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TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
BACKGROUND	3
OBJECTIVES	3
METHODS	3
RESULTS	5
DISCUSSION	8
AUTHORS' CONCLUSIONS	8
ACKNOWLEDGEMENTS	8
REFERENCES	9
CHARACTERISTICS OF STUDIES	11
DATA AND ANALYSES	18
Analysis 1.1. Comparison 1 Patient education compared with usual treatment, no intervention or control, Outcome 1 Mood - depression.	18
Analysis 1.2. Comparison 1 Patient education compared with usual treatment, no intervention or control, Outcome 2 Health beliefs -attitudes (medical services) - no time point.	18
Analysis 1.3. Comparison 1 Patient education compared with usual treatment, no intervention or control, Outcome 3 Health beliefs - attitudes (medication use) - no time point.	19
Analysis 2.1. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 1 Pain frequency (% pain days).	20
Analysis 2.2. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 2 Pain severity (emotion).	20
Analysis 2.3. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 3 Pain severity (sensation).	21
Analysis 2.4. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 4 Coping strategies.	21
Analysis 2.5. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 5 Health service utilisation (emergency visits).	21
Analysis 2.6. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 6 Health service utilisation (hospital admissions).	21
Analysis 2.7. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 7 Health service utilisation (outpatient clinic visits).	22
Analysis 2.8. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 8 Quality of life - daily function.	22
Analysis 2.9. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 9 Health beliefs - locus of control (chance).	22
Analysis 2.10. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 10 Health beliefs - locus of control (powerful others).	22
Analysis 2.11. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 11 Health beliefs - locus of control (internal).	22
Analysis 2.12. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 12 Mental health.	23
APPENDICES	23
WHAT'S NEW	24
HISTORY	24
CONTRIBUTIONS OF AUTHORS	25
DECLARATIONS OF INTEREST	25
SOURCES OF SUPPORT	25
INDEX TERMS	26

[Intervention Review]

Psychological therapies for sickle cell disease and pain

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ABSTRACT

Background

Sickle cell disease comprises a group of genetic blood disorders. It occurs when the sickle haemoglobin gene is inherited from both parents. The effects of the condition are: varying degrees of anaemia which, if severe, can reduce mobility; a tendency for small blood capillaries to become blocked causing pain in muscle and bone commonly known as 'crises'; damage to major organs such as the spleen, liver, kidneys, and lungs; and increased vulnerability to severe infections. There are both medical and non-medical complications, and treatment is usually symptomatic and palliative in nature. Psychological interventions for individuals with sickle cell disease might complement current medical treatment, and studies of their efficacy have yielded encouraging results. This is an update of a previously published Cochrane Review.

Objectives

To examine the evidence that psychological interventions improve the ability of people with sickle cell disease to cope with their condition.

Search methods

We searched the Cochrane Cystic Fibrosis and Genetic Disorders Group Haemoglobinopathies Trials Register, which comprises references identified from comprehensive electronic database searches and the Internet, handsearches of relevant journals and abstract books of conference proceedings.

Date of the most recent search of the Group's Haemoglobinopathies Trials Register: 17 February 2015.

Selection criteria

All randomised or quasi-randomised controlled trials comparing psychological interventions with no (psychological) intervention in people with sickle cell disease.

Data collection and analysis

Both authors independently extracted data and assessed the risk of bias of the included studies.

Main results

Twelve studies were identified in the searches and seven of these were eligible for inclusion in the review. Five studies, involving 260 participants, provided data for analysis. One study showed that cognitive behaviour therapy significantly reduced the affective component of pain (feelings about pain), mean difference -0.99 (95% confidence interval -1.62 to -0.36), but not the sensory component (pain intensity), mean difference 0.00 (95% confidence interval -9.39 to 9.39). One study of family psycho-education was not associated with a reduction in depression. Another study evaluating cognitive behavioural therapy had inconclusive results for the assessment of coping strategies,

and showed no difference between groups assessed on health service utilisation. In addition, family home-based cognitive behavioural therapy did not show any difference compared to disease education. One study of patient education on health beliefs showed a significant improvement in attitudes towards health workers, mean difference -4.39 (95% CI -6.45 to -2.33) and medication, mean difference -1.74 (95% CI -2.98 to -0.50). Nonetheless, these results may not apply across all ages, severity of sickle cell disease, types of pain (acute or chronic), or setting.

Authors' conclusions

Evidence for the efficacy of psychological therapies in sickle cell disease is currently limited. This systematic review has clearly identified the need for well-designed, adequately-powered, multicentre randomised controlled trials assessing the effectiveness of specific interventions in sickle cell disease.

PLAIN LANGUAGE SUMMARY

Psychological therapies for sickle cell disease and pain

Sickle cell disease is a group of blood disorders. It can cause anaemia, which if severe can reduce mobility. It may also allow small blood vessels to become blocked causing pain in muscle and bone and it can damage major organs such as the spleen, liver, kidneys, and lungs. People with sickle cell disease are more vulnerable to severe infections. Treatment is usually in response to symptoms and designed to ease pain. Psychological treatment to help people cope with sickle cell disease might complement current medical treatment. There are four types of treatment: patient education; cognitive therapy (to do with thoughts and feelings); behavioural therapy (to do with actions); psychodynamic psychotherapy (talking to relieve emotional pain). We searched for randomised or quasi-randomised controlled trials which compared psychological treatments to each other or to no treatment in sickle cell disease. We included seven studies in the review, of which five, with 260 people, had data we could enter into the review. One study showed that cognitive behaviour therapy reduced the affective part of pain (feelings about pain), but not the sensory part (pain intensity). Another study of this therapy had inconclusive results for coping strategies and showed no difference on how different groups used the health service. A study using cognitive behavioural therapy with teenagers and their families at home did not show any difference when compared with education about sickle cell disease. One education study did not show a reduction in depression. Furthermore, one study in patient education helped improve attitudes to healthcare workers and medication use in adolescents and young adults. The authors believe that some patient education seems relevant for children, adolescents and young adults, while methods to improve the ability to cope in both children and adults are important. Nonetheless, these results may not apply to across all ages, clinical severity, types of pain (acute or chronic) that people with sickle cell disease have, or which country they live in. More research needs to be done in this area.

BACKGROUND

Description of the condition

Sickle cell disease comprises a group of genetic disorders of haemoglobin predominantly affecting people originating from areas where malaria is found. The sickle cell gene, being an adaptation against malaria, is prevalent in Africa, Asia, the Caribbean, Middle East, Mediterranean and Southern Europe. Nonetheless, global migration appears to be changing the distribution (Piel 2014). The global affected population appears to be on the increase, and is now estimated at over 300,000 (Piel 2013).

Sickle cell disease occurs when the haemoglobin variant HbS gene is inherited from both parents, i.e. sickle cell anaemia (HbSS), which is the most common (Serjeant 2001), or when the HbS gene is inherited from one parent and another haemoglobin variant gene from the other, such as haemoglobin sickle cell disease (HbSC) or sickle- β -thalassaemia (S- β -Thal). Sickle cell trait, the 'carrier' state, is the inheritance of the HbS gene from one parent and the normal haemoglobin (HbA) gene from the other. These individuals are free of symptoms relating to sickle cell disease (Serjeant 2001).

Sickle cell disease causes a lot of problems for affected individuals. The effects of the illness are: varying degrees of anaemia, which if severe reduce the capacity for mobility; intermittent obstruction of blood vessels causing attacks of pain in muscle and bone, known as vaso-occlusive 'crises'; damage to major organs such as the brain, liver, kidneys, lungs and spleen; and increased vulnerability to severe infections. Numerous complications can occur and affect any organ of the body. Life threatening complications include acute chest syndrome, splenic or hepatic sequestration and stroke (Yawn 2014). Also, children may be at risk of cognitive impairment as a result of strokes or subtle neurological conditions (Daly 2011).

Current treatment is mainly aimed at reducing symptoms of sickle cell disease: pain is controlled with analgesics, hydration, application of heat, and other complementary methods; transfusions are given to correct severe anaemia, prevent strokes, and for other complications such as acute chest syndrome; infections are treated with antibiotics (Yawn 2014). Bone marrow transplantation can prevent, stabilise or reverse complications associated with sickle cell disease, and has an expanded role in recent times (Bolaños-Meade 2012). This is a major procedure, which cannot be routinely offered because of age restrictions and the difficulty of finding suitable donors. Treatment with hydroxyurea has been shown to raise the level of foetal haemoglobin (HbF) and decrease cellular dehydration in people with HbSS (Cokic 2003). It is therefore very effective in preventing and reducing the rate of painful episodes and the subsequent number of hospitalisations (Charache 1995).

Pain is one of the most significant symptoms experienced in the daily lives of affected individuals. Its onset, chronicity and severity are unpredictable, idiosyncratic and distinguishable from other types of pain. Painful episodes have been reported to be highest among those aged 20 to 29 years and are a predictor of early death, decreasing steadily after 30 years (Platt 1991). Although sickle cell pain may not be present all the time, recurrent acute episodes occur throughout life and may require frequent hospitalisations (Aljuburi 2012; Ballas 2012).

Description of the intervention

Psychologically, there is considerable variability in the ability of people with sickle cell disease to cope with painful episodes (Anie 2005; Gil 1989). Some people with sickle cell disease cope relatively well with pain: they work; are active socially and recreationally; and are well adjusted psychologically. Others cope poorly; they lead more limited lives and are very reliant on acute services for their pain management, thus posing a challenge to clinicians. Distress, disability and reduced quality of life as a result of pain associated with sickle cell disease are common (Ballas 2014).

As in other chronic pain conditions, cognitive and behavioural therapies have been considered as adjuncts to routine medical treatment for the management of sickle cell pain. These interventions aimed to improve the ability of people with sickle cell disease to cope with their pain, have shown encouraging results in children and adults (Gil 1997; Thomas 1999), and with incorporated treatment manuals (Anie 2002).

Why it is important to do this review

This review, an update of previous publications, assesses the contribution of psychological interventions used for managing sickle cell pain and the psychological impact of sickle cell disease (Anie 2000; Anie 2012). We also intended to determine the effects of different therapy formats (e.g. individual versus group) on the outcome of sickle cell disease and pain.

OBJECTIVES

The purpose of this review was to assess whether psychological therapies for sickle cell disease and pain can improve the ability of people with sickle cell disease to cope with their condition. The main objectives were to determine:

1. whether psychological therapies are effective in the management of sickle cell disease and related pain;
2. which psychological intervention is most effective for sickle cell disease and related pain;
3. the best way of delivering psychological therapies.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised controlled trials (RCTs) and controlled clinical trials (CCTs) published and unpublished have been included.

Trials where quasi-randomisation methods were used would have been analysed separately, but only if there was sufficient evidence that the treatment and non-treatment groups were comparable in terms of clinical features.

Types of participants

All children and adults diagnosed with sickle cell disease, irrespective of phenotype, age, gender, race, ethnic origin and setting.

Types of interventions

This review focuses on four main types of psychological interventions. All studies that included one or more of the following

therapies for managing sickle cell disease and related pain were considered.

Patient education

1. Sickle cell disease and sickle cell pain
2. Psychological theories of pain experience and pain control

Cognitive therapy

1. Focusing on ways of thinking, e.g. automatic thoughts and negative thoughts
2. Monitoring thoughts and feelings
3. Challenging and re-framing inappropriate thoughts
4. Attention diversion and distraction
5. Imagery and hypnosis

Behavioural therapy

1. Activity monitoring and re-scheduling
2. Stress monitoring and reduction
3. Relaxation and biofeedback
4. Communication skills training including assertiveness training
5. Goal setting
6. Enhancing motivation
7. Problem solving

Psychodynamic psychotherapy

1. Focus on childhood development and early life experiences
2. Insight into previous traumatic events

Types of outcome measures

The following outcomes in people with sickle cell disease were assessed. All included studies reported on at least one of the outcomes below.

Primary outcomes

1. Pain status (frequency, duration, severity, location, precipitating factors, modulating factors)
2. Mood (anxiety, depression)
3. Coping strategies (behavioural responses, cognitive strategies)
4. Health service utilisation (frequency of Accident & Emergency department visits and hospital admissions, duration of hospitalisations, consultations with doctors (including general practitioners))

Secondary outcomes

1. Quality of life (physical and social function, ability to fulfil roles, life satisfaction)
2. Health beliefs (locus of control)
3. General health (including mental health)

Search methods for identification of studies

Electronic searches

Relevant studies were identified from the Group's Haemoglobinopathies Trials Register using the terms: sickle cell AND psychology.

The Haemoglobinopathies Trials Register is compiled from electronic searches of the Cochrane Central Register of Controlled Trials (CENTRAL) (updated each new issue of *The Cochrane Library*) and weekly searches of MEDLINE. Unpublished work is identified by searching the abstract books of five major conferences: the European Haematology Association conference; the American Society of Hematology conference; the British Society for Haematology Annual Scientific Meeting; the Caribbean Health Research Council Meetings; and the National Sickle Cell Disease Program Annual Meeting. For full details of all searching activities for the register, please see the relevant section of the [Cystic Fibrosis and Genetic Disorders Group Module](#).

We also searched the following databases: Embase (1974 to 2014 Week 36) (searched 05 September 2014) which yielded up to 1941 abstracts ([Appendix 1](#)); PsycINFO (1967 to September Week 1 2014) (searched 05 September 2014) yielded up to 125 abstracts ([Appendix 2](#)).

Date of the most recent search of the Group's Haemoglobinopathies Trials Register: 17 February 2015.

Searching other resources

Attempts were also made to identify any unpublished trials through contact with experts in the field and personal communication with known authors.

Data collection and analysis

Selection of studies

Each author independently selected the studies to be included in this review.

Data extraction and management

Each author independently extracted data using standard data acquisition forms. No disagreement occurred, so no other expert in the field was invited to make an independent assessment based on the selection criteria.

We intended to group these outcomes into time periods - short term (up to three months), medium term (between three months and six months) and long term (over six months). However, insufficient information was available to allow analysis in this way.

Assessment of risk of bias in included studies

Each author independently assessed the risk of bias in each included trial using a simple form, which follows the domain-based evaluation described in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). The overall risk of bias comprises five 'risk domains', with each domain classified as 'low risk', 'high risk', or 'unclear risk' of bias. The five risk of bias domains are:

1. generation of the allocation sequence (does the trial use an acceptable method of generating the random sequence for allocating participants to treatment arm?);
2. concealment of allocation (was the allocation sequence adequately concealed? Methods such as centralised allocation and sequentially numbered opaque sealed envelopes would be considered adequate);

3. blinding (was knowledge of the allocated interventions adequately prevented among participants, personnel and outcome assessors during the study?);
4. incomplete outcome data (were incomplete outcome data a problem in the trial and were the trial methods of dealing with these missing data adequate?);
5. selective outcome reporting (are reports of the study free from suggestions of selective outcome reporting? For example were all the primary endpoints pre-specified in the trial protocol reported?).

Additionally, a sixth risk domain is used to describe any other potential source of bias not covered by the first five risk domains.

Measures of treatment effect

No binary outcome measures were found in the included studies, in future updates, if such measures are included, we will summarise these in terms of risk ratios (RR) by extracting numbers in each group. For continuous outcomes, we recorded either mean change from baseline for each group or mean post-treatment or intervention values and standard deviation for each group. We also intended to compute a pooled estimate of treatment effect by calculating the mean difference (MD) with 95% confidence intervals (CI); however, we were unable to do this because of insufficient data.

Unit of analysis issues

We do not intend to include crossover studies since psychological interventions cannot be 'washed out' after these have been administered.

Dealing with missing data

If data which we required for our analysis were not reported in the study reports, we contacted the lead author of the study for these.

Assessment of heterogeneity

We were unable to combine any data in a meta-analysis, therefore we could not assess heterogeneity between study results using a standard chi-squared test as intended. If we are able to combine data in future updates of this review, we will also use the I^2 statistic of a measure of heterogeneity (Higgins 2003). We will define levels of heterogeneity as follows:

- 0% to 40%: might not be important;
- 30% to 60%: may represent moderate heterogeneity;
- 50% to 90%: may represent substantial heterogeneity;
- 75% to 100%: considerable heterogeneity.

We recognise that the importance of the observed value of I^2 depends on the magnitude and direction of effects and also the strength of evidence for heterogeneity (e.g. P value from the chi-squared test, or a confidence interval for I^2).

Assessment of reporting biases

There were no published protocols for the included studies; nonetheless for each study, we examined outcomes described in the 'Methods' section and compared these with the 'Results' section. We reviewed the studies to extract the number and characteristics of reported outcomes (including statistical significance, level of reporting, and specification as primary,

secondary, or unspecified according to the text). Furthermore, we contacted authors to list any outcomes that were not reported in the published papers and to indicate for each unreported outcome whether it reached statistical significance ($P < 0.05$) in any inter-group comparison; whether it was a primary, secondary, or unspecified outcome according to the protocol; whether it was of little, moderate, or high clinical importance; and the reasons for not reporting it. We did not receive any replies.

Data synthesis

We intended to analyse the results using a fixed-effect model if we performed a meta-analysis, and plan to employ a random-effects model if we identify significant heterogeneity (as defined above) in future updates.

Subgroup analysis and investigation of heterogeneity

If, in future updates of the review, we identify substantial heterogeneity and there are sufficient studies included (at least 10), we plan to undertake the following subgroup analyses: age; gender; ethnic origin.

Sensitivity analysis

We were unable to perform a sensitivity analysis based on the risk of bias of the studies; however, if in future sufficient studies are included, we will undertake this analysis.

RESULTS

Description of studies

Please refer to the relevant tables ([Characteristics of included studies](#); [Characteristics of excluded studies](#)).

Results of the search

Twelve potentially relevant RCTs were identified in the search (Applegate 2003; Barakat 2007; Barakat 2010; Boroffice 1991; Broome 2001; Gil 1996; Gil 1997; Kaslow 2000; Ketchen 2006; Kinlow 2001; Thomas 1999; Yerys 2003).

Included studies

Seven studies were eligible for inclusion in the review (Barakat 2010; Boroffice 1991; Broome 2001; Gil 1996; Gil 1997; Kaslow 2000; Thomas 1999). Five studies (Barakat 2010; Boroffice 1991; Broome 2001; Kaslow 2000; Thomas 1999) with a total of 260 participants provided suitable data for entry into Review Manager (Review Manager 2011). For two studies (Gil 1996; Gil 1997), insufficient data on post-intervention outcome measures were reported (no means and standard deviations). We have tried to contact the authors of the studies for further information, but received no reply. Therefore, no data from these two studies could be entered into Review Manager (Review Manager 2011) and results are reported narratively.

Participants and setting

Participants in all the studies had sickle cell disease and included both genders. Five studies were conducted in the USA (Barakat 2010; Broome 2001; Gil 1996; Gil 1997; Kaslow 2000), one in the UK (Thomas 1999) and one in Nigeria (Boroffice 1991).

Type of intervention

Patient education

1. Group therapy - (no time period reported), adolescents and young adults (Boroffice 1991)
2. Family group therapy - six sessions, children and adolescents with family members (Kaslow 2000)
3. Family home-based group therapy - three two-weekly sessions plus one booster session (one month later), adolescents with family members (Barakat 2010).

Cognitive behavioural therapy

1. Individual therapy - one session plus one review session the following week, children and adolescents (Gil 1997)
2. Group therapy - four sessions over four weeks, children and adolescents (Broome 2001)
3. Individual therapy - three sessions over three weeks with home practice tapes, adults (Gil 1996)
4. Group therapy - eight sessions over eight weeks, adults (Thomas 1999)
5. Family home-based group therapy - three two weekly sessions plus one booster session (one month later), adolescents with family members (Barakat 2010).

Excluded studies

Five studies were excluded; one since the intervention was aimed at the parents and not children with sickle cell disease (Applegate 2003); two were not randomised (Ketchen 2006; Kinlow 2001); one did not contain an intervention (Barakat 2007); one was not related to pain (Yerys 2003).

Risk of bias in included studies

Allocation

Allocation concealment and generation of the randomisation sequence were judged to be adequate in one study as random number tables were used to label cards, which were placed in sealed envelopes (Thomas 1999); we therefore judged this study to have a low risk of bias from generation and concealment of the allocation sequence. In the remaining six studies generation of sequence was described as 'randomised' but no further details were given and the concealment of the allocation sequence was not discussed; we therefore judged these studies to have an unclear risk of bias (Barakat 2010; Boroffice 1991; Broome 2001; Gil 1996; Gil 1997; Kaslow 2000) - see [Characteristics of included studies](#).

Blinding

Due to the nature of the interventions, it was not possible to blind the participants or the clinicians to the treatment group; besides, the outcome assessors were not blinded in any of the studies. Therefore, we judged all seven studies to have a risk of bias due to lack of blinding.

Incomplete outcome data

We judged two studies to have a risk of bias due to incomplete data (Boroffice 1991; Gil 1996). The Nigerian study did not present any data on withdrawals and although this information was requested from the authors, it has not been received (Boroffice 1991). The Gil study did not report the number of participants in each of the study groups after randomisation (Gil 1996).

We are cautious about the results of two studies and judge them to have an unclear risk of bias (Broome 2001; Thomas 1999). In the Broome study, there were no data reported on 10 children who were excluded from the initial 75 study participants after randomisation because of non-attendance, and full data were not reported on 32 of the remaining 65 children (Broome 2001). In addition, data reported on 32 adolescents in this study were excluded because of the lack of a control group (Broome 2001). In the Thomas study, the authors did not report data on 38 out of 59 (39%) participants who were excluded from the study after randomisation (15 because they did not fully meet the inclusion criteria, and 23 who were classified as 'dropouts') (Thomas 1999). We contacted the authors for additional results, but the data we received were still incomplete, and the representativeness of the study sample could not be assessed. In neither study was an intention-to-treat analysis carried out (Broome 2001; Thomas 1999).

Three studies were judged to be adequate for outcome data reported (Barakat 2010; Gil 1997; Kaslow 2000).

Selective reporting

The risk of bias in selective reporting was classified to be uncertain in four studies (Boroffice 1991; Broome 2001; Gil 1996; Thomas 1999); because exclusions and attrition were not fully reported as described above. Three studies were considered to be acceptable for selective reporting (Barakat 2010; Gil 1997; Kaslow 2000).

Other potential sources of bias

We did not identify any studies that were not reported because of language.

Therapists' training and materials

The competence of therapists and materials used were not fully reported in all the studies. Experienced or trained psychologists were reported to be employed in four studies, i.e. the family educational programme using a manual (Kaslow 2000), and cognitive behavioural therapy (Gil 1996; Gil 1997; Thomas 1999). Doctoral students in clinical psychology were utilised together with trained psychologists in one study for both patient education and cognitive behavioural therapy (Barakat 2010). Trained nurses were employed in another study for cognitive behavioural therapy (Broome 2001). In all studies of cognitive behavioural therapy, protocols were used but these were not described, although one study validated the credibility of treatment with an independent psychologist (Thomas 1999). The competence of the therapists was not stated in the other patient education study, even though the educational protocol was described (Boroffice 1991).

Effects of interventions

Data were reported on different outcome measures in the seven studies, therefore no comparisons were made. Furthermore, five studies provided suitable data for analysis (Barakat 2010; Boroffice 1991; Broome 2001; Kaslow 2000; Thomas 1999). The results by type of intervention and outcomes are summarised below.

Patient education

Primary outcomes

1. Pain status

This was not reported in any of the studies.

2. Mood

This was assessed in one study (Kaslow 2000). Mood was measured on the Child Depression Inventory (27 items ranging from 0 to 54, with higher scores indicating more depressive symptoms). Family psycho-education assisted with a therapy manual compared with usual treatment in children did not show any significant reduction in depression, mean difference (MD) -0.60 (95% confidence interval (CI) -4.53 to 3.33) (Kaslow 2000) (Analysis 1.1).

3. Coping strategies

This was not reported in any of the studies.

4. Health service utilisation

This was not reported in any of the studies.

Secondary outcomes

1. Quality of life

This was not reported in any of the studies.

2. Health beliefs

Boroffice used a specially designed 11-item, 3-point Likert scale questionnaire to measure attitudes to medical services (Boroffice 1991). Scores range from 0 to 33, with higher scores denoting more negative attitudes. The effect of a patient educational programme (with an intervention group of lecture and group interaction, and one control group) in providing information led to a significant improvement in attitudes towards health service personnel, MD -4.39 (95% CI -6.45 to -2.33) and medication, MD -1.74 (95% CI -2.98 to -0.50) (Analysis 1.2; Analysis 1.3). It also revealed that the two intervention methods were effective in enhancing positive attitudes.

3. General health

This was not reported in any of the studies.

Cognitive behavioural therapy

Primary outcomes

1. Pain status

This was assessed in four studies (Gil 1996; Gil 1997; Thomas 1999; Barakat 2010). Gil examined experimental pain sensitivity calibrated to noxious stimulation in both studies, with results indicating reduction in the tendency to report laboratory pain following coping skills training in children or adolescents (Gil 1997), and adults (Gil 1996) compared with control conditions (didactic discussion sessions). However, data reported could not be entered into the statistical analysis.

Pain frequency was assessed in one study with a pain diary by calculating the proportion (percentage) of days with pain (Barakat 2010). Cognitive behavioural family therapy compared with attention control did not reduce pain frequency post intervention, MD -0.69 (95% CI -13.56 to 12.18) or at 12 months follow up, MD 8.87 (95% CI -3.33 to 21.07) (Analysis 2.1).

The total score of 15 pain descriptor words rated from zero (no pain) to three (severe pain) on the Short Form McGill Pain Questionnaire was used to assess pain severity. Cognitive behavioural group therapy as opposed to no intervention significantly reduced the affective component, MD -0.99 (95% CI -1.62 to -0.36) but not the

sensory component of pain severity, MD 0.00 (95% CI -9.39 to 9.39) (Thomas 1999) (Analysis 2.2; Analysis 2.3).

2. Mood

This was not reported in any of the studies.

3. Coping strategies

These were evaluated in five studies (Gil 1996; Gil 1997; Thomas 1999; Broome 2001; Barakat 2010). Gil used the CSQ-SCD for both studies (Gil 1996; Gil 1997). In children or adolescents (Gil 1997) and adults (Gil 1996), brief training in coping skills compared with control conditions (didactic discussions) increased coping attempts, and decreased negative thinking. Data reported could not be entered into the statistical analysis.

Thomas also used the CSQ-SCD. However, data reported from the analysis of this questionnaire were insufficient to ascertain whether cognitive behavioural therapy improved coping ability compared to no intervention (Thomas 1999). Data reported from this instrument were ordinal categorical, which could not be entered into the statistical analysis.

Broome used the Schoolagers' Coping Strategies Inventory (Broome 2001). This is a 26-item self-report instrument designed to yield two scores of frequency and effectiveness of coping strategies used by children (including distraction, relaxation, social support and drawing). Data on two scores of frequency and effectiveness were not reported either at baseline or post-intervention. Thus, we were unable to determine whether cognitive behavioural techniques helped with coping as compared to no intervention.

Bakarat employed the CSQ-SCD (Barakat 2010). Cognitive behavioural therapy compared with attention control did not reveal any significant improvements in coping attempts post intervention, MD 3.03 (95% CI -17.73 to 23.79) or at 12 months follow up, MD 11.50 (95% CI -9.35 to 32.35) (Analysis 2.4).

4. Health service utilisation

This was measured in four studies (Broome 2001; Gil 1996; Thomas 1999; Barakat 2010). However, in two studies insufficient outcome data were reported to determine whether cognitive behavioural therapy compared with control or no intervention had an effect on health service utilisation (Gil 1996; Thomas 1999). As a result, no data were entered into the statistical analysis for either study.

Broome measured: the number of visits to hospital emergency departments; to outpatient clinics; and hospital admissions for 12 months prior to the intervention. Compared with controls, children did not show any significant changes in health service utilisation according to these measures: emergency visits, MD -0.30 (95% CI -2.04 to 1.44); hospital admissions, MD 1.00 (95% CI -1.91 to 3.91); clinic visits, MD 1.40 (95% CI -1.42 to 4.22) (Broome 2001) (Analysis 2.5; Analysis 2.6; Analysis 2.7).

Bakarat reviewed medical charts for 12 months SCD outpatient clinic visits pre- and post-baseline (Barakat 2010). Cognitive behavioural therapy compared with attention control did not significantly reduce health service utilisation at 12 months post-baseline, MD 0.45 (95% CI -5.06 to 5.96) (Analysis 2.7).

Secondary outcomes

1. Quality of life

This was measured by Thomas using the Pain Self-Efficacy Questionnaire, with a total score of 10 items rated from zero (not at all confident) to six (completely confident) (Thomas 1999). Participants had higher scores on daily function indicating that they felt significantly more confident after cognitive behavioural therapy but not after a non-interventional control, MD 15.00 (95% CI 7.84 to 22.16) (Thomas 1999) (Analysis 2.8).

2. Health beliefs

This was measured by Thomas using the Beliefs About Pain Control Questionnaire, which comprises three subscales of 13 items (from one equalling disagree strongly to six equalling agree strongly) (Thomas 1999). Cognitive behavioural therapy compared with no intervention showed a significant reduction in the role of external factors on the control of pain in both the role of chance events or happenings, MD -4.50 (95% CI -7.19 to -1.81), and in the role of powerful others, MD -4.50 (95% CI -6.84 to -2.16) (Analysis 2.9; Analysis 2.10). A significant increase in internal locus of control beliefs about pain was also observed, MD 3.80 (95% CI 1.55 to 6.05) (Thomas 1999) (Analysis 2.11).

3. General health

There was no difference in the mental health of participants (measured on the General Health Questionnaire-28) as a result of treatment with cognitive behavioural therapy or no treatment, MD -1.50 (95% CI 5.75 to -2.75) (Thomas 1999) (Analysis 2.12).

DISCUSSION

People with sickle cell disease and their families have to cope with a chronic condition, which causes psychological distress and affects their quality of life. Therefore, psychological interventions are indicated to complement medical treatment for effective management. These studies suggest that interventions, which focus on education about sickle cell disease, are effective in improving knowledge and attitudes about the condition in both children and adolescents (young people) and carers. Such educational programmes could perhaps be used as the first step in psychological interventions for people with sickle cell disease. Cognitive and behavioural therapies may also be helpful but their effectiveness still remains unclear because of the poor quality of the studies.

These findings need to be interpreted with caution because the results cannot necessarily be generalised across all ages, clinical severity, types of pain (acute or chronic) experienced by people with sickle cell disease, or patient populations.

AUTHORS' CONCLUSIONS

Implications for practice

The quality of the studies included in this review was not sufficient to allow firm conclusions about the efficacy of psychological interventions to be made at the present time. Nonetheless, patient education seems relevant for children and adolescents, while methods to improve the ability to cope in both children and adults are important.

Implications for research

More research is needed using a structured approach to assess psychological therapies, taking into account both demographic and clinical variables. Well-designed, adequately-powered studies should incorporate treatment manuals for consistency and to allow replication. Future studies should also help in identifying the most important components of psychological interventions relevant to different sickle cell populations, and in testing the efficacy of different therapy formats, e.g. individual versus group. Similar outcome measures should also be used, both within and between different sickle cell patient groups. Multicentre collaboration, perhaps international, may be needed for this purpose.

Subsequent reviews such as this would be improved if future trial publications reported data more fully.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Barakat 2010

Methods	Setting: USA, urban.
Participants	Diagnosis: SCD. N = 53. Sex: male & female. Ethnicity: African American. Age: 12 to 18 years. Excluded:132
Interventions	Family home-based approach. 1. Pain management - 4 sessions (3 x two-weekly plus 1 month later) n = 27. 2. Disease education - 4 sessions (3 x two-weekly plus 1 month later) n = 26.
Outcomes	1. Pain status - pain days and medication use (pain diary) 2. Health service utilisation - SCD clinic visits, other outpatient clinic visits 3. School attendance 4. Coping strategies 5. SCD knowledge - SCD knowledge, transition knowledge 6. Disease self-efficacy 7. Quality of life Unable to use Health-related hindrance - not administered to all participants
Notes	
Risk of bias	
Bias	Authors' judgement Support for judgement

Barakat 2010 (Continued)

Random sequence generation (selection bias)	Unclear risk	Reported as randomised, but no further details provided.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Raters	High risk	Raters not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Exclusions & attrition were fully reported.
Selective reporting (reporting bias)	Low risk	Exclusions & attrition were fully reported.

Boroffice 1991

Methods	Setting: Nigeria, urban.
Participants	Diagnosis: SCD. N = 60. Sex: male & female. Ethnicity: Nigerian Age: 13 to 22 years. Marital status: single. Excluded: 2.
Interventions	Group Approach. 1. Patient education - lecture (n = 17).* 2. Patient education - lecture & group interaction (n = 19).* 3. Control - nothing (n = 20).
Outcomes	1. Attitudes to medical services. 2. Attitudes to medication.
Notes	* Full data not reported - review authors have assumed that the numbers of participants in each group were balanced at the start of study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Reported as randomised, but no further details provided.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Raters	High risk	Raters not blinded.

Boroffice 1991 (Continued)

Incomplete outcome data (attrition bias) All outcomes	High risk	Data on withdrawals were not reported. This information was requested from the authors, but not received.
Selective reporting (reporting bias)	Unclear risk	Exclusions and attrition were not fully reported.
Other bias	Unclear risk	Competence of therapists and materials used were not fully reported, although the educational protocol was described.

Broome 2001

Methods	Setting: USA, urban.
Participants	Diagnosis: SCD. N = 65. Sex: male & female. Ethnicity: African American. Age: 6 to 12 years. Excluded: 10.
Interventions	Group approach. 1. Cognitive behavioural - 4 x weekly sessions (n = 22). 2. Art therapy - 4 x weekly sessions (n = 18). 3. Attention control - 4 x weekly sessions (n = 9).
Outcomes	1. Coping strategies. 2. Health service utilisation - ER visits, clinic visits, hospital admissions.
Notes	*Full data not reported - reviewers have assumed that participants in each group were not balanced at the start of the study.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Reported as randomised, but no further details provided.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Raters	High risk	Raters not blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No data were reported on 10 children who were excluded from the initial 75 study participants after randomisation because of non-attendance, & full data were not reported on 32 of the remaining 65 children. In addition, data reported on 32 adolescents in this study were excluded because of the lack of a control group. We are very cautious about the results of this study. An intention-to-treat analysis was not carried out.

Broome 2001 (Continued)

Selective reporting (reporting bias)	Unclear risk	Exclusions and attrition were not fully reported.
Other bias	Unclear risk	Competence of therapists (trained nurses) and materials used were not fully reported.

Gil 1996

Methods	Setting: USA, urban.
Participants	Diagnosis: SCD. N = 64. Sex: male & female. Age: mean 33.3 (SD 9.9) years. Ethnicity: African American. Excluded: 2.
Interventions	Individual Approach. 1. Cognitive behavioural - 3 x weekly 45-min sessions & home practice tapes. 2. Control - disease education - 3 x weekly 45-min didactic sessions & home reading materials.
Outcomes	Unable to use - 1. Pain sensitivity. 2. Pain status (frequency, duration, intensity). Mean & SD not reported. 4. Health service utilisation (hospital visits & health care provider calls or visits). No outcome data reported.
Notes	Full data not reported on N in each group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Reported as randomised, but no further details provided.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Raters	High risk	Raters not blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	The number of participants in each of the study groups after randomisation was not reported.
Selective reporting (reporting bias)	Unclear risk	Exclusions and attrition were not fully reported.
Other bias	Unclear risk	Competence of therapists (experienced or trained psychologists) and materials used were not fully reported.

Gil 1997

Methods	Setting: USA, urban.
Participants	Diagnosis: SCD. N = 49. Sex: male & female. Ethnicity: African American. Age: 8 to 17 years.
Interventions	Individual Approach. 1. Cognitive behavioural - 1 x 45 min session, 1 review session (n = 25). Control - nothing (n = 24).
Outcomes	Unable to use - 1. Pain sensitivity. 2. Coping strategies. 3. Disease severity (complications in previous 12 months). Mean & SD not reported.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Reported as randomised, but no further details provided.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Raters	High risk	Raters not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judged to be adequate for outcome data reported.
Selective reporting (reporting bias)	Low risk	Judged to be acceptable.
Other bias	Unclear risk	Competence of therapists (experienced or trained psychologists) and materials used were not fully reported.

Kaslow 2000

Methods	Setting: USA, urban.
Participants	Diagnosis: SCD. N = 39. Sex: male & female. Age: 7 to 16 years.

Kaslow 2000 (Continued)

Ethnicity: African American
Excluded: 20.

Interventions	Group Approach (family). 1. Psycho-education - 6 x sessions (n = 14). 2. Control - nothing (n = 14).
Outcomes	1. Child and parent disease knowledge. 2. Child depression. 3. Child behaviour. 4. Family functioning. 5. Family support. 6. Family resources.

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Reported as randomised, not matched, no further details provided.
Allocation concealment (selection bias)	Unclear risk	Not discussed.
Blinding (performance bias and detection bias) Raters	High risk	Raters not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Judged to be adequate for outcome data reported.
Selective reporting (reporting bias)	Low risk	Judged to be acceptable.
Other bias	Unclear risk	Competence of therapists (experienced or trained psychologists) & materials used were not fully reported.

Thomas 1999

Methods	Setting: UK, urban.
Participants	Diagnosis: SCD. N = 59. Sex: male & female. Age: 15 to 35 years. Ethnicity: African and Caribbean. Excluded: 38.
Interventions	Group Approach. 1. Cognitive-behaviour - 8 x weekly 60 min sessions (n = 19). 2. Attention placebo - 8 x weekly 60 min sessions (n = 14).

Psychological therapies for sickle cell disease and pain (Review)

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Thomas 1999 (Continued)

3. Control - nothing (n = 26).

Outcomes

1. General health.
2. Coping strategies.
3. Self-efficacy.
4. Pain.
5. Pain control beliefs.

Unable to use.

1. Health service utilisation. - Mean & SD not reported.

Notes
Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random number table to label cards in sealed envelopes.
Allocation concealment (selection bias)	Low risk	Sealed envelopes used.
Blinding (performance bias and detection bias) Raters	High risk	Raters not blinded.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Data were not reported on 38 out of 59 (39%) participants who were excluded from the study after randomisation (15 because they did not fully meet the inclusion criteria, and 23 who were classified as 'dropouts'). We contacted the authors for additional results, but the data we received were still incomplete. The representativeness of the study sample could not be assessed. We are therefore cautious about the results of this study. An intention-to-treat analysis was not carried out.
Selective reporting (reporting bias)	Unclear risk	Exclusions and attrition were not fully reported.
Other bias	Unclear risk	Competence of therapists (experienced or trained psychologists) and materials used were not fully reported. Credibility of treatment validated with an independent psychologist.

ER: emergency room

min: minute

SCD: sickle cell disease

SD: standard deviation

UK: United Kingdom

USA: United States of America

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Applegate 2003	Intervention is for parents not children.

Study	Reason for exclusion
Barakat 2007	Non-interventional.
Ketchen 2006	Not randomised.
Kinlow 2001	Not randomised.
Yerys 2003	Not related to pain.

DATA AND ANALYSES

Comparison 1. Patient education compared with usual treatment, no intervention or control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mood - depression	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 At 6 weeks	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Health beliefs -attitudes (medical services) - no time point	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3 Health beliefs - attitudes (medication use) - no time point	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

Analysis 1.1. Comparison 1 Patient education compared with usual treatment, no intervention or control, Outcome 1 Mood - depression.

Study or subgroup	Patient education		Control		Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)		
1.1.1 At 6 weeks						
Kaslow 2000	19	41.8 (5.5)	18	42.4 (6.6)		-0.6[-4.53,3.33]
					Favours education	Favours control

Analysis 1.2. Comparison 1 Patient education compared with usual treatment, no intervention or control, Outcome 2 Health beliefs -attitudes (medical services) - no time point.

Study or subgroup	Patient education		Control		Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
Boroffice 1991	19	14.1 (2.2)	20	18.5 (4.1)		0%	-4.39[-6.45,-2.33]
					Favours education	Favours control	

Analysis 1.3. Comparison 1 Patient education compared with usual treatment, no intervention or control, Outcome 3 Health beliefs - attitudes (medication use) - no time point.

Study or subgroup	Patient education		Control		Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
	N	Mean(SD)	N	Mean(SD)			
Boroffice 1991	19	9.1 (0.8)	20	10.9 (2.7)		0%	-1.74[-2.98,-0.5]
					Favours education		Favours control

Comparison 2. Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain frequency (% pain days)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 Post intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 At 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Pain severity (emotion)	1		Std. Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 At 2 months	1		Std. Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 Pain severity (sensation)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 At 2 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Coping strategies	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Post intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4.2 At 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Health service utilisation (emergency visits)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 At 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Health service utilisation (hospital admissions)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 At 12 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Health service utilisation (outpatient clinic visits)	2		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
7.1 At 12 months	2		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 Quality of life - daily function	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 At 2 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Health beliefs - locus of control (chance)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
9.1 At 2 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
10 Health beliefs - locus of control (powerful others)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
10.1 At 2 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
11 Health beliefs - locus of control (internal)	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
11.1 At 2 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
12 Mental health	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
12.1 At 2 months	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 2.1. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 1 Pain frequency (% pain days).

Study or subgroup	CBT		Control		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
2.1.1 Post intervention						
Barakat 2010	17	16.6 (16.6)	20	17.3 (23.2)		-0.69[-13.56,12.18]
2.1.2 At 12 months						
Barakat 2010	17	16.7 (23)	20	7.8 (12.3)		8.87[-3.33,21.07]

Analysis 2.2. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 2 Pain severity (emotion).

Study or subgroup	CBT		Control		Std. Mean Difference	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
2.2.1 At 2 months						
Thomas 1999	19	1.9 (2.1)	26	4.9 (3.5)		-0.99[-1.62,-0.36]

Analysis 2.3. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 3 Pain severity (sensation).

Analysis 2.4. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 4 Coping strategies.

Analysis 2.5. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 5 Health service utilisation (emergency visits).

Analysis 2.6. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 6 Health service utilisation (hospital admissions).

Analysis 2.7. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 7 Health service utilisation (outpatient clinic visits).

Analysis 2.8. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 8 Quality of life - daily function.

Analysis 2.9. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 9 Health beliefs - locus of control (chance).

Analysis 2.10. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 10 Health beliefs - locus of control (powerful others).

Analysis 2.11. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 11 Health beliefs - locus of control (internal).

Analysis 2.12. Comparison 2 Cognitive behavioural therapy (CBT) compared with usual treatment, no intervention or control, Outcome 12 Mental health.

APPENDICES

Appendix 1. EMBASE (OvidSP)

Search:		
#	Searches	Results
1	sickle cell.mp.	29529
2	psychology.mp.	45429
3	therapy.mp.	1146528
4	pain.mp.	210766
5	1 and 2	17
6	1 and 3	1532
7	1 and 4	1941

Appendix 2. PsycINFO (OvidSP)

Search:		
#	Searches	Results
1	sickle cell.mp.	1070
2	psychology.mp.	22301
3	therapy.mp.	57891
4	pain.mp.	18108
5	1 and 2	3

(Continued)

6	1 and 3	41
7	1 and 4	125

WHAT'S NEW

Date	Event	Description
8 May 2015	New citation required but conclusions have not changed	Following the updated searches, one new study (n = 53) has been included in the review (Barakat 2010). While minor changes have been made throughout, no major amendments to the conclusions of the review were made.
8 May 2015	New search has been performed	Following a search of the Cochrane Cystic Fibrosis and Genetic Disorders Group's Haemoglobinopathies Trials Register, one new trial has been included in the update of the review (Barakat 2010) and an additional reference to an already excluded trial has been added to the Barakat trial (Barakat 2007).

HISTORY

Protocol first published: Issue 1, 2000

Review first published: Issue 3, 2000

Date	Event	Description
24 January 2013	Amended	Contact details updated.
1 December 2011	New citation required but conclusions have not changed	Minor update. No new information has been included in the review.
4 November 2011	New search has been performed	A search of the Cochrane Cystic Fibrosis and Genetic Disorders Group's Haemoglobinopathies Trials Register did not identify any relevant trials for possible inclusion in the review.
8 September 2010	Amended	Contact details updated.
7 September 2009	New search has been performed	A search of the Group's Haemoglobinopathies Register identified four references; none of which were eligible for inclusion in the review (Barakat 2007 ; Ketchen 2006 ; Kinlow 2001 ; Yerys 2003).
1 October 2008	Amended	Converted to new review format. The 'Synopsis' has been replaced by a 'Plain Language Summary'.
2 April 2007	New search has been performed	The search of the Group's Haemoglobinopathies Trials Register identified eleven new references (to five trials) all of which were not eligible for inclusion in the review.
3 April 2006	New search has been performed	The search of the Group's Haemoglobinopathies Trials Register identified one new reference (Applegate 2003) which has been listed under Excluded studies.

Date	Event	Description
2 May 2005	New search has been performed	The search of the Group's Haemoglobinopathies Trials Register identified no new trials eligible for inclusion within the review.
1 March 2004	New search has been performed	The search of the Groups trials register found one reference to the already included Thomas 1999 trial. This reference did not provide any additional information not already included within the review.
1 May 2003	New search has been performed	<p>A new study has been added to the "Included Studies" section of this review (Broome 2001). However, there have been no substantive changes made to the conclusions of this review.</p> <p>Gil 1996 and Gil 1997 have been moved from 'Studies awaiting assessment' to 'Included studies', but there is insufficient data to be entered into RevMan for analysis.</p> <p>An additional reference [abstract] to the already included study by Kaslow has been incorporated into the review (Kaslow 2000).</p> <p>The 'Results' section of the review and the MetaView has been changed in order to more closely reflect the structure of the 'Types of Interventions'.</p>
8 February 2002	New search has been performed	Additional data have been gained from primary authors since the initial publication of this review. Therefore, three studies previously included in the 'Studies Awaiting Assessment' section are now in the 'Included Studies' section (Boroffice 1991; Thomas 1999; Kaslow 2000).

CONTRIBUTIONS OF AUTHORS

The review authors worked together on the search strategy initially and also examined the identified studies for methodological quality to arrive at a consensus for inclusion or exclusion.

Dr Kofi Anie then took the lead in writing the original review and the updated versions.

DECLARATIONS OF INTEREST

Kofi Anie: none known.

John Green: none known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

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- National Institute for Health Research, UK.

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INDEX TERMS

Medical Subject Headings (MeSH)

*Adaptation, Psychological; Depression [psychology] [therapy]; Hemoglobin SC Disease [*therapy]; Outcome Assessment, Health Care; Pain [psychology]; Pain Management [*methods]; Psychotherapy [*methods]; Randomized Controlled Trials as Topic

MeSH check words

Adolescent; Adult; Child; Humans