Brief psychological interventions for psychiatric disorders in young people with long term physical health conditions: a systematic review and meta-analysis

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Introduction

Rates of psychiatric disorders such as depression (Pinquart & Shen, 2011c), disruptive behaviour disorders (i.e. oppositional and conduct disorders) (Pinquart & Shen, 2011b), post-traumatic stress (Pinquart, 2018), anxiety (Pinquart & Shen, 2011a) and eating disorders (Conviser, Fisher, & McColley, 2018) are significantly elevated in young people with long term physical health conditions (Almane et al., 2019; Chun et al., 2015; Khanna et al., 2019; Quilter, Hiraki, & Korczak, 2019). This is a public health concern as large numbers of children and young people have long term physical health conditions, with prevalence rates of up to 23% in the UK (Brooks, Magnusson, Klemera, Spencer, & Morgan, 2011) and 25% in the US (Van Cleave, Gortmaker, & Perrin, 2010; van der Lee, Mokkink, Grootenhuis, Heymans, & Offringa, 2007). Untreated co-morbid psychiatric disorders in paediatric patients have been associated with more impaired physical functioning (Ding, Hall, Jacobs, & David, 2008), lower quality of life (Johnson, Jones, Seidenberg, & Hermann, 2004), sub-optimal disease management (Sildorf et al., 2018) and increased mortality during admission to hospital (Olusunmade, Qadir, Akyar, Farid, & Aggarwal, 2019). The impact can extend to the whole family. Higher rates of parenting stress (Cousino & Hazen, 2013) and emotional problems in siblings (Sharpe & Rossiter, 2002) have been found in families of children with a long term physical condition compared to those without. There is evidence to suggest that this higher rate of emotional problems in siblings can persist in the long term (O'Neill & Murray, 2016). There are also economic costs of co-morbidity, as those with comorbid psychiatric disorders in the context of chronic physical illness experience more frequent and longer admissions to hospital, which can be up to 5 times more expensive than those of their peers without a psychiatric co-morbidity (Zima et al., 2016). For frequency of hospital admissions, this is especially true in young people where the psychiatric comorbidity is a developmental disorder, attention deficit hyperactivity disorder or anxiety disorder (Zima et al., 2016).

In the UK, psychiatric disorders in children and young people are treated within specialist Child and Adolescent Mental Health Services. Yet, accessibility of treatments in the community appears limited. For example, for 78% of young people referred to Child and Adolescent Mental Health Services with problems in addition to their long term physical health condition, the outcome of the referral was not known (Children's Commissioner, 2016). Even for the few who access treatment, research in this area suggests that interventions received are patchy, inconsistent and not always compliant with NICE guidelines (Welch, Shafran, Heyman, Coughtrey, & Bennett, 2018). For mild depression in children and young people, NICE recommend as first line treatment a psychological intervention such as digital cognitive–behavioural therapy (CBT), group CBT, group non-directive supportive therapy (NDST) or group interpersonal psychotherapy (IPT) for 8 - 12 sessions (NICE, 2019); for anxiety disorders, individual CBT of 8−12 sessions of 45 minutes' duration (for social anxiety) or group CBT (NICE, 2013b); for disruptive behaviour disorders (conduct disorder or ODD) (NICE, 2013a) and challenging behaviour in young people with an intellectual disability (NICE, 2015) parent training interventions. Poor access to evidence-based mental health support is not due to a lack of known effective treatments for young people (Weisz et al., 2017). Evidence suggests that cognitive behavioural therapy (CBT) treatments may be effective in young people with mental health needs in addition to long term physical health conditions. This has been explored for a range of conditions – for example epilepsy, inflammatory bowel disease, functional symptoms and chronic pain (Moore et al., 2019) and may require practical adaptations, such as more flexibility around appointments (Bennett, Shafran, Coughtrey, Walker, & Heyman, 2015). Some psychological interventions included adaptations to content to take account of the long term physical health condition (for example in the PASCET-PI studies by Szigethy and colleagues, adaptations to content included information about inflammatory bowel disease, techniques for coping with abdominal pain, identifying negative cognitions about inflammatory bowel disease), but at present there is insufficient evidence to know whether these are required or improve efficacy (Moore et al., 2019). There was insufficient evidence to assess whether these interventions

are cost-effective (Moore et al., 2019). It is likely that barriers to accessing care, although compounded by a long term physical health condition, are similar to those of young people without a long term physical health condition. These include a lack of trained therapists, costs, logistical issues like child care, transport, work demands and time (Owens et al., 2002).

A promising approach to increase access to evidence-based therapy for adults with co-morbid long-term conditions and anxiety/depression (Kellett et al., 2016), involves using 'brief' CBT interventions as part of stepped care. This model has been extended to young people with anxiety/depression/disruptive behaviour in the absence of a co-morbid long term physical health condition, with similar results (Edbrooke-Childs, Calderon, Wolpert, & Fonagy, 2015). Although the definitions of 'brief' vary, they usually involve ≤10 sessions with ≤6 hours of therapist contact per patient often include self-help materials, and can be delivered by mental health workers with less specialist training (Cape & Kendall, 2011; Stallard, 2017). This is in contrast to traditional 'high-intensity' therapies that typically involve 12-16 hour-long sessions, by a highly trained mental health professional.

Brief interventions have the potential to reach more people. The mechanisms may include a reduction in time spent travelling to clinic for patients, travel costs, time off work or school (Stallard, 2017). These benefits are likely to be particularly important to families who already have to attend a number of appointments for their child's physical illness. Moreover, they allow mental health workers with less specialist training to deliver interventions with similar outcomes at a reduced cost to society (Creswell et al., 2017), thereby increasing capacity and as a result reducing waiting times.

In order to determine what brief evidence-based psychological treatments for paediatric hospital patients are effective, a review of the evidence is needed. There have been reviews in children and adolescents of specific forms of brief CBT in specific long term physical

health conditions, such as e-health interventions for anxiety and depression (Thabrew et al., 2017), or remotely delivered interventions for chronic pain/headache (Fisher, Law, Palermo, & Eccleston, 2015). A subgroup analysis of a broader review of psychological interventions for young people with long term physical health conditions looked at “brief” therapy, defined as <6 sessions or <6 hours, rather than ‘brief’ as defined above. In this particular subgroup analysis, Thabrew and colleagues synthesised different types of psychological therapies in the same meta-analysis (e.g. CBT and family therapy) (Thabrew et al., 2018), which precluded examining differential efficacy of individual modalities, as in reviews of high intensity interventions for young people with long term physical health conditions these have differed (Moore et al., 2019). Finally, this was done two years ago in a fast moving field and important additional papers have been published since then.

To our knowledge none have reviewed brief interventions (including guided self-help) in long term physical health conditions in young people with elevated psychiatric symptoms as a whole.

Objectives

This systematic review aimed to explore:

- the efficacy of brief interventions targeting elevated symptoms of psychiatric disorders for young people with long term physical health conditions versus any comparator.
- the effects of such interventions on other key aspects of individual functioning (e.g. quality of life or physical health).
- factors that may moderate the efficacy or acceptability of these interventions.

Methods

Protocol pre-registration and outcome reporting

The review protocol was registered to PROSPERO on the 22/03/2019 (PROSPERO ID: CRD42019121299). Outcomes were reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement (Moher, Liberati, Tetzlaff, Altman, & Group, 2009).

Criteria for considering studies for this review

Inclusion criteria

Population

- Studied participants up to 18 years of age.
- Participants either had a psychiatric disorder or elevated symptoms of a psychiatric disorder at baseline (defined as the mean of the sample in each arm being above an accepted cut off for a validated mental health measure).
- Participants all diagnosed with a long term physical health condition.
    - We defined long term physical health conditions as lasting for at least 3 months, causing functional impairment, necessitating medical care and where cure is considered unlikely. This definition was in line with that of a recent evidence synthesis on the topic (Moore et al., 2019) . Moore and colleagues (2019) report defining long term physical health conditions, by drawing on a systematic review of definitions of chronic health conditions in childhood (van der Lee et al., 2007) and selecting a combination of those most frequently cited. Conditions included in the search: AIDS and HIV, asthma, cancer, chronic pain, cleft palate, cystic fibrosis, deafness/hearing impairment, diabetes, epilepsy, headache, heart disease, inflammatory bowel disease (IBD), kidney disease, liver disease, migraine, sickle cell anaemia, spina bifida and visual impairment.

Intervention

- Studied a brief intervention defined as: interventions involving ≤10 sessions with ≤6 hours of therapist contact per patient (Cape & Kendall, 2011; Stallard, 2017). In the case of group treatments, we multiplied the total number of hours of the group by the number of therapists and then divided it by the average number of patients in the group (Rodgers et al., 2012).
    - This included all brief interventions with a cognitive and/or behavioural component (e.g. CBT, parenting interventions), relational/insight-oriented component (family/systemic therapy, psychodynamic therapy), as well as interventions using physiological, sensory and/or complementary approaches (e.g. music therapy, massage therapy, biofeedback, hypnosis) to target symptoms of psychiatric disorders and reduce distress/impairment.

Comparator

- Any control group (e.g. treatment as usual, waitlist control, other psychological therapy, pharmacological therapy or other).

Outcomes

- Reported a child-related mental health measure (the measure had to relate to the mental health of the child and not the parent/carer, although parent-reports of child health/behaviour were acceptable) at post-intervention and/or follow-up (any length).
    - *Examples of outcome measures include: symptoms of depression (e.g. Beck Depression Inventory for Youth), anxiety (e.g. State-Trait Anxiety Inventory for Children) behavioural disorders (e.g. Child Behaviour Checklist).*

Study design

- *Randomised controlled trials (RCTs) only.*

Exclusion criteria

We excluded studies that were not in a language that was known to the reviewers (i.e. studies not in Italian, French or English).

Search Methods

Electronic Searches, citation searches, reference list searches and grey literature searches were independently undertaken by MC and MP (a psychological wellbeing practitioner).

Electronic searches

EMBASE, MEDLINE, PsycINFO databases were searched from inception to 12/02/2020. Grey/unpublished literature was also included, through searches of PsycExtra, Google and Google Scholar. Broadly, the search terms were categorised into 5 primary areas; (1) Children and young people, (2) Brief psychological interventions (3) Psychiatric disorders (4) Chronic illness 5) RCT. Please see supplementary materials for the full electronic search strategy.

Other searches

Additional literature was found through reviewing the reference lists of relevant systematic reviews in the area.

Data collection and analysis

Study selection

Study selection was performed independently by two reviewers, MC and MP. The kappa agreement for included/excluded studies at the full-text article screening stage was 0.879

(P<0.001; substantial agreement). Where disagreements arose this was resolved through discussion with SB.

Data extraction and management

A data extraction form was developed and adapted from the Cochrane handbook template (Higgins et al., 2019). Data on study details and aims, participants, mental health measures at baseline, intervention, number of sessions, and duration of sessions, outcome measures, findings and study quality were extracted independently by two reviewers, MC and CS (a clinical psychologist). The kappa agreement for extraction of the primary mental health outcome measure between the two independent reviewers was 0.833 (p<0.001; substantial agreement). Where disagreements arose this was resolved through discussion with SB.

Assessment of risk of bias in included studies

Risk of bias was independently assessed by two reviewers (MC and CS) using the Cochrane Risk of Bias Tool (Higgins et al., 2011). This assesses allocation concealment, sequence generation, blinding, selective outcome reporting and incomplete outcome reporting. The kappa agreement for risk of bias ratings between the two independent reviewers was 0.648 (p<0.001; substantial agreement). Studies with no obvious evidence of selective reporting required a protocol to cross-check this, otherwise they were coded as 'unclear risk of bias' in that domain. Studies where only self-report measures were used, were coded as unclear risk of bias, unless a blind assessor was used, in which case they were coded as low risk of bias. Where disagreements arose this was resolved through discussion with SB.

Data synthesis

The meta-analysis was carried out using Review Manager 5 (RevMan), according to the Cochrane guidelines (Higgins et al., 2019). For each relevant outcome, post-intervention mean, standard deviation and sample size were extracted. Comparisons of clinical efficacy

were summarised with the standardised mean difference (Hedges' g) between intervention and control group post-intervention as studies assessed similar outcomes but measured them in a variety of ways (e.g. different self-report questionnaires for anxiety symptoms) (Higgins et al., 2019). Hedges' g was used to calculate effect size at post-intervention, with 95% confidence intervals (CIs) and p-values. A meta-analysis was considered feasible where multiple studies examined the same type of intervention (e.g. CBT) and used the same outcome category (e.g. anxiety measure). A random-effects model was used to pool effect sizes, due to no two studies addressing the research question using the same methodology. When a quantitative synthesis was not possible, due to insufficient suitable studies for a meta-analysis or where certain outcomes were not reported (e.g. standard deviation), these were synthesised narratively.

We contacted authors for apparent missing data. As this was unsuccessful, we reported missing data as 'not reported' in Tables 1 and 2. Heterogeneity was calculated using Tau^2 and I^2. As per the Cochrane guidelines, I^2 was roughly interpreted as follows:

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

All meta-analysis, forest plots and related calculations were done using Review Manager 5.3 (Revman version 5.3). Assessment of Publication bias was planned by examining funnel plots for asymmetry in Revman 5.3, but this was not possible due to the limited number of studies with similar characteristics entered in the meta-analysis. For the same reason regression-based assessments of publications bias were unable to be used.

Summary of findings

The GRADE system (Schünemann, Brożek, Guyatt, & Oxman, 2013) was used to assess quality of the body of evidence, using GRADEpro (version 3.6). Four categories are used in this approach (high, moderate, low and very low) to rate the quality of the evidence available. All RCTs start at a high level. Evidence from RCTs can be downgraded if there are indications of low quality such as high risk of bias or small sample sizes. Where this occurred it was noted in the footnotes of the 'Summary of findings' table (Table 4).

Results

Description of studies

The initial search identified 944 papers after duplicates had been removed (see PRISMA flow diagram, Figure 1). A total of 12 studies (with 425 children and adolescents) were found to meet the inclusion criteria of the review (Bennett, 2017; Bufalini, 2009; Field et al., 1998; Freedenberg, Hinds, & Friedmann, 2017; Hains, 2000; Hickman, Jacobson, & Melnyk, 2015; Jastrowski Mano et al., 2013; Liossi & Hatira, 1999; Scharff, Marcus, & Masek, 2002; Sharma, Mehta, & Sagar, 2017; Yetwin, 2011; Zhang, Mo, Torres, & Huang, 2019). Study characteristics were summarised in Table 1.

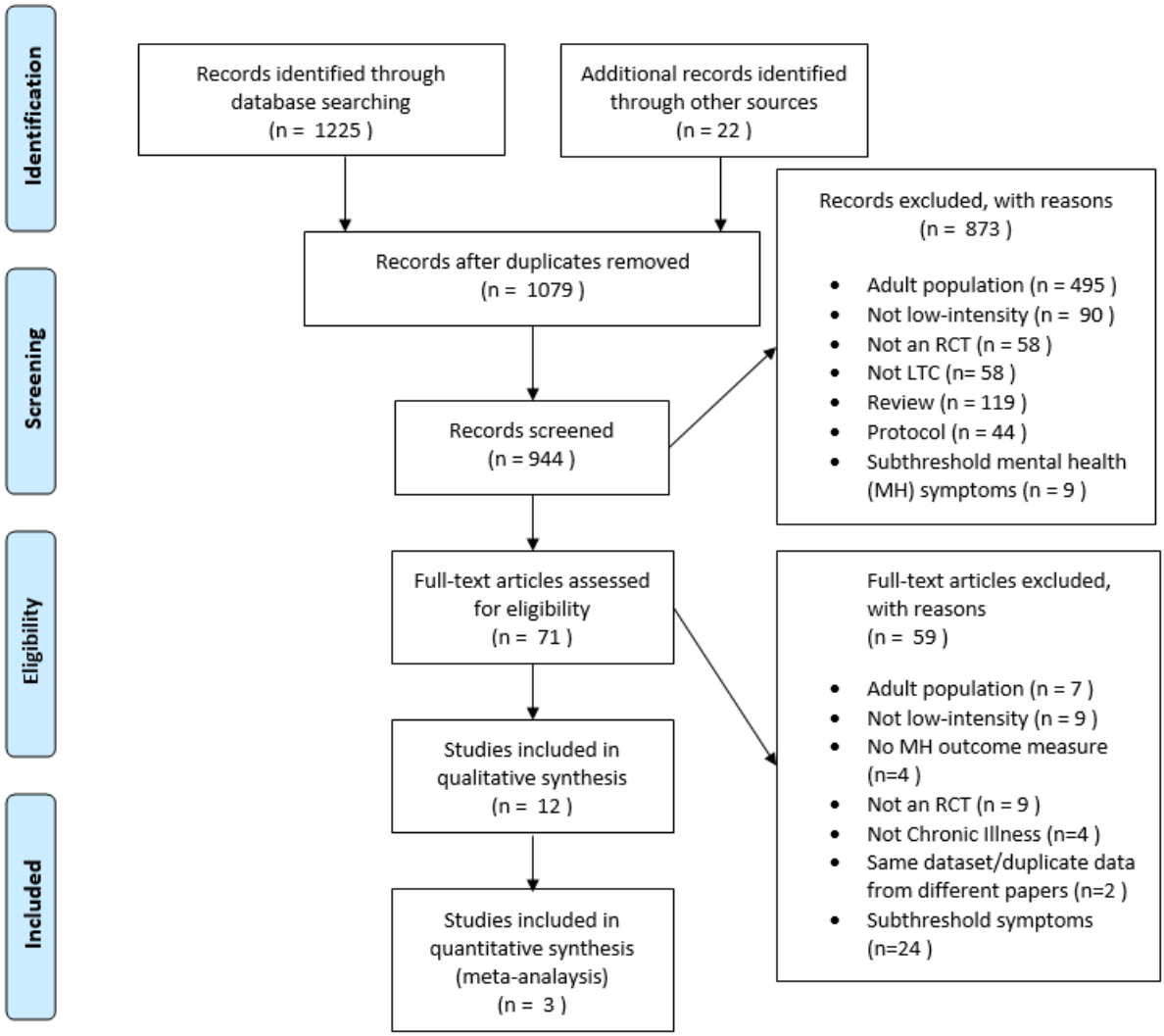

Figure 1. PRISMA flow diagram of included studies in the review

Table 1. Characteristics of included studies

Study	Participant n (% female)	Age of Participants M years (SD)	Psychiatric disorder	Long Term Condition	Intervention	Intervention provider	Intervention structure	Dose (hours)	Intervention recipient	Delivery method	Delivery format	Comparator	Site	Time points	Country
Bennett (2017)	34 (50%)	11.28 (3.29)	Anxiety, depression and disruptive behavior	Neurological conditions (88% epilepsy)	Cognitive Behavioural Therapy guided self-help	Trained research assistants supervised by clinical psychologist (who also took on cases)	Up to 10 sessions of 30minutes (total 5 hours max.)	5 hours (max)	Parent and/or child	Phone	Individual	Waitlist control	Hospital	Pre-, post- and 3-months	UK
Bufalini et. al. (2009)	39 (39%)	6.7 (SD not reported)	Procedural anxiety	Cancer	Interactive Music therapy	Doctor trained in music therapy	15min prior to procedure and up to sedation. (total time not reported)	Not reported	Child	f2f	Individual	Treatment as usual (usual sedation)	Hospital	T1;T2;T3;T4 (4 time points from beginning to end of intervention)	Italy
Field et. al. (1998)	32 (38%)	9.15 (SD not reported ; range: 4 -14)	Anxiety	Asthma	Massage therapy	Massage therapist taught parent of child to administer massages	One-off demonstration, written instructions and a videotaped demo were given to parents who then massaged child 30mins a night for 30days (total time not reported)	Not reported	Child	f2f	Individual	Progressive Muscle Relaxation	Hospital	Pre- and post-	USA
Hains et. al. (2000)	15 (53%)	Not reported (range:12-15)	Anxiety	Type I Diabetes	Group Cognitive Behavioural Therapy	2x Psychology PhD	6x 1 hour sessions per group of 4 youths	1h30mins	Child	f2f	Group	Waitlist control	Hospital	Pre-, post- and 1 month	USA
Hickman et. al. (2015)	32 (72%)	Intervention group: 15.38 (0.96) Control: 14.8 (1.17)	Depression	Headaches	Cognitive behavioural skills building	Neurology Nurse trained in Cognitive behavioural skills building	three office sessions of 30 minutes and four telephone sessions of 20 minutes over seven weeks (total 2h50mins)	2h50mins	Child	Blended phone/f2f	Individual	Headache education program	Hospital	Pre- and post-	USA

Freedenberg et. al. (2017)	46 (63%)	MBSR group: 15.1 (1.8) Video group: 14.5 (1.6)	Anxiety	Congenital Heart Disease	Mindfulness-Based Stress Reduction	Nurse trained in MBSR	6 x 1.5 hour group sessions (7-10 per group)	1h	Child	f2f	Group	Online video support group	Hospital	Pre-, post- and 6 months	USA
Jastrowski et. al. (2013)	6 (83%)	Intervention group: 15 (2.16) Control: 12.5 (0.71)	Anxiety	Chronic pain	Mindfulness-Based Stress Reduction	MBSR practitioner	6x 90 minutes group sessions (4 per group)	2h25mins	Child	f2f	Group	Psychoeducation group	Hospital	Pre-, post-, 1 month and 3 months	USA
Liossi et. al. (1998)	30 (43%)	8 (2.5)	Procedural anxiety	Leukaemia	Hypnosis	Clinical Psychologist	2x30 minute sessions	1hour	Child and Parent	f2f	Individual	CBT and control	Hospital	Pre- and post-	UK
Scharff et.al. (1999)	36 (66%)	Intervention group: 13.3 (2.5) Handcooling biofeedback group: 13.2 (2.0) Control: 12.0 (2.7)	Anxiety	Migraine	Thermal biofeedback and cognitive behavioural stress management training	PhD psychologist	4x1 hour sessions in 6 weeks	4 hours	Child	f2f	Individual	Handcooling biofeedback and Waitlist control	Hospital	Pre-, post-, 3 months and 6 months	USA
Sharma et. al. (2017)	63 (48%)	13.90 (2.60)	Anxiety	Headache	Transdiagnostic group Cognitive Behavioural Therapy	Doctoral level students used to delivering CBT, supervised by a clinical psychologist and psychiatrist	12x 2 hour group sessions (5-6 young people per group)	4h30mins	Child	f2f	Group	Treatment as usual (pharmacotherapy)	Hospital	Pre- and post-	India
Yetwin (2011)	19 (76%)	14.1 (1.91)	Anxiety	Chronic pain	Heart rate variability Biofeedback	PhD psychologist	4 treatment sessions, lasting 30-60mins	45mins x 4 = 3 hours	Child	f2f	Individual	Waitlist control	Hospital	Pre- and post-	USA

Zhang et. al. (2019)	108 (51%)	NR (range:8-18)	Anxiety	Cancer	Cognitive Behavioural Therapy	CBT therapist	5 sessions over 5 weeks (1 assessment, 3 treatment sessions and 1 to collect questionnaires)	Not reported	Child and Parent	f2f	Individual	Treatment as usual	Hospital	Pre- and post-	China

CBT: Cognitive Behavioural Therapy; **f2f**: Face-to-face; **MBSR** Mindfulness-Based Stress Reduction; **SD:** Standard deviation; **T1:** Time point 1

All studies involved different combinations of long term physical health conditions, psychiatric disorders and intervention types. Ten studies looked at anxiety, one at depression and one at 'emotional and behavioural' problems. The most common long term physical health conditions were cancer and headache. The majority of studies were delivered face-to-face and on an individual basis. Five studies were based on Cognitive Behavioural principles. Average therapist time per patient was 3 hours, in studies where this was reported. Two of the included studies were unpublished doctoral theses (Bennett, 2017; Yetwin, 2011).

Risk of bias

Risk of bias was assessed in accordance to Cochrane's 'risk of bias tool (Higgins et al., 2011) and summarised in Figures 2 and 3. Overall, there was evidence of risk of bias in all studies, due to difficulty in blinding participants and personnel. No studies had low risk of bias in all other domains. Interventions based on CBT principles tended to have a lower risk of bias.

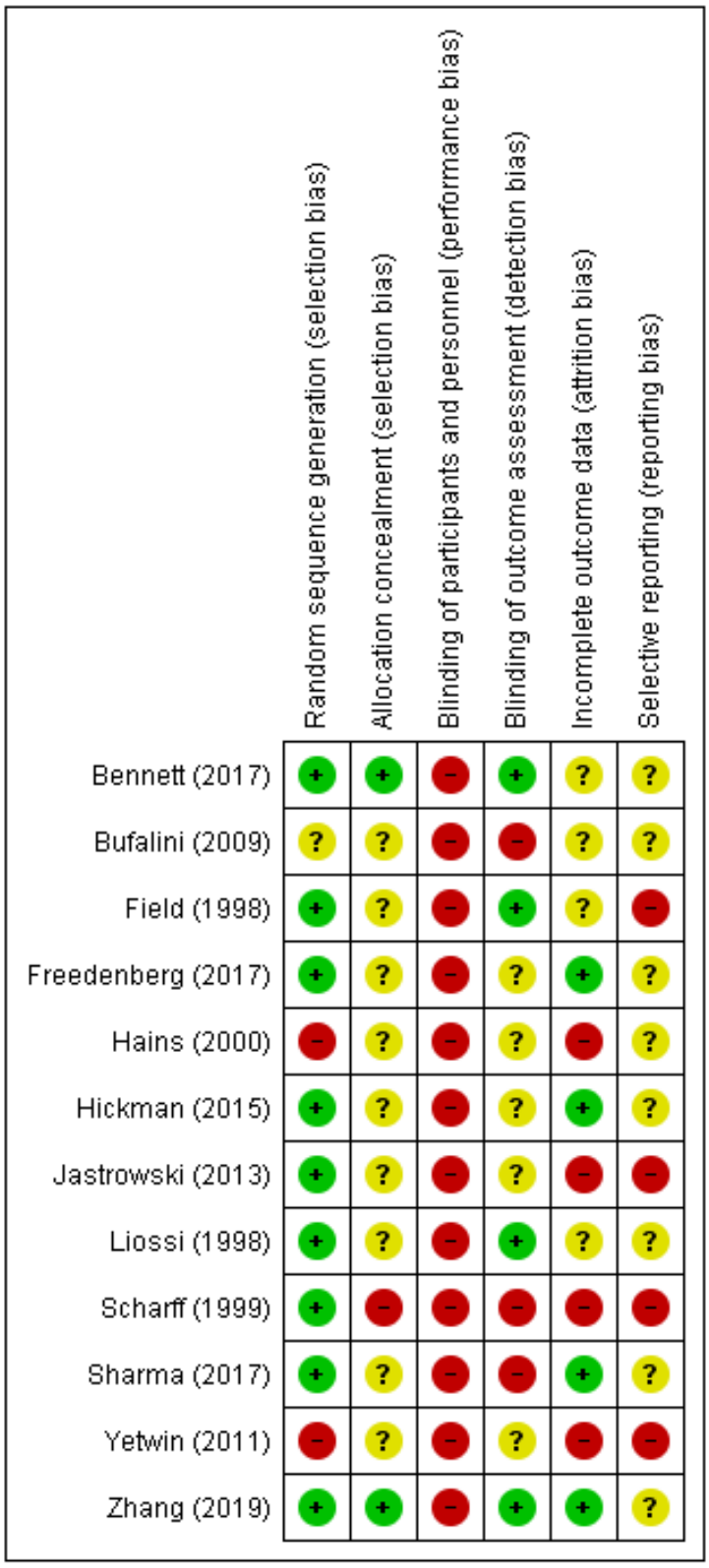

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study

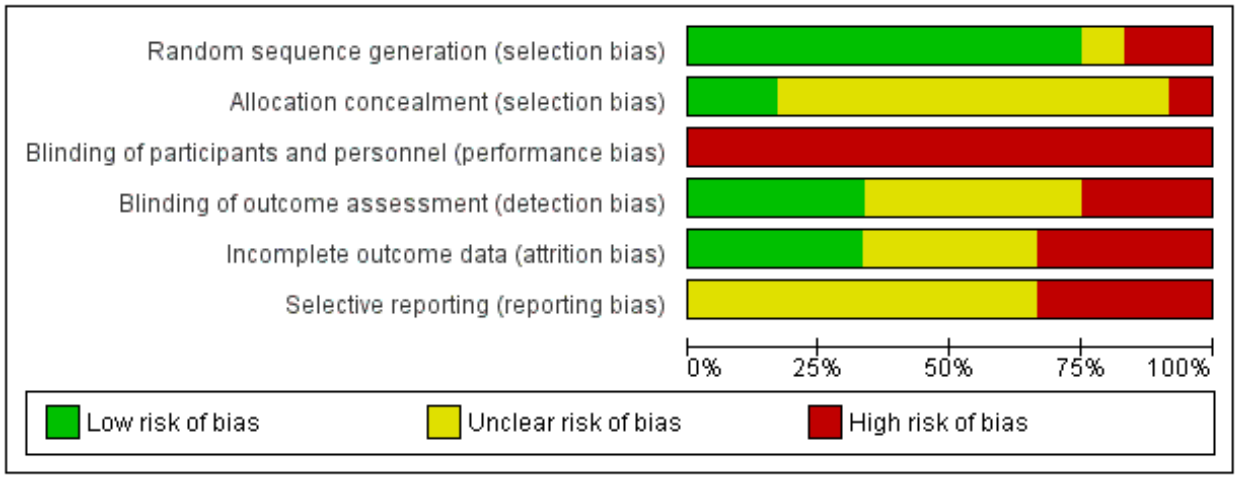

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies

Efficacy

Definitive conclusions cannot be drawn from the available evidence as most studies had small sample sizes and as a result were likely to be underpowered to detect statistically significant between group differences. Mental health outcomes of the included studies are summarised in Table 2. Other outcomes are summarised in Table 3. A summary of findings table for the main comparison: ‘Brief interventions compared to any comparator for psychiatric disorders in children with long term physical health conditions is presented in Table 4.

Table 2. Summary of mental health outcome measures of included studies

		Intervention				Control				Both groups	
Study	**Outcome measure**	**Intervention name**	**N**	**Pre (SD)**	**Post (SD)**	**Comparator name**	**N**	**Pre**	**Post**	**g [95% CI]**	**Summary for MH measure**
Bennett (2017)	SDQ-P total	Cognitive Behavioural therapy guided self-help	17	22.41(3.50)	18.78 (1.77)	Waitlist control	17	21.94(3.96)	19.13(4.30)	- 0.10 [-0.78, 0.57]	SDQ total scores demonstrated change across time, and a medium/large effect size was noted (d = 1.308, 95% CI: 0.568 to 2.049). There was no significant difference between groups.
	SDQ-P impact		17	5.94 (2.36)	5.07 (1.93)	Waitlist control	17	5.88 (2.71)	3.95 (2.22)	0.53 [-0.16, 1.21]	The SDQ impact scale similarly demonstrated a significant effect of time, but no statistically significant difference between groups.
Bufalini, et al. (2009)	m-YPAS	Interactive Music therapy	20	Measured at 4 time points up until procedure	Measured at 4 time points up until procedure	Treatment as usual	19	Measured at 4 time points up until procedure	Measured at 4 time points up until procedure	Not reported/insufficient data to calculate	Significant decrease in procedural anxiety at all 4 time points for intervention group compared to controls.
Field et. al. (1998)	STAI-C	Massage therapy	8	32.60 (SD NR)	27.9 (SD NR)	Progressive muscle relaxation	8	30.70 (SD NR)	28.8 (SD NR)	Not reported/insufficient data to calculate	Significant decrease in reported anxiety in the older children and their parents immediately after massage therapy.
Freedenberg et.al. (2017)	HADS (anxiety)	Mindfulness-Based Stress Reduction	26	10.5(4.0)	9.9 (4.0)	Online video support group	20	7.1 (6.2)	6.8 (5.3)	0.66 [0.06, 1.26]	Anxiety scores did not change significantly from before to after the interventions. The pre–post by group interaction revealed that anxiety did not change differently in the two groups.
Hains et.al. (2000)	STAI-state	Cognitive behavioural skills building	8	39.00 (7.45)	33.75 (6.43)	Waitlist control	7	38.5 (8.74)	39.67 (10.93)	-0.63 [-1.68, 0.41]	Significant within group differences on state anxiety. No statistically significant difference between groups.
Hickman et.al. (2015)	BYI-depression	Group cognitive behavioural therapy	16	60 (4.51)	51.69 (6.65)	Education group	16	57.56 (3.35)	49.69 (6.46)	0.30 [-0.40, 0.99]	No statistically significant difference was found in post-intervention depression controlling for baseline differences in depression scores.
Jastrowski et. al. (2013)	STAI-C	Mindfulness-Based Stress Reduction	4	Not reported	Not reported	Not reported	2	Not reported	Not reported	Not reported/insufficient data to calculate	Due to very high attrition levels, statistical analyses could not be carried out and means (SD) were not reported.

Liossi et. al. (1998)	Wong-Baker FACES	Hypnosis	10	4.5 [þ] (IQR not reported)	0.5 [þ] (IQR not reported)	Cognitive Behavioural Therapy	10	5 [þ] (IQR not reported)	3.5 [þ] (IQR not reported)	Not reported/insufficient data to calculate	The individual comparisons between groups were significant for anxiety scores.
						Control	10	4.5 [þ] (IQR not reported)	5.0 [þ] (IQR not reported)	Not reported/insufficient data to calculate	The individual comparisons between groups were significant for anxiety scores.
Scharff et. al.	STAI-C	Thermal biofeedback and cognitive behavioural stress management training	12	32.2 (12.2)	Not reported	Hand cooling Biofeedback	11	34.6(8.5)	Not reported	Not reported/insufficient data to calculate	Reported no significant difference in STAIC score change between groups (pre, post)
	STAI-C		12	32.2 (12.2)	Not reported	Waitlist control	12	37.7 (10.6)	Not reported	Not reported/insufficient data to calculate	Reported no significant difference in STAIC score change between groups (pre, post)
Sharma et.al. (2017)	STAI-state	Transdiagnostic group CBT	32	41.00(9.39)	29.16 (5.97)	Treatment as usual	31	42.42(8.71)	40.13 (9.02)	-1.42 [-1.98, -0.86]	Participants in the TCBT condition showed significant improvement in state anxiety, while no significant change in state anxiety was observed for participants in the TAU condition.
Yetwin (2011)	CASI	HRV Biofeedback	9	29.78 (7.48)	28.67 (7.26)	Waitlist control	10	31.90 (8.17)	28.60 (7.55)	0.01 [-0.89, 0.91]	No significant between group difference on anxiety sensitivity.
Zhang et.al. (2019)	DASS (anxiety)	CBT	53	11.53 (7.52)	5.83 (3.07)	Treatment as usual	53	9.49 (4.61)	8.66 (4.92)	-0.69 [-1.08, -0.29]	Participants in the CBT group showed significant improvement in anxiety, while no significant change in anxiety was observed for participants in the TAU condition.

BYI: Beck Youth Inventory; **CASI:** Childhood Anxiety Sensitivity Index; **CBT:** Cognitive Behavioural Therapy; **DASS:** Depression Anxiety Stress Scale; **f2f**: Face-to-face; **HADS:** Hospital Anxiety and Depression scale; **HRV:** Heart Rate Variability; **IQR:** Interquartile range; **MBSR** Mindfulness-Based Stress; **m-YPAS:** modified Yale Preoperative Anxiety Scale; Reduction; **NR:** Not reported; **SD:** Standard Deviation; **SDQ-P:** Strengths and Difficulties Questionnaire Parent; **STAI:** State-Trait Anxiety Inventory; **STAIC:** State-Trait Anxiety Inventory Child; **TAU:** treatment as usual; **TCBT:** Transdiagnostic cognitive behavioural therapy

The two studies with the largest sample sizes and a relatively low risk of bias were Sharma and colleagues (2017) and Zhang and colleagues (2019). Zhang and colleagues (2019) showed that 5 sessions of CBT in young people with cancer significantly improved symptoms of anxiety compared to treatment as usual (n=106 in the completers analysis). In Sharma et al. (2017) (n=63) a transdiagnostic CBT group intervention significantly improved symptoms of anxiety in young people with a headache disorder compared to treatment as usual.

Evidence for the effect of CBT on anxiety in children with a long term physical health condition and any comparator was investigated further by meta-analysing outcomes for three studies: Hains and colleagues (2000), Sharma and colleagues (2017) and Zhang and colleagues (2019). We did not include the study by Bennett and colleagues (2017), as the only mental health measure where participants had above threshold symptoms in both arms at baseline was the Strengths and Difficulties Questionnaire. Although the Strengths and Difficulties Questionnaire covers anxiety, it is a summary measure of emotional and behaviour symptoms and therefore was deemed too different from the DASS (anxiety) and STAI-state used in the included studies, which specifically measure symptoms of anxiety. A large effect size in favour of brief CBT was found ($g = - 0.95$, CI -1.49 to -.041; $p < 0.01$) with non-significant moderate-substantial heterogeneity ($I^2 = 58\%$; $p = 0.09$). The interventions included young people with three different long term physical health conditions: paediatric cancer, headache and type I diabetes and two different control groups (pharmacotherapy as part of treatment as usual for two studies and waitlist control for ones). The results of the meta-analysis are summarised in a forest plot (see Figure 4).

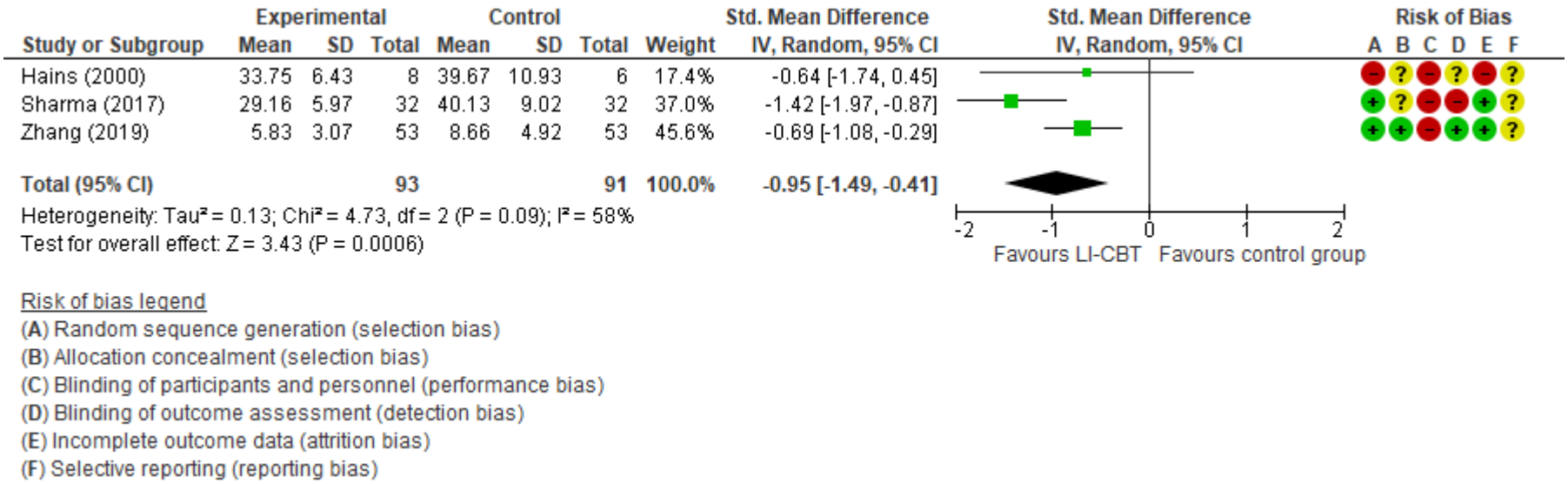

Figure 4. Forest plot of comparison: CBT vs any comparator, outcome: anxiety post-intervention

Mindfulness-based stress reduction interventions in one case showed no effect on anxiety or depression (Freedenberg et al., 2017) and in the other (Jastrowski Mano et al., 2013) considerable attrition meant effect sizes could not be calculated. Both biofeedback interventions found no significant between group difference on anxiety scores (Scharff et al., 2002; Yetwin, 2011). Massage therapy (Field et al., 1998), hypnosis (Liossi & Hatira, 1999) and music therapy (Bufalini, 2009) all reported significant differences between groups for anxiety scores. However, these studies had a higher risk of bias, small sample sizes and lacked replication for the particular intervention type. There was insufficient evidence to comment on whether brief interventions have an effect on physical health outcomes or quality of life. Similarly, a lack of evidence precluded conclusions on possible moderators of efficacy.

Table 3. Summary of physical health and other outcomes of included studies

	Other physical health outcomes	Other outcomes
Bennett (2017)	No significant between group difference in: ▪ Health-related quality of life (PedsQL)	The intervention had high acceptability: mean score 16.88 (SD:1.26) out of 18 on the evaluation of service questionnaire Significant reduction in mean total number of psychiatric diagnoses from 1.47 to 0.62 in completer's analysis, but not ITT No significant between group difference in: ▪ Subthreshold total anxiety and depression (RCADS)
Bufalini, et al. (2009)	Children in the intervention group were significantly more likely to be compliant with anaesthesia	The intervention had high acceptability: ▪ 80% of parents described it as very useful
Field et. al. (1998)	Significant improvement in younger age group's: ▪ All tested pulmonary function tests ▪ Child attitudes to asthma Significant improvement in older age group's: ▪ Forced expiratory flow only ▪ Child attitudes to asthma only	Significant reduction in cortisol limited to younger age group at post-treatment.
Hains et. al. (2000)	No significant between group difference in: ▪ Diabetes stress ▪ Metabolic control	No significant between group difference in: ▪ Coping score (negative, positive or behavioural)

Hickman et.al. **(2015)**	▪ Significant within, but not between group difference in self-reported reduction of headache-related disability ▪ Significant between group difference in self-reported increase in beliefs about teen's ability to lead a healthy lifestyle in intervention group but not in comparison group. ▪ No significant change in parent-reported reduction in parent perception of pain interference	The intervention had high acceptability: ▪ 94% rated the COPE-HEP intervention as helpful ▪ 100% of parents and adolescents would recommend the intervention to a friend ▪ 100% adolescents completed all 7 sessions, although at varying times
Freedenberg et.al. **(2017)**	Significant within, but not between group difference in illness-related stress Significant within, but not between, group differences in secondary coping	Predictors of increased reduction in anxiety/depression symptoms: ▪ Higher baseline levels of anxiety/depression respectively ▪ Greater use of coping of coping skills
Jastrowski et. al. **(2013)**	Due to very high attrition levels, statistical analyses could not be carried out and means (SD) were not reported.	Due to very high attrition levels, statistical analyses could not be carried out and means (SD) were not reported.
Liossi et. al. **(1998)**	Significant reduction in self-reported pain: ▪ Between Hypnosis and control ▪ Between CBT and control No significant difference between hypnosis and CBT for self-reported pain	No significant between group difference (CBT vs Hypnosis) in correlations between hypnotisability and clinical outcomes
Scharff et.al. **(1999)**	Significant between group difference in biofeedback groups compared to WLC in reduced: ▪ headache frequency ▪ headache index Within group gains maintained at 3- and 6- month follow-up. No significant between group difference in headache variables at 3- or 6- months follow-up between biofeedback groups	None.

Sharma et.al. (2017)	Significant within and between group difference in: ▪ Self-reported reduction of headache impact on daily life (in both groups from pre- to post-, but significantly greater for those receiving TCBT than for those in the TAU condition)	Significant within and between group difference in: ▪ Clinician-rated improvement in young person's global functioning (in both groups from pre- to post-, but significantly greater for those receiving TCBT than for those in the TAU condition)
Yetwin (2011)	Significant between group difference in: ▪ Self-reported reduction in pain intensity ▪ Self-reported reduction in 'current pain' (PPQ) ▪ Self-reported increase in school functioning (PedsQL) No significant between group difference in: ▪ Sleep quality ▪ Self-reported 'worst pain' (PPQ) ▪ Self-reported 'Total', 'physical', 'emotional' and 'social' functioning (PedsQL)	No significant between group difference in: ▪ Subthreshold depression
Zhang et.al. (2019)	None	Significant between group difference in: ▪ Reduction of subthreshold symptoms of low mood and stress ▪ Increase in psychological resilience

CBT: Cognitive Behavioural Therapy; **COPE-HEP:** Creating Opportunities for Personal Empowerment Headache Education Program; **ITT:** Intention-to-treat; **NR:** Not reported; **PEDSQL:** Paediatric Quality of Life Inventory; **PPQ:** Paediatric Pain Questionnaire; **RCADS:** Revised Children's Anxiety and Depression Scale; **SD:** Standard Deviation; **TAU:** treatment as usual; **TCBT:** Transdiagnostic cognitive behavioural therapy; **WLC:** Waitlist control;

Table 4. Summary of Findings table

Brief interventions compared to any comparator for psychiatric disorders in children with long term conditions

Patient or population: Children and adolescents with psychiatric disorders and long term conditions
Settings:
Intervention: brief therapy
Comparison: any comparator

Outcomes	Anticipated absolute effects (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Anxiety post-intervention: CBT vs any comparator		The mean anxiety post-intervention: cbt vs any comparator in the intervention groups was **0.95 standard deviations lower** (1.49 to 0.41 lower)	184 (3 studies)	⊕⊕⊕⊖ **moderate**[1,2,3]	SMD -0.95 (-1.49 to -0.41)
Anxiety post-intervention: MBSR vs any comparator	See comment	See comment	52 (2 studies)	⊕⊕⊖⊖ **low**[4]	No significant between group difference.
Anxiety post-intervention: Biofeedback vs any comparator	See comment	See comment	43 (2 studies)	⊕⊖⊖⊖ **very low**[2,5]	No significant between group difference.
Anxiety post-intervention: Other brief therapy (music therapy, massage therapy and hypnosis) vs any comparator	See comment	See comment	75 (3 studies)	⊕⊖⊖⊖ **very low**[1,2,6]	Significant reduction in anxiety in intervention groups.

CI: Confidence interval ; **SMD:** Standardised Mean Difference ; **MBSR:** Mindfulness-based stress reduction; **CBT:** Cognitive Behavioural Therapy

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.

[1] Unclear or high risk of bias in a number of domains
[2] Small sample sizes in included studies
[3] Large pooled effect size
[4] Very high attrition in one study.
[5] High or unclear risk of bias in most domains across studies.
[6] No replication of therapy type by independent group (e.g. only one study looking at massage therapy)

Discussion

Summary of main results

This review and meta-analysis provide preliminary evidence that brief interventions based on cognitive behavioural principles may benefit young people with a long term physical health conditions who also present with elevated symptoms of anxiety.

There was insufficient evidence to assess whether this held true for depression, disruptive behaviour/oppositional defiant disorder, other psychiatric disorders, health-related quality of life or physical health. Similarly there was insufficient evidence to establish possible moderators of treatment efficacy or acceptability.

Music therapy, hypnosis and massage therapy showed some promise, but studies looking at these interventions displayed high risk of bias, small sample sizes and lacked replication by independent research groups, so more research is needed in this area. However, we also recognise that it may be difficult to maintain low bias in all areas, particularly in blinding participants, for these types of intervention. At present there is insufficient evidence to recommend mindfulness-based stress reduction, biofeedback, hypnosis, music therapy or massage therapy as brief interventions for this population.

Limitations

The findings from the meta-analysis must be interpreted with caution due to high risk of bias in 6 domains across the three included studies, small number of included studies and sample sizes (pooled intervention arm: n = 93 and pooled comparator arm: n = 91) and differences in chronic conditions (cancer, headache and type 1 diabetes) and control groups (pharmacotherapy as part of treatment as usual for two studies and waitlist control for one).

One of the studies included in this review was conducted by four of the review authors (SB, AC, IH, RS; (Bennett, 2017), which may be a potential source of bias. However, data

extraction and risk of bias were conducted independently by two authors who had no involvement with the original study. Two of the included studies were unpublished and so did not undergo peer review. We could not formally assess publication bias due to the limited number of studies in the meta-analysis and as a result cannot exclude the possibility of publication bias. However, we did run pre-defined searches in a number of databases and searched grey literature to try and minimise the risk. It is possible that the search terms we selected biased the findings in favour of cognitive behavioural therapy. All studies used self-report measures for the outcomes of interest and were therefore at risk of 'halo effects' and other response biases.

Agreements and disagreements with other studies or reviews

In keeping with previous reviews in the area (Bennett et al., 2015; Moore et al., 2019; Thabrew et al., 2018; Thabrew et al., 2017) we found tentative evidence for CBT-based interventions. Our findings diverged from those found in a review by Thabrew and colleagues (2018) who conducted a subgroup analysis to establish the effects of 'brief' CBT for anxiety in young people with a long term physical health condition. In their meta-analysis a non-significant between group difference was found between brief psychological treatments (<6 hours or <6 sessions) versus any comparator at post-treatment. The difference is likely due to methodological differences in the reviews. For example, we only included studies in which symptoms of anxiety were elevated above a clinical cut-off on a validated measure. We also did not synthesise different types of psychological therapies in the same meta-analysis (e.g. CBT and family therapy). Moreover, we considered group treatment as brief (if it met our criteria of ≤10 sessions with ≤6 hours of therapist contact per patient). This for example, led to one study (Sharma et al., 2017), being classed as 'longer therapy' in Thabrew and colleagues (2018), but as 'brief' in our review. Future work should look towards obtaining a consensus as to what comprises a 'brief' intervention and how it applies to group treatment. Finally, we found an additional RCT published since their review: Zhang and colleagues (2019).

Compared to the evidence synthesis by Moore et.al. (2019) who found tentative evidence for CBT for depression, we only found one study using brief CBT, in which symptoms of depression were above threshold and it showed no between-group differences when correcting for baseline differences in depression (Hickman et al., 2015). The main reason for excluding many of the studies from our review were either to do with the interventions being high-intensity (e.g. several of the inflammatory bowel disease interventions) or due to the sample means being below threshold for a psychiatric disorder. Again, the main divergence here were to do with methodological differences and the scope of the reviews.

In keeping with a previous review by Bennett et. al (2015), study authors reported having to make allowances for young people and families living with long term physical health conditions; for example cancellations were common (Hickman et al., 2015). In certain studies, telephone therapy was used to make appointments more accessible (Bennett, 2017). Others reflected post-hoc that including more telephone sessions, might increase feasibility (Hickman et al., 2015).

Implications for practice and future research

The findings from this review suggest that brief CBT may be an effective way to increase access to treatment for elevated symptoms of anxiety in young people with a long term physical health condition. These could be delivered in a group or individual format. Brief CBT treatments for anxiety may form part of a 'stepped care approach' in existing paediatric services.

Trials of brief parenting interventions for disruptive behaviour and brief interventions for depression need to be carried out, as these have been shown to be effective in young people without a long term physical health condition (Bennett et al., 2019) and/or in a high-intensity format in children with a long term physical health condition (Moore et al., 2019). A

greater number of appropriately powered trials with mental health as the primary outcome are also required. This review focused on children that were above threshold for a mental health disorder, but there is an important public health impact of improving mental health in those with long term physical health conditions even if they are subthreshold, so additional syntheses of those studies would be useful. Larger, high quality trials targeting elevated anxiety symptoms need to replicate the preliminary findings in this review and include longer term follow-ups. As a number of evidence-based brief treatments for anxiety for children without a long term physical health condition already exist, these could be adapted and tested in future trials. Trials evaluating stepped care approaches for young people with a long term physical health condition need to be conducted to establish who benefits from brief therapy, who may need to be 'stepped up' and how services can best be organised to meet rising demands.

At a time when child and adolescent mental health services have been publicly described as "a car crash waiting to happen"(Doward, 2016), funding and research into brief CBT interventions may provide some of the increased access that is so urgently required.

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Tables

1. *Characteristics of included studies*
2. *Summary of mental health outcome measures of included studies*
3. *Summary of physical health and other outcomes of included studies*
4. *Summary of Findings table*

Figures

1. *PRISMA flow diagram of included studies in the review*
2. *Risk of bias summary: review authors' judgements about each risk of bias item for each included study*
3. *Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies*
4. *Forest plot of comparison: CBT vs any comparator, outcome: anxiety post-intervention*

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