal costs using conservative assumptions: either 10% of depressed children who are left untreated become unemployed in adulthood where society suffers up to 5-years of their work absence as a consequence, or the burden on parents effected by childhood depression equates to functionally the same proportion of work absences.

This indicates that it may be 10-times cheaper to treat depressed children than to leave them untreated in adulthood. Even if 1/1000 depressed children who would otherwise incur work absences in adulthood are treated, the result will be cost-effective. Equally, where parents incur the 5-year work absences, it will be cost-effective to treat the children at the maximum level of care to the extent needed by the individual.

Because this analysis is the first to present total cost for childhood depression by age and treatment estimations for the UK, it is not without limitations. This model tests the consequences of 1% of severely-, mildly- and moderately-depressed individuals receiving only a 1.5-yr course of fluoxetine. It tests the financial consequences of 10% of depressed children and adolescents receiving, on average, 15 sessions of CBT. Finally, this model tests the financial consequences of 10% of children and adolescents receiving both CBT and fluoxetine treatments. However, not every child with mild depression will necessarily require or receive up to 15 sessions of CBT, a full course of fluoxetine, or any treatment at all. The point is to show, for costing purposes, that a full course of expensive treatment for all depressed children under the age of 18 years is cost-effective in light of the high cost due to work absences in not treating this population.
9.1.4 Conclusions

Efficient service utilisation based upon rigorous health economic evaluations on the cost-effectiveness of treating in childhood versus adulthood would reduce the social and economic burden of depression, to ensure optimal care is delivered within the constraints of the national budget.
10 Summary of Recommendations

[To be included for publication, please refer to recommendations in chapters for this consultation]
11 References


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Committee on Safety of Medicines. Use of selective serotonin reuptake inhibitors (SSRIs) in children and adolescents with major depressive disorder (MDD). www.mhra.gov.uk


Income data services. 9 June 2004. [http://www.incomesdata.co.uk/index/html](http://www.incomesdata.co.uk/index/html)


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12 Abbreviations and glossary of terms

Abbreviations

AD Antidepressant
ADHD Attention deficit hyperactivity disorder
AGREE Appraisal of Guidelines Research and Evaluation
AMED Allied and Complementary Medicine Database
APA American Psychiatric Association
AUC Area under the curve

BDI Beck Depression Inventory
BNF British National Formulary
BPS British Psychological Society

CAMHS Child and Adolescent Mental Health Services
CAPA The Child and Adolescent Psychiatric Assessment
CBT Cognitive behavioural therapy
CDI Children’s Depression Inventory
CD-MDD Comorbid conduct disorder
CDRS-R Children’s Depression Rating Scale Revised
CEBMH University of Oxford Centre for Evidence-Based Mental Health
CEFAHP Clinical Effectiveness Forum for the Allied Health Professions
CEMH Centre for Economics in Mental Health
CES-D The Center for Epidemiological Studies- Depression Scale
CGAS Child Global Assessment Scale
CI Confidence interval
CINAHL Cumulative Index to Nursing and Allied Health Literature
CORE Centre for Outcomes Research and Effectiveness, British Psychological Society
COT College of Occupational Therapists
CPA Care Programme Approach
CRU College Research Unit, Royal College of Psychiatrists
CSM Committee on Safety of Medicines

DA Dopamine
DALY Disability-adjusted life
DFES Department for Education and Skills
DICA-R The Diagnostic Interview for Children and Adolescents-Revised
DISC The Diagnostic Interview Schedule for Children
DSM Diagnostic and Statistical Manual of the American Psychiatric Association
<table>
<thead>
<tr>
<th>Acronym</th>
<th>Full Form</th>
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<tr>
<td>NNT</td>
<td>Number needed to treat</td>
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<tr>
<td>NSF</td>
<td>National Service Framework (for children)</td>
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<td>PCT</td>
<td>Primary Care Trust</td>
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<td>PRU</td>
<td>Pupil Referral Units</td>
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<tr>
<td>PsycINFO</td>
<td>An abstract (not full text) database of psychological literature from the 1800s to the present</td>
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<td>RADS</td>
<td>The Reynolds Adolescent Depression Scale</td>
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<tr>
<td>Rcpsych</td>
<td>Royal College of Psychiatrists</td>
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<tr>
<td>RCGP</td>
<td>Royal College of General Practitioners</td>
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<tr>
<td>RCN</td>
<td>Royal College of Nursing</td>
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<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
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<td>RPS</td>
<td>Royal Pharmaceutical Society</td>
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<tr>
<td>RR</td>
<td>Relative risk (risk ratio)</td>
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<tr>
<td>SD</td>
<td>Standard deviation</td>
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<td>SE</td>
<td>Standard error</td>
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<tr>
<td>SENC0</td>
<td>Special Educational Needs Co-ordinator</td>
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<td>SIGLE</td>
<td>System for Information on Grey Literature in Europe</td>
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<td>SIGN</td>
<td>Scottish Intercollegiate Guidelines Network</td>
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<tr>
<td>SMD</td>
<td>Standardised mean difference</td>
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<td>SSRIs</td>
<td>Selective serotonin reuptake inhibitors</td>
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<td>TADS</td>
<td>Treatment for Adolescents With Depression Study</td>
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<tr>
<td>TCA</td>
<td>Tricyclic antidepressant</td>
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<td>TG</td>
<td>Topic Group</td>
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<tr>
<td>WHO</td>
<td>World Health Organisation</td>
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<tr>
<td>WMD</td>
<td>Weighted mean difference</td>
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Glossary of terms

**Adherence:** The behaviour of taking medicine according to treatment dosage and schedule as intended by the prescriber. In this guideline, the term adherence is used in preference to the term compliance, but is not synonymous with concordance, which has a number of different uses/meanings.

**Adverse events:** Any undesirable experience that results in any of the following outcomes: death, a life-threatening experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

**Affective Disorder:** A syndrome in which an individual experiences a significant alteration in affect or mood. Whether depressed or elated, this change of mood is accompanied by alteration in the individuals activity levels.

**Atypical depression:** A sub-type of major depressive disorder in which patients have reactive mood and at least two of the following four symptoms: hyperphagia, hypersomnia, leaden paralysis, or a lifetime history of interpersonal sensitivity to rejection, resulting in functional impairment.

**Bipolar disorder:** this condition is also known as manic depression. It is an illness that affects mood, causing a person to switch between feeling very low (depression) and very high (mania).

**Care Programme Approach (CPA):** Introduced in 1991, this approach was designed to ensure that different community services are coordinated and work together towards a particular person’s care. This approach requires that professionals from the health authority and local authority get together to arrange care, and applies to all patients accepted for care by the specialist mental health services.

**Child:** an individual aged 5 to 11 years old

**Chronic depression:** a form of depression, which is marked by a course of illness lasting 2 years or more.

**Clinical questions:** questions posed by the guideline development group which are used to guide the identification and interrogation of the evidence-base relevant to the topic of the guideline.

**Clinical significance:** Where the effect of a treatment is large enough to be of real benefit to a patient, for example in terms of reduced symptoms or improved quality of life.
Cognitive behavioural therapies (CBT): Discrete, time-limited, structured psychological interventions, derived from the cognitive-behavioural model of affective disorders in which the patient: (1) works collaboratively with a therapist to identify the types and effects of thoughts, beliefs and interpretations on current symptoms, feelings states and/or problem areas; (2) develops skills to identify, monitor and then counteract problematic thoughts, beliefs and interpretations related to the target symptoms/problems; and (3) learns a repertoire of coping skills appropriate to the target thoughts, beliefs and/or problem areas.

Cohort study (also known as follow-up, incidence, longitudinal, or prospective study): An observational study in which a defined group of people (the cohort) is followed over time. Outcomes are compared in subsets of the cohort who were exposed or not exposed (or exposed at different levels) to an intervention or other factor of interest.

Committee on Safety of Medicines (CSM): The CSM is one of the independent advisory committees established under the Medicines Act (Section 4) which advises the UK Licensing Authority (Government Health Ministers) on the quality, efficacy and safety of medicines in order to ensure that appropriate public health standards are met and maintained.

Comorbidity: Two or more diseases or conditions occurring at the same time, such as depression and anxiety.

Confidence interval (CI): The range within which the ‘true’ values (e.g. size of effect of an intervention) are expected to lie with a given degree of certainty (e.g. 95% or 99%). (Note: confidence intervals represent the probability of random errors, but not systematic errors or bias).

Costs (direct): The costs of all the goods, services and other resources that are consumed in the provision of a health intervention. They can be medical or non-medical.

Costs (indirect): The lost productivity suffered by the national economy as a result of an employee’s absence from the workplace through illness, decreased efficiency or premature death.

Depression unresponsive to treatment: A term used to describe depression that has failed to respond to two or more antidepressants at an adequate dose for an adequate duration given sequentially.

Double blind (also termed double masked): A trial in which neither the participants nor the investigators (outcome assessors) are aware of which intervention the participants are given. The purpose of blinding the participants (recipients and providers of care) is to prevent performance bias.
The purpose of blinding the investigators (outcome assessors) is to protect against detection bias.

**Dysphoria:** An emotional state characterized by malaise, anxiety, depression or unease.

**Dysthymia:** A chronic lowering of mood that does not fulfil the criteria for recurrent depressive disorder, in terms of either severity or duration of individual episodes. There are variable phases of minor depression and comparative normality. Despite tiredness, feeling down and not enjoying very much, people with dysthymia are usually able to cope with every day life.

**Effect size:** An estimate of the size of the effect that a given treatment has compared with a control treatment (for example, another active treatment, no treatment or ‘treatment as usual’). Examples of effect sizes are the relative risk statistic (used for dichotomous outcomes), and the weighted mean difference and standardised mean difference statistics (both used for continuous outcomes).

**Effectiveness:** The extent to which a specific intervention, when used under ordinary circumstances, does what it is intended to do. Clinical trials that assess effectiveness are sometimes called management trials.

**Efficacy:** The extent to which an intervention produces a beneficial result under ideal conditions. Clinical trials that assess efficacy are sometimes called explanatory trials and are restricted to participants who fully co-operate. The randomised controlled trial is the accepted ‘gold standard’ for evaluating the efficacy of an intervention.

**Electroconvulsive therapy (ECT)** (also termed convulsive therapy, electroshock therapy or shock therapy): A therapeutic procedure in which an electric current is briefly applied to the brain to produce a seizure. This is used for treatment of severe depression symptoms or to ease depression that is not responding well to other forms of treatment.

**Family therapy:** Family sessions with a treatment function based on systemic, cognitive behavioural or psychoanalytic principles, which may include psychoeducational, problem-solving and crisis management work and specific interventions with the identified patient.

**Forest plot:** A graphical display of results from individual studies on a common scale, allowing visual comparison of trial results and examination of the degree of heterogeneity between studies.

**Funnel plot:** A scatter plot used to assess publication bias within a set of studies in a meta-analysis. Publication bias can occur when studies finding a favourable result are published in favour of those finding an unfavourable
result. It plots estimated treatment effects against a measure of studies’ sample sizes. If no publication bias is present, the plot should resemble an inverted funnel with the results of smaller studies being more widely scattered than those of larger studies.

**Good practice point (GPP):** Recommended good practice based on the clinical experience of the Guideline Development Group.

**Guided self-help (GSH):** A self-administered intervention designed to treat depression, which makes use of a range of books or a self-help manual that is based on an evidence-based intervention and is designed specifically for the purpose.

**Guideline development group (GDG):** The group of academic experts, clinicians and patients responsible for developing the guideline.

**Guideline recommendation:** A systematically developed statement that is derived from the best available research evidence, using predetermined and systematic methods to identify and evaluate evidence relating to the specific condition in question.

**Health Technology Appraisal (HTA):** The process of determining the clinical and cost effectiveness of a health technology in order to develop recommendations on the use of new and existing medicines and other treatments within the NHS in England and Wales.

**Heterogeneity:** term used to illustrate the variability or differences between studies in the estimates of effects.

**Homogeneity:** term used to illustrate when there are no or minor variations in the directions and degrees of results between individual studies that are included in the systematic review.

**Interpersonal psychotherapy (IPT):** A discrete, time-limited, structured psychological intervention, derived from the interpersonal model of affective disorders that focuses on interpersonal issues and where: (1) therapist and patient work collaboratively to identify the effects of key problematic areas related to interpersonal conflicts, role transitions, grief and loss, and social skills, and their effects on current symptoms, feelings states and/or problems; (2) they seek to reduce symptoms by learning to cope with or resolve these interpersonal problem areas.

**Kiddie Schedule for Affective Disorders and Schizophrenia for School Age Children (K-SADS):** An interviewer led procedure for diagnostic assessment of depression including the severity of current episode designed to be used by
trained individuals with some clinical experience for use with participants aged 6 to 17 years.

**Major depression** (also called **clinical depression** or **major depressive disorder**): The guideline uses the ICD 10 definition in which ‘an individual usually suffers from depressed mood, loss of interest and enjoyment, and reduced energy leading to increased fatiguability and diminished activity. Marked tiredness after only slight effort is common. Other symptoms are: (a) reduced concentration and attention; (b) reduced self-esteem and self-confidence; (c) ideas of guilt and unworthiness (even in a mild type of episode); (d) bleak and pessimistic views of the future; (e) ideas or acts of self-harm or suicide; (f) disturbed sleep; (g) diminished appetite.’

**Meta-analysis:** The use of statistical techniques in a systematic review to integrate the results of several independent studies.

**Mild depression:** The guideline uses the ICD 10 definition of 4-6 depressive symptoms.

**Moderate depression:** The guideline uses the ICD 10 definition of 7-9 depressive symptoms.

**Monoamine oxidase inhibitors (MAOIs):** A class of antidepressants that help brain neurotransmitters remain active longer, which may lead to a reduction in symptoms of depression.

**Mood and Feelings Questionnaire for Children (MFQ -C):** A self-report measure used to screen for depression.

**Mood and Feelings Questionnaire for Parents (MFQ -P):** A self-report measure used by parents to screen for depression in their child.

**NICE 2002:** In this guideline, the reference used to cite recommendations from NICE technology appraisals.

**Placebo:** A non-drug, or physically inactive substance, which is given as part of a clinical research trial. It has no specific pharmacological activity against illness.

**Placebo response (or placebo effect):** A phenomenon in which a placebo a substance like sugar, distilled water, or saline solution -- can improve a patient's condition simply because the person has the expectation that it will be helpful. Expectation to plays a potent role in the placebo effect.

**Psychodynamic psychotherapy:** psychological interventions, derived from a psychodynamic/psychoanalytic model in which: (1) therapist and patient explore and gain insight into conflicts and how these are represented in
current situations and relationships including the therapy relationship (e.g. transference and counter-transference); (2) patients are given an opportunity to explore feelings, and conscious and unconscious conflicts, originating in the past, with the technical focus on interpreting and working through conflicts; (3) therapy is non-directive and patients are not taught specific skills such as thought monitoring, re-evaluation or problem-solving.

**Psychoeducation:** Programmes for individual patients or groups of patients that involve an explicitly described educational interaction between the intervention provider and the patient or carer as the prime focus of the study.

**Psychosis:** a condition in which an individual isn't in contact with reality. This can include: sensing things that aren't really there (hallucinations); having beliefs that aren't based on reality (delusions); problems in thinking clearly; and not realising that there is anything wrong with themselves (called ‘lack of insight’).

**Racial identity status:** An individual’s perception of himself or herself as belonging to a racial group; also the beliefs, morals and attitudes that one shares with a particular racial group in contrast with other groups. It has been suggested that racial identity is integral to personality and is a key dynamic factor in psychotherapeutic dyads.

**Randomisation:** A method used to generate a random allocation sequence, such as using tables of random numbers or computer-generated random sequences. The method of randomisation should be distinguished from concealment of allocation, because if the latter is inadequate, selection bias may occur despite the use of randomisation. For instance, a list of random numbers may be used to randomise participants, but if the list were open to the individuals responsible for recruiting and allocating participants, those individuals could influence the allocation process, either knowingly or unknowingly.

**Randomised controlled trial (RCT) (also termed randomised clinical trial):** An experiment in which investigators randomly allocate eligible people into groups to receive or not to receive one or more interventions that are being compared. The results are assessed by comparing outcomes in the different groups. Through randomisation, the groups should be similar in all aspects apart from the treatment they receive during the study.

**Recurrent depression:** the development of a depressive disorder in a person who has previously suffered from depression.

**Relapse:** The reappearance of disease signs and symptoms after apparent recovery. The definitions of relapse used in the review in the guideline were those adopted by the individual studies and varied between studies.
Relative risk (RR): Also known as risk ratio; the ratio of risk in the intervention group to the risk in the control group. The risk (proportion, probability or rate) is the ratio of people with an event in a group to the total in the group. A relative risk (RR) of 1 indicates no difference between comparison groups. For undesirable outcomes, an RR that is less than 1 indicates that the intervention was effective in reducing the risk of that outcome.

Remission: Diminution or disappearance of symptoms.

Risk profiling: A structured assessment and analysis of those factors in the child/young person’s environment and history that are known to increase the risk of depression.

Screening: Screening is defined by the guideline development group as a simple test performed on a large number of people to identify those who have depression.

Selective serotonin reuptake inhibitors (SSRIs): A class of antidepressant medications that increase the level of serotonin (a neurotransmitter believed to influence mood) in the brain.

Self-help: Any activity or lifestyle choice that an individual makes in the belief that it will confer therapeutic benefit.

Sleep hygiene: Behavioural practices that promote continuous and effective sleep.

Standard care: The usual care given to those suffering from acute psychiatric episodes in the area concerned.

Standard doses: The recommended dose range listed in the British National Formulary; this normally reflects the information contained in the manufacturers’ Summary of Product Characteristics (SPC) as well as advice from an external panel of experts.

Statistical significance: An effect size that is statistically significant is one where the probability of achieving the result by chance is less than 5% - i.e. a p-value less than 0.05.

Stepped care: A considered, organised, co-ordinated approach to screening, assessment, treatment and onward referral by an individual practitioner, team or care provider organisation, within the parameters of defined protocols or pathways. These approaches may or may not be provided within the context of a fixed budget (for example, the Health Maintenance Organisation (HMO) in the USA). Primary Care Trusts are required to develop protocols for the...
treatment of depression in primary care within the National Service Framework for Mental Health.

**Stepped care model:** A sequence of treatment options to offer simpler and less expensive interventions first and more complex and expensive interventions if the patient has not benefited, based on locally agreed protocols.

**Sub-syndromal depression** (also termed *sub-threshold depression*): Depression symptoms that fail to meet criteria for major depressive disorder.

**Suicidal ideation:** Thoughts about suicide or of taking action to end one's own life.

**Tier 1 CAMHS:** Primary care services including GP’s, health visitors, school nurses, social workers, teachers, juvenile justice workers, voluntary agencies and social services.

**Tier 2 CAMHS:** Services provided by professionals relating to workers in primary care including clinical child psychologists, paediatricians, educational psychologists, child and adolescent psychiatrists, child and adolescent psychotherapists, community nurses/ nurse specialists and family therapists.

**Tier 3 CAMHS:** Specialised services for more severe, complex or persistent disorders including child and adolescent psychiatrists, clinical child psychologists, nurses (community or in-patient), child psychotherapists, occupational therapists, speech and language therapists, art, music and drama therapists, family therapists.

**Tier 4 CAMHS:** Tertiary level services such as day units, highly specialised outpatient teams and in-patient units.

**Tricyclic antidepressants (TCAs):** The original class of antidepressants used to treat depression by increasing levels of the neurotransmitters serotonin and norepinephrine.

**Wait list control:** A term used in controlled trials when participants are allocated to a 'wait list' condition. Outcome measures are taken from these participants at the end of the waiting period and compared to those from participants who received the treatment. The wait list participants then receive the treatment.
**Watchful waiting:** an intervention in which no active treatment is offered to the child or young person with depression if in the opinion of the healthcare professional the person may recover without a specific intervention. All such patients should be offered a follow up appointment.

**Young person:** an individual aged 12 to 18 years old.

Appendices A–N, O, and P–R are in separate files for consultation.