Depression in children and adolescents: complementary therapies

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Philip Hazell

ABSTRACT

INTRODUCTION: Depression is the world's leading cause of disability-adjusted life years lost among adolescents. Depression may affect 2% to 8% of children and adolescents, with a peak incidence around puberty. It may be self-limiting, but about 40% of affected children experience a recurrent attack, one third of affected children will make a suicide attempt, and 3% to 4% will die from suicide. METHODS AND OUTCOMES: We conducted a systematic overview, aiming to answer the following clinical question: What are the effects of complementary treatments for depression in children and adolescents? We searched: Medline, Embase, The Cochrane Library, and other important databases up to August 2014 (BMJ Clinical Evidence overviews are updated periodically; please check our website for the most up-to-date version of this overview). RESULTS: At this update, searching of electronic databases retrieved 141 studies. After deduplication and removal of conference abstracts, 103 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 60 studies and the further review of 43 full publications. Of the 43 full articles evaluated, two systematic reviews were added at this update. CONCLUSIONS: In this systematic overview, we categorised the efficacy for six interventions based on information about the effectiveness and safety of glutamine, light therapy, omega-3 polyunsaturated fatty acids, s-adenosylmethionine, St John's wort (Hypericum perforatum), and vitamin C.

QUESTIONS

INTERVENTIONS

Key points

- Depression in children and adolescents may have a more insidious onset than in adults, with irritability a more prominent feature than sadness.

  Depression may affect 2% of children and 4% to 8% of adolescents, with a peak incidence around puberty.

  It may be self-limiting, but about 40% of affected children experience a recurrent attack, one third of affected children will make a suicide attempt, and 3% to 4% will die from suicide.
- In the previous version of this overview, we examined the evidence for a broad range of therapies, including pharmacological, psychological, and combination treatments for depression in children and adolescents. For this update we have focused on selected complementary therapies.
- Up to 20% of young people with depression may be taking complementary treatments. Benefit in treating depression has been claimed for at least 70 complementary treatments, but efficacy studies have been conducted for only a minority of these agents.
- We searched for RCTs and systematic reviews of RCTs on the effectiveness of six complementary therapies for depression in children and adolescents.

  We found little evidence that met our inclusion criteria.
- We don't know whether glutamine, omega-3 polyunsaturated fatty acids, s-adenosylmethionine, St John's wort, or vitamin C are beneficial.
- There is some evidence from small studies that light therapy may be beneficial in reducing depression symptoms in young people with seasonal affective disorder (SAD), but we don't know if these benefits generalise to young people with major depression.
- As complementary treatments are generally classified as dietary supplements, there is no regulatory requirement or financial incentive to provide clinical trial evidence of efficacy and safety. The conduct of such trials would not be technically difficult.

Clinical context

GENERAL BACKGROUND

Depression may affect 2% to 8% of children and adolescents, with a peak incidence around puberty. In 2014, it was reported as the world's leading cause of disability-adjusted life years lost among adolescents.

FOCUS OF THE REVIEW

In the previous version of this overview, we examined the evidence for a broad range of therapies, including pharmacological, psychological, and combination treatments for depression in children and adolescents. For this update we have focused on selected complementary therapies because up to 20% of young people with depression may be using them. It is possible that some people prefer to take complementary treatments because of concern about the well-publicised potential adverse effects of antidepressant medications. Multiple complementary medicines or homeopathic remedies have been used, for which claims of antidepressant effect have been made. A systematic review included in this overview found that, for nearly all of these agents, no studies of any kind were found to support the claim of efficacy. As a starting point, we have focused on six complementary treatments for which the review identified at least one efficacy study in young people.

COMMENTS ON EVIDENCE

Many of the trials identified in the literature search did not meet the inclusion criteria for this overview. Some studies of light therapy suggest benefit in reducing depressive symptoms, but the participants in these trials were mostly suffering seasonal affective disorder. The studies are out of scope, as the focus of the chapter is treatment for major depression. The only trial of omega-3 polyunsaturated fatty acids did not meet *BMJ Clinical Evidence* inclusion criteria as the attrition rate of the sample exceeded 20%. Studies of glutamine, s-adenosylmethionine, St John's wort (*Hypericum perforatum*), and vitamin C were not RCTs. Most complementary treatments are classified as dietary supplements rather than pharmaceuticals; hence, manufacturers are not obliged to provide evidence of efficacy and safety prior to marketing. There is no financial incentive to run any clinical trials; therefore, it is unsurprising that evidence is sparse. One way to stimulate more clinical trials of complementary treatments would be to require the manufacturers of dietary supplements to provide the same level of evidence to support claims of efficacy as that required of manufacturers of pharmaceutical products. As this would drive up prices, it might not be popular with consumers.

SEARCH AND APPRAISAL SUMMARY

The update literature search for this overview was carried out from the date of the last search, July 2011, to August 2014. A back search from 1966 was performed for the new options added to the scope at this update. For more information on the electronic databases searched and criteria applied during assessment of studies for potential relevance to the overview, please see the Methods section. Searching of electronic databases retrieved 141 studies. After deduplication and removal of conference abstracts, 103 records were screened for inclusion in the overview. Appraisal of titles and abstracts led to the exclusion of 60 studies and the further review of 43 full publications. Of the 43 full articles evaluated, two systematic reviews were added at this update.

ADDITIONAL INFORMATION

Complementary treatments are not inert pharmacologically; therefore, there is the potential for interaction with pharmaceuticals. Prior to prescribing medication, clinicians should ask all patients whether they have been taking complementary treatment.

DEFINITION

Depression is the world's leading cause of disability-adjusted life years lost among adolescents. [1] Compared with adult depression (see overviews Depression in adults: drug and physical treatments and Depression in adults: psychological treatments), depression in children (6–12 years) and adolescents (13–18 years) may have a more insidious onset, may be characterised more by irritability than by sadness, and occurs more often in association with other conditions such as anxiety, conduct disorder, hyperkinesis, and learning problems. [2] [3] The term 'major depression' is used to distinguish discrete episodes of depression from mild, chronic (1 year or longer) low mood or irritability, which is known as 'dysthymia'. [2] [3] The severity of depression may be defined by the level of impairment and the presence or absence of psychomotor changes and somatic symptoms. In some studies, severity of depression is defined according to cut-off scores on depression rating scales. Definitions of refractory depression (also known as treatment-resistant depression) vary, but in this overview it refers to depression that has failed to respond, or has only partially responded, to an adequate trial of at least two recognised treatments. [4] For the purposes of this overview, we excluded studies if the population was entirely made up of children and adolescents with refractory depression, but we included studies that had mixed populations of refractory and non-refractory depression. **Complementary treatments** may be defined as those involving practices and beliefs that are not upheld by the dominant health systems in Western countries. [5] Complementary medicines (as opposed to physical treatments) may also be defined as products that are marketed as nutraceuticals. Up to 20% of young people with depression may be using complementary treatments. [5] It is possible that some people prefer to take complementary treatments because of concern about the well-publicised potential adverse effects of antidepressant medications. [5] One systematic review included in this overview [5] identified 70 complementary medicines or homeopathic remedies, for which claims of antidepressant effect have been made. For nearly all

these agents, no studies of any kind were found to support the claim of efficacy. In this overview, we have concentrated on six complementary treatments, for which the review identified at least one efficacy study in young people. [5]

INCIDENCE/ PREVALENCE

The prevalence of major depression is estimated to be approximately 2% in children and 4% to 8% in adolescents. [3] Pre-adolescent boys and girls are affected equally by the condition, but in adolescents, depression is more common among girls than boys. [3]

AETIOLOGY/ RISK FACTORS

Depression in children usually arises from a combination of genetic vulnerability, suboptimal early developmental experiences, and exposure to stresses. However, depressive syndromes sometimes occur as sequelae to physical illness, such as viral infection, and may overlap with fatigue syndromes. [6] The heritability of depression may increase with age, [7] but the findings from genetics studies are inconsistent. Recurrent depression seems to have a stronger familial association compared with single-episode depression. [8] Depression-prone individuals have a cognitive style characterised by an overly pessimistic outlook on events. [9] This cognitive style precedes the onset of depression and seems independent of recent life events and ongoing stresses. [10] Stressful life events may trigger the first occurrence of depression, but are rarely sufficient on their own to cause depression. After a first incidence of depression, lower levels of stress are needed to provoke subsequent episodes of illness. [2] Enduring problems in the relationship with the primary carers is an important risk factor for depression, but such difficulties also predispose to other psychiatric disorders. [2]

PROGNOSIS

In children and adolescents, the recurrence rate after a first depressive episode is 40%. [11] Young people experiencing a moderate to severe depressive episode may be more likely than adults to have a manic episode within the following few years. [2] [3] [12] Trials of treatments for child and adolescent depression have found high rates of response to placebo (as much as two-thirds of people in some inpatient studies), suggesting that episodes of depression may be self-limiting in many cases. [13] One third of young people who experience a depressive episode will make a suicide attempt at some stage, and 3% to 4% of those who experience depression will die from suicide. [14]

AIMS OF INTERVENTION

To improve mood, social and occupational functioning, and quality of life; to reduce morbidity and mortality; to prevent recurrence of depressive disorder, with minimal adverse effects.

OUTCOMES

Symptom improvement Primarily measured by developmentally specific pseudo-continuous outcome measures such as the Children's Depression Rating Scale and the Children's Depression Inventory, although some studies of adolescents use scales developed for use in adults, such as the Hamilton Rating Scale for Depression. Symptom improvement may also be measured by pseudo-continuous outcome measures reported by parents, such as the Children's Depression Inventory for Parents. Categorical outcomes are sometimes expressed as children and adolescents no longer meeting specified criteria for depression on a structured psychiatric interview, such as the Kiddie-Schedule for Affective Disorders and Schizophrenia (Kiddie-SADS), which combines data from children and their parents. Global improvement in symptoms, as judged by an investigator, is sometimes reported using the Clinical Global Impressions Scale or the Children's Global Assessment Scale (see table 1, p 9). **Quality of life**; **adverse effects**.

METHODS

Search strategy *BMJ Clinical Evidence* search and appraisal date August 2014. Databases used to identify studies for this systematic overview include: Medline 1966 to August 2014, Embase 1980 to August 2014, The Cochrane Database of Systematic Reviews 2014, issue 8 (1966 to date of issue), the Database of Abstracts of Reviews of Effects (DARE), and the Health Technology Assessment (HTA) database. **Inclusion criteria** Study design criteria for inclusion in this systematic overview were systematic reviews and RCTs published in English, and containing 20 or more individuals, of whom more than 80% were followed up. There was no minimum length of follow-up. We included studies described as 'open', 'open label', or not blinded. *BMJ Clinical Evidence* does not necessarily report every study found (e.g., every systematic review). Rather, we report the most recent, relevant, and comprehensive studies identified through an agreed process involving our evidence team, editorial team, and expert contributors. **Evidence evaluation** A systematic literature search was conducted by our evidence team, who then assessed titles and abstracts, and finally selected articles for full text appraisal against inclusion and exclusion criteria agreed *a priori* with our expert contributor. In consultation with the expert contributor, studies were selected for inclusion and all data relevant to this overview extracted into the benefits and harms section of the review. In addition, information that did not meet our pre-defined criteria for inclusion in the benefits and harms section may have been reported in the 'Further information on studies' or 'Comment' section. **Adverse effects** All serious adverse effects, or those adverse effects reported as statistically significant, were included in the harms section of the overview. Pre-specified adverse effects

identified as being clinically important were also reported, even if the results were not statistically significant. Although *BMJ Clinical Evidence* presents data on selected adverse effects reported in included studies, it is not meant to be, and cannot be, a comprehensive list of all adverse effects, contraindications, or interactions of included drugs or interventions. A reliable national or local drug database must be consulted for this information. **Comment and Clinical guide sections** In the Comment section of each intervention, our expert contributors may have provided additional comment and analysis of the evidence, which may include additional studies (over and above those identified via our systematic search) by way of background data or supporting information. As *BMJ Clinical Evidence* does not systematically search for studies reported in the Comment section, we cannot guarantee the completeness of the studies listed there or the robustness of methods. Our expert contributors add clinical context and interpretation to the Clinical guide sections where appropriate. **Structural changes this update** At this update we have removed the following previously reported questions: What are the effects of pharmacological, psychological, and combination treatments for depression in children and adolescents? What are the effects of treatments for refractory depression in children and adolescents? We have focused on the following question: What are the effects of complementary treatments for children and adolescents with depression? We have added four new interventions as follows: glutamine, light therapy, s-adenosylmethionine, and vitamin C. **Data and quality** To aid readability of the numerical data in our overviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). *BMJ Clinical Evidence* does not report all methodological details of included studies. Rather, it reports by exception any methodological issue or more general issue that may affect the weight a reader may put on an individual study, or the generalisability of the result. These issues may be reflected in the overall GRADE analysis.

QUESTION What are the effects of complementary treatments for depression in children and adolescents?

OPTION GLUTAMINE New

- We found no direct information from RCTs about glutamine in the treatment of depression in children or adolescents.

Benefits and harms

Glutamine:

We found one systematic review (search date 2006) evaluating complementary and self-help treatments in the treatment of depression in children and adolescents. [5] The review identified no RCTs on the effects of glutamine in the treatment of depression in children or adolescents.

Comment: The rationale for glutamine supplementation is the finding of altered glutamine levels in some people with depression.

OPTION LIGHT THERAPY New

- We found no direct information from RCTs about light therapy in the treatment of depression in children or adolescents.
- Three RCTs were identified by two systematic reviews that did not meet *BMJ Clinical Evidence* inclusion criteria because they either had too few participants, were in young adults only (over 18 years old), or only considered light therapy in people with winter depression.
- There is some evidence from small studies that light therapy may be beneficial in reducing depression symptoms in young people with seasonal affective disorder (SAD), but we don't know if these benefits generalise to young people with major depression.

Benefits and harms

Light therapy:

We found two systematic reviews (search dates 2006; [5] and 2008 [15]) evaluating light therapy in the treatment of depression in children and adolescents. The first review [5] identified two RCTs, and the second review [15] identified one RCT of light therapy in the treatment of depression in children or adolescents. None of the three RCTs met *BMJ Clinical Evidence* reporting criteria. However, we have included more details on these RCTs in the Comment section. We found no subsequent RCTs meeting *BMJ Clinical Evidence* inclusion criteria.

Comment:

The three RCTs identified by the two systematic reviews did not meet *BMJ Clinical Evidence* inclusion criteria because they either had too few participants, were in young adults only (>18 years old), or only considered light therapy in people with winter depression.

The first RCT of light therapy included in the first systematic review [5] compared light therapy (2 hours in the evening) with relaxation training in five patients described as having 'winter depression' and four patients with non-seasonal depression. [16] The trial used a single-blind crossover design. The review reported that the RCT found a significant improvement in the patients with winter depression treated with light therapy, but not in the patients with non-seasonal depression. The second RCT included in the first review [5] compared light therapy (2 hours in the early morning plus 1 hour in the evening) with placebo (wearing clear goggles for 1 hour plus 5 minutes low-intensity dawn simulation) in 28 patients with winter depression. [17] The trial used a double-blind crossover design. The review reported that the RCT found a significant improvement in parents' reports of symptoms, but only a non-significant trend in symptoms reported by the children themselves.

The second review found one RCT that compared bright light therapy (10,000 lux bright light for 30 minutes/day) with control (exposure to a deactivated negative ion generator for 30 minutes/day) in 40 young adults (aged 18 to 22 years) with SAD for 3 weeks. [18] Outcomes included depressive symptoms using the Beck Depression Inventory second edition (BDI-II) and the Structured Interview Guide for the Hamilton Depression Rating-Seasonal Affective Disorder (SIGH-SAD), with a 50% reduction of symptoms considered to represent remission. After 3 weeks of treatment, there were significantly more people in remission in the bright light treatment group compared with control (80% in the bright light therapy group *v* 0% in the control group; P <0.001).

Evidence of benefit of light therapy for non-seasonal depression in adults would give some indication whether the findings of the studies of light therapy in young people with SAD might generalise to young people with non-seasonal depression. A review of light therapy for non-seasonal depression in adults found evidence of modest benefit. [19] However, in most included studies light therapy was adjunctive to other treatments, meaning that they would not meet *BMJ Clinical Evidence* inclusion criteria. At the time of publication, the generalisability of the studies in young people with SAD to young people with major depression is, therefore, unknown.

Clinical guide

Use of a light box is classified as a self-help strategy in the NICE guideline on depression in children and young people, [20] with the goal being to improve circadian rhythms, rather than to impact on depression symptoms directly. The guideline positions self-help after 4 weeks of watchful waiting and before the introduction of specific psychological therapies in the management of depression in young people.

OPTION OMEGA-3 POLYUNSATURATED FATTY ACIDS (FISH OIL)

- We found no direct information from RCTs about omega-3 polyunsaturated fatty acids in the treatment of depression in children or adolescents.

Benefits and harms

Omega-3 polyunsaturated fatty acids:

We found one systematic review (search date 2006) evaluating complementary and self-help treatments in the treatment of depression in children and adolescents. [5] The review identified one RCT on the effects of omega-3 polyunsaturated fatty acids in the treatment of depression in children or adolescents, but it did not meet *BMJ Clinical*

Evidence inclusion criteria. We have included some information on this RCT in the Comment section. We found no subsequent RCTs.

Comment: At present, there is insufficient evidence to support the use of omega-3 polyunsaturated fatty acids in the treatment of depression in children and adolescents. The RCT included in the systematic review compared omega-3 fatty acids (both eicosapentaenoic acid [EPA] and docosahexaenoic acid [DHA]) with placebo in children aged 6 to 12 years. [21] It did not meet *BMJ Clinical Evidence* inclusion criteria because the rate of attrition was higher than our requirement for inclusion. A total of 20 out of the 28 children randomised were included in the analysis. The review reported that the RCT found 7 out of 10 children in the omega-3 fatty acid group had a reduction of 50% or more in scoring on the Children's Depression Scale compared with no reduction in the placebo group, with no reported adverse effects.

Clinical guide
The NICE guideline on depression in children and young people [20] classifies omega-3 fatty acids as a form of self-help; therefore, it is positioned after watchful waiting and before specific psychological therapies in the management of depression. In practice, many patients would take omega-3 fatty acids as adjunctive treatment in addition to specific psychological therapy and/or antidepressant medication.

OPTION ST JOHN'S WORT (HYPERICUM PERFORATUM)

- We found no direct information from RCTs about St John's wort (*H perforatum*) in the treatment of depression in children or adolescents.

Benefits and harms

St John's wort:

We found one systematic review (search date 2006) evaluating complementary and self-help treatments in the treatment of depression in children and adolescents. [5] The review identified no RCTs on the effects of St John's wort in the treatment of depression in children or adolescents.

Comment: At present, there is insufficient evidence to support the use of St John's wort (*H perforatum*) in the treatment of depression in children and adolescents. St John's wort is pharmacologically active. It can potentiate serotonergically active drugs including antidepressants, increasing the risk of a serotonin syndrome. In addition, St John's wort induces metabolic enzymes, reducing the efficacy of a range of therapeutic agents. [22]

Clinical guide
Consistent with the NICE guideline on depression in children and young people, [20] St John's wort may be positioned as a self-help strategy in the management of depression in young people. Because of potential interactions, St John's wort must be ceased prior to the introduction of serotonergically active antidepressant medications.

OPTION S-ADENOSYLMETHIONINE New

- We found no direct information from RCTs about S-adenosylmethionine in the treatment of depression in children or adolescents.

Benefits and harms

S-adenosylmethionine:

We found one systematic review (search date 2006) evaluating complementary and self-help treatments in the treatment of depression in children and adolescents. [5] The review identified no RCTs on the effects of S-adenosylmethionine in the treatment of depression in children or adolescents.

Comment: One systematic review has found S-adenosylmethionine to be of likely benefit in the treatment of depression in adults. [23] It is reasonable to think the treatment could also be effective for depression in children and adolescents.

OPTION VITAMIN C New

- We found no direct information from RCTs about vitamin C in the treatment of depression in children or adolescents.

Benefits and harms

Vitamin C:

We found one systematic review (search date 2006) evaluating complementary and self-help treatments in the treatment of depression in children and adolescents. [5] The review identified no RCTs on the effects of vitamin C in the treatment of depression in children or adolescents.

Comment: A small trial of vitamin C versus placebo augmentation of fluoxetine therapy in paediatric patients with depression found that the group receiving vitamin C had a greater reduction in depression symptoms. [24] It is possible, therefore, that vitamin C has an antidepressant effect in its own right.

GLOSSARY

Pseudo-continuous outcome measure The strict definition of a continuous outcome is one measured on a scale that is continuously variable, good examples being height or systolic blood pressure. In addition, there is an assumption that an increase in 1 unit in one region is equivalent to an increase of 1 unit in another region of the scale. In the case of psychometric scales made up of a series of questions, the latter assumption is not always valid, in which case the scale may be referred to as a pseudo-continuous measure. Caution needs to be applied in interpreting the magnitude of change reported on such measures.

SUBSTANTIVE CHANGES

Glutamine New option. One systematic review added. [5] Categorised as 'unknown effectiveness'.

Light therapy New option. Two systematic reviews added. [5] [15] Categorised as 'unknown effectiveness'.

S-adenosylmethionine New option. One systematic review added. [5] Categorised as 'unknown effectiveness'.

Vitamin C New option. One systematic review added. [5] Categorised as 'unknown effectiveness'.

Omega-3 polyunsaturated fatty acids (fish oil) One systematic review added. [5] Categorisation unchanged (unknown effectiveness).

St John's wort One new systematic review added. [5] Categorisation unchanged (unknown effectiveness).

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Philip Hazell
Conjoint Professor of Child & Adolescent Psychiatry
Discipline of Psychiatry
Sydney Medical School
Sydney
Australia

Competing interests: PH's employer has received funds for his participation in a speakers' bureau for Lilly, and a speakers' bureau and advisory board for Shire. PH is an author of references cited in this overview.

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TABLE 1 **Summary of outcome measures commonly used in trials of treatments for depression in children and adolescents (see text).**

Outcome measure	Description	Scoring system
Children's Depression Rating Scale (Revised)	Semi-structured interview with child, supplemented with information from parents or significant others; assesses 17 symptoms, including those that serve as DSM criteria for depressive disorders; based on how the child has felt over previous 2 weeks. Can be used as a depression screening instrument, a confirmatory diagnostic tool, and a measure of treatment response in children. Good interrater (0.74–0.96) and test–retest (0.80–0.96) reliability, sound internal consistency (0.70), insensitive to age of child.	Items scored on a scale of 1 (least difficulties) to 5 or 7 (greatest difficulties). The summary score (range 17–113) is then transformed into a t score. Scores below 55 are unlikely to be associated with depressive disorder, scores 55–64 indicate possible risk, and scores above 65 are likely to be associated with depressive disorder.
Children's Depression Inventory	Self-report questionnaire (administrator may read aloud while child fills in) consisting of 27 items. For each item, the child chooses one of 3 statements describing how he or she has felt over the previous 2 weeks. Covers most DSM criteria for depressive disorder. Can be used as a depression screening instrument, a confirmatory diagnostic tool, and a measure of treatment response in children. Variable test–retest reliability (0.38–0.87) but sound internal consistency (0.59–0.88).	Items scored on a scale of 0 (least difficulties) to 2 (greatest difficulties). An aggregate score (range 0–54) of 11 or greater is associated with depressive disorder (sensitivity 0.67, specificity 0.60). Items load onto 5 factors: dysphoric mood, acting out, loss of personal and social interest, self-depreciation, and vegetative symptoms.
Hamilton Rating Scale for Depression (Revised)	Designed to assess adult depressive symptomatology but has been widely used with adolescent populations. Clinician rating based on interview with person and a self-report problem inventory. Can be used as a depression screening instrument, a confirmatory diagnostic tool, and a measure of treatment response. Excellent interrater reliability (0.90+), and moderate to good internal consistency (0.45–0.90).	Items are scored on a 3–5 point scale of 0 (absent) to 2 or 4 (clearly present/severe). An aggregate score (range 0–64) of 11 is regarded as indicative of a diagnosis of depression.
Children's Depression Inventory for Parents	Modified version of the Child Depression Inventory completed by parents, which describes the child over the previous 2 weeks. May be used as a confirmatory diagnostic tool and is sensitive to treatment response. Moderate test–retest reliability (0.54–0.75), sound internal consistency (0.82–0.85). Generally moderate to good mother–father total score correlation (0.54–0.64), but variable parent–child correlation (0.03–0.74).	Items scored on a scale of 0 (least difficulties) to 2 (greatest difficulties). An aggregate score (range 0–54) of 12 or greater is associated with depressive disorder but does not discriminate well between depression and presentations of other psychiatric conditions (sensitivity 0.87; specificity 0.24).
Kiddie-Schedule for Affective Disorders and Schizophrenia (Kiddie-SADS)	Semi-structured diagnostic interview for children and adolescents, completed with child and parents. Covers most childhood disorders. Current and lifetime assessment versions available. Used in research trials as a standard method of diagnostic assessment. Good interrater reliability (0.86–0.89) and moderate to good test–retest reliability of individual items (0.41–0.81), and for categorical depression diagnosis (0.54). Moderate internal consistency of depression items (0.60–0.84).	Items are scored on a 2- or 3-point scale (not present, subthreshold, threshold). Some versions include a 0–6 point scale to assess severity (not at all/normal to extreme).
Clinical Global Impressions Scale	Clinician ratings to assess overall severity of symptoms in reference to baseline functioning. Interrater reliability high when clinicians are trained, and it has moderate to good test–retest reliability.	Consists of 3 global measures, which include severity of illness (scale 1–7; "normal" to "extremely ill"); global improvement (scale 1–7; "very much improved" to "very much worse"); and the efficacy index (scale 1–4; compares improvement in symptoms to adverse effects, from "none" to "outweighs therapeutic effect"). Higher scores indicate greater symptomatology and impairment; or not much change from baseline (before treatment).
Depression Checklist Scores	Includes 10 major symptoms of depression, as used by DSM III, and as appropriate for children. Each symptom category is anchored by characteristic behaviours of that symptom. The symptom category is checked as positive if any of the presentations are evident. Has been used as a confirmatory diagnostic tool and a measure of treatment response. No information available regarding reliability or consistency.	Total scores (range 0–10) reflect the number of depressive symptoms evident. Follows a DSM approach to diagnosis: if a child has enough symptoms reaching threshold for a period of 1 month, and these represent a change from usual behaviour, then the child can be given a diagnosis of depression.
Longitudinal Interval Follow-up Evaluation Interview for DSM-III-R	Clinician-rated semi-structured interview with patient, which assesses the longitudinal course of mental illness. Excellent interrater reliability for the psychiatric symptom ratings and the global assessment scores (0.90).	Sections are rated on various scales that range from 1 and have variable end points. Low scores indicate no symptomatology/high functioning, and high scores indicate severe symptomatology/diagnostic criteria met/low functioning.

Outcome measure	Description	Scoring system
Children's Global Assessment Scale	Clinician rating of the subject's most impaired level of functioning over the previous month on a hypothetical continuum of health–illness, irrespective of treatment or prognosis. Test–retest reliability is high, making the instrument a good measure of change over time. Interrater reliability is only modest.	A single score is made in the range 100–1, with 0 indicating inadequate information. A score in the range 100–91 indicates superior functioning, 90–81 good functioning in all areas, 80–71 no more than slight impairment, 70–61 difficulties in a single area, 60–51 variable functioning with sporadic difficulties in several areas, 50–41 moderate degree of impairment in most or severe impairment in one area of functioning, 40–31 major impairment in functioning in several areas or unable to function in one, 30–21 unable to function in most areas, 20–11 needs considerable supervision to prevent harm to self or others, 10–1 needs constant supervision because of severely aggressive or self-destructive behaviour, or other disorder. The use of intermediary levels (e.g., 35, 58, 62) is encouraged to reflect finer grading of impairment.
Global Assessment of Functioning Scale	Clinician rating of psychological, social, and occupational functioning on a hypothetical continuum of health–illness. Does not include impairment in functioning due to physical or environmental limitations. Psychometric data on children and adolescents are limited for this instrument.	A single score is made in the range 100–1, with 0 indicating inadequate information. The scoring ranges are similar to those for the Children's Global Assessment Scale.

DSM, Diagnostic and statistical manual.