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Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents (Review)

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[Intervention Review]

Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

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ABSTRACT

Background

This is the first update of a review published in 2015, Issue 1. Chronic pain is common during childhood and adolescence and is associated with negative outcomes, such as increased severity of pain, reduced function, and low mood. Psychological therapies, traditionally delivered face-to-face with a therapist, are efficacious at reducing pain intensity and disability. To address barriers to treatment access, such as distance and cost of treatment, technology is being used to deliver these psychological therapies remotely. Therapies delivered remotely, such as via the Internet, computer-based programmes, and smartphone applications, can be used to deliver treatment to children and adolescents with chronic pain.

Objectives

To determine the efficacy of psychological therapies delivered remotely compared to waiting list, treatment as usual, or active control treatments, for the management of chronic pain in children and adolescents.

Search methods

We searched four databases (CENTRAL, MEDLINE, Embase, and PsycINFO) from inception to May 2018 for randomised controlled trials (RCTs) of remotely-delivered psychological interventions for children and adolescents with chronic pain. We searched for chronic pain conditions including, but not exclusive to, headache, recurrent abdominal pain, musculoskeletal pain, and neuropathic pain. We also searched online trial registries, reference sections, and citations of included studies for potential trials.

Selection criteria

We included RCTs that investigated the efficacy of a psychological therapy delivered remotely via technology in comparison to an active, treatment as usual, or waiting-list control. We considered blended treatments, which used a combination of technology and up to 30% face-to-face interaction. Interventions had to be delivered primarily via technology to be included, and we excluded interventions delivered via telephone. We included studies that delivered interventions to children and adolescents (up to 18 years of age) with a chronic pain condition or where chronic pain was a primary symptom of their condition (e.g. juvenile arthritis). We included studies that reported 10 or more participants in each comparator arm, at each extraction point.

Data collection and analysis

We combined all psychological therapies in the analyses. We split pain conditions into headache and mixed (non-headache) pain and analysed them separately. We extracted pain severity/intensity, disability, depression, anxiety, and adverse events as primary outcomes, and satisfaction with treatment as a secondary outcome. We considered outcomes at two time points: first immediately following the end of treatment (known as 'post-treatment'), and second, any follow-up time point post-treatment between three and 12 months (known as 'follow-up'). We assessed risk of bias and all outcomes for quality using the GRADE assessment.

Main results

We found 10 studies with 697 participants (an additional 4 studies with 326 participants since the previous review) that delivered treatment remotely; four studies investigated children with headache conditions, one study was with children with juvenile idiopathic arthritis, one included children with sickle cell disease, one included children with irritable bowel syndrome, and three studies included children with different chronic pain conditions (i.e. headache, recurrent abdominal pain, musculoskeletal pain). The average age of children receiving treatment was 13.17 years.

We judged selection, detection, and reporting biases to be mostly low risk. However, we judged performance and attrition biases to be mostly unclear. Out of the 16 planned analyses, we were able to conduct 13 meta-analyses. We downgraded outcomes for imprecision, indirectness of evidence, inconsistency of results, or because the analysis only included one study.

Headache conditions

For headache pain conditions, we found headache severity was reduced post-treatment (risk ratio (RR) 2.02, 95% confidence interval (CI) 1.35 to 3.01); P < 0.001, number needed to treat to benefit (NNTB) = 5.36, 7 studies, 379 participants; very low-quality evidence). No effect was found at follow-up (very low-quality evidence). There were no effects of psychological therapies delivered remotely for disability post-treatment (standardised mean difference (SMD) -0.16, 95% CI -0.46 to 0.13; P = 0.28, 5 studies, 440 participants) or follow-up (both very low-quality evidence). Similarly, no effect was found for the outcomes of depression (SMD -0.04, 95% CI -0.15 to 0.23, P = 0.69, 4 studies, 422 participants) or anxiety (SMD -0.08, 95% CI -0.28 to 0.12; P = 0.45, 3 studies, 380 participants) at post-treatment, or follow-up (both very low-quality evidence).

Mixed chronic pain conditions

We did not find any beneficial effects of psychological therapies for reducing pain intensity post-treatment for mixed chronic pain conditions (SMD -0.90, 95% CI -1.95 to 0.16; P = 0.10, 5 studies, 501 participants) or at follow-up. There were no beneficial effects of psychological therapies delivered remotely for disability post-treatment (SMD -0.28, 95% CI -0.74 to 0.18; P = 0.24, 3 studies, 363 participants) and a lack of data at follow-up meant no analysis could be run. We found no beneficial effects for the outcomes of depression (SMD 0.04, 95% CI -0.18 to 0.26; P = 0.73, 2 studies, 317 participants) and anxiety (SMD 0.53, 95% CI -0.63 to 1.68; P = 0.37, 2 studies, 370 participants) post-treatment, however, we are cautious of our findings as we could only include two studies in the analyses. We could not conduct analyses at follow-up. We judged the evidence for all outcomes to be very low quality.

All conditions

Across all chronic pain conditions, six studies reported minor adverse events which were not attributed to the psychological therapies. Satisfaction with treatment is described qualitatively and was overall positive. However, we judged both these outcomes as very low quality.

Authors' conclusions

There are currently a small number of trials investigating psychological therapies delivered remotely, primarily via the Internet. We are cautious in our interpretations of analyses. We found one beneficial effect of therapies to reduce headache severity post-treatment. For the remaining outcomes there was either no beneficial effect at post-treatment or follow-up, or lack of evidence to determine an effect. Overall, participant satisfaction with treatment was positive. We judged the quality of the evidence to be very low, meaning we are very uncertain about the estimate. Further studies are needed to increase our confidence in this potentially promising field.

PLAIN LANGUAGE SUMMARY

Psychological therapies (remotely-delivered) for the management of chronic and recurrent pain in children and adolescents

Background

Experiencing long-term pain during childhood is common. Children and adolescents (< 18 years of age) with long-term pain often report intense pain which negatively impacts their lives. The pain can affect their ability to function physically, can limit their ability to go to school, and can leave them feeling anxious or depressed. The most common types of chronic pain in children and adolescents are headaches, recurrent abdominal pain, musculoskeletal pain, and back pain. Normally, a therapist, physically together with a patient or family (a method often called face-to-face) delivers psychological therapies, such as cognitive behavioural therapy (e.g. coping skills, activity pacing) or behavioural therapy (e.g. relaxation exercises). We know that face-to-face therapies can reduce pain intensity and improve physical functioning in children. Technology (e.g. the Internet, computer programmes, and smartphone applications) now allows therapy to be delivered without needing to be face-to-face with a therapist. Therapies delivered remotely promise to make treatments easier to access because they remove the need for travel. They may also be less expensive.

We set out to understand if psychological therapies, delivered remotely using technology, can help children and adolescents with long-term pain to have less pain, to improve physical functioning, and to have fewer symptoms of depression and anxiety, compared to children who are waiting to be treated (waiting-list control), or being treated in other ways (active control, e.g. receiving education about long-term pain).

Study characteristics

For this update, we conducted the search through to May 2018. We found 10 studies including 697 children and adolescents; four of these studies (326 participants) were new for this update. Four studies treated children with headache, one study treated children with juvenile idiopathic arthritis, one treated children with sickle cell disease, one included children with irritable bowel syndrome, and three studies included mixed samples of children, some who had headache and some with other chronic pain conditions. All studies delivered cognitive behavioural therapy. The average age of children receiving the interventions was 13 years. We looked at six outcomes: pain, physical functioning, depression, anxiety, side effects, and satisfaction with treatment.

Key results

We split the painful conditions into two groups and looked at them separately. The first group included children with headache. The second group included children with other painful conditions (e.g. frequent stomach pain, musculoskeletal pain), known as 'mixed chronic pain'. Psychological therapies delivered remotely (primarily via the Internet) were helpful at reducing pain for children and adolescents with headache when assessed immediately following treatment. However, we did not find a beneficial effect for these children at follow-up. We found no beneficial effect of therapies for reducing pain intensity for children with other types of pain. Further, we did not find beneficial effects of remotely-delivered therapies on physical functioning, depression, or anxiety post-treatment for headache and mixed chronic pain conditions. However, there were limited data for mixed chronic pain conditions to draw conclusions from these outcomes, particularly at follow-up. Satisfaction with treatment was described in the trials and was generally positive. Six trials described side effects which were not linked to receiving psychological therapies.

Currently, there are very few studies investigating this treatment. Caution should be taken when interpreting these results as they are based on a small number of studies with few children. Further studies in this area are likely to change our findings and may show this to be a useful treatment for reducing pain and improving functioning in children with long-term pain.

Quality of the evidence

We rated the quality of the evidence from studies using four levels: very low, low, moderate, or high. Very low-quality evidence means that we are very uncertain about the results. High-quality evidence means that we are very confident in the results. We judged the quality of evidence as very low, downgraded due to differences between studies and assessments for the same outcomes, as well as differences identified in the statistical tests. However, this is a growing field and more trials with more participants using cognitive behavioural therapy and other psychological therapies are needed to determine if remotely-delivered therapies are helpful for young people with long-term pain.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Psychological therapies delivered remotely compared with any control for children with headache conditions

Patient or population: children or adolescents with headaches
Settings: home
Intervention: psychological therapies delivered remotely via technology
Comparison: any control

Outcomes	Probable outcome with control	Probable outcome with intervention	NNT/Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)
Achievement of at least 50% reduction in headache severity Post-treatment Higher scores indicate more children with reduced headache	**125 per 1000**	**271 per 1000**	**NNTB = 5.36** **RR 2.02** (1.35 to 3.01)	7 studies (379 participants)	⊕◯◯◯ **Very low**[b,c]
Achievement of at least 50% reduction in headache severity Follow-up Higher scores indicate more children with reduced headache	**168 per 1000**	**262 per 1000**	**NNTB = 6.29** **RR** 1.76 (0.88 to 3.52)	4 studies (230 participants)	⊕◯◯◯ **Very low**[a,c,d]
Disability Post-treatment Lower scores indicate lower levels of disability		The mean disability in the intervention groups was 0. 16 lower (-0.46 to 0.13)		5 studies (440 participants)	⊕◯◯◯ **Very low**[a,c,d]
Disability Follow-up Lower scores indicate lower levels of disability		The mean disability in the intervention groups was 0.16 lower (-0.38 to 0.05)		3 study (341 participants)	⊕◯◯◯ **Very low**[a,d,e]

Depression Post-treatment Lower scores indicate lower levels of depression		The mean depression in the intervention groups was 0.04 lower (-0.15 to 0.23)		4 studies (422 participants)	⊕◯◯◯ **Very low**[b,d]
Anxiety Post-treatment Lower scores indicate lower levels of anxiety		The mean anxiety in the intervention groups was 0.08 lower (-0.28 to 0.13)		3 studies (380 participants)	⊕◯◯◯ **Very low**[b,d]
Anxiety Follow-up Lower scores indicate lower levels of anxiety		The mean anxiety in the intervention groups was 0.01 lower (-0.22 to 0.20)		3 studies (360 participants)	⊕◯◯◯ **Very low**[b,d]

CI: confidence interval; **NNT:** number needed to treat to benefit; **RR:** risk ratio

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low quality: we are very uncertain about the estimate.

[a]Downgraded once due to indirectness of evidence.
[b]Downgraded twice due to indirectness of evidence.
[c]Downgraded once due to unexplained heterogeneity or inconsistency of results.
[d]Downgraded once due to imprecision of results.
[e]Downgraded once due to probability of reporting bias.

BACKGROUND

This is the first update of a review published in 2015, Issue 1 (Fisher 2015).

Description of the condition

Episodes of chronic pain are surprisingly common during childhood and adolescence (Perquin 2000). About 5% to 8% of youth with chronic pain experience significant pain-related disability (Huguet 2008). The most commonly reported chronic pain problems are headache, recurrent abdominal pain, musculoskeletal pain, and back pain (King 2011). Epidemiological studies report that girls experience more pain than boys and that pain increases during early adolescence (King 2011). Paediatric chronic pain is also among the most costly chronic health conditions, with an estimated economic cost of USD 19.5 billion annually in the US alone (Groenewald 2014). Chronic pain can interfere with many aspects of daily life for children, and is associated with elevated symptoms of depression and anxiety as well as difficulty participating in school, sports, and activities with friends and family (Cohen 2011; Gauntlett-Gilbert 2007; Kaczynski 2011). The detrimental effects of chronic pain can also impact parents, who report significant distress and anxiety (Jordan 2007; Maciver 2010). Longitudinal studies indicate that children with chronic pain are at risk for pain, psychiatric comorbidities, and pain-related disability in adulthood (Noel 2016; Shelby 2013; Walker 2012). Appropriate treatment of chronic pain in childhood has the potential to disrupt long-term trajectories of pain and disability in adulthood.

Description of the intervention

Psychological therapies, delivered individually or in groups to children and families, can reduce pain and disability in children with chronic pain (Fisher 2018). However, most children do not receive psychological treatment for chronic pain due to barriers to access including geographic distance from treatment centres, cost, and stigma against mental health treatment (Palermo 2013; Peng 2007). This has led to consideration of innovative methods of remote treatment delivery, such as via the Internet, computer, or smartphone devices (Palermo 2009). For example, the Internet is widely available to a large number of children and adolescents; in the US 95% of teenagers have access to the Internet through smartphones (Anderson 2018).

Different terms are used within this growing field, broadly described as e-health, m-health, telemedicine, telecare, minimal therapist contact, and distance treatment. Here, we adopt the term 'remotely-delivered therapies' to refer to psychological therapies delivered via technology, such as the Internet, smart phone applications, or CD-ROMs. In clinical practice, these technology-delivered programmes may replace or supplement face-to-face treatment for the child's pain problem. We distinguish remotely-delivered therapies from those that rely on clinician contact, such as telemedicine and telecare, where the technology is used to bring the clinician to the patient. In contrast, remotely-delivered therapies are flexible, self-guided treatments most typically delivered without contact with a clinician.

How the intervention might work

Psychological therapies are used in paediatric pain practice to reduce pain symptoms, disability, and negative mood associated with pain conditions, and to modify social-environmental factors to enhance the child's adaptive functioning (Fisher 2018). This field is currently dominated by cognitive behavioural therapies (CBTs) and behavioural therapies that typically include components such as pain education, relaxation training, biofeedback, hypnosis, cognitive coping skills, behavioural activation, healthy lifestyle habits, and parent operant strategies.

Recognising the advantages of reaching more children in their homes with remotely-delivered interventions, early studies relied on low levels of technology, including written self-help manuals, portable biofeedback monitors, and relaxation audiotapes (e.g. Burke 1989; McGrath 1992). As technological advances became available, intervention delivery options expanded to personal computers via CD-ROM applications and then to programmes/applications via the Internet. The delivery of psychological therapies over the Internet is becoming more common (March 2008; Richardson 2010; Tait 2010). The potential benefits of a successful programme include improved access, improved scale of coverage, and lowered cost (Marks 2009; Palermo 2009). However, the change of a delivery mechanism from face-to-face delivery to remote delivery via technology arguably changes the content, intensity, and force of a treatment. The move away from face-to-face delivery is not simply a change in the route of administration. The transformation of a treatment to a reliance on communication technology (instead of face-to-face interaction with a therapist) may involve critical changes in aspects of the treatment thought crucial to its success. For example, treatment where a therapist is not present may influence treatment participation and impact treatment outcomes (Fry 2009). At the same time, technology platforms may offer critical benefits that are not available in face-to-face models of care, such as 24-7 access to skills training.

There may also be different therapeutic opportunities available using interactive and communication technologies. As described in the behavioural change model for Internet interventions (Ritterband 2009), user characteristics interact with website characteristics to produce behaviour change. For example, Internet-delivered therapies may work by better matching and designing technology to maximise the therapeutic benefits (e.g. 24-hour access to skills training), or there may be a blend to these solutions that function differently dependent upon user characteristics.

Why it is important to do this review

Psychological therapies delivered remotely (principally but not exclusively via the Internet) have now developed into stand-alone treatments, and are investigated as stand-alone treatments. A Cochrane Review has previously summarised the evidence of psychological therapies for the management of chronic pain in children and adolescents (Fisher 2018). This was first authored in 2003, and updated in 2009, 2012, 2014, and most recently in 2018. Earlier updates combined remote and face-to-face treatment delivery. However, we believe it is important to separate them so that the evidence can be separately evaluated. This review should be considered a sister review to the Fisher 2018 update, which now excludes treatments delivered via technology. A similar distinction has also been made in the Cochrane Reviews on psychological therapies for the management of chronic pain in adults: face-to-face in Williams 2012 and Internet delivered in Eccleston 2014.

OBJECTIVES

To determine the efficacy of psychological therapies delivered remotely compared to waiting list, treatment as usual, or active control treatments, for the management of chronic pain in children and adolescents.

METHODS

Criteria for considering studies for this review

Types of studies

We searched for randomised controlled trials (RCTs) that delivered psychological therapies remotely to children and adolescents with chronic pain.

Types of participants

We included studies of children and adolescents under the age of 18 years. The intervention had to primarily target the child or adolescent with chronic or recurrent pain, defined as pain lasting for three months or longer. Pain conditions typically (but not exclusively) fall into the categories of headache, musculoskeletal pain, neuropathic pain, and recurrent abdominal pain. We excluded pain associated with life-limiting conditions (e.g. cancer) or where pain is not a primary symptom of the condition (e.g. diabetes). For the trial to be included, we required 10 or more participants to be in each arm of the trial at each extracted time point of post-treatment or follow-up.

Types of interventions

We included studies that delivered primarily psychological treatments and included recognisable psychotherapeutic content, or were based on an existing psychological framework. We included only RCTs with at least one comparator arm. Therapies had to aim to improve pain outcomes, function, or both; we excluded therapies that solely aimed to manage child or adolescent mood. Psychological therapies had to be delivered remotely, using technology, such as the Internet, computer programme, or smartphone application. In previous versions of this review, we included interventions delivered remotely but not via technology, such as by telephone, audiotapes and self-help books. In order to reduce heterogeneity and keep the review contemporary, we have excluded studies of therapies delivered remotely but not via technology in this update. This follows our protocol for this review. Therapies delivered face-to-face and by remote, non-technology modalities are included in Fisher 2018, and are not included in this review. We also considered therapies that used blended treatments, combining both face-to-face contact and a remote component for inclusion in this review. However, the intention of included trials (stated or inferred) was to deliver the majority of the treatment remotely from the therapist. As a guide, we excluded studies where over 30% of contact time (assessment or therapy) was face-to-face. We excluded interventions that had a primary aim to monitor symptoms or aid communication (such as with a treatment team). We included waiting list, treatment as usual, or active control as comparison conditions. We excluded equivalence trials where the control was another active therapy.

Types of outcome measures

Primary outcomes

We extracted five primary outcomes from each study.

- Pain symptoms
- Disability
- Depression
- Anxiety
- Adverse events

Secondary outcomes

We extracted satisfaction with treatment as a secondary outcome.

Search methods for identification of studies

Electronic searches

We searched the following databases for studies for this update.

- CENTRAL (CRSO) searched to 1 May 2018.
- MEDLINE (OVID) 1946 to April week 3 2018.

- Embase (OVID) 1974 to 2018 week 18.
- PsycINFO (OVID) 1806 to April week 4 2018.

We devised a search strategy for MEDLINE which we adapted for the other databases listed (see Appendix 1 for all search strategies).

Searching other resources

We conducted a reference search and citation search of all included studies in order to identify additional studies not found in our database search. We examined relevant reviews retrieved by the database searches to identify any further trials. In addition, we searched trial registries, including the metaRegister of controlled trials (mRCT) (www.controlled-trials.com/mrct/), ClinicalTrials.gov (clinicaltrials.gov), and the World Health Organization International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/en/) for trials in May 2018. We did not impose any limitations on publication date or language.

Data collection and analysis

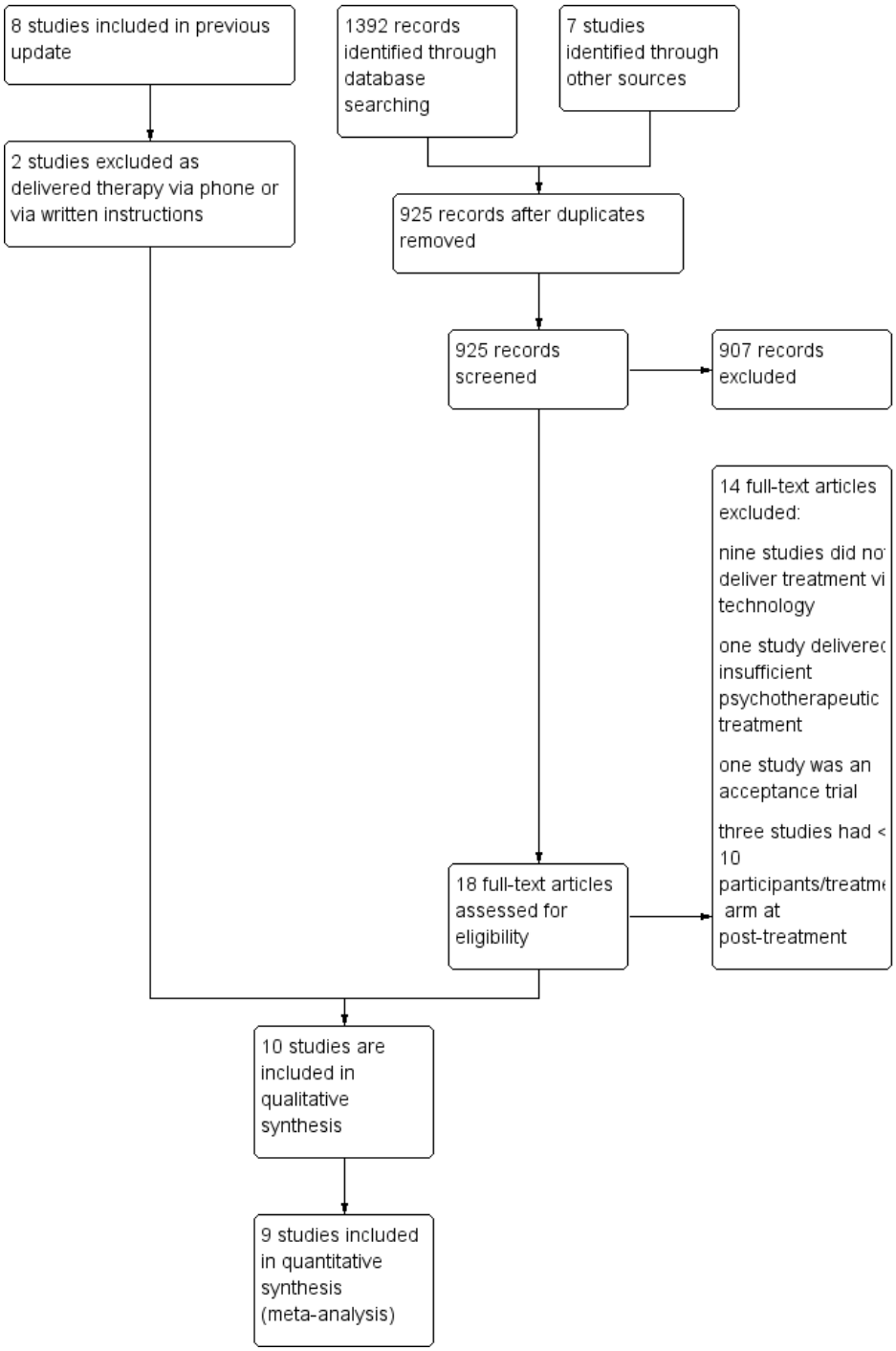
Selection of studies

For this update, two review authors (EF, JD) independently selected and read potential studies for inclusion. A third review author (TP) arbitrated any disagreements. We selected studies according to the following criteria.

- Children and adolescents under the age of 18 years with a chronic pain condition.
- N $\geq$ 10 in each arm of the trial at each extracted time point.
- A primarily psychological therapy used in at least one arm of each included trial.
- Therapies with a primary aim to change thoughts or behaviours of the child to assist with the management of, or coping with, chronic pain.
- Therapies that were principally delivered remotely, via technology.

See PRISMA flow diagram for search results (Figure 1), as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

Figure 1. Study flow diagram.



Data extraction and management

Two review authors (EF, EL) independently extracted data from the studies. JD extracted data from studies in which EL was an author. EF and EL discussed disagreements, and then a third review author (TP or CE) arbitrated if no agreement could be found. We extracted study characteristics from each of the studies. These included patient demographics and characteristics of the psychological therapies including delivery type, duration of treatment, when and where treatment was accessed, engagement in treatment, type of control condition, and follow-up periods. We then extracted data for each of the five primary outcomes and secondary outcome at post-treatment and follow-up. We contacted study authors via email if studies reported incomplete outcome data.

Assessment of risk of bias in included studies

We assessed risk of bias using Cochrane's 'Risk of bias' tool. This outlines four biases: selection bias, performance and detection bias, attrition bias, and reporting bias.

Selection bias

Random sequence generation (checking for possible selection bias): we assessed the method used to generate the allocation sequence as: low risk of bias (any truly random process, e.g. random number table; computer random number generator); unclear risk of bias (method used to generate sequence not clearly stated). We excluded studies using a non-random process (e.g. odd or even date of birth; hospital or clinic record number).

Allocation concealment (checking for possible selection bias): we judged the method used to conceal allocation to interventions prior to assignment determines whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment. We assessed the methods as low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes) or unclear risk of bias (method not clearly stated). We judged studies that do not conceal allocation (e.g. open list) as high risk of bias.

Performance and detection bias

Blinding of participants and personnel (checking for possible performance bias): we assessed the methods used to blind study participants and personnel from knowledge of which intervention a participant received. We assessed methods as low risk of bias (study states that it was blinded and describes the method used to achieve blinding) or unclear risk of bias (study that is not clear regarding whether they blinded participants). We did not rate any studies as high risk of bias due to the nature of psychological treatments being extremely difficult to blind.

Blinding of outcome assessment (checking for possible detection bias). We assessed the methods used to blind study participants and outcome assessors from knowledge of which intervention a participant received. We assessed the methods as: low risk of bias (study has a clear statement that outcome assessors were unaware of treatment allocation, or describes how this was achieved, e.g. completed assessments online); unclear risk of bias (study states that outcome assessors were blind to treatment allocation but lacks a clear statement on how it was achieved, or if this is not described). We judged studies where outcome assessment was explicitly not blinded as high risk of bias.

Attrition bias

We assessed the methods used to deal with incomplete data as: low risk of bias (authors reported attrition with reasons, and reported no differences between completers and non-completers); unclear risk of bias (authors reported attrition but did not report any differences between completers and non-completers); high risk of bias (attrition was not reported).

Reporting bias

We assessed whether studies reported all outcomes in their manuscripts that they stated in their methods. We judged studies as low risk of bias if all data were reported in the manuscripts, unclear risk of bias if they provided data on request, and high risk of bias if they did not respond to data requests.

Measures of treatment effect

We categorised chronic pain conditions into headache and mixed chronic pain conditions (e.g. musculoskeletal pain, recurrent abdominal pain), and analysed these studies separately. Due to the small number of studies in this area, we combined mixed chronic pain conditions (excluding headache) in analyses to provide the overall effectiveness of psychological therapies delivered remotely. If a study included children with both headache and mixed chronic pain conditions, we entered data into both analyses where appropriate. We analysed the effect of treatment on children's pain symptoms, disability, depression, and anxiety at two time points (post-treatment and follow-up). We extracted adverse events and described these narratively. We defined satisfaction with treatment as any patient self-reported measure that evaluated how useful the treatment was, satisfaction with the outcome of therapy, or likeability and preference for the treatment. When studies used more than one measure for a given outcome, we extracted the most reliable or commonly used.

We defined post-treatment as the time point immediately following treatment. Follow-up was defined as the time point between three and 12 months following post-treatment. If more than one time point was available, the latter of the two was extracted. Due to this novel method of delivery of psychological interventions, there are currently only a small number of studies that can be included in analyses. Therefore, we did not categorise studies by therapy type or control type (i.e. active versus waiting list). In total, there are 20 possible analyses, categorised by four headings.

- Treatment versus control, post-treatment, headache conditions
- Treatment versus control, follow-up, headache conditions
- Treatment versus control, post-treatment, mixed chronic pain conditions
- Treatment versus control, follow-up, mixed chronic pain conditions

Unit of analysis issues

Randomisation occurred at the individual level. We included studies of children with headache and mixed chronic pain in both sets of analyses (headache and mixed chronic pain conditions).

Dealing with missing data

We contacted study authors for outcome data if they were missing from manuscripts.

Assessment of heterogeneity

We assessed heterogeneity by assessing the I^2 of the analyses. We interpreted these according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011):

- 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.

Assessment of reporting biases

We assessed reporting biases as part of the 'Risk of bias' assessment. We planned to use funnel plot analyses following guidelines in Chapter 10.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We did not, however, have sufficient data to conduct these analyses.

Data synthesis

We pooled data using Review Manager 5 (Review Manager 2014). Headache conditions are typically reported with dichotomous data for pain symptoms defined by a 50% reduction of pain symptoms. Mixed chronic pain conditions (e.g. musculoskeletal pain, neuropathic pain, and recurrent abdominal pain) are typically reported with continuous data for pain symptoms. We calculated risk ratios (RRs), 95% confidence intervals (CIs) and number needed to treat to benefit (NNTB) for dichotomous data. We reported standardised mean differences (SMDs) and 95% CIs for continuous data. We used Mantel-Haenszel methods to analyse dichotomous data and random-effects models to analyse continuous data.

Quality of the evidence

Two review authors (EF, JD) independently rated the quality of the outcomes. We used GRADE to rank the quality of the evidence using the Review Manager software (Review Manager 2014), and the guidelines provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011).

The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness, and reporting bias) to assess the quality of the body of evidence for each outcome. The GRADE system uses the following criteria for assigning grade of evidence.

- High quality: further research is very unlikely to change our confidence in the estimate of effect.
- Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- Very low quality: we are very uncertain about the estimate.

The GRADE system uses the following criteria for assigning a quality level to a body of evidence (Chapter 12, Higgins 2011).

- High: randomised trials; or double-upgraded observational studies.
- Moderate: downgraded randomised trials; or upgraded observational studies.
- Low: double-downgraded randomised trials; or observational studies.
- Very low: triple-downgraded randomised trials; or downgraded observational studies; or case series/case reports.

Factors that may decrease the quality level of a body of evidence are:

- limitations in the design and implementation of available studies suggesting high likelihood of bias;
- indirectness of evidence (indirect population, intervention, control, outcomes);
- unexplained heterogeneity or inconsistency of results (including problems with subgroup analyses);
- imprecision of results (wide confidence intervals);
- high probability of reporting bias.

Factors that may increase the quality level of a body of evidence are:

- large magnitude of effect;

- all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results show no effect;
- dose-response gradient.

We decreased the grade rating by one (- 1) or two (- 2) (up to a maximum of - 3 to 'very low') if we identified:

- serious (- 1) or very serious (- 2) limitation to study quality;
- some (-1) or considerable (-2) inconsistency of results;
- some (- 1) or major (- 2) uncertainty about directness;
- serious (-1) or very serious (- 2) concerns about imprecision of data, which could include a small number of participants or wide confidence intervals;
- some (-1) or considerable (-2) probability of reporting bias.

There are sometimes reasons to downgrade an outcome to 'very low quality' as recommended by GRADE guidelines (Guyatt 2013). We downgraded outcomes immediately to 'very low' when the total sample size was lower than the optimal information size (OIS; Schünemann 2013), or when only one study was included in analyses. Where outcomes exceeded the OIS, we downgraded outcomes once or twice if clinical decisions would change if we relied on the upper versus the lower 95% confidence interval (imprecision of results). The judgement was based on how much the confidence intervals differed.

'Summary of findings' table

We included two 'Summary of findings' tables to present the main findings in a transparent and simple tabular format. One 'Summary of findings' table provides quality of evidence for headache conditions, and the second shows quality of evidence for mixed chronic pain conditions. We included key information concerning the quality of evidence, the magnitude of effect of the interventions examined, and the sum of available data on the outcomes. We included 50% reduction in headache severity (headache conditions) or pain intensity (mixed chronic pain conditions), and disability at post-treatment and follow-up, and anxiety and depression post-treatment in all tables. We included anxiety or depression at follow-up in each 'Summary of findings' table, dependent on the outcome with the most participants, as we are limited to seven outcomes per table.

Subgroup analysis and investigation of heterogeneity

We planned subgroup analyses to investigate the technology type (e.g. Internet versus mobile app). We also planned to determine the difference in effect between trials that included a human support component (blended therapy) versus those without human support that were exclusively delivered remotely, as additional support during trials delivered via the Internet has been found to influence outcomes of participants (Law 2012). We were unable to conduct these analyses due to the small number of trials.

Sensitivity analysis

We planned to conduct sensitivity analyses in smaller ($n \leq 20$ participants/arm) versus larger ($n > 20$ participants/arm) trials, and in those trials with an active control versus waiting-list controls. However, there are currently insufficient data to conduct these meaningfully. We will consider conducting these in future updates.

RESULTS

Description of studies

See Characteristics of included studies; Characteristics of excluded studies.

Results of the search

We have conducted two searches to date. The first search was conducted from inception to June 2014 (see Appendix 2) and the latest search for this update was conducted in May 2018 (Figure 1). In the previous review, we included eight studies with 371 participants. Due to the changes in the inclusion criteria with this update, we excluded two studies because they did not deliver treatment via technology (Cottrell 2007; McGrath 1992). In the updated search, we found 1392 abstracts through database searches and seven studies through additional searches (925 abstracts after duplication), and we included an additional four new studies to this update (Bonnert 2017; Law 2015; Palermo 2016; Schatz 2015), resulting in 10 studies included in total (Bonnert 2017; Connelly 2006; Hicks 2006; Law 2015; Palermo 2009; Palermo 2016; Rapoff 2014; Schatz 2015; Stinson 2010; Trautmann 2010).

Included studies

We found 10 studies that met the inclusion criteria for this review (697 participants at post-treatment, an additional four studies and 326 participants from the previous review). Four studies investigated psychological therapies delivered remotely for children with headache (Connelly 2006; Law 2015; Rapoff 2014; Trautmann 2010), one assessed juvenile idiopathic arthritis (Stinson 2010), one included children with sickle cell disease (Schatz 2015), and one included children with irritable bowel syndrome (Bonnert 2017). Finally, three included headache and mixed chronic pain conditions (i.e. recurrent abdominal pain and musculoskeletal pain) meaning that we entered them in both headache and mixed chronic pain analyses where appropriate (Hicks 2006; Palermo 2009; Palermo 2016). Children were recruited via hospitals or clinics (8 studies), adverts in the media or community (1 study), or a combination of advertisements in clinics and the community (1 study). All children recruited into trials were diagnosed with their primary condition by a medical professional. A total of 830

participants entered into treatment and 697 participants finished, giving a retention rate of 84%. Girls (66%) outnumbered boys (34%). The mean age of participants was 13.17 years (standard deviation (SD) 1.85).

Most treatments were delivered via the Internet (Bonnert 2017; Hicks 2006; Law 2015; Palermo 2009; Palermo 2016; Stinson 2010; Trautmann 2010), one study delivered the intervention through a smartphone (Schatz 2015), and two studies delivered treatment via CD-ROM (Connelly 2006; Rapoff 2014). Control conditions differed between studies. Two studies used a waiting-list control (Bonnert 2017; Palermo 2009), and the remaining studies used active controls. The active controls included treatment as usual (Connelly 2006; Hicks 2006; Law 2015; Schatz 2015), Internet-delivered psychoeducation (Palermo 2016; Trautmann 2010), or via CD-ROM (Rapoff 2014), and telephone-delivered supportive care (Stinson 2010). All participants completed treatment in their homes and included phone calls, emails, or a combination of both on a weekly basis to deliver treatment, check engagement, or answer questions. See Table 1 for a summary of the characteristics of treatment and control conditions.

Five trials were supported by grants from the National Institutes of Health (Law 2015; Palermo 2009; Palermo 2016; Rapoff 2014; Schatz 2015). One trial was funded by a pharmaceutical and biologics company (Connelly 2006). The remaining trials were supported by research foundations, government-backed research councils, or awards (Bonnert 2017; Hicks 2006; Stinson 2010; Trautmann 2010). Four studies did not have a statement about conflict of interest, five studies declared that the authors did not have a conflict of interest, one study stated that authors were members of research funding bodies (see Characteristics of included studies for more detail).

Excluded studies

We excluded 14 articles in this update, resulting in 18 in total. We excluded two studies (previously included in the review) as they did not deliver the intervention remotely through technology, as defined in the update of this review (Cottrell 2007; McGrath 1992). We also excluded a further seven studies due to this reason (Greenley 2015; Kroner-Herwig 2002; Larsson 1987a; Larsson 1987b; Larsson 1990; Levy 2017; van Tilburg 2009). We excluded one study as it was conducted as an open trial (Bonnert 2014), and another as it was an acceptance paper with no useable data (Armbrust 2015). We excluded Long 2009 which evaluated the usability of an online study already included in the review (Palermo 2009). We excluded another study due to insufficient psychotherapeutic content (Ahola Kohut 2016). We excluded a further five studies as they included fewer than 10 participants in at least one arm of the trial at an extraction time point (McClellan 2009; Merlijn 2005; Palermo 2018; Trautmann 2008; Voerman 2015).

Risk of bias in included studies

We conducted 'Risk of bias' assessments on all included studies (for a summary see Figure 2 and Figure 3) following guidelines from the recommended 'Risk of bias' tool (Higgins 2011). More detail on the 'Risk of bias' judgements can be found in the Characteristics of included studies.

Figure 2. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

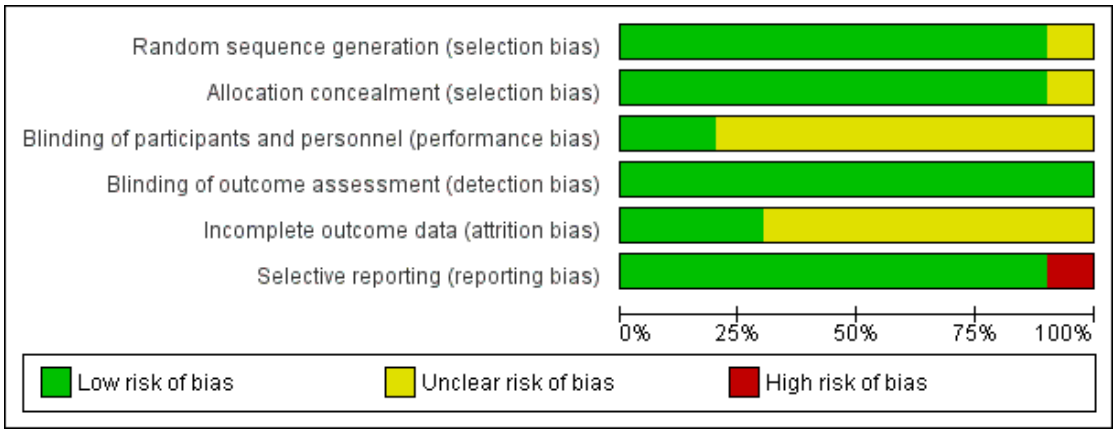
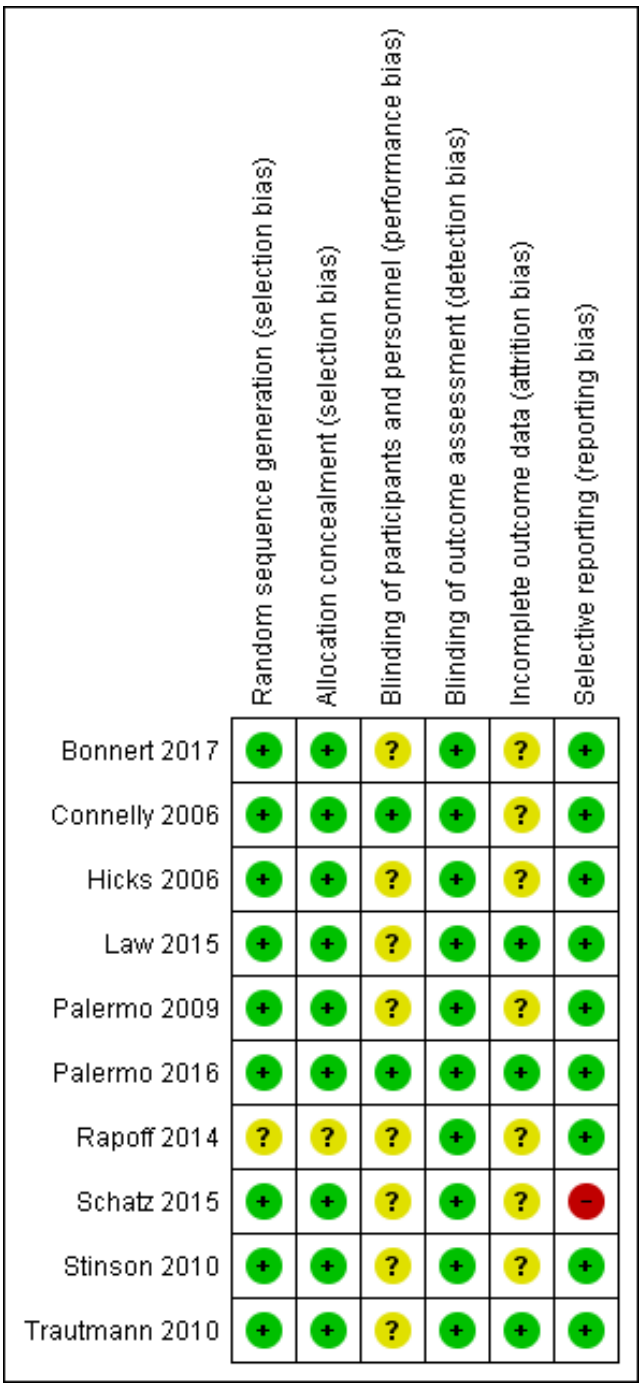


Figure 3. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Random sequence generation

We found nine studies to be at low risk of bias for random sequence generation. We judged the remaining study at unclear risk of bias because the trialists did not give a sufficient explanation of how they randomly allocated participants.

Allocation concealment

For allocation concealment, we judged nine studies to have low risk of bias, and one study as unclear as the trialists did not describe how allocation concealment was achieved.

Blinding

Blinding of participants and personnel (performance bias)

We judged two studies as having low risk of bias for blinding participants and personnel. We judged the remaining studies at unclear risk of bias as there was no clear description of how study authors blinded the participants and personnel.

Blinding of outcome assessment (detection bias)

We judged all studies to blind outcome assessors as participants complete their questionnaires electronically.

Incomplete outcome data

For attrition bias, we found that seven out of 10 studies were unclear on attrition. We judged three studies to be at low risk of bias as they fully reported attrition in studies and reported no differences between completers and non-completers.

Selective reporting

We judged nine studies as low risk of bias for selective reporting bias, as they reported all data in the manuscripts. We judged one study to be high risk of bias as study authors did not report full data in manuscripts and did not respond to data requests.

Effects of interventions

See: **Summary of findings for the main comparison** Summary of findings for children with headache conditions; **Summary of findings 2** Summary of findings for children with mixed chronic pain conditions

The pain outcomes extracted below differ between headache and mixed conditions (see Table 2 for a scorecard of results). For headache conditions we extracted dichotomous outcomes. For mixed chronic pain conditions we extracted continuous pain outcomes.

The International Headache Society and American Headache Society provide guidance on how to measure headache pain in adults and children. Guidelines for trials of behavioural and pharmacological treatments for chronic and recurrent headache recommend reporting headache frequency as the primary outcome variable and pain intensity and duration as secondary outcome variables (Andrasik 2005; Penzien 2005; Tfelt-Hansen 2012). Therefore, we preferentially extracted data for children and adolescents who reported at least 50% reduction of headache frequency in both the treatment and control groups; this was possible in four studies (Connelly 2006; Law 2015; Rapoff 2014; Trautmann 2010). When headache frequency was not reported or available, we extracted data for children and adolescents who reported at least 50% reduction in pain intensity in both the treatment and control groups (Hicks 2006; Palermo 2009; Palermo 2016). Headache pain outcomes are hereby known as 'headache severity'. For mixed chronic pain conditions, we extracted mean pain intensity across all trials. Nine studies are included in the analyses; Schatz 2015 did not present any analysable data.

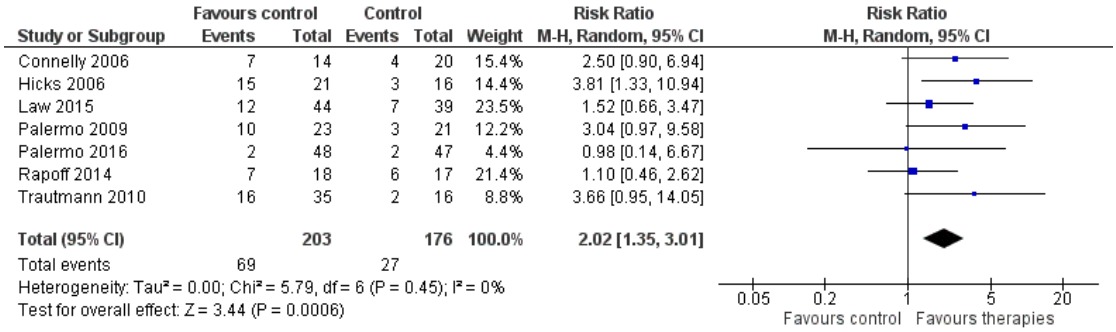
Treatment versus control for headache conditions

Primary outcomes

Headache severity

We found seven studies (379 participants) that reported whether psychological therapies delivered remotely reduced headache frequency in children with headache conditions post-treatment, and four studies (230 participants) at follow-up. Psychological therapies delivered remotely have a beneficial effect at achieving at least 50% reduction of headache severity post-treatment (risk ratio (RR) 2.02, 95% confidence interval (CI) 1.35 to 3.01; $P < 0.001$), number needed to treat to benefit (NNTB) = 5.36; Analysis 1.1; Figure 4). This effect was not maintained at follow-up (RR 1.76, 95% CI 0.88 to 3.52; P = 0.11, NNTB = 6.29; Analysis 2.1; Summary of findings for the main comparison).

Figure 4. Forest plot of comparison: 1 Headache conditions treatment versus control (post-treatment), outcome: Achievement of at least 50% reduction in headache severity.



We calculated the optimal information size (OIS) based on the primary headache severity outcome and found the OIS was 80 participants/arm. We judged the quality of evidence for headache severity post-treatment and at follow-up as very low, meaning we are very uncertain about the estimate. We downgraded the post-treatment outcome once for inconsistency of results and twice for indirectness of evidence. At follow-up, we downgraded the outcome once for indirectness of evidence, once for inconsistency of results, and once for imprecision of results. Specifically the clinical decision would be different depending on the interpretation of the upper versus the lower confidence interval.

Disability

We found five studies (440 participants) that evaluated whether psychological therapies delivered via technology were beneficial at reducing disability post-treatment. We did not detect a beneficial treatment effect (standardised mean difference (SMD) -0.16, 95% CI -0.46 to 0.13; P = 0.28; Analysis 1.2). At follow-up, we found three studies (341 participants) that also did not detect a beneficial treatment effect (SMD -0.16, 95% CI -0.38 to 0.05; P = 0.14; Analysis 2.2). We judged disability outcomes at both time points to be very low-quality. We downgraded the quality of evidence at both time points once for indirectness of evidence and once for imprecision. We downgraded the outcome at post-treatment once more for inconsistency of results. We also downgraded the follow-up outcome once for probability of reporting bias.

Depression

For depression, we found four studies (442 participants) had data available to determine whether psychological therapies were beneficial at reducing depressive symptoms post-treatment. We did not detect a beneficial effect of treatment (SMD -0.04, 95% CI -0.15 to 0.23; P = 0.69; Analysis 1.3). At follow-up, we found two studies (320 participants), and we did not detect a beneficial effect of treatment (SMD 0.03, 95% CI -0.19 to 0.25; P = 0.80; Analysis 2.3). We judged depression outcomes as very low quality. We downgraded both outcomes twice for indirectness of evidence and once for imprecision.

Anxiety

We found three studies that investigated the effect of psychological therapies on reducing anxiety symptoms post-treatment (380 participants) and at follow-up (360 participants). We did not find a beneficial treatment effect at either time point (post-treatment SMD -0.08, 95% CI -0.28 to 0.13; P = 0.46; Analysis 1.4; follow-up SMD -0.01, 95% CI -0.22 to 0.20; P = 0.91, Analysis 2.4). Similar to other headache outcomes, we judged the quality of evidence for anxiety as very low quality. We downgraded both outcomes twice for indirectness of evidence and once for imprecision.

Adverse events

Law 2015 and Palermo 2016 reported that no study-related adverse events occurred during the treatment. The remaining trials did not report if any adverse events occurred in the trial reports. Connelly 2006, Rapoff 2014 and Trautmann 2010 gave full reasons for dropouts. However, the remaining trials did not give full reasons for dropouts. We rated this outcome at very low quality, downgraded twice due to indirectness of evidence and once for inconsistency of results.

Secondary outcome

Satisfaction with treatment

Satisfaction was assessed in five studies (Hicks 2006; Law 2015; Palermo 2009; Palermo 2016; Trautmann 2010). We were unable to meta-analyse the data due to the heterogeneity of measures

used and the use of waiting-list controls (satisfaction ratings are inappropriate to measure in this group).

Hicks 2006 measured satisfaction in the treatment group using a visual analogue scale and reported that child and parent satisfaction were positively correlated. Law 2015 reported that adolescents and parents were generally satisfied with treatment on a scale of 1 to 5 (youth M = 3.35, SD = 0.50; parent M = 3.73, SD = 0.47). Palermo 2009 measured satisfaction for the treatment group using the Treatment Evaluation Inventory - Short Form (Kelley 1989), and reported global satisfaction of children and parents in the treatment group as moderate to high. Palermo 2016 reported that adolescents and parents in the treatment group reported significantly higher satisfaction (range 9 to 45) with treatment compared to those in the control group (treatment group adolescents M = 32.2, SD = 4.7; control group adolescents: M = 29.9, SD = 5.0; treatment group parent: M = 33.0, SD = 4.5; control parent: M = 30.2, SD = 4.9). Finally, Trautmann 2010, who included two treatment arms and a control asked all participants and their parents to report their degree of satisfaction. The findings revealed that the applied relaxation (treatment) group were more satisfied compared to the education (control) group. However, there were no significant differences between the cognitive behavioural (treatment) group and the applied relaxation (treatment) group or the education (control) group.

Connelly 2006 and Rapoff 2014 did not report satisfaction outcomes. We rated this outcome at very low quality, downgraded twice due to indirectness of evidence and once for inconsistency of results.

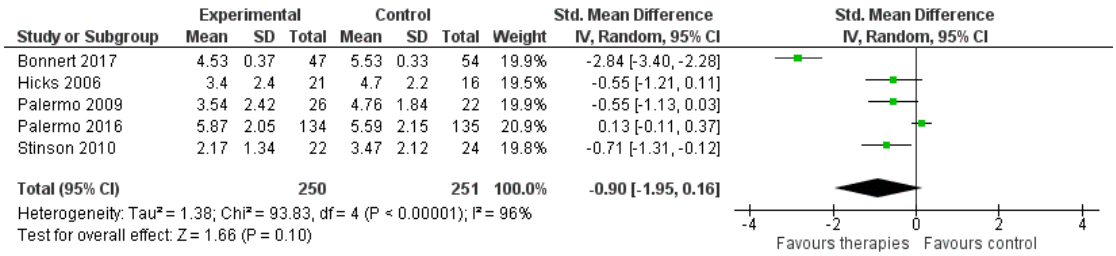
Treatment versus control for mixed chronic pain conditions

Primary outcomes

Pain intensity

We found five studies (501 participants) that reported whether psychological therapies reduced pain intensity for children with mixed chronic pain conditions at post-treatment, and two studies (301 participants) at follow-up. We did not find a beneficial effect post-treatment (SMD -0.90, 95% CI -1.95 to 0.16; P = 0.10; Analysis 3.1, Figure 5). We also did not find a beneficial effect of treatment at follow-up (SMD -0.41, 95% CI -1.62 to 0.79; P = 0.50; Analysis 4.1; Summary of findings 2). Both analyses had substantial heterogeneity (> 80%).

Figure 5. Forest plot of comparison: 3 Mixed conditions: treatment versus control (post-treatment), outcome: 3.1 Pain intensity.



We calculated the OIS based on the primary pain intensity outcome and found the OIS was 117 participant/arm. We judged pain intensity post-treatment and at follow-up to be very low quality. We downgraded both the pain intensity post-treatment and at follow-up twice for inconsistency of results, and once for imprecision.

Disability

We found three studies (363 participants) that reported disability outcomes post-treatment and one study (269 participants) at follow-up. We did not find a beneficial effect of psychological interventions at reducing disability for children with chronic pain post-treatment (SMD -0.28, 95% CI -0.74 to 0.18; P = 0.24; Analysis 3.2). We judged disability at post-treatment and follow-up as very low quality. At post-treatment, we downgraded once for indirectness of evidence, inconsistency of results, and once for imprecision of results. At follow-up, we downgraded immediately to very low quality due to only being able to include one study in the analysis.

Depression

We found two studies that reported on depression outcomes at post-treatment (317 participants), and we did not detect a beneficial effect of treatment (SMD 0.04, 95% CI -0.18 to 0.26; P = 0.73; Analysis 3.3). We only found one study that could be included in the follow-up analysis, and therefore we did not conduct an analysis. We judged post-treatment and follow-up outcomes of depression as very low quality. We downgraded the post-treatment outcome once due to imprecision and twice due to probability of reporting bias. At follow-up, we downgraded immediately to very low quality due to only being able to include one study in the analysis.

Anxiety

We found two studies (370 participants) that assessed anxiety post-treatment, and we did not detect a beneficial effect of treatment (SMD 0.53, 95% CI -0.63 to 1.68; P = 0.37; Analysis 3.4). We graded the quality of evidence for post-treatment and follow-up as very low. At post-treatment, we downgraded the outcome twice due to inconsistency of results and once due to imprecision. At follow-up, we downgraded immediately to very low quality due to only being able to include one study in the analysis.

Adverse events

Of the eight studies investigating children with mixed chronic pain conditions, only Palermo 2016 reported that no study-related adverse events occurred during the study and reported reasons for dropouts. Stinson 2010 gave full reasons regarding participants who dropped out, however the remaining studies did not report full reasons for dropouts. We rated this outcome at very low quality, downgraded three times due to only one study being able to be included in the analysis.

Secondary outcome

Satisfaction with treatment

Five studies reported results on satisfaction (Bonnert 2017; Hicks 2006; Palermo 2009; Palermo 2016; Stinson 2010). Hicks 2006, Palermo 2009 and Palermo 2016 are described above.

Bonnert 2017 reported a high level of satisfaction with treatment with 83% of adolescents in the Internet-cognitive behavioural therapy (CBT) treatment group reporting good or excellent treatment, 91% reported good or excellent support from therapists, and 81% reported being satisfied or very satisfied with treatment.

Stinson 2010 used a questionnaire developed by the investigators of the trial. The study reported that participants in the treatment group were satisfied with treatment. No information is provided regarding the satisfaction of the 'own best efforts' control group. Similar to the headache group, satisfaction data could not be entered into a meta-analysis.

Schatz 2015 did not include a satisfaction questionnaire.

We rated this outcome at very low quality, downgraded twice due to indirectness of evidence and once for inconsistency of results.

ADDITIONAL SUMMARY OF FINDINGS [Explanation]

Psychological therapies delivered remotely compared with any control for children with mixed chronic pain conditions

Patient or population: children or adolescents with mixed chronic pain conditions
Settings: home
Intervention: psychological therapies delivered remotely via technology
Comparison: any control

Outcomes	Probable outcomes with intervention	No of Participants (studies)	Quality of the evidence (GRADE)
Pain intensity Post-treatment Lower scores indicate lower levels of pain intensity	The mean pain intensity in the intervention groups was 0.90 lower (-1.95 to 0.16)	501 participants (5 studies)	⊕◯◯◯ **Very low**[c,d]
Pain intensity Follow-up Lower scores indicate lower levels of pain intensity	The mean pain intensity in the intervention groups was 0.41 lower (-1.62 to 0.79)	301 participants (2 studies)	⊕◯◯◯ **Very low**[c,d]
Disability Post-treatment Lower scores indicate lower levels of disability	The mean disability in the intervention groups was 0.28 lower (-0.74 to 0.18)	363 participants (3 studies)	⊕◯◯◯ **Very low**[a,b,d]
Disability Follow-up Lower scores indicate lower levels of disability	Meta-analysis could not be conducted	269 participants (1 study)	⊕◯◯◯ **Very low**[g]
Depression Post-treatment Lower scores indicate lower levels of depression	The mean depression in the intervention groups was 0.04 higher (-0.18 to 0.26)	317 participants (2 studies)	⊕◯◯◯ **Very low**[d,f]

Anxiety Post-treatment Lower scores indicate lower levels of anxiety	The mean anxiety in the intervention groups was 0.53 higher (-0.63 to 1.68)	370 participants (2 studies)	⊕◯◯◯ **Very low**[c,d]
Anxiety Follow-up Lower scores indicate lower levels of anxiety	Meta-analysis could not be conducted	269 participants (1 study)	⊕◯◯◯ **Very low**[g]

GRADE Working Group grades of evidence
High quality: further research is very unlikely to change our confidence in the estimate of effect
Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low quality: we are very uncertain about the estimate.

[a] Downgraded once due to indirectness of evidence.
[b] Downgraded once due to unexplained heterogeneity or inconsistency of results.
[c] Downgraded twice due to unexplained heterogeneity or inconsistency of results.
[d] Downgraded once due to imprecision of results.
[e] Downgraded once due to probability of reporting bias.
[f] Downgraded twice due to probability of reporting bias.
[g] Downgraded three times to very low-quality due to only including one study in analysis.

DISCUSSION

Summary of main results

This updated systematic review included a total of 10 trials with 697 participants (this included an additional 4 studies with 326 participants from the previous review) that delivered psychological therapies remotely to children and adolescents with chronic pain. We conducted separate analyses for children and adolescents with headache conditions and mixed chronic pain conditions (including juvenile idiopathic arthritis, musculoskeletal pain, recurrent abdominal pain, and sickle cell disease). The body of evidence in this field is still limited, heterogeneous, and very low quality, and therefore our conclusions are cautious. Currently, our analyses indicate that psychological treatments delivered remotely may reduce headache severity post-treatment, although this is not maintained at follow-up. We did not find evidence for a beneficial effect of remotely-delivered psychological therapies on pain intensity in children with mixed chronic pain conditions. Similarly, we did not find a beneficial effect of treatment for improving disability across all conditions. There are limited data, and therefore we do not know the effects of psychological treatments on depression and anxiety across headache and other types of chronic pain, and for any outcome in children with mixed chronic pain at follow-up. Our narrative review of treatment satisfaction data suggests that children and parents are satisfied with remotely-delivered treatments. We found that no study-related adverse events occurred in half of the included studies. However, we are cautious about interpreting these data, given the limited available information. Due to a small number of trials and participants in this review, and the heterogeneous nature of the data to date, it was not possible to conduct subgroup or sensitivity analyses as planned.

These findings do not indicate that treatments delivered remotely are redundant. To date, there are 10 trials that met this criteria, and although we did not detect a beneficial treatment effect on most of the outcomes evaluated in this review, this field is growing. Importantly, we judged low risk of bias across most studies for randomisation, allocation concealment, blinding of outcome assessors, and selective reporting biases. Further, most studies used an active control condition, meaning we can determine whether psychological therapies are more beneficial than giving participants something else (e.g. education).

Overall completeness and applicability of evidence

Similar to other reviews investigating psychological therapies for children with chronic pain (Fisher 2014; Fisher 2018), the studies included in this review were dominated by cognitive behavioural or behavioural treatments. Therefore, it is difficult to comment on whether other types of psychological therapies could be effective if delivered remotely. As we have highlighted in previous reviews (Fisher 2014; Fisher 2018), clinical trials for children with chronic pain should include core outcomes as recommended by PedIMMPACT (McGrath 2008), including anxiety and depression outcomes. Most included studies had publication dates after this guidance was published, yet many omit key recommended clinical trial outcomes. We were unable to conduct meta-analyses for most depression and anxiety outcomes due to lack of data. Mood outcomes are very important when considering children with chronic pain and functional disability; they have been found to be associated with disability outcomes (Simons 2012). Further, follow-up data are critical to determine the long-term effects of these interventions. Satisfaction should also be measured in both the treatment and active control groups to determine whether satisfaction with treatment delivered remotely is higher compared to an active control.

Quality of the evidence

In this update we conducted GRADE assessments on the quality of evidence. Overall, we found very low-quality evidence, meaning we are very uncertain about the estimate. We downgraded outcomes for imprecision, indirectness of evidence, inconsistency of results, or because the analysis only included one study. The rating of very low quality is unsurprising as the body of evidence is still relatively small and so to draw strong conclusions and rate the evidence as moderate or high quality would be premature at this time.

We conducted 'Risk of bias' assessments for all included studies. Overall, we judged the risk of bias as low. However, similar to the original version of this review, there were two noticeable 'Risk of bias' categories where the majority of studies did not have a low risk of bias, reducing the quality of the studies. First, only two studies gave an adequate description of blinding of participants (Connelly 2006; Palermo 2016). Second, attrition was incompletely reported in most of the included trials. Authors should analyse and report data between completers and non-completers of treatment to ensure that they are not retaining a particular type of patient. Achieving a low 'Risk of bias' judgement across all 'Risk of bias' categories is attainable if authors are clear, transparent, and attentive when conducting and reporting trials.

Potential biases in the review process

We tried to limit the bias in this review by independently sifting and extracting information, and checking data. Two review authors (TP, EL) of this review authored three studies that are included. These review authors were not involved in extracting their data or completing 'Risk of bias' assessments for these studies.

Agreements and disagreements with other studies or reviews

This review is intended to be a sister review to Fisher 2018, which assesses psychological interventions delivered face-to-face, over the telephone with a therapist, or via written instructions for children with chronic pain. These interventions have previously been the 'go-to' delivery type in this field and therefore, unsurprisingly, Fisher 2018 included over four times as many studies and participants (47 studies, 2884 participants). Similar to the current review, the Fisher 2018 review split pain conditions by headache and mixed/non-headache pain conditions, revealing six effects of psychological treatments. For headache conditions, psychological interventions were found to have a beneficial effect on pain post-treatment and for disability at follow-up. For non-headache/mixed chronic pain conditions, three beneficial effects were found post-treatment for pain intensity, disability, and anxiety (Fisher 2018). The beneficial effects were maintained at follow-up for disability. However, in the latest update of this review, subgroup analyses of smaller ($n \leq 20$ participants/arm) versus larger ($n > 20$ participants/arm) trials revealed that whilst analyses including smaller studies showed a beneficial effect, this was not the same for larger studies. Other aspects of studies included in both reviews were similar, including age, gender, recruitment methods, and therapies delivered.

A systematic review investigating the overall efficacy of psychological therapies delivered face-to-face and remotely has been conducted (Fisher 2014). Further, this review summarises the evidence by pain condition and finds results similar to Fisher 2018.

Other systematic reviews have investigated the efficacy of remotely-delivered or Internet-delivered psychological therapies to both children and adults (e.g. Buhrman 2016; Eccleston 2014; Macea 2010; Stinson 2009). Buhrman 2016 evaluated Internet interventions for adults and children with chronic pain and found 22 trials, two of which delivered treatment to children and are included in this review. Overall, the findings across studies were positive in favour of cognitive behavioural therapy (CBT), including beneficial effects for pain, disability, catastrophising, anxiety, and depression. Eccleston 2014 summarised evidence from 15 studies that delivered therapy for adults with chronic pain via the Internet and found seven effects. First, therapies reduced pain and disability post-treatment for those adults with a headache condition. For adults with non-headache pain conditions, beneficial effects were found for pain, disability, depression, and anxiety post-treatment, and for disability at follow-up. Macea 2010 investigated web-based cognitive behavioural therapy (CBT) interventions for adults and children with chronic pain. Eleven studies were identified and a meta-analysis revealed small reductions in pain symptoms for the web-based CBT conditions. Other outcomes (e.g. disability, mood) were not investigated. Summaries of the literature have also been conducted exclusively for children. Stinson 2009 searched for interventions that were delivered via the Internet for subacute or chronic health conditions. Other forms of technology (e.g. CD-ROM) were excluded. Nine studies met the inclusion criteria, of which one study included pain patients (Hicks 2006; also included in this review). Due to the heterogeneity of outcome measures and conditions, data could not be synthesised in a meta-analysis.

Internet-delivered psychological interventions have been conducted in other areas, such as depression and anxiety disorders. One review investigating the efficacy of seven studies (569 children and adolescents) and found that Internet-delivered psychological therapies decreased anxiety symptoms but not depressive symptoms in children, adolescents, and young adults (Ye 2014). The authors did not conduct quality assessment on the included trials. A separate meta-analysis using a broader criterion of remotely delivered or e-therapies for anxiety and depression revealed 26 studies (NCCMH). The strongest evidence found that computerised CBTs were beneficial for children and adolescents with depression and for decreasing anxiety in general populations. However, the evidence was judged to be low quality. Finally, a review included 25 studies of children with psychiatric and somatic conditions who received Internet-delivered CBT (Vigerland 2016). The authors found moderate effect sizes for CBT for both psychiatric conditions (e.g. anxiety) and somatic conditions including chronic pain (Vigerland 2016).

AUTHORS' CONCLUSIONS

Implications for practice

For children and adolescents with chronic pain

There is insufficient evidence to confidently say whether psychological therapies delivered via technology can reduce pain intensity/severity, or other symptoms associated with chronic pain. Preliminary evidence suggests that these treatments may reduce pain severity immediately following treatment for children with headache, but these effects are not maintained after at least three months. The overall quality of the evidence is very low, meaning we are very uncertain of the estimates of effects and more trials are needed. We found that there are relatively few adverse events associated with these treatments. However, the studies included here all delivered cognitive behavioural therapy (CBT) and therefore, we are uncertain about whether other forms of psychological therapy could be more effective across more outcomes.

For clinicians

Remotely-delivered therapies may be useful for some children and adolescents with chronic pain, particularly those who have poor access to face-to-face treatment. However, none of the interventions included in this review are available to the public. Many of

the trials in this review delivered active control, and therefore receiving an active control (e.g. psychoeducation) may also be beneficial for this population. Receiving some form of CBT remotely may reduce pain in the short term, but there is insufficient evidence to show long-term effects. We did not find any other effects, and there was a distinct lack of evidence for mood outcomes. We judged the quality of evidence as very low, meaning we are very uncertain about the estimates of effects.

For policy makers

We judged the quality of evidence as very low, meaning we are very uncertain about the estimate of effects and there is currently insufficient evidence. However, waiting lists to access chronic pain clinics are typically long (28 to 140 days (Fashler 2016); 197.5 days (Palermo 2019)), and there is an opportunity to deliver psychological therapies at low cost to a wide range of children whilst they wait to see a clinician. The preliminary evidence suggests that these interventions may decrease headache pain in the short term, although more evidence is needed before we can be confident about the estimate of effects for outcomes included in this review. Further, parents may also benefit from psychological interventions, as shown in Fisher 2018 and Eccleston 2015. Funding in this area should be channeled into the stakeholder advised and iterative development of technology-delivered psychological therapies, and for large, high quality trials that investigate remotely-delivered therapies via technology. This would increase our confidence of the effects of these interventions.

For funders for the intervention

Currently, the quality of evidence for remote interventions delivered to children with chronic pain is very low. This is due to the small and fairly heterogeneous field, and therefore we need more randomised controlled trials (RCTs) to increase our confidence in the efficacy of these treatments. This modality of intervention is potentially very powerful at reaching and treating large numbers of children and adolescents with chronic pain (i.e. > 160 participants), and should be considered in funding agendas. We encourage further exploration of CBT interventions in this area, but also alternative therapies to reduce the negative impact of chronic pain on children and their families.

Implications for research

General

Many of our suggestions from the previous version of this review remain relevant. This field is still small but growing. Preliminary findings presented in this review are promising but future studies should build on this base of knowledge and the proposals outlined here. This field has been heavily dominated by CBTs. Other types of therapies delivered remotely should be tested to investigate whether they can produce equivalent or increased effects for children with chronic pain. Remotely-delivered therapies are likely, eventually, to be provided as the first choice of treatment for many and it would be helpful to investigate whether particular therapies are more relevant for particular patients (Morley 2013).

Design

We encourage multicentre RCTs of remotely-delivered psychological interventions for children with chronic pain. We propose that future RCTs should include the following components.

- At least two arms, including (at minimum) a treatment group and a placebo comparator. Placebo comparators that control for technology use (e.g. online education) will strengthen the study designs.
- The optimal information size for headache trials should be 80 participants or more per arm and 117 participants or more per arm for mixed chronic pain conditions.
- Trialling of fully automated interventions (without any human support) would provide a more scalable option by lessening the burden on therapists and other healthcare professionals.
- Including full descriptions of technology components (e.g. interactive elements, human support, etc.) to allow for better understanding of potentially effective features of remotely-delivered interventions.
- Trialling of other psychological therapies (beyond CBT) for children and adolescents with chronic pain.

Measurement

With regard to measurement, we encourage trials with the following measurement elements.

- Trials should assess the outcome domains recommended by McGrath 2008 for inclusion in clinical trials of children and adolescents with chronic pain. At minimum, trials should measure and report pain intensity, disability, depression, and anxiety outcomes. Assessment of adverse events should be mandatory and reported in published manuscripts.
- Trials should report a 50% reduction in pain frequency, intensity, and duration for headache trials and intensity for mixed chronic pain conditions between baseline and post-treatment/follow-up for intervention and control groups. For mixed conditions, a consensus should be met so that pain measures are standardised within pain conditions.
- Trials should also report satisfaction with treatment in both treatment and control arms of trials, so that we are able to assess whether adolescents are more satisfied with psychological therapies compared to control arms.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Bonnert 2017

Methods	RCT. 2 arms. Assessed at pretreatment, post-treatment, 6 months
Participants	End of treatment: N = 95, 6-month follow-up (tx only) N = 42 Start of treatment: N = 101 Sex: 62 F, 39 M Mean age: 15.54, SD = 1.56 (range 13-17) Source: primary, secondary, and tertiary care clinics Diagnosis: irritable bowel syndrome Mean years of pain: 23 participants reported symptoms from 2 to 11 months, 78 reported symptoms for more than 12 months. Mean durations of symptoms reported by parents = 5.12 (SD = 4.11) years
Interventions	"Exposure-based Internet-CBT with therapist support" "Wait-list control". Participants in the waiting list were asked not to initiate any psychological treatment during the waiting list period of 10 weeks
Outcomes	**Primary pain outcome:** Faces Pain Scale-revised **Primary disability outcome:** none **Primary depression outcome:** none **Primary anxiety outcome:** Spence Children's Anxiety Scale **Primary satisfaction outcome:** Client Satisfaction Questionnaire **Measures reported:** Gastrointestinal Symptom Rating Scale-IBS version Faces Pain Scale-revised Pediatric Quality of Life Inventory Children's Somatization Inventory School absence IBS-Behavioral Responses Questionnaire Visceral Sensitivity Index Perceived Stress Scale Spence Children's Anxiety Scale Client Satisfaction Questionnaire
Notes	**Funding source:** Jan and Dan Olsson Foundation (4-1559/2013), the Swedish Research Council (521-2013-2846), the Kempe-Carlgren Foundation, the Ruth and Richard Julin Foundation (2012Juli0048), the Majblomman Foundation, the Ishizu Matsumurais Donation, the Ihre Foundation (SLS-331861), the Ihre fellowship in Gastroenterology, the Gadelius Foundation, the Samariten Foundation, the Värkstadsstiftelsen Foundation, the Swedish Research Council for Health, Working life and Welfare (2014-4052), the Swedish Society of Medicine (SLS-331681 SLS-410501), and the Stockholm County Council (ALF). Financial support was also provided through the regional agreement on medical training and clinical research between Stockholm County Council and Karolinska Institutet (20130129). None of the funding bodies had any influence on study design, implementation, data analysis, or interpretation

Bonnert 2017 (*Continued*)

	Declarations of interest: authors declare no conflicts of interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Participants were consecutively randomized to either exposure-based Internet-CBT or wait-list. The randomization was conducted by an independent researcher, who received lists with anonymous study ID numbers and used a random number service (www.random.org)" Comment: probably done
Allocation concealment (selection bias)	Low risk	"The randomization was conducted by an independent researcher, who received lists with anonymous study ID numbers and used a random number service (www.random.org) to allocate participants, thus ensuring concealment of allocation." Comment: probably done
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description found in text Comment: probably not done
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Measures completed online
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Attrition is described, however significant descriptions between completers and non-completers were not reported
Selective reporting (reporting bias)	Low risk	Data were fully reported

Connelly 2006

Methods	RCT. 2 arms. Assessed at pretreatment, post-treatment, 2 months, 3 months
Participants	End of treatment: N = 36 Start of treatment: N = 37 Sex: 18 F, 19 M Mean age: 10.0 (range 7-12) Source: clinic Diagnosis: headache Mean years of pain: not given

Connelly 2006 (*Continued*)

Interventions	"CD-ROM behavioural" "Wait-list neurology TAU"
Outcomes	**Primary pain outcome:** clinical reduction in headache frequency **Primary disability outcome:** Ped-MIDAS **Primary depression outcome:** none **Primary anxiety outcome:** none **Primary satisfaction outcome:** none **Measures reported:** total pain (headache diary) Pediatric Migraine Disability Assessment (Ped-MIDAS)
Notes	**Funding source:** educational grant from AstraZeneca LP **Declarations of interest:** none stated

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Randomly assigned to one of two groups by a research assistant using a uniform random numbers table." Comment: probably done
Allocation concealment (selection bias)	Low risk	"Randomly assigned to one of two groups by a research assistant using a uniform random numbers table." Comment: probably done
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Study neurologists remained blind to randomisation condition throughout the study. Chances of unbinding were limited because follow-up appointments with the study neurologist were scheduled for 2 months following the initial assessment." Comment: probably done
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Measures completed at home and mailed back
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Attrition is described, however significant descriptions between completers and non-completers were not reported
Selective reporting (reporting bias)	Low risk	Data were fully reported

Hicks 2006

Methods	RCT. 2 arms. Assessed at pretreatment, 1 month post-treatment, 3 months
Participants	End of treatment: N = 37; 1-month follow-up N = 37, 3-month follow-up N = 32 Start of treatment: N = 47 Sex: 30 F, 17 M Mean age: 11.7 (range 9 to 16) Source: advertisements in media, physicians' offices and school Diagnosis: headache and RAP Duration (mean): 3 years
Interventions	"Internet CBT (with Internet and phone)" "Standard Care (Wait List)"
Outcomes	**Primary pain outcome:** clinical reduction in headache frequency (headache analysis) and mean pain intensity (mixed chronic pain conditions analysis) **Primary disability outcome:** none **Primary depression outcome:** none **Primary anxiety outcome:** none **Primary satisfaction outcome:** satisfaction **Measures reported:** pain diary numeric rating scale frequency numeric rating scale intensity Pediatric Quality of Life Inventory Parental Quality of Life treatment expectation participant feedback (including satisfaction)
Notes	**Funding source:** Peter Samuelson STARBRIGHT Foundation 2002 Dissertation Award in paediatric psychology and the Canadian Pain Society Small Grant for Local and Regional Initiatives. McGrath is supported by a Canada Research Chair **Declarations of interest:** none stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"The 47 participants were stratified by age and pain severity and randomly assigned by blocks to either the treatment condition or the standard medical care wait-list condition." Comment: probably done
Allocation concealment (selection bias)	Low risk	"The 47 participants were stratified by age and pain severity and randomly assigned by blocks to either the treatment condition or the standard medical care wait-list condition."

Hicks 2006 (*Continued*)

		Comment: probably done
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description found in text Comment: probably not done
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Measures completed at home and submitted online
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Attrition completely reported; significant differences between completers and non-completers were not reported
Selective reporting (reporting bias)	Low risk	Data were fully reported

Law 2015

Methods	RCT. 2 arms. Assessed at pretreatment, 1 month post-treatment, 3 months
Participants	End of treatment: N = 59; 3-month follow-up N = 49 Start of treatment: N = 83 Sex: 68 F, 15 M Mean age: 14.5, SD = 1.7, (range 11-17) Source: multidisciplinary paediatric headache clinic Diagnosis: migraine, tension-type headache, other headache disorder Duration (mean): not reported
Interventions	"Internet CBT (WebMAP) + specialized headache treatment" "Specialized headache treatment"
Outcomes	**Primary pain outcome:** clinical reduction in headache frequency (headache analysis) **Primary disability outcome:** Child Activity Limitations Interview-21 **Primary depression outcome:** Children's Depression Inventory **Primary anxiety outcome:** Revised Children's Manifest Anxiety Scale, 2nd edition **Primary satisfaction outcome:** Treatment Evaluation Inventory-Short Form **Measures reported:** Treatment Evaluation Inventory-Short Form headache frequency headache Pain Intensity Child Activity Limitations Interview-21 Revised Children's Manifest Anxiety Scale, 2nd edition Children's Depression Inventory Adult Responses to Children's Symptoms total sleep time sleep onset sleep efficiency

Law 2015 (*Continued*)

Notes	**Funding source:** this research was supported by Grant K24HD060068 from the National Institutes of Health/National Institute of Child Health and Human Development (PI: Palermo) **Declarations of interest:** none stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Blocked randomization with blocks of 10 was used to assign participants to one of the two treatment conditions. An online number generator was used to produce the blocked randomization. Participants were allocated in a 1:1 ratio." Comment: probably done
Allocation concealment (selection bias)	Low risk	"Group assignments were identified by ID number in an excel spreadsheet that was password protected and accessible only to a research coordinator who was blinded to participant recruitment, screening, and informed consent. Following completion of all pre-treatment assessments, the research coordinator accessed the excel spreadsheet to reveal the group assignment. This information was then programmed into the Web-MAP system, which generated a message on the website to each study participant revealing the instructions for their treatment assignment." Comment: probably done
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	"Because of the nature of the intervention, it was not possible to blind participants or research staff to group status."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"A research coordinator who was blinded to group status conducted all assessment procedures that occurred in the clinic." Comment: probably done
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition is fully reported and authors report that there were no differences between completers and non-completers
Selective reporting (reporting bias)	Low risk	Data were fully reported

Palermo 2009

Methods	RCT. 2 arms. Assessed at pretreatment and post-treatment
Participants	End of treatment: N = 44 Start of treatment: N = 48 Sex: 35 F, 13 M Mean age: 14.8 (SD 2.0) Source: medical centre in the Pacific Northwest USA Diagnosis: headache (25% of the sample), abdominal pain (50% of the sample), or musculoskeletal pain (25% of the sample) Mean years of pain: 30 months
Interventions	"Internet-delivered family cognitive-behavioural therapy" "Wait-list control group"
Outcomes	**Primary pain outcome:** clinical reduction in headache frequency (headache analysis) and mean pain intensity (mixed chronic pain conditions analysis) **Primary disability outcome:** Child Activity and Limitations Interview **Primary depression outcome:** Revised Child Anxiety and Depression Scale **Primary anxiety outcome:** none **Primary satisfaction outcome:** treatment acceptability and satisfaction **Measures reported:** daily pain intensity NRS (averaged over 7 days) usual pain intensity over the past month NRS Child Activity Limitations Interview Revised Child Anxiety and Depression Scale Protect subscale from Adult Responses to Children's Symptoms treatment acceptability and satisfaction
Notes	**Funding source:** National Institutes of Health/National Institute of Child Health and Human Development (Grant HD050674; PI: Palermo) and by a grant from the Doernbecher Foundation **Declarations of interest:** authors have no conflicts of interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"A fixed allocation randomisation scheme was used. Specifically, we used blocked randomisation with blocks of 10 to assign participants to the two treatment conditions during the course of randomisation. An online random number generator was used to produce the blocked randomisation. Group assignments were identified by ID number in sealed envelopes. Following completion of all pre-treatment assessments, a research coordinator opened the sealed envelope to reveal the group assign-

Palermo 2009 (*Continued*)

		ment." Comment: probably done
Allocation concealment (selection bias)	Low risk	"A fixed allocation randomisation scheme was used. Specifically, we used blocked randomisation with blocks of 10 to assign participants to the two treatment conditions during the course of randomisation. An online random number generator was used to produce the blocked randomisation. Group assignments were identified by ID number in sealed envelopes. Following completion of all pre-treatment assessments, a research coordinator opened the sealed envelope to reveal the group assignment." Comment: probably done
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description found in text Comment: probably not done
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Measures completed at home and submitted online or mailed back
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Attrition completely reported; significant differences between completers and non-completers were not reported
Selective reporting (reporting bias)	Low risk	Data were fully reported

Palermo 2016

Methods	RCT. 2 arms. Assessed at pretreatment, post-treatment, 6 months, 12 months (12-month data not published)
Participants	End of treatment: N = 258, 6 months = 257 Start of treatment: N = 273, 266 received treatment Sex: 205 F, 68 M Mean age: 14.71, SD = 1.62 Source: 15 interdisciplinary paediatric pain clinics at academic medical centres across the US and Canada Diagnosis: headache (7% of the sample), abdominal pain (11% of the sample), or musculoskeletal pain (42% of the sample), Multiple pain sites (40% of the sample) Mean years of pain: not reported

Palermo 2016 (*Continued*)

Interventions	"Internet-delivered family cognitive-behavioural therapy (WebMAP)" "Internet-delivered pain education"
Outcomes	**Primary pain outcome:** pain intensity (NRS 0 -11) over 7 days **Primary disability outcome:** Child Activity and Limitations Interview **Primary depression outcome:** Bath Adolescent Pain Questionnaire-Depression subscale **Primary anxiety outcome:** Bath Adolescent Pain Questionnaire-General Anxiety subscale **Primary satisfaction outcome:** Treatment Evaluation Inventory-Short Form **Measures reported:** daily pain intensity NRS (averaged over 7 days) Child Activity Limitations Interview Bath Adolescent Pain Questionnaire (social functioning, physical functioning, depression, general anxiety, pain-specific anxiety, family functioning, development subscales) Adolescent Sleep Wake Scale Adult Responses to Children's Symptoms Helping for Health Inventory Treatment Evaluation Inventory-Short Form website satisfaction treatment engagement treatment expectations
Notes	**Funding source:** research reported in this study was supported by the Eunice Kennedy Shriver National Institute of Child Health & Human Development of the National Institutes of Health under Award Number R01HD062538 (T.M.P. [principal investigator]) **Declarations of interest:** authors have no conflicts of interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomization was implemented using a computer-generated randomization schedule to derive a randomization assignment to 2 treatment conditions in blocks of 4 for each ID number." Comment: probably done
Allocation concealment (selection bias)	Low risk	"The randomization assignment was programmed into the Web-MAP2 system. After pretreatment assessments, the group assignment was provided to each participant on the Web site with instructions on how to proceed during the treatment phase." Comment: probably done

Palermo 2016 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Participants were blinded to whether they were receiving an active or control treatment."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Assess- ments were completed online through our secure, password-protected Web site independently by adolescents and parents (using separate login procedures) at baseline before randomization, after completion of the 8 to 10 week intervention (immediately after treatment) and at 2 longer-term follow-up periods (6 and 12 months). Because all study assessments were completed independently online, there was no possible examiner bias in outcome assessments." Comment: probably done
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition is fully reported and authors report that there were no differences between completers and non-completers
Selective reporting (reporting bias)	Low risk	Data were fully reported

Rapoff 2014

Methods	RCT. 2 arms. Assessed at pretreatment and post-treatment
Participants	End of treatment: N = 22 Start of treatment: N = 35 Sex: 25 F, 10 M Mean age: 10.2 (SD 1.75) Source: paediatric headache clinics at 1 university and 2 children's hospitals Diagnosis: headache Mean years of pain: unknown
Interventions	"Headstrong programme" "Education"
Outcomes	**Primary pain outcome:** none **Primary disability outcome:** Pediatric Migraine Disability Assessment **Primary depression outcome:** none **Primary anxiety outcome:** none **Primary satisfaction outcome:** none **Measures reported:** headache diaries including frequency, intensity/severity, and duration Pediatric Migraine Disability Assessment Pediatric Quality of Life Inventory

Rapoff 2014 (*Continued*)

Notes	**Funding source:** National Institutes of Health (National Institute of Neurological Disorders and Stroke), R01-NS046641 (PI: Michael Rapoff) **Declarations of interest:** authors have no conflicts of interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	"Participants were stratified by age (7-9 and 10-12) and randomly assigned following baseline to one of the two groups (education control or Headstrong)." Comment: probably done; description of randomisation not provided
Allocation concealment (selection bias)	Unclear risk	No description found in text Comment: probably not done
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description found in text Comment: probably not done
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Measures completed at home and mailed back
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Attrition completely reported; significant differences between completers and non-completers were not reported
Selective reporting (reporting bias)	Low risk	Data were fully reported

Schatz 2015

Methods	RCT. 2 arms. Assessed at pretreatment and post-treatment
Participants	End of treatment: N = 46 Start of treatment: N = 48 Sex: 27 F, 19 M Mean age: 13.04 (SD 2.5) Source: clinic Diagnosis: sickle cell disease Mean years of pain: lifelong
Interventions	"CBT coping skills training" "Waitlist standard care"

Schatz 2015 (*Continued*)

Outcomes	**Primary pain outcome:** pain intensity **Primary disability outcome:** activity score from daily diary **Primary depression outcome:** none **Primary anxiety outcome:** none **Primary satisfaction outcome:** none **Measures reported:** daily pain diary and activity log Coping Strategies Questionnaire
Notes	**Funding statement:** this work was supported by the National Institutes of Health, National Heart, Lung, and Blood Institute (R21HL0923365 to J.S. and C.B.M. and T32 GM081740 and F31HL108582 to A.M.S.) **Declaration of interest:** the authors declare no conflicts of interest

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomization was achieved by drawing colored marbles out of an opaque bag (wave 1) or by computer software using blocks of 10 (wave 2)."
Allocation concealment (selection bias)	Low risk	"A researcher not involved in study data collection prepared sequentially numbered, opaque, sealed envelopes that assigned each participant and were opened by the youth. "
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description found in text Comment: probably not done
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Participants completed questionnaires electronically
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Attrition completely reported; significant differences between completers and non-completers were not reported
Selective reporting (reporting bias)	High risk	Data incompletely reported

Stinson 2010

Methods	RCT. 2 arms. Assessed at pretreatment and post-treatment
Participants	End of treatment: N = 39 Start of treatment: N = 46 Sex: 31 F, 15 M Mean age: 14.6 (SD 1.5) Source: 4 paediatric tertiary care centres Diagnosis: juvenile idiopathic arthritis Mean years of pain: 6.4 (SD 4.6)
Interventions	"Internet treatment" "Attentional control group"
Outcomes	**Primary pain outcome:** Recall Pain Inventory **Primary disability outcome:** Juvenile Arthritis Quality of Life Questionnaire **Primary depression outcome:** none **Primary anxiety outcome:** Perceived Severity of Stress Questionnaire **Primary satisfaction outcome:** none **Measures reported:** Recall Pain Inventory Juvenile Arthritis Quality of Life Questionnaire Perceived Severity of Stress Questionnaire Medical Issues, Exercise, Pain and Social Support Questionnaire Children's Arthritis Self-Efficacy scale JIA-specific Child Adherence Report Questionnaire Parent Adherence Report Questionnaire
Notes	**Funding source:** The Canadian Arthritis Network and The Arthritis Society **Declarations of interest:** Drs. Feldman and McGrath (co-authors) hold Canada Research Chairs

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"A fixed allocation randomisation scheme was used. Specifically, blocked randomisation was employed. An online random number generator was used to produce the blocked randomisation. Group assignments were identified by ID number in sealed envelopes during the recruitment period." Comment: probably done
Allocation concealment (selection bias)	Low risk	"A fixed allocation randomisation scheme was used. Specifically, blocked randomisation was employed. An online random number generator was used to produce

Stinson 2010 (*Continued*)

		the blocked randomisation. Group assignments were identified by ID number in sealed envelopes during the recruitment period." Comment: probably done
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description found in text Comment: probably not done
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Measures completed at home and submitted online
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Attrition completely reported; significant differences between completers and non-completers were not reported
Selective reporting (reporting bias)	Low risk	Data were fully reported

Trautmann 2010

Methods	RCT. 3 arms. Assessed at pretreatment, post-treatment, 6 months
Participants	End of treatment: N = 55; follow-up N = 40 Start of treatment: N = 68 Sex: 36 F, 30 M Mean age: 12.7 (SD 2.2) Source: newspaper adverts and websites Diagnosis: headache (migraine, tension type headache or combined headache) Mean years of pain: 2.8 (SD 3.0)
Interventions	"Cognitive behavioural therapy, self-help and management" "Applied relaxation group" "Education"
Outcomes	**Primary pain outcome:** clinical reduction in headache frequency **Primary disability outcome:** none **Primary depression outcome:** Children's Depression Inventory **Primary anxiety outcome:** Pain Catastrophising Scale **Primary satisfaction outcome:** none **Measures reported:** Children's Depression Inventory pain diary Children's Depression Inventory Pain Catastrophising Scale health-related quality of life (KINDL-R) Strengths and Difficulties Questionnaire

Trautmann 2010 (*Continued*)

Notes	**Funding source:** German Research Foundation (Number: KR756/16-2) **Declarations of interest:** none stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"All participants were randomly assigned to one of the three conditions. The randomly ordered list of groups was used to assign sequentially enrolled participants to two intervention groups and the active control condition." Comment: probably done
Allocation concealment (selection bias)	Low risk	"The first author randomly selected participants according to a computer-generated randomisation list by using the 'select cases' random selection option." Comment: probably done
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	No description found in text Comment: probably not done
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Measures completed at home and mailed back
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition is described. "Furthermore, no significant differences were found between dropouts and completers"
Selective reporting (reporting bias)	Low risk	Data were fully reported

CBT: cognitive behavioural therapy
F: female
M: male
N: number of participants
NRS: numerical rating scale
JIA: juvenile idiopathic arthritis
Ped-MIDAS: Pediatric Migraine Disability Assessment
RAP: recurrent abdominal pain
RCT: randomised controlled trial
SD: standard deviation
TAU: treatment as usual
Tx: treatment

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Ahola Kohut 2016	Insufficient psychotherapeutic treatment
Armbrust 2015	Acceptance paper
Bonnert 2014	Open trial, no control group
Cottrell 2007	Did not deliver treatment via technology
Greenley 2015	Did not deliver treatment via technology
Kroner-Herwig 2002	Did not deliver treatment via technology
Larsson 1987a	Did not deliver treatment via technology
Larsson 1987b	Did not deliver treatment via technology
Larsson 1990	Did not deliver treatment via technology
Levy 2017	Did not deliver treatment via technology
Long 2009	Usability evaluation of online treatment
McClellan 2009	N < 10 in at least 1 arm of the trial at post-treatment
McGrath 1992	Did not deliver treatment via technology
Merlijn 2005	N < 10 in at least 1 arm of the trial at post-treatment
Palermo 2018	N < 10 in at least 1 arm of the trial at post-treatment
Trautmann 2008	N < 10 in at least 1 arm of the trial at post-treatment
van Tilburg 2009	Did not deliver treatment via technology
Voerman 2015	Insufficient number of participants at post-treatment

DATA AND ANALYSES

Comparison 1. Headache conditions: treatment versus control (post-treatment)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Achievement of at least 50% reduction in headache severity	7	379	Risk Ratio (M-H, Random, 95% CI)	2.02 [1.35, 3.01]
2 Disability	5	440	Std. Mean Difference (IV, Random, 95% CI)	-0.16 [-0.46, 0.13]
3 Depression	4	422	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.15, 0.23]
4 Anxiety	3	380	Std. Mean Difference (IV, Random, 95% CI)	-0.08 [-0.28, 0.13]

Comparison 2. Headache conditions: treatment versus control (follow-up)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Achievement of at least 50% reduction in headache severity	4	230	Risk Ratio (M-H, Random, 95% CI)	1.76 [0.88, 3.52]
2 Disability	3	341	Std. Mean Difference (IV, Random, 95% CI)	-0.16 [-0.38, 0.05]
3 Depression	2	320	Std. Mean Difference (IV, Random, 95% CI)	0.03 [-0.19, 0.25]
4 Anxiety	3	360	Std. Mean Difference (IV, Random, 95% CI)	-0.01 [-0.22, 0.20]

Comparison 3. Mixed chronic pain conditions: treatment versus control (post-treatment)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain intensity	5	501	Std. Mean Difference (IV, Random, 95% CI)	-0.90 [-1.95, 0.16]
2 Disability	3	363	Std. Mean Difference (IV, Random, 95% CI)	-0.28 [-0.74, 0.18]
3 Depression	2	317	Std. Mean Difference (IV, Random, 95% CI)	0.04 [-0.18, 0.26]
4 Anxiety	2	370	Std. Mean Difference (IV, Random, 95% CI)	0.53 [-0.63, 1.68]

Comparison 4. Mixed chronic pain conditions: treatment versus control (follow-up)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Pain intensity	2	301	Std. Mean Difference (IV, Random, 95% CI)	-0.41 [-1.62, 0.79]
2 Disability	1	269	Std. Mean Difference (IV, Random, 95% CI)	-0.15 [-0.39, 0.09]
3 Depression	1	269	Std. Mean Difference (IV, Random, 95% CI)	0.01 [-0.23, 0.25]
4 Anxiety	1	269	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.22, 0.26]

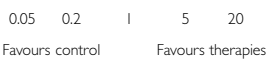
Analysis 1.1. Comparison 1 Headache conditions: treatment versus control (post-treatment), Outcome 1 Achievement of at least 50% reduction in headache severity.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 1 Headache conditions: treatment versus control (post-treatment)

Outcome: 1 Achievement of at least 50% reduction in headache severity

Study or subgroup	Favours control n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Connelly 2006	7/14	4/20		15.4 %	2.50 [0.90, 6.94]
Hicks 2006	15/21	3/16		14.4 %	3.81 [1.33, 10.94]
Law 2015	12/44	7/39		23.5 %	1.52 [0.66, 3.47]
Palermo 2009	10/23	3/21		12.2 %	3.04 [0.97, 9.58]
Palermo 2016	2/48	2/47		4.4 %	0.98 [0.14, 6.67]
Rapoff 2014	7/18	6/17		21.4 %	1.10 [0.46, 2.62]
Trautmann 2010	16/35	2/16		8.8 %	3.66 [0.95, 14.05]
Total (95% CI)	**203**	**176**		**100.0 %**	**2.02 [1.35, 3.01]**
Total events: 69 (Favours control), 27 (Control)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 5.79, df = 6 (P = 0.45); I^2 =0.0%					
Test for overall effect: Z = 3.44 (P = 0.00059)					
Test for subgroup differences: Not applicable					



Analysis 1.2. Comparison 1 Headache conditions: treatment versus control (post-treatment), Outcome 2 Disability.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 1 Headache conditions: treatment versus control (post-treatment)

Outcome: 2 Disability

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Connelly 2006	14	12.2 (9.92)	17	10.74 (11.61)		13.0 %	0.13 [-0.58, 0.84]
Law 2015	20	4.83 (4.78)	37	4.86 (4.4)		18.7 %	-0.01 [-0.55, 0.54]
Palermo 2009	26	3.6 (2.86)	22	6.62 (4.76)		16.8 %	-0.77 [-1.36, -0.18]
Palermo 2016	134	5.68 (4.38)	135	5.65 (4.69)		37.4 %	0.01 [-0.23, 0.25]
Rapoff 2014	18	7.82 (10.59)	17	12.29 (12.94)		14.1 %	-0.37 [-1.04, 0.30]
Total (95% CI)	**212**		**228**			**100.0 %**	**-0.16 [-0.46, 0.13]**

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 6.90$, df = 4 (P = 0.14); $I^2 = 42\%$

Test for overall effect: Z = 1.08 (P = 0.28)

Test for subgroup differences: Not applicable

Analysis 1.3. Comparison 1 Headache conditions: treatment versus control (post-treatment), Outcome 3 Depression.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 1 Headache conditions: treatment versus control (post-treatment)

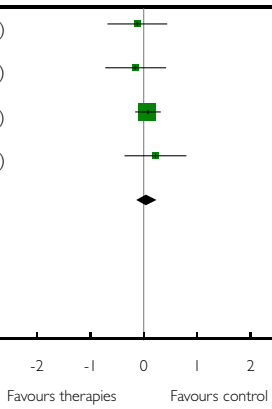
Outcome: 3 Depression

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Law 2015	27	46.3 (10.03)	23	47.48 (9.5)		12.0 %	-0.12 [-0.68, 0.44]
Palermo 2009	26	58.96 (13.1)	22	61.59 (18.67)		11.5 %	-0.16 [-0.73, 0.41]
Palermo 2016	134	9.71 (5.1)	135	9.32 (5.37)		65.1 %	0.07 [-0.16, 0.31]
Trautmann 2010	38	9.47 (9.09)	17	7.7 (5.2)		11.3 %	0.22 [-0.36, 0.79]
Total (95% CI)	**225**		**197**			**100.0 %**	**0.04 [-0.15, 0.23]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.24$, df = 3 (P = 0.74); $I^2 = 0.0\%$

Test for overall effect: Z = 0.40 (P = 0.69)

Test for subgroup differences: Not applicable



Analysis 1.4. Comparison 1 Headache conditions: treatment versus control (post-treatment), Outcome 4 Anxiety.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 1 Headache conditions: treatment versus control (post-treatment)

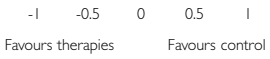
Outcome: 4 Anxiety

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Law 2015	30	46.33 (8.99)	25	48.32 (10.81)		14.6 %	-0.20 [-0.73, 0.33]
Palermo 2016	134	10.56 (5.91)	135	10.85 (6.1)		72.3 %	-0.05 [-0.29, 0.19]
Trautmann 2010	38	30.9 (7.95)	18	31.7 (8.3)		13.1 %	-0.10 [-0.66, 0.46]
Total (95% CI)	**202**		**178**			**100.0 %**	**-0.08 [-0.28, 0.13]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.26$, df = 2 (P = 0.88); $I^2 = 0.0\%$

Test for overall effect: Z = 0.74 (P = 0.46)

Test for subgroup differences: Not applicable



Analysis 2.1. Comparison 2 Headache conditions: treatment versus control (follow-up), Outcome 1 Achievement of at least 50% reduction in headache severity.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 2 Headache conditions: treatment versus control (follow-up)

Outcome: 1 Achievement of at least 50% reduction in headache severity

Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Hicks 2006	13/18	2/14		18.2 %	5.06 [1.36, 18.82]
Law 2015	19/44	10/39		36.8 %	1.68 [0.89, 3.17]
Palermo 2016	3/49	1/44		8.1 %	2.69 [0.29, 24.96]
Rapoff 2014	7/11	7/11		36.9 %	1.00 [0.53, 1.88]
Total (95% CI)	**122**	**108**		**100.0 %**	**1.76 [0.88, 3.52]**

Total events: 42 (Experimental), 20 (Control)

Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 6.17$, df = 3 (P = 0.10); $I^2 = 51\%$

Test for overall effect: Z = 1.61 (P = 0.11)

Test for subgroup differences: Not applicable

Analysis 2.2. Comparison 2 Headache conditions: treatment versus control (follow-up), Outcome 2 Disability.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 2 Headache conditions: treatment versus control (follow-up)

Outcome: 2 Disability

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Law 2015	28	5.19 (5.02)	22	5.27 (4.61)		14.6 %	-0.02 [-0.57, 0.54]
Palermo 2016	134	5.46 (4.32)	135	6.16 (5.04)		79.4 %	-0.15 [-0.39, 0.09]
Rapoff 2014	11	0.91 (1.45)	11	3.5 (4.86)		6.1 %	-0.69 [-1.56, 0.17]
Total (95% CI)	**173**		**168**			**100.0 %**	**-0.16 [-0.38, 0.05]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.73$, df = 2 (P = 0.42); $I^2 = 0.0\%$

Test for overall effect: Z = 1.49 (P = 0.14)

Test for subgroup differences: Not applicable

Analysis 2.3. Comparison 2 Headache conditions: treatment versus control (follow-up), Outcome 3 Depression.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 2 Headache conditions: treatment versus control (follow-up)

Outcome: 3 Depression

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Law 2015	28	44.75 (9.52)	23	43.74 (6.45)		15.8 %	0.12 [-0.43, 0.67]
Palermo 2016	134	9.55 (5.13)	135	9.49 (5.58)		84.2 %	0.01 [-0.23, 0.25]
Total (95% CI)	**162**		**158**			**100.0 %**	**0.03 [-0.19, 0.25]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.13$, df = 1 (P = 0.72); $I^2 = 0.0\%$

Test for overall effect: Z = 0.25 (P = 0.80)

Test for subgroup differences: Not applicable

Analysis 2.4. Comparison 2 Headache conditions: treatment versus control (follow-up), Outcome 4 Anxiety.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 2 Headache conditions: treatment versus control (follow-up)

Outcome: 4 Anxiety

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Law 2015	28	45.82 (10.96)	22	45.36 (9.9)		14.2 %	0.04 [-0.52, 0.60]
Palermo 2016	134	10.35 (6.12)	135	10.23 (5.45)		77.3 %	0.02 [-0.22, 0.26]
Trautmann 2010	31	24.95 (7)	10	28.1 (9.9)		8.6 %	-0.40 [-1.12, 0.32]
Total (95% CI)	**193**		**167**			**100.0 %**	**-0.01 [-0.22, 0.20]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 1.22$, df = 2 (P = 0.54); $I^2 = 0.0\%$

Test for overall effect: Z = 0.11 (P = 0.91)

Test for subgroup differences: Not applicable

Analysis 3.1. Comparison 3 Mixed chronic pain conditions: treatment versus control (post-treatment), Outcome 1 Pain intensity.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 3 Mixed chronic pain conditions: treatment versus control (post-treatment)

Outcome: 1 Pain intensity

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Bonnert 2017	47	4.53 (0.37)	54	5.53 (0.33)		19.9 %	-2.84 [-3.40, -2.28]
Hicks 2006	21	3.4 (2.4)	16	4.7 (2.2)		19.5 %	-0.55 [-1.21, 0.11]
Palermo 2009	26	3.54 (2.42)	22	4.76 (1.84)		19.9 %	-0.55 [-1.13, 0.03]
Palermo 2016	134	5.87 (2.05)	135	5.59 (2.15)		20.9 %	0.13 [-0.11, 0.37]
Stinson 2010	22	2.17 (1.34)	24	3.47 (2.12)		19.8 %	-0.71 [-1.31, -0.12]
Total (95% CI)	**250**		**251**			**100.0 %**	**-0.90 [-1.95, 0.16]**

Heterogeneity: $Tau^2 = 1.38$; $Chi^2 = 93.83$, df = 4 (P<0.00001); $I^2 = 96\%$

Test for overall effect: Z = 1.66 (P = 0.096)

Test for subgroup differences: Not applicable

Analysis 3.2. Comparison 3 Mixed chronic pain conditions: treatment versus control (post-treatment), Outcome 2 Disability.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 3 Mixed chronic pain conditions: treatment versus control (post-treatment)

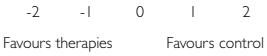
Outcome: 2 Disability

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Palermo 2009	26	3.6 (2.86)	22	6.62 (4.76)		27.5 %	-0.77 [-1.36, -0.18]
Palermo 2016	134	5.68 (4.38)	135	5.65 (4.69)		44.5 %	0.01 [-0.23, 0.25]
Stinson 2010	22	1.95 (1.4)	24	2.27 (1.21)		27.9 %	-0.24 [-0.82, 0.34]
Total (95% CI)	**182**		**181**			**100.0 %**	**-0.28 [-0.74, 0.18]**

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 5.94$, df = 2 (P = 0.05); $I^2 = 66\%$

Test for overall effect: Z = 1.18 (P = 0.24)

Test for subgroup differences: Not applicable



Analysis 3.3. Comparison 3 Mixed chronic pain conditions: treatment versus control (post-treatment), Outcome 3 Depression.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 3 Mixed chronic pain conditions: treatment versus control (post-treatment)

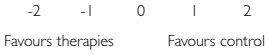
Outcome: 3 Depression

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Palermo 2009	26	58.96 (13.1)	22	61.59 (18.67)		15.0 %	-0.16 [-0.73, 0.41]
Palermo 2016	134	9.71 (5.1)	135	9.32 (5.37)		85.0 %	0.07 [-0.16, 0.31]
Total (95% CI)	**160**		**157**			**100.0 %**	**0.04 [-0.18, 0.26]**

Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.57$, df = 1 (P = 0.45); $I^2 = 0.0\%$

Test for overall effect: Z = 0.34 (P = 0.73)

Test for subgroup differences: Not applicable



Analysis 3.4. Comparison 3 Mixed chronic pain conditions: treatment versus control (post-treatment), Outcome 4 Anxiety.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 3 Mixed chronic pain conditions: treatment versus control (post-treatment)

Outcome: 4 Anxiety

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Bonnert 2017	47	25.23 (2.38)	54	22.62 (2.22)		48.9 %	1.13 [0.71, 1.55]
Palermo 2016	134	10.56 (5.91)	135	10.85 (6.1)		51.1 %	-0.05 [-0.29, 0.19]
Total (95% CI)	**181**		**189**			**100.0 %**	**0.53 [-0.63, 1.68]**

Heterogeneity: $Tau^2 = 0.66$; $Chi^2 = 22.60$, df = 1 (P<0.00001); $I^2 = 96\%$

Test for overall effect: Z = 0.90 (P = 0.37)

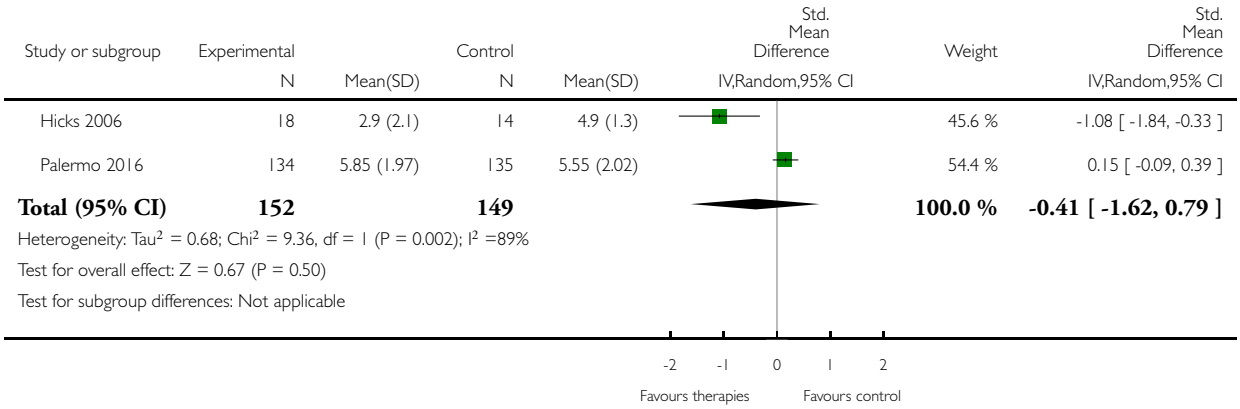
Test for subgroup differences: Not applicable

Analysis 4.1. Comparison 4 Mixed chronic pain conditions: treatment versus control (follow-up), Outcome 1 Pain intensity.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 4 Mixed chronic pain conditions: treatment versus control (follow-up)

Outcome: 1 Pain intensity



Analysis 4.2. Comparison 4 Mixed chronic pain conditions: treatment versus control (follow-up), Outcome 2 Disability.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 4 Mixed chronic pain conditions: treatment versus control (follow-up)

Outcome: 2 Disability

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Palermo 2016	134	5.46 (4.32)	135	6.16 (5.04)		100.0 %	-0.15 [-0.39, 0.09]
Total (95% CI)	**134**		**135**			**100.0 %**	**-0.15 [-0.39, 0.09]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.22 (P = 0.22)

Test for subgroup differences: Not applicable

Analysis 4.3. Comparison 4 Mixed chronic pain conditions: treatment versus control (follow-up), Outcome 3 Depression.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 4 Mixed chronic pain conditions: treatment versus control (follow-up)

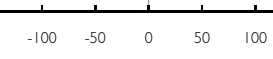
Outcome: 3 Depression

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Palermo 2016	134	9.55 (5.13)	135	9.49 (5.58)		100.0 %	0.01 [-0.23, 0.25]
Total (95% CI)	**134**		**135**			**100.0 %**	**0.01 [-0.23, 0.25]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.09 (P = 0.93)

Test for subgroup differences: Not applicable

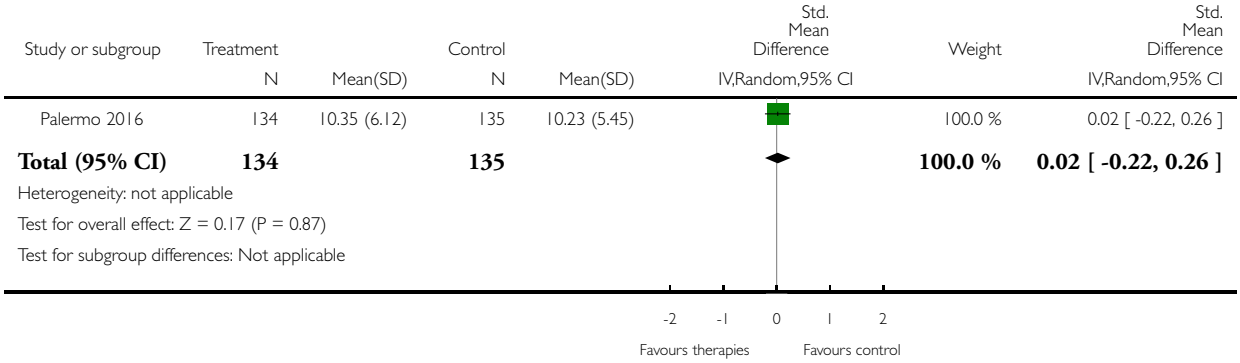


Analysis 4.4. Comparison 4 Mixed chronic pain conditions: treatment versus control (follow-up), Outcome 4 Anxiety.

Review: Psychological therapies (remotely delivered) for the management of chronic and recurrent pain in children and adolescents

Comparison: 4 Mixed chronic pain conditions: treatment versus control (follow-up)

Outcome: 4 Anxiety



ADDITIONAL TABLES

Table 1. Description of remotely-delivered treatments

Study	Description of treatment	Description of control
Bonnert 2017	**Name of treatment programme:** Internet CBT **Therapy type:** CBT **Mode of delivery:** Internet **Content:** children completed 10 weekly modules that provided instruction in using exposure exercises to reduce symptom-fear and avoidance. Parents completed 5 modules focusing on supporting their child to engage in the challenging exposure exercises **Support:** clinical psychologists provided weekly online support which included feedback, assistance in planning homework assignments, and answering questions. Text messages and phone calls were used to remind participants to log on to the platform but not to provide therapy **Programme features:** modules included short texts, examples, audio files, and videos and ended with homework assignments that had to be completed before the next module could be accessed **Duration:** 10 modules completed by children and 5	**Control type:** waiting-list control **Mode of delivery:** N/A **Content:** participants were asked not to initiate any psychological treatment during the waiting-list period of 10 weeks but were free to use any other treatment **Duration:** 10 weeks. After the post-treatment assessment, waiting-list participants were crossed over to Internet CBT

Table 1. Description of remotely-delivered treatments (*Continued*)

	modules completed by parents over 10 weeks	
Connelly 2006	**Name of treatment programme:** Headstrong **Therapy type:** CBT **Mode of delivery:** CD-ROMs, plus weekly telephone calls with a study therapist **Content:** children completed 3 modules: education, relaxation, and thought-changing. Parents completed 1 module on pain behaviour modification. Each module included assignments for home practice **Support:** weekly telephone calls with a study therapist were used to answer questions **Programme features:** all components of the CD-ROMs were fully narrated and included developmentally appropriate graphics, language and music **Duration:** 4 modules completed over 4 weeks plus weekly phone calls from a study therapist (unknown duration). Each module could be completed in 1 hour	**Control type:** waiting-list control **Mode of delivery:** N/A **Content:** participants continued with the recommendations of their neurologist, and were contacted weekly by phone by study staff to encourage completion of assessments **Duration:** 2 months, after which participants were offered the Headstrong programme
Hicks 2006	**Name of treatment programme:** Help Yourself Online **Therapy type:** CBT **Mode of delivery:** Internet plus personalised relaxation tape and weekly email or telephone calls with a study therapist **Content:** children completed 7 online chapters covering pain education, relaxation techniques, cognitive strategies, activity pacing, lifestyle choices, and relapse prevention. Parents completed 2 online chapters focused on encouraging healthy behaviour. Each chapter ended with a knowledge quiz. Children were assigned skills to practice each week, which were then reviewed with the study therapist via alternating email or telephone contact **Support:** study staff contacted parents twice during the treatment period **Duration:** 1 chapter per week for 7 weeks plus email or telephone contact with the study therapist. Average duration of contact with the study therapist was 187 minutes per family **Programme features:** each chapter included a knowledge quiz. All participants received a personalised relaxation tape	**Control type:** waiting-list control **Mode of delivery:** N/A **Content:** participants were reminded by study staff to see their physician, as needed, while waiting to start the treatment programme **Duration:** 7 weeks, after which participants were offered the Help Yourself Online programme
Law 2015	**Name of treatment programme:** Web-based Management of Adolescent Pain (Web-MAP) **Therapy type:** CBT **Mode of delivery:** Internet **Content:** the programme was identical to the one used in Palermo 2009; see below for details	**Control type:** treatment as usual at a specialised headache clinic **Mode of delivery:** face-to-face **Content:** participants received one or more of the following interventions as recommended by their providers at the headache clinic, including medication

Table 1. Description of remotely-delivered treatments (*Continued*)

	Support: online coaches provided personalised feedback on behavioural assignments via a message centre **Programme features:** the website included interactive fields, which allowed for tailored and personalised assignments and instructions, interactive animations, audio files of relaxation exercises, and video files of peer models **Duration:** children and parents each completed 8 modules over 8 to 10 weeks. Each module could be completed in 30 minutes	management, psychological therapy, and physical therapy **Duration:** 8 to 10 weeks, after which participants were offered Web-MAP
Palermo 2009	**Name of treatment programme:** Web-based Management of Adolescent Pain (Web-MAP) **Therapy type:** CBT **Mode of delivery:** Internet **Content:** Web-MAP includes separate websites for children and parents. Children completed 8 modules on pain education, recognising stress and negative emotions, relaxation methods, distraction methods, cognitive methods, sleep hygiene and lifestyle factors, staying active, and relapse prevention. Parents completed 8 modules on pain education, recognising stress and negative emotions, operant training, modelling, sleep hygiene and lifestyle, communication, and relapse prevention. Each module included a knowledge quiz and a behavioural assignment **Support:** online coaches provided personalised feedback on behavioural assignments via a message centre **Duration:** children and parents each completed 8 modules over 8 to 10 weeks. Each module could be completed in 30 minutes **Programme features:** the website included interactive fields, which allowed for tailored and personalised assignments and instructions, interactive animations, audio files of relaxation exercises, and video files of peer models	**Control type:** waiting-list control **Mode of delivery:** N/A **Content:** participants continued with standard care offered through the pain clinic, although were asked not to start psychotherapy for pain management during the 8-week period **Duration:** 8 to 10 weeks, after which participants were offered Web-MAP
Palermo 2016	**Name of treatment programme:** Web-based Management of Adolescent Pain-2 (Web-MAP2) **Therapy type:** CBT **Content:** The design and treatment content of Web-MAP2 was adapted from the version of the programme tested in Palermo 2009 (see above for details). Adolescents and parents received access to the full Web-MAP2 programme including education about chronic pain, training in behavioural and cognitive coping skills, instruction in increasing activity participation, and education about pain behaviours and parental operant and communication strategies	**Control type:** active (education control) **Mode of delivery:** Internet **Content:** The control version of the Web-MAP study website had 2 functional components: 1) modules with information compiled from publicly available websites about paediatric chronic pain management, and 2) diary and assessments. The control website did not provide behavioural and cognitive skills training, or access to an online coach **Duration:** adolescents and parents were instructed to log into the web programme weekly at the same interval as the CBT group to read information about paediatric

Table 1. Description of remotely-delivered treatments (*Continued*)

	Support: online coaches provided personalised feedback on behavioural assignments via a message centre **Programme features:** participants had access to 5 functional components of the web programme: 1) treatment modules, 2) assessments and daily diaries, 3) compass (audio files of relaxation exercises), 4) passport (progress tracker), and 5) a message centre to correspond with the online coach. Vignettes, videos of peer models, illustrations, interactive fields, and reinforcing quizzes are used throughout the programme **Duration:** children and parents each completed 8 modules over 8 to 10 weeks. Each module could be completed in 30 minutes	chronic pain
Rapoff 2014	**Name of treatment programme:** Headstrong **Therapy type:** CBT **Mode of delivery:** CD-ROMs plus workbook and weekly phone calls with a study therapist **Content:** children completed 3 modules: education, relaxation, and problem solving and stress management. Parents completed 1 module on pain behaviour modification. The workbook included supplementary materials **Duration:** each module was divided into six 10-minute lessons. Children completed one 10-minute lesson per day for 4 weeks. Parents completed one 10-minute lesson per day for one week. Each lesson included a knowledge quiz and homework assignment **Support:** weekly phone calls with study therapist were used to answer questions about the CD-ROMs and to remind participants about record keeping **Programme features:** graphics, audio narration, music, clickable progress controls, passwords to mark progress through the programme, and homework assignments. A workbook had supplementary material required to complete the treatment. Parents were given a manual containing instructions and technical assistance information	**Control type:** active (education control) **Mode of delivery:** CD-ROM **Content:** children completed modules on education about primary headaches and health habits. Parents were given a manual on how to use the educational programme **Duration:** each module was divided into six 10-minute lessons. Children completed one 10-minute lesson per day for 4 weeks
Schatz 2015	**Name of treatment programme:** CBT Coping Skills Training **Therapy type:** CBT **Content:** one in-person CBT training session was delivered by a licensed clinical psychologist or doctoral student and involved pain education, explained active versus passive coping methods, and introduced CBT techniques that would be used at home including progressive muscle relaxation, deep breathing, guided imagery, and distraction. After the training session, chil-	**Control type:** waiting-list control **Mode of delivery:** N/A **Content:** standard care in a sickle cell disease specialty clinic **Duration:** 8 weeks, after which they were offered the CBT coping skills training

Table 1. Description of remotely-delivered treatments (*Continued*)

	dren were provided with a smart phone loaded with a coping skills programme. The coping skills programme was designed to facilitate skills practice and included audio files of relaxation exercises as well as a daily pain diary **Support:** families were contacted by phone weekly to address questions and ensure implementation of skills. Telephone, email and text message were used to assess barriers to adherence to the pain diary **Programme features:** the programme used an application that provided icons the child could click on to start audio files. For example, clicking on a picture of a balloon would initiate the audio file for deep breathing **Duration:** In-person CBT training was 46-60 minutes, followed by smartphone training (30-40 minutes). The treatment took place over 8 weeks, but unknown number of modules and duration	
Stinson 2010	**Name of treatment programme:** Teens Taking Charge: Managing Arthritis Online **Therapy type:** CBT **Mode of delivery:** Internet, plus weekly telephone calls from a study therapist **Content:** adolescents completed 12 modules, which included education about arthritis, managing symptoms (pain, stiffness, fatigue), managing stress and negative thoughts, relaxation, distraction, other types of care (exercise, nutrition, splints), self-monitoring and supports, lifestyle issues, and issues related to transition to adulthood. Parents completed 2 modules focused on encouraging healthy behaviour. Each module includes a knowledge quiz and homework assignments. Parents were also able to view the materials on the teen website **Support:** weekly scripted telephone calls with a study coach were used to review homework assignments, quiz responses, module content, and problem-solve around skills implementation. The website also included a discussion board that was monitored by the study coach **Duration:** children completed 12 modules over 12 weeks. Each module took between 20 and 30 minutes to complete. Participants received an average of 1.6 telephone calls per week with the average duration of calls being 17.3 minutes (range 7 to 30 minutes) **Programme features:** the web programme is multilayered and interactive, and includes a discussion board monitored by a study coach. Adolescents use a progress tracker in the web programme to monitor progress on personal goals	**Control type:** active (attention control) **Mode of delivery:** telephone **Content:** adolescents received weekly phone calls from a research assistant to discuss their "own best efforts" at managing their arthritis **Duration:** participants received a mean of 1.4 phone calls per week. Average duration of calls was 3 minutes (range 2 to 6 minutes)

Table 1. Description of remotely-delivered treatments (*Continued*)

Trautmann 2010	**Name of treatment programme:** Internet-based self-help training **Therapy type:** CBT **Mode of delivery:** Internet and a relaxation CD **Content:** there were 2 treatment groups in this trial; cognitive behavioural group (CBG) and applied relaxation group (APG) The CBG completed modules on headache education, stress management, progressive relaxation techniques, cognitive restructuring, self-assurance, and problem solving. Participants received a CD with relaxation instructions, and children could download relaxation instructions from a website The APG completed modules on headache education, progressive relaxation, cue-controlled relaxation, and an applied relaxation CD **Support:** both groups received weekly email support from study therapists. Emails were standardised and included a knowledge quiz to determine whether participants had read the assigned material and completed the assigned exercises. Participants also received 2 booster emails after the completion of treatment focused on reminders of skills learned and encouragement to continue daily practice **Duration:** participants completed 1 module per week for 6 weeks. Participants received weekly email support from study therapists during treatment and 2 booster emails after the completion of treatment **Programme features:** relaxation CD, email support from study therapists, option to download and print material from the website to review and practice	**Control type:** active (education control) **Mode of delivery:** Internet **Content:** adolescents received access to the headache education module and had weekly email contact with study therapists. Emails focused on review of headache diary from the previous week **Duration:** weekly email contact with study therapists

CBT: cognitive behavioural therapy
N/A: not applicable

Table 2. Scorecard of results

Psychological therapies (remotely delivered) for the management of chronic pain in children				
	Headache		**Mixed chronic pain conditions**	
	Post-treatment	**Follow-up**	**Post-treatment**	**Follow-up**
Pain	Effect (7)	No effect (4)	No effect (5)	No effect (2)
Disability	No effect (5)	No effect (3)	No effect (3)	No data (1)

Table 2. Scorecard of results (*Continued*)

Depression	No effect (4)	No effect (2)	No effect (2)	No data (1)
Anxiety	No effect (3)	No effect (3)	No effect (2)	No data (1)

Number indicated in brackets denotes number of studies entered into analyses.

APPENDICES

Appendix 1. Search strategies

CENTRAL (CRSO) search strategy

1. MeSH DESCRIPTOR Pain EXPLODE ALL TREES
2. MeSH DESCRIPTOR Headache Disorders EXPLODE ALL TREES
3. MeSH DESCRIPTOR Fibromyalgia
4. ((pain* or headache* or migraine* or fibromyalgia* or neuralgia*)):TI,AB,KY
5. #1 OR #2 OR #3 OR #4
6. MeSH DESCRIPTOR Child EXPLODE ALL TREES
7. MeSH DESCRIPTOR adolescent
8. MeSH DESCRIPTOR Infant
9. ((child* or infant* or baby or babies or preschooler* or pre-schooler* or toddler* or schoolchild* or girl* or boy* or adolescen* or teen*)):TI,AB,KY
10. #6 OR #7 OR #8 OR #9
11. MeSH DESCRIPTOR Internet EXPLODE ALL TREES
12. ((internet or web or blog* or "social media" or online or www or email* or e-mail*)):TI,AB,KY
13. MeSH DESCRIPTOR Telecommunications EXPLODE ALL TREES
14. ((telemedicine or tele-medicine)):TI,AB,KY
15. ((telehealth or tele-health)):TI,AB,KY
16. ((ehealth or e-health)):TI,AB,KY
17. ((mobile health or mhealth or m-health)):TI,AB,KY
18. ICT:TI,AB,KY
19. (((inform* or communicat* or interact*) near6 (computer* or technolog* or software))):TI,AB,KY
20. (((health* or treat* or therap* or intervention* or assist* or selfmanag* or self-manag*) near6 (computer* or technolog* or software))):TI,AB,KY
21. ("world wide web"):TI,AB,KY
22. ((telephone* or phone* or mobile* or cellphone* or apps or text* or SMS or smartphone*)):TI,AB,KY
23. ((virtual reality or augmented reality or VR or AR)):TI,AB,KY
24. #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23
25. #5 AND #10 AND #24

MEDLINE (OVID) search strategy

1 exp Pain/
2 exp Headache Disorders/
3 Fibromyalgia/
4 (pain* or headache* or migraine* or fibromyalgia* or neuralgia*).tw.
5 or/1-4

6 exp Child/
7 Adolescent/
8 Infant/
9 (child* or infant* or baby or babies or preschooler* or pre-schooler* or toddler* or schoolchild* or girl* or boy* or adolescen* or teen*).tw.
10 or/6-9
11 exp Internet/
12 (Internet or web or blog* or "social media" or online or www or email* or e-mail*).tw.
13 exp Telecommunications/
14 (telemedicine or tele-medicine).tw.
15 (telehealth or tele-health).tw.
16 (ehealth or e-health).tw.
17 (mobile health or mhealth or m-health).tw.
18 ICT.tw.
19 ((inform* or communicat* or interact*) adj6 (computer* or technolog* or software)).tw.
20 ((health* or treat* or therap* or intervention* or assist* or selfmanag* or self-manag*) adj6 (computer* or technolog* or software)).tw.
21 "world wide web".tw.
22 (telephone* or phone* or mobile* or cellphone* or apps or text* or SMS or smartphone*).tw.
23 (virtual reality or augmented reality or VR or AR).tw.
24 or/11-23
25 5 and 10 and 24
26 randomized controlled trial.pt.
27 controlled clinical trial.pt.
28 randomized.ab.
29 placebo.ab.
30 drug therapy.fs.
31 randomly.ab.
32 trial.ab.
33 or/26-32
34 exp animals/ not humans.sh.
35 33 not 34
36 25 and 35

Embase (OVID) search strategy

1. exp Pain/
2. exp Headache Disorders/
3. Fibromyalgia/
4. (pain* or headache* or migraine* or fibromyalgia* or neuralgia*).tw.
5. or/1-4
6. exp Child/
7. Adolescent/
8. Infant/
9. (child* or infant* or baby or babies or preschooler* or pre-schooler* or toddler* or schoolchild* or girl* or boy* or adolescen* or teen*).tw.
10. or/6-9
11. exp Internet/
12. (internet or web or blog* or "social media" or online or www or email* or e-mail*).tw.
13. exp Telecommunications/
14. (telemedicine or tele-medicine).tw.
15. (telehealth or tele-health).tw.
16. (ehealth or e-health).tw.
17. (mobile health or mhealth or m-health).tw.
18. ICT.tw.
19. ((inform* or communicat* or interact*) adj6 (computer* or technolog* or software)).tw.

20. ((health* or treat* or therap* or intervention* or assist* or selfmanag* or self-manag*) adj6 (computer* or technolog* or software)).tw.
21. "world wide web".tw.
22. (telephone* or phone* or mobile* or cellphone* or apps or text* or SMS or smartphone*).tw.
23. (virtual reality or augmented reality or VR or AR).tw.
24. or/11-23
25. 5 and 10 and 24
26. random$.tw.
27. factorial$.tw.
28. crossover$.tw.
29. cross over$.tw.
30. cross-over$.tw.
31. placebo$.tw.
32. (doubl$ adj blind$).tw.
33. (singl$ adj blind$).tw.
34. assign$.tw.
35. allocat$.tw.
36. volunteer$.tw.
37. Crossover Procedure/
38. double-blind procedure.tw.
39. Randomized Controlled Trial/
40. Single Blind Procedure/
41. or/26-40
42. (animal/ or nonhuman/) not human/
43. 41 not 42
44. 25 and 43

PsycINFO (OVID) search strategy

1. exp Pain/
2. exp Headache/
3. Fibromyalgia/
4. (pain* or headache* or migraine* or fibromyalgia* or neuralgia*).tw.
5. or/1-4
6. (child* or infant* or baby or babies or preschooler* or pre-schooler* or toddler* or schoolchild* or girl* or boy* or adolescen* or teen*).tw.
7. exp Internet/
8. (internet or web or blog* or "social media" or online or www or email* or e-mail*).tw.
9. exp Telecommunications/
10. (telemedicine or tele-medicine).tw.
11. (telehealth or tele-health).tw.
12. (ehealth or e-health).tw.
13. (mobile health or mhealth or m-health).tw.
14. ICT.tw.
15. ((inform* or communicat* or interact*) adj6 (computer* or technolog* or software)).tw.
16. ((health* or treat* or therap* or intervention* or assist* or selfmanag* or self-manag*) adj6 (computer* or technolog* or software)).tw.
17. "world wide web".tw.
18. (telephone* or phone* or mobile* or cellphone* or apps or text* or SMS or smartphone*).tw.
19. (virtual reality or augmented reality or VR or AR).tw.
20. or/7-19
21. 5 and 6 and 20
22. clinical trials/
23. (randomis* or randomiz*).tw.
24. (random$ adj3 (allocat$ or assign$)).tw.
25. ((clinic$ or control$) adj trial$).tw.
26. ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.

27. (crossover$ or "cross over$").tw.
28. random sampling/
29. Experiment Controls/
30. Placebo/
31. placebo$.tw.
32. exp program evaluation/
33. treatment effectiveness evaluation/
34. ((effectiveness or evaluat$) adj3 (stud$ or research$)).tw.
35. or/22-34
36. 21 and 35

Appendix 2. Previous search findings

2014 Search: we conducted a search of four databases that produced 1384 papers after duplicates were removed. A further two were identified from other sources. From the 12 papers identified and read in full, eight were included and four were excluded.

WHAT'S NEW

Date	Event	Description
26 June 2018	New search has been performed	We updated this review to include the results of a new search on 1 May 2018
12 June 2018	New citation required but conclusions have not changed	We included four new studies with 326 additional participants

HISTORY

Protocol first published: Issue 5, 2014

Review first published: Issue 3, 2015

Date	Event	Description
9 February 2016	Review declared as stable	See Published notes.

CONTRIBUTIONS OF AUTHORS

Emma Fisher oversaw the project, contributed to the design, analysis and authoring of the text, and is responsible for any future update of this review.

Tonya Palermo, Emily Law, Joanne Dudeney, and Christopher Eccleston all contributed to the design, analysis, and authoring of the text.

DECLARATIONS OF INTEREST

EF: none known

EL: Emily Law is a paediatric psychologist who provides evaluation and treatment for children with chronic pain at Seattle Children's Hospital. Dr Law is an author on three of the included trials (Law 2015; Palermo 2009; Palermo 2016), and was not involved in data extraction or assessments of these studies. During the completion of this work, EL received salary support from the National Institutes of Health/National Institute of Neurological Disorders and Stroke (K23NS089966, PI: Law).

JD: none known. Joanne Dudeney is a clinical psychologist working on clinical trials of CBT for chronic pain.

CE: none known

TP: none known; Tonya Palermo is an author on three studies included in this review (Law 2015; Palermo 2009; Palermo 2016), and was not involved in data extraction or assessments of these studies. During the completion of this work, TP received salary support from the National Institutes of Health/National Institute of Child Health, Behavior and Development (K24HD060068, PI: Palermo).

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Internal sources

- No sources of support supplied

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- National Institutes of Health, USA.

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- National Institutes of Health, USA.

Emily Law was supported by grant number K23-NS089966 from the National Institute of Neurological Disorders and Stroke

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the protocol, we stated that interventions delivered by audiotapes or written manuals were included in Fisher 2018. For Fisher 2015, the review author team decided to include this mode of remotely-delivered intervention, as some interventions included audiotapes or written material in combination with another form of intervention (e.g. telephone calls). However, in this update of this review, we reversed this decision in order to fit with the protocol and conduct this review in the spirit that was intended. Defining what is classed as 'remote' is a difficult and potentially contentious issue, however, we have chosen to define this as being delivered using technology for at least 70% of contact time.

Further changes from Fisher 2015 to the current update include the following.

- We have updated the Background section with more current literature and references.

- We have provided additional detail regarding the types of conditions that will be included.
- We have provided more detail regarding 'Risk of bias' assessment.
- We have included 'Summary of findings' tables and included methods to assess quality of evidence as required by Cochrane.
- We have provided more information regarding unit of analyses, dealing with missing data, assessment of heterogeneity, assessment of reporting biases, and sensitivity analyses in the methods; these sections were previously incomplete. We have removed conducting a subgroup analysis by 'intensity of treatment'; the authors agreed this would be difficult to define and it is not practical.

INDEX TERMS

Medical Subject Headings (MeSH)

Abdominal Pain [psychology; therapy]; Anxiety [therapy]; Arthritis, Juvenile [psychology; therapy]; Chronic Pain [psychology; *therapy]; Cognitive Behavioral Therapy [methods]; Depression [therapy]; Headache [psychology; *therapy]; Internet; Musculoskeletal Pain [psychology; therapy]; Pain Management [*methods]; Patient Satisfaction; Psychotherapy [*methods]; Randomized Controlled Trials as Topic; Recurrence; Relaxation Therapy [methods]; Telemedicine [*methods]; Treatment Outcome

MeSH check words

Adolescent; Child; Humans