Computerised therapies for anxiety and depression in children and young people: A systematic review and meta-analysis

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Abstract

One quarter of children and young people (CYP) experience anxiety and/or depression before adulthood, but treatment is sometimes unavailable or inadequate. Self-help interventions may have a role in augmenting treatment and this work aimed to systematically review the evidence for computerised anxiety and depression interventions in CYP aged 5-25 years old. Databases were searched for randomised controlled trials and 27 studies were identified. For young people (12-25 years) with risk of/diagnosed anxiety disorders or depression, computerised CBT (cCBT) had positive effects for symptoms of anxiety (SMD -0.77, 95% CI -1.45 to -0.09, k=6, N=220) and depression (SMD -0.62, 95% CI -1.13 to -0.11, k=7, N=279). In a general population study of young people, there were small positive effects for anxiety (SMD -0.15, 95% CI -0.26 to -0.03; N=1,273) and depression (SMD -0.15, 95% CI -0.26 to -0.03; N=1,280). There was uncertainty around the effectiveness of cCBT in children (5-11 years). Evidence for other computerised interventions was sparse and inconclusive. Computerised CBT has potential for treating and preventing anxiety and depression in clinical and general populations of young people. Further program development and research is required to extend its use and establish its benefit in children.

Keywords: Anxiety; Depression; Meta-analysis; Child psychology; Adolescent psychology; Internet-delivered cognitive behavior therapy

Introduction

One quarter of children and young people suffer anxiety disorders or depression by adulthood (Copeland, Shanahan, Costello, & Angold, 2011; Kessler, Avenevoli, & Ries Merikangas, 2001; Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1993). Around 3% of children have an anxiety disorder at any one time, but rates of depression are relatively low (<1%) (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Ford, Goodman, & Meltzer, 2003). In adolescence, rates of anxiety disorders remain similar and rates of depression rise to 3% (Costello et al., 2003; Ford et al., 2003; Lewinsohn et al., 1993), with cumulative prevalence of anxiety disorders and depression of around 10% and 25% respectively by 18 years (Lewinsohn et al., 1993; Merikangas, He, Burstein, et al., 2010). Both anxiety disorders and depression in children and young people are associated with significant adverse mental health and life course outcomes, with the onset of the majority of adult anxiety disorders and depression occurring in childhood or adolescence (Kim-Cohen et al., 2003; Pine, Cohen, Gurley, Brook, & Ma, 1998; Woodward & Fergusson, 2001). Collectively, these considerations highlight the significant public health burden of anxiety disorders and depression in children and young people, and the importance of access to effective treatment.

Guidelines that include children and young people recommend psychological interventions as a first line approach for anxiety disorders and depression (Connolly & Bernstein, 2007; NICE., 2005a, 2005b, 2005c). However, there is evidence that many children and young people with anxiety disorders and depression do not receive evidence-based treatment (Kataoka, Zhang, & Wells, 2002; Merikangas, He, Brody, et al., 2010; Stallard, Udwin, Goddard, & Hibbert, 2007; Wang et al., 2007). This may be due to a lack of symptom awareness, poor access to services or, where services are not provided, the cost of intervention. Where mental health services are delivered, these are commonly inadequate (Wang et al., 2007). In the case of Cognitive Behavioural Therapy (CBT), which is recommended for the treatment of both anxiety disorders and depression in children and young people (Connolly & Bernstein, 2007; NICE., 2005a, 2005b, 2005c), barriers to treatment include a lack of training, infrastructure and funding (Gunter & Whittal, 2010; Stallard et al., 2007).

It has been proposed that self-help strategies may relieve some of the burden on health care services (Jorm & Griffiths, 2006) and, with the increasing use of internet and computer technologies, the computerisation of psychological interventions appears a logical step to achieve the provision of cost-effective help to all. There is a relatively large amount of research showing the effectiveness of computerised therapy for anxiety and depression in adults (Andersson & Cuijpers, 2009; Andrews, Cuijpers, Craske, McEvoy, & Titov, 2010; Reger & Gahm, 2009). Children and young people have shown favourable attitudes towards these types of intervention (Stallard, Velleman, & Richardson, 2010), but systematic reviews of internet-based therapies in children and young people do not include recent research and cover a limited range of computerised therapies (Calear & Christensen, 2010; Richardson, Stallard, & Velleman, 2010). The current review aims to comprehensively review the evidence for all types of computerised therapy for anxiety and depression in children and young people.

Methods

Study selection

A systematic search for English language studies was conducted in the following databases from database inception to June 2013: Australian Education Index (AEI), Applied Social Sciences Index and Abstracts (ASSIA), British Education Index (BREI), British Humanities

Index (BHI), Education Resources in Curriculum (ERIC), Cochrane Central Database of Controlled Trials (CENTRAL) [Cochrane Library], Cumulative Index to Nursing and Allied Health Literature (CINAHL), Education Resources Information Center (ERIC), Embase, International Bibliography of Social Science (IBSS), Medline, PAIS International, PreMedline, PsycINFO, Social Services Abstracts (SSA) and Sociological Abstracts. Studies were identified using search terms for disorders of "anxiety or depression" appended to "computerised therapy" (see appendix 1 for details of the full list of search terms used). Reference lists of included studies and previous reviews were also searched for additional evidence. Citations were screened and hard copies of potentially relevant studies obtained.

Inclusion criteria

Randomised controlled trials of any computerised psychological therapies, for example, CBT, problem solving therapy and interpersonal psychotherapy, in children (5 to 11 years old) and young people (12 to 25 years old) (CYP) were included in the review. Computerised therapies could be delivered via the Internet, downloadable software, CD-ROMs or smartphone applications. Studies only including adults >25 years of age, or mixed populations where the mean age was >18 years, were excluded. Studies in CYP with diagnosed depression or an anxiety disorder, studies in at risk populations (with elevated depression or anxiety symptom scores) and studies of preventative interventions in general, non-clinical, populations were included. Studies of any computerised therapy were included, provided the majority of the intervention (>50%) was undertaken without the input of a therapist. Studies where a larger proportion of the intervention was delivered directly by a therapist (and not via a computer) were excluded from the review. Studies comparing an intervention with a non-therapeutic control (e.g. wait-list or no treatment) and studies comparing an intervention with another active intervention (e.g. face-to-face therapy), were included in the review. For the purposes of this review, we focused on outcomes that were a direct assessment of mental health and studies reporting only outcomes related to potential mechanisms of change (e.g. improvements in psychometric training tests) were not included.

Data extraction

Data extraction was conducted by one reviewer and checked by a second and any disagreements were resolved by consensus. Information on participant and study characteristics and mental health outcomes were extracted into an excel spreadsheet, previously piloted on typical studies. Study characteristics included the country, setting, inclusion and exclusion criteria, duration and components of the intervention and control conditions, numbers of participants randomised, rates of attrition and sources of funding. Participant characteristics included age, gender, primary disorder and co-morbidities and baseline severity score. Data for self- (primary outcome) and clinician- (secondary outcome) rated outcomes were extracted. Where studies were relevant but data could not be obtained from the publication, authors were contacted to obtain the data. For interventions aimed at treating anxiety, the critical outcome was symptoms of anxiety and, for interventions aimed at treating depression, the critical outcome was symptoms of depression. For interventions aimed at treating both anxiety and depression, symptoms of anxiety and depression were included.

Quality assessment

Risk of bias for each study was assessed with the Cochrane tool (Higgins & Green, 2011) by one reviewer and checked by a second and any disagreements were resolved by consensus. This tool assesses risk of bias in randomised controlled trials in domains relating to the allocation of participants to groups (selection bias), exposure to care or other factors in

addition to the intervention of interest (performance bias), independence of outcome assessment (detection bias) and the presence of loss to follow-up (attrition bias) and selective outcome reporting (reporting bias). The overall risk of bias was judged on the basis of whether any source of bias was likely to have had a significant impact on the findings (not simply on a count of the number of sources of bias). The overall quality of the evidence for each outcome was assessed using the GRADE approach (Guyatt, Oxman, Schunemann, Tugwell, & Knottnerus, 2011). Evidence was downgraded by one or two levels based on the following factors: a) risk of bias, b) inconsistency of results (heterogeneity between study effect sizes; defined as $I^2 > 50\%$), c) indirectness (poor applicability) of the population, intervention, control or outcomes (e.g. when the intervention involved significant therapist input), d) imprecision of results (judged to be poor when the number of participants was less than the optimum information size, conservatively assumed to be N=400) or e) suspected publication bias. In cases where risk of bias and indirectness were not considered severe enough to warrant downgrading for each, outcomes were downgraded once for the combination of weaknesses. After all factors had been considered, certainty in the effect estimates was categorised as: 1) 'high' (very certain that the true effect lies close to that of the estimate of the effect); 2) 'moderate' (moderately certain of the effect estimate and the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different); 3) 'low' (certainty of the effect estimate is limited and the true effect may be substantially different from the estimate of the effect); or 4) 'very low' (very little certainty of the effect estimate and the true effect is likely to be substantially different from the estimate of effect) (Balshem et al., 2011).

Data analysis

Data were entered into RevMan (The Cochrane Collaboration, 2012) and, where possible, random effects meta-analysis was conducted to summarise findings using the standardised mean difference (SMD). Where data were available, post-treatment means and standard deviations (SD) were compared. In the absence of means and SD, where p values for post-treatment comparisons were available, these were converted into SMD so that data could be combined in the meta-analysis. The I² statistic (Higgins & Thompson, 2002) was calculated to assess the degree of heterogeneity within meta-analyses and, where I² exceed 50%, formal investigation of heterogeneity was conducted. Studies of children (5-11 years) and young people (12-25 years) were considered separately in the analysis. Comparisons of interventions with non-therapeutic controls e.g. waiting list or no treatment, were grouped together in the analysis. Comparisons of computerised interventions with other therapeutic interventions were grouped separately.

For studies of computerised CBT (cCBT) in young people, subgroup analysis was conducted to try to explain the observed heterogeneity. Previous work has indicated that the degree of therapist input may be an important moderating factor in the effectiveness of computerised programs (Griffiths, Farrer, & Christensen, 2010) and this was therefore pre-specified as an a priori investigation of heterogeneity. Studies of cCBT for anxiety and depression were classified as 'low' (no contact with therapists for the majority of sessions), 'some' (indirect contact e.g. weekly emails or phone conversations) or 'high' (therapist was in attendance at the time of program use) therapist input and subgroup analysis was conducted to determine whether the degree of therapist input was a source of heterogeneity. Due to the large amount of unexplained heterogeneity remaining, a post hoc subgroup analysis was also conducted, to investigate the effect of age (studies of young people aged 12-18 versus 18-25 years) and severity (young people with only elevated symptom scores versus those with diagnosed disorders).

Results

Study selection

Of 9,330 citations obtained through the searches, 6,989 remained after removing duplicates and, on screening, 6,798 were excluded as there was sufficient information in the abstract to be certain that they were not relevant to the review. 195 were selected for hard-copy review. Of these, 168 were excluded because they did not meet the inclusion criteria (detailed above) for the intervention (N=89), population (N=42), study design (N=12) or outcomes (N=18), or because data could not be obtained from publications (N=7) (Figure 1). Twenty seven studies were included in the review (Table 1).

Study characteristics

cCBT

Fourteen studies investigated the efficacy of ten computerised cognitive behavioural therapy (cCBT) programs for anxiety disorders and/or depression. These programs implemented CBT through a variety of approaches, some using relatively straight-forward replications of CBT in a computerised format, and some using more dynamic, gaming-type, approaches. Two of these programs were for anxiety disorders in children: BRAVE for children-ONLINE (March, Spence, & Donovan, 2009) and Camp Cope-A-Lot (Khanna & Kendall, 2010) and both were evaluated in populations at high risk of, or diagnosed, anxiety disorder. Eight programs were for young people. Two of these programs were for anxiety disorders: BRAVE for teenagers-ONLINE (Spence et al., 2011) and Cool Teens (Wuthrich et al., 2012) and both were conducted with populations diagnosed with a range of anxiety disorders. Three programs were for depression: The Journey (Stasiak, Hatcher, Frampton, & Merry, 2014), SPARX (Fleming, Dixon, Frampton, & Merry, 2012; Merry et al., 2012) and Mood Helper (Clarke et al., 2009) and were conducted in populations at high risk of (Clarke et al., 2009; Fleming et al., 2012; Merry et al., 2012) or diagnosed with (Stasiak et al., 2014) depression. Two programs were for both anxiety disorders and depression: MoodGym (Calear, Christensen, Mackinnon, Griffiths, & O'Kearney, 2009; Ellis, Campbell, Sethi, & O'Dea, 2011; Sethi, 2013; Sethi, Campbell, & Ellis, 2010) and Think Feel Do (Stallard, Richardson, Velleman, & Attwood, 2011) and were conducted in a general population of young people (Calear et al., 2009) or populations at risk of depression or an anxiety disorder (Ellis et al., 2011; Sethi, 2013; Sethi et al., 2010). One program was specifically for young adults with a diagnosis of social anxiety disorder (unnamed) (Tillfors et al., 2011).

Of the two studies of cCBT in children, one was considered to have high therapist input (Khanna & Kendall, 2010) and the other was considered to have some therapist input (March et al., 2009). All studies of cCBT for anxiety in young people were considered to have some therapist input (Spence et al., 2011; Wuthrich et al., 2012). Of the studies of cCBT for depression in young people, all were considered to have low therapist input (Clarke et al., 2009; Fleming et al., 2012; Stasiak et al., 2014). For cCBT for both anxiety and depression in young people, in the general population study (Calear et al., 2009), there was low therapist input, but all studies in populations at risk of anxiety and depression were considered to have some therapist input (Ellis et al., 2011; Sethi, 2013; Sethi et al., 2010; Stallard et al., 2011).

Attention bias modification and cognitive bias modification of interpretations

Three studies were of attention bias modification (ABM). ABM is based on the principle that anxious individuals have a bias in attention towards threat stimuli and aims to alter this bias by training individuals to seek positive stimuli out of groups of negative stimuli. In all three studies, this was done using the Dot Probe Task, where individuals were trained to attend to non-threatening faces presented alongside threatening faces. One study was in young people

at risk of social anxiety (Li, Tan, Qian, & Liu, 2008), and the remaining two were in children at risk of (Bar-Haim, Morag, & Glickman, 2011) or diagnosed with (Waters, Pittaway, Mogg, Bradley, & Pine, 2013) anxiety disorders in general. Five studies were of cognitive bias modification of interpretations (CBM-I). These studies used sentence completion tasks to modify bias in interpretation of ambiguous information (participants added words into gaps in sentences in a way that made them positive interpretations in order to proceed to the next sentence). One CBM-I study was in young people with anxiety disorders (Fu, Du, Au, & Lau, 2013), one in an unselected general population of young people (Salemink & Wiers, 2011), one in young people with diagnosed depression (Micco, Henin, & Hirshfeld-Becker, 2013), one in young people at risk of developing OCD (Clerkin & Teachman, 2011) and one in young people with spider phobia (Teachman & Addison, 2008). One study was of combined ABM and CBM-I in young people with social and/or test anxiety (Sportel, de Hullu, de Jong, & Nauta, 2013).

Other computerised interventions

One study was of computerised problem solving therapy (cPST) in young people at risk of anxiety and depression (Hoek, Schuurmans, Koot, & Cuijpers, 2012), where participants completed exercises, such as devising problem-solving strategies and developing plans for future solutions. One study was of a mobile phone application in young people with psychological distress (Kauer et al., 2012), where participants were prompted to enter data on mood, life events and lifestyle. Data was reported and later reviewed with their GP. One study was of computerised exposure for spider phobia in children and young people (Muris, Merckelbach, Holdrinet, & Sijsenaar, 1998), where participants were presented with spiders ranging from low- to high-fear potential on a computer screen. One study was of a CBT website for adolescents at risk of PTSD, where cognitive and resiliency theory-based information and exercises were provided to normalise and promote recovery (Cox, Kenardy, & Hendrikz, 2010).

Evidence quality

Based on the GRADE approach, confidence in the evidence for each outcome is shown in Table 2 (outcomes compared to non-therapeutic control) and Table 3 (outcomes compared to an active intervention). Some cCBT studies were associated with risk of bias, frequently due to a lack of participant and outcome assessor blinding. Some studies used a waitlist control group and/or had additional therapist input alongside the program and these aspects were considered to introduce indirectness. In the overall assessment of evidence quality, most outcomes were downgraded for sub-optimal sample size, risk of bias or indirectness, or a combination of these. In some cases, there was important heterogeneity in the meta-analysis and these outcomes were also downgraded for inconsistency.

Outcomes

The effect sizes for the self- and, where reported, clinician-rated outcomes for each intervention are shown in Table 2 and Table 3.

Anxiety

In the two trials of cCBT in children with diagnosed anxiety disorders, there was a favourable effect on anxiety for cCBT compared with a non-therapeutic control (computer-assisted education, support and attention program or waitlist) when rated by clinicians, but was inconclusive when self-rated (Table 2, Figure 2). Only one of these trials compared cCBT to face-to-face CBT, and interventions had similar effects on self- and clinician-rated anxiety severity (Table 3, Figure 3). Confidence in the evidence for all these comparisons was low.

In the six trials of young people diagnosed with anxiety disorders or with elevated anxiety scores, the evidence favoured cCBT when compared to a non-therapeutic control (waitlist or no treatment) for self-rated anxiety (Table 2, Figure 2), but confidence in the evidence was low. Two of the studies, reported clinician-rated severity and evidence favoured cCBT compared to the waitlist control (Table 3, Figure 3). When compared to face-to-face CBT, cCBT had similar effects in three trials on self-rated anxiety and, in one trial, on clinician-rated anxiety (Table 3, figure 3), but confidence in the evidence for these comparisons was low.

In a general population study of young people, cCBT gave a small improvement in self-rated anxiety compared to the waitlist control (Table 2, Figure 4) and confidence in the evidence was moderate.

Comparisons of ABM, CBM-I, cPST and a mobile phone application with non-therapeutic controls generally showed inconclusive findings (Figure 2). In one trial that reported clinician-rated severity scores, anxiety improved following ABM compared with control (Table 2), but confidence in the evidence was low.

Depression

In the seven trials of young people with depression or with elevated depression scores, cCBT improved self-rated depression compared with non-therapeutic controls (waitlist, no treatment, treatment as usual or computerised attention program) (Table 2, Figure 5). In two of these trials, depression severity was also assessed by clinicians and showed a large effect in favour of cCBT, but the finding was inconclusive (Table 2). Confidence in the evidence was low for both outcomes.

In two trials, cCBT was compared with face-to-face CBT and the effect favoured face-to-face therapy for self-rated symptoms of depression (Table 3, Figure 3). In one trial, cCBT was compared with face-to-face counselling and interventions had similar effects on self- and clinician-rated depression severity (Table 3, Figure 3). Again, confidence in the evidence was low.

In a general population study of young people, cCBT gave a small improvement in self-rated depression symptoms compared to the waitlist control (Table 2, Figure 4) and confidence in the evidence was moderate.

In single studies of CBM-I, cPST and the mobile phone application, the evidence suggested little difference on self-rated depression compared with non-therapeutic controls (Table 2, Figure 5), but the estimates were imprecise and confidence in the evidence was low.

Social anxiety

Studies of computerised interventions for social anxiety generally showed inconclusive findings (Table 2, Figure 6). In one trial of cCBT for social anxiety compared to a waitlist control in young people, self-rated social anxiety symptoms were improved, but confidence in the evidence was low.

Phobia, OCD and PTSD

No interventions for phobia, OCD or PTSD showed benefits compared with non-therapeutic controls (Table 2, Figure 7) or equivalence with active interventions (Table 3, Figure 3), but estimates were imprecise and confidence in the evidence for some comparisons was very low.

cCBT for anxiety or depression in young people subgroup analysis

To explore the heterogeneity observed in studies of cCBT for young people, studies were subgrouped according to the degree of therapist input (a priori investigation) and participant severity and age (post-hoc investigations).

All studies of cCBT for anxiety in young people were classed as having some therapist input and therefore none of the observed heterogeneity could be explained by this factor. Three studies of cCBT for depression in young people were classed as having low therapist input and four were classed as having some therapist input, but there was no conclusive difference between subgroups (I^2 for subgroup differences=0%). Heterogeneity remained in both the low therapist input (SMD -0.39, 95% CI -0.86 to -0.08, k=3, N=173, I^2 =48%) and some therapist input (SMD -0.78, 95% CI -1.70 to 0.14, k=4, N=106, I^2 =78%) subgroups, suggesting that there were other important sources of heterogeneity.

In the studies of cCBT for anxiety, there were significantly greater effects (p=0.005) for the three studies (N=91) in young people with only elevated symptom scores (SMD -1.43, 95% CI -2.05 to -0.80) compared with the three studies (N=129) of young people with diagnosed anxiety disorders, in whom the effect of the intervention was not significant (SMD -0.20, 95% CI -0.78 to 0.38). However, for studies of cCBT for depression, although there was a trend towards an increased effect in undiagnosed populations, there was no significant difference between subgroups (p=0.21).

In studies of cCBT for anxiety, a moderating effect was also observed for age, where intervention effect was greater in studies in young people aged 18-25 years compared to those in young people aged 12-17 years (p for subgroup differences=0.005). However, these were the same subgroups of studies as for severity. There was no moderating effect observed when studies of cCBT for depression were subgrouped by age (p for subgroup differences=0.81).

Iatrogenic effects

Iatrogenic effects were not reported by the included studies except for one cCBT study (Merry et al., 2012), where it was report that there were no differences in possible intervention-related adverse effects between intervention and control groups.

Discussion

The review highlighted the potential benefit of cCBT programs for treating anxiety and depression in young people. Anxiety and depression were improved with medium effect sizes in mild to moderately anxious or depressed populations and also with small effect sizes in general populations, indicating potential public health as well as treatment benefits for these types of programs. cCBT for social anxiety disorder in young people showed some indication of being effective but data came from one small study and further research would be needed to confirm this finding. For cCBT programs for anxiety disorders in children, there were less data and the evidence was weaker than for cCBT in young people.

There was limited evidence for other (non cCBT) interventions. Although attention bias modification and cognitive bias modification of interpretations have been shown to improve outcomes of attention and interpretation bias (Beard, Sawyer, & Hofmann, 2012; Lau, 2013), no conclusive benefits were observed for direct measurements of anxiety or depression in the studies reviewed. The duration of training in some trials was short (single session) and the volume of evidence for any single indication was low. No other computerised therapy interventions for depression or anxiety disorders appeared to show much promise, largely because the evidence is lacking. As such, the true benefit of the interventions identified (computerised problem solving therapy, mobile phone self-monitoring, computerised exposure and a CBT website) cannot currently be determined.

Comparison with previous reviews

Our findings for cCBT are consistent with other, more general, systematic reviews of psychological interventions where potential benefit has been shown for the prevention of depression (Merry et al., 2011) and treatment of anxiety (James, James, Cowdrey, Soler, & Choke, 2013) in CYP. Neither of these reviews sub-grouped children and young people separately but James and colleagues, using meta-regression, found that age explained little heterogeneity between studies of CBT in CYP. This suggests that, in general, CBT may be as effective for children as for young people. This finding differs from findings in the current review, where no strong evidence for cCBT in children was found. However, there were only a small number of studies in the current review and so the effectiveness of cCBT in children could not be discounted.

The review by Merry et al. (2011) grouped prevention studies as 'targeted' or 'universal'. Targeted interventions included both selective programmes (those that focus on populations with a risk factor for disorder) and indicated programmes (those that focus on populations with symptoms or signs suggestive of incipient disorder). Universal interventions were those in general, unselected, populations of CYP. The results suggested that both targeted and universal interventions may have benefits, consistent with the current review.

Merry and colleagues also raised the issue of whether studies may have involved secondary prevention (i.e. prevention of future disturbance among children or young people with a history of anxiety or depression). As noted by Merry et al., studies did not typically include assessments of participants' past history and it was not possible to specifically explore the role of CBT in secondary prevention. Similarly, in the present review, it was not possible to explore this empirically because past history was not typically reported.

There have been two other reviews of computerised cCBT for anxiety and depression in CYP, both published in 2010 (Calear & Christensen, 2010; Richardson et al., 2010). Almost all of the current evidence has been published since this date and, with the limited robust data available, the reviews concluded that cCBT appears to be acceptable and effective in CYP but that further rigorous research was needed. Some of this research has now been done and the current review may allow a more optimistic view of the potential of cCBT for treating and preventing anxiety and depression in young people.

Limitations

Despite these encouraging findings, there are several limitations. This review was not able to determine the long-term impact of these types of interventions. Only four cCBT studies in young people reported longer term follow-up (past the end of treatment), the longest being 12 months post-treatment (Spence et al., 2011). Although one small study showed no advantage of cCBT at follow-up (Stasiak et al., 2014), one large study did show sustained effects in a general population compared to a waitlist control (Calear et al., 2009) and two studies showed similar effects at follow-up compared to counselling (Merry et al., 2012) and face-to-face CBT (Spence et al., 2011). Further research on the-long term effects of programs would help to establish their sustained effect.

Some caution is also needed in discerning the likely magnitude of effects due to the predominantly low quality of the evidence and important heterogeneity associated with a number of outcomes

Moderators of effectiveness

Sub-group analysis was conducted to investigate sources of heterogeneity. Severity of disorder has been shown to moderate the effectiveness of psychological treatments in CYP,

with reduced efficacy in clinically diagnosed populations compared to populations where not all participants were diagnosed (Weisz et al., 2013). Age may also potentially be a moderating factor, and the current review included a broad age range of young people (12-25 years). Therefore, post-hoc analysis was conducted to investigate severity of condition (all diagnosed versus not all diagnosed) and age (12-17 versus 18-25 years) as moderating factors in studies of cCBT in young people.

Significant subgroup differences were found when studies of anxiety were separated by age (greater effect in 18-25 compared to 12-17 year olds) and severity (greater effect in young people with elevated symptom scores compared to diagnosed anxiety) but no differences were observed for studies of depression. This post-hoc analysis contained a small number of studies and the anxiety subgroups contained the same groups of studies for both age and severity. Conclusions about moderating factors cannot therefore be drawn from this work but future research, examining the impact of patient severity and age, is likely to be important in determining the specific populations in whom cCBT is most effective.

Additionally, intervention-related factors, such as duration of intervention and the amount of help/guidance given to participants, are also likely to be important. Many of the interventions were not purely 'self-help and included input from therapists during the intervention. This often involved weekly phone conversations or emails but, in some cases, input was even greater, with therapists being present for the duration of the computerised therapy. cCBT studies in children tended to have a high degree of therapist input. For cCBT in young people, all anxiety treatment studies had some degree of therapist input and there was therapist input in around half of depression treatment studies. To examine the impact of therapist input on treatment effectiveness, this variable was pre-specified as a potential moderator and investigated in a subgroup analysis of studies of cCBT in young people. Because all anxiety studies were classed as having some therapist input, only the depression studies could be included in the subgroup analysis. For these, there was no significant difference between 'minimal' and 'some' therapist input studies. However, the number of studies was small and therapist input may still be an important intervention component, as previously observed in a larger meta-analysis of computerised interventions for depression in adults and children (Richards & Richardson). For cCBT in children, additional parental input may be a valuable tool. A number of parent-implemented bibliotherapy/face-to-face programs have been shown to be effective in children (Cobham, 2012; Lyneham & Rapee, 2006; Thirlwall et al., 2013), and the translation of these types of interventions into computerised formats may bring beneficial computerised treatment. However, the evidence for these types of treatment is limited and further research is required to develop, and determine the effectiveness of, computerised parent-focussed interventions for childhood anxiety disorders.

Future product development

The design and content of the cCBT program itself is likely to be important in determining its effectiveness. It is important that cCBT products are interactive, engaging and up-to-date with current technology, and give young people autonomy (NCCMH, 2014) and individualisation of therapy (Knowles et al., 2014). For the further development of computerised therapies for children and young people, specialist technical input is likely to be needed for products to meet the expressed needs of this group. This is a rapidly changing field, with continuous updates in software products, hardware and smart phone technology. Online or computer-based therapies will need specialist input in designing the structure, function and form of software, alongside specialist psychological input for the content of programs. Attention should be given to identifying evidence-based components which can be effectively combined as part of an intervention package, where the principles governing

models of combinations of e-modules are also evidence based (Weisz et al., 2012). Further, independent, high quality evaluation is needed to assess whether products improve outcomes in practice in clinical, non-clinical and general populations. Despite these uncertainties, a conservative conclusion may be that there are likely to be small to medium sized benefits for the treatment of diagnosed or at risk young people and small benefits for general populations of young people, at least in the shorter-term and possibly long-term. The evidence for cCBT compared to face-to-face therapies is limited and the current data does not provide sufficient evidence to support the use of cCBT as a replacement to face-to-face CBT. However, it provides the potential to improve access to CBT, where face-to-face therapy is not available or delayed.

Conclusion

In conclusion, computerised CBT shows promise as an effective intervention for anxiety and depression in young people. The magnitude of effect is uncertain but this review highlights the potential for computerised CBT programs to treat young people with anxiety and depression, both as a part of broader conventional therapeutic programme and as a possible public health intervention for the large numbers of young people with mental health problems who do not access mental health support. Further product development, in line with current technologies and the preferences of young people, gives opportunities to bring improvements in anxiety and depression to clinical and general populations. Evidence is weaker for cCBT in children but there are opportunities for further research and development of child and parent-focussed interventions that may provide effective computerised treatments for children too. The evidence for other interventions is sparse and inconclusive, highlighting the need for increased and ongoing evaluation of computerised therapies.

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Table 1 Study characteristics

Study		Populati	ion		Intervention			Comparato	ors		Assessmen	t (weeks)
_	N	Mean age (SD), range	Diagnosis	% Male	Туре	n	Components	Type	n	Components	Post- treatment	Follow- up
Compute	erised cog	gnitive beh	avioural therap	y in chil	dren							
Khanna et al. (2010)	RCT (49)	10.1 (1.6), 7-13	Diagnosed anxiety disorder	67	cCBT program for anxiety (Camp Cope-A-Lot)	16	Text, animation with cartoon characters, photographs, videos and rewards. Twelve weekly 35 minute sessions. First 6 sessions completed independently. Final 6 sessions completed with the help of a therapist. Parents	Computer control	16 17	Computer-assisted education, support and attention. Twelve weekly 50 minute sessions	12	13
							received two sessions with therapist	face CBT	17	minute sessions		
March et al. (2009)	al. (73) (009) 7		Anxiety diagnosis and 'clinical'or 'at risk' symptoms of anxiety (ADIS-C/P ≥4)	45	cCBT program for anxiety (BRAVE for Children- ONLINE)	30	Consecutive web pages with reading, exercises, games, quizzes and homework. Children: Ten weekly 60 minute sessions. Parents: Six weekly 60 minute sessions. Therapists gave homework feedback and two phone calls to parents and children	Waitlist control	29	No additional treatment	10	26
Compute			avioural therap		<u> </u>							
Spence et al. (2011)	RCT (115)	14.0 (1.6), 12-18	Diagnosed anxiety disorder	41	cCBT for anxiety (BRAVE for	44	Adolescents: Ten weekly 60 minute sessions. Booster sessions at 1 and 3 months after	Waitlist control	27	No additional treatment	12	52
					Teenagers-ONLINE)		treatment. Parents: Five 60 minute sessions. Email feedback on homework and phone calls from therapist	Face-to- face CBT	44	Adolescents: Ten weekly 60 minute sessions, booster sessions at 1 and 3 months after treatment Parents: Five 60 minute sessions		

Study		Populati	ion		Intervention			Comparato	rs		Assessmer	nt (weeks)
-	N	Mean age (SD), range	Diagnosis	% Male	Туре	n	Components	Type	n	Components	Post- treatment	Follow- up
Wuthri ch et al. (2012)	RCT (43)	15.2 (1.1), 14-17	Diagnosed anxiety disorder	37	cCBT for anxiety (Cool Teens, CD-ROM)	24	Eight 30 minute sessions over 12 weeks. Parents received information booklet. Phone calls to adolescents and parents throughout from a dedicated therapist	Waitlist control	19	No additional treatment	12	None
Stasiak et al. (2014)	RCT (34)	15.2 (1.5), 13-18	≥30 on CDRS-R or ≥76 on RADS-2	59	cCBT program for depression (The Journey)	17	Interactive fantasy adventure game. Seven modules conducted over 4-10 weeks. No therapist input except in cases where participant requested counselling	Computer control	17	Program with psycho-educational content	10	4
Merry et al. (2012)	RCT (187)	15.6 (1.6), 12-19	10-19 on the PHQ-9 or troubling symptoms of depression		cCBT program for depression (SPARX)	94	Interactive fantasy game. Seven modules completed over 4-7 weeks	Treatment as usual	93	Most commonly face-to-face therapy	7	13
Flemin g et al. (2012)	RCT (32)	14.9 (0.8), 12-16	CDRS-R score >30	56	cCBT program for depression (SPARX)	19	Interactive fantasy game. Seven modules completed over 5 weeks at education sites. Sites visited or phoned weekly by therapist	Waitlist control	11	No additional treatment	5	None
Clarke et al. (2009)	RCT (160)	22.6 (2.5), 18-24	Diagnosed depression or at risk of depression (elevated health care utilization)		cCBT program for depression (MoodHelpe r)	83	Information pages, depression monitor, diary, counter-thought generator, behaviour therapy tutorials with automated feedback. Used cCBT program as frequently as wished	Treatment as usual	77	No additional treatment	5, 10, 16 and 32	None

Study		Population	on		Intervention			Comparato	rs		Assessmen	t (weeks)
-	N	Mean age (SD), range	Diagnosis	% Male	Туре	n	Components	Type	n	Components	Post- treatment	Follow- up
Sethi et al. (2010)	RCT (38)	19.5 (1.6), 18-23	Mild/ moderate anxiety or depression	34	cCBT program for anxiety and depression	9	Reading, demonstrations, quizzes and homework. Five modules. Five 45 minute sessions over 3 weeks.	No treatment	10	No additional treatment	3	None
			(DASS-21: 10-20 for depression,		(MoodGym)		First session guided by therapist, available to help if needed in subsequent sessions	Face-to face CBT	9	Five 45 minute sessions over 3 weeks		
			8-14 for anxiety)					Combined face-to-face and cCBT	10	Five 45 minute sessions over 3 weeks		
Ellis et al.	RCT (39)	19.7 (1.7),	Low/ moderate	23	cCBT program for	13	Reading, demonstrations, quizzes and homework. Five	No treatment	13	No additional treatment	3	None
(2011)		18-25	psychologi cal distress (identified with K10)		anxiety and depression (MoodGym)		modules completed in 3 60 minute sessions over 3 weeks. Researcher present in all sessions	Mood Garden	13	Online peer support group		
Sethi et al. (2013)	RCT (89)	20.2 (1.29), 18-25	Mild/ moderate anxiety or	33	cCBT program for anxiety and	23	Reading, demonstrations, quizzes and homework. Five modules completed in 5 60	Waitlist control	23	No additional treatment	5	None
` '			depression (DASS-21: 10-20 for depression, 8-14 for anxiety)		depression (MoodGym)		minute sessions over 5 weeks. Researcher present in all sessions	Face-to face CBT	21	Five 60 minute sessions over 5 weeks		
Calear et al. (2009)	RCT (1,477)	14.3 (0.8), 12-17	None, general school population	44	cCBT for anxiety and depression (MoodGym)	563	Reading, demonstrations, quizzes and homework. Five modules completed in 5 45 minute sessions over 5 weeks. Teacher present to help with technical issues and monitor the class	Waitlist control	914	No additional treatment	5	26

Study		Populati	ion		Intervention			Comparato	ors		Assessmen	t (weeks)
	N	Mean age (SD), range	Diagnosis	% Male	Type	n	Components	Type	n	Components	Post- treatment	Follow up
Stallard et al. (2011)	RCT (20)	NR (NR), 11-17	Anxiety disorder or mild/ moderate depression	67	cCBT program for anxiety and depression (Think, Feel, Do)	6	Six 30-45 minute sessions over six weeks, commonly in participant's homes. Each session facilitated by a psychology assistant, teacher or nurse	Waitlist control	9	No additional treatment	6 (waitlist control 4)	None
Tillfors et al. (2011)	RCT (19)	16.5 (1.6), 15-21	Diagnosis of social anxiety	11	cCBT program for social anxiety	9	Information pages and homework of essay questions and quizzes. Nine weekly sessions. Therapists reviewed homework and gave email feedback	Waitlist control	9	No additional treatment	9	None
Bar- Haim et al. (2011)	RCT (35)	10.1 (0.5), NR	High anxiety (top 50% of sample distributio n on SCARED)	42	ABM Dot probe task with face stimuli	18	Four 60 minute sessions over 2 weeks	Neutral training	16	Four 60 minute sessions over 2 weeks	2	None
Waters et al. (2013)	RCT (37)	9.6 (1.3), 7-13	Clinically anxious (ADIS-C/P ≥4)	38	ABM Dot probe task with face stimuli	18	Four sessions a week for 3 weeks	Attention training	19	Four sessions a week for 3 weeks	3	None
Li et al. (2008)	RCT (24)	NR (NR), 18-22	Social anxiety (27% with highest scores on SIAS)	58	ABM Dot probe task with face stimuli	12	One 20 minute session per day for 1 week	Neutral training	12	One 20 minute session per day for 1 week	1	None

Study		Populat	ion		Intervention			Comparato	rs		Assessmen	t (weeks)
·	N	Mean age (SD), range	Diagnosis	% Male	Туре	n	Components	Type	n	Components	Post- treatment	Follow- up
Sportel et al. (2013)	RCT (240)	14.1 (0.7), 12-15	Social and/or test anxiety (RCADS: girls >10, boys >9; TAI: girls >43, boys >38)	28	ABM dot probe tasks and CBM-I Word fragment completion	86	Two sessions per week for 10 weeks	No treatment Group CBT	70	No additional treatment Therapist-delivered, 3-10 per group. One 1.5 hour session per week for 10 weeks	12	26 and 52
Fu et al. (2013)	RCT (28)	14.5 (1.8), 12-17	Anxiety disorder (Chinese version of SCARED >23)	46	CBM-I Word fragment completion	16	Single session. Positive completion tasks	Neutral training	12	Single session. Positive and negative completion tasks	Post- session	None
Salemi nk et al. (2011)	RCT (170)	14.5 (0.5), 14-16	General population	46	CBM-I Word fragment completion	73	Single session, 45 minutes. Positive completion tasks	Neutral training	75	Single session. Positive and negative completion tasks	Post- session	None
Teach man et al. (2008)	RCT (61)	18.6 (0.9), NR	Very high spider fear (Fear Survey Schedule- III ≥5)	26	CBM-I Word fragment completion	20	Single session, 40 minutes. Positive completion tasks	Neutral training No training	21 20	Single session. Positive and negative completion tasks. No additional treatment	Post- session	None
Clerkin et al. (2011)	RCT (100)	18.8 (1.0), NR	High in OCD symptoms (>28 on the OCI-R)	45	CBM-I Word fragment completion	50	Single session. Positive completion tasks	Neutral training	50	Single session. Positive and negative completion tasks	Post- session	None

Study		Populat	ion		Intervention			Comparato	rs		Assessmen	t (weeks)
	N	Mean age (SD), range	Diagnosis	% Male	Type	n	Components	Type	n	Components	Post- treatment	Follow- up
Micco et al. (2013)	RCT (45)	18.3 (1.9), 14-21	BDI-II ≥ 14	27	CBM-I Word fragment completion	23	Four 30 minute sessions over the course of 2 weeks. Positive completion tasks	Neutral training	22	Four 30 minute sessions over the course of 2 weeks. Neutral filler scenarios	2	2
			ing therapy									
Hoek et al. (2012)	RCT (45)	16.1 (2.3), 12-21	Mild/ moderate anxiety or depression (CES-D >40, HADS-A >14)	24	Computerise d problem solving therapy	22	One lesson per week for 5 weeks	Waitlist control	23	No additional treatment	5	12
Mobile p		f-monitori										
Kauer et al. (2012)	RCT (118)	18.0 (3.2), 14-24	Mild or moderate mental health difficulties (K10>16)	30	Self- monitoring with mobile phone	50	Recording of mood and related behaviours over 2-4 weeks	Non- therapeutic mobile phone use	33	Recording of non- emotional factors over 2-4 weeks	2-4	6
Compute	rised exp	osure	,									
Muris et al. (1998)	RCT (26)	12.6 (2.5), 8-17	Diagnosis of spider phobia rated by	0	Computerise d exposure to spiders	8	2.5 hour single session	In vivo spider exposure	9	2.5 hour single session	Post- session	None
			the DISC-R					EMDR	9	2.5 hour single session		
CBT wel			-		-	-		-			-	
Cox et al. (2010)	RCT (85)	10.9 (2.2), 7-16	Hospitalise d overnight following an	69	Cognitive and resiliency theory-based	29	Participants could access the website as often as they wished Parents sent an information booklet	No treatment	27	No additional treatment	4-6	22-24

Study		Populat	ion		Intervention	l		Comparat	ors		Assessment	t (weeks)
	N	Mean age (SD), range	Diagnosis	% Male	Type	n	Components	Type	n	Components	Post- treatment	Follow- up
			unintention al injury		website							

Note. ABM=Attention bias modification; ADIS-C/P=Anxiety Disorders Interview Schedule for DSM-IV: Child and Parent Version; BDI=Beck Depression Inventory; CBM-I=Cognitive bias modification of interpretations; cCBT=Computerised cognitive behavioural therapy; CDRS-R=Children's Depression Rating Scale-Revised; Depression CES-D=Centre for Epidemiologic Studies Depression Rating Scale; DASS-21=Depression Anxiety Stress Scale-21; DSM=Diagnostic and Statistical Manual of Mental Disorders; EMDR=Eye movement desensitisation and reprocessing; HADS-A=Hospital Anxiety and Depression Scale; K10=Kessler Psychological Distress Scale; N=Number of participants randomised; n=Number of participants in the analysis for intervention or control group; NR=Not reported; OCD=Obsessive compulsive disorder; OCI-R=Obsessive compulsive inventory – revised; PHQ-9=Patient Health Questionnaire depression scale; RADS-2=Reynolds' Adolescent Depression Scale-2nd Edition; RCADS=Revised Children's Anxiety and Depression Scale; SCARED=Screen for Child Anxiety Related Emotional Disorders; SIAS=Social Interaction Anxiety Scale; TAI=Test Anxiety Inventory.

Table 2 Evidence summary for interventions versus non-therapeutic control

Intervention	Study	Reason for downgrading	GRADE evidence quality	Se	lf-rated	l outcome		Cli	nician	-rated outcome	_
				k	N	SMD (95% CI)	I^2	k	N	SMD (95% CI)	I^2
cCBT for anxiety in children	Khanna 2010 March 2009	Insufficient sample size, indirect intervention (high therapist input)	Low	2	91	-0.20 (-0.62, 0.21)	0%	2	91	-0.75, (-1.27, -0.24)	26%
cCBT for anxiety in young people	Ellis 2011 Sethi 2010 Sethi 2013 Spence 2011 Stallard 2011 Wuthrich 2012	Insufficient sample size, indirect intervention (therapist input in all studies), important inconsistency ¹	Low	6	220	-0.77 (-1.45, -0.09)	81%	2	114	-1.09 (-1.49, -0.68)	0%
cCBT for anxiety in young people (general population)	Calear 2009	Indirect comparator (waitlist control)	Moderate	1	1,273	-0.15 (-0.26, -0.03)	N\A				
cCBT for depression in young people	Clarke 2009 Ellis 2011 Fleming 2012 Sethi 2010 Sethi 2013 Stallard 2011 Stasiak 2014	Insufficient sample size, important inconsistency	Low	7	279	-0.62 (-1.13, -0.11)	73%	2	64	-1.29 (-2.87, 0.29)	86%
cCBT for depression in young people (general	Calear 2009	Cluster randomised study with waitlist control	Moderate	1	1,280	-0.15 (-0.26, -0.03)	N/A				

population)											
cCBT for social anxiety in young people	Tillfors 2011	Insufficient sample size, indirect intervention (some therapist input) and comparator (waitlist control)	Low	1	18	-1.22 (-2.25, -0.19)	N/A				
ABM for mixed anxiety disorders in children	Bar-Haim 2011 Waters 2013	Insufficient sample size	Moderate	2	68	-0.19 (-0.69, 0.32)	9%	1	34	-0.95 (-1.66, -0.23)	N/A
ABM for social anxiety in young people	Li 2008	Insufficient sample size	Low	1	24	-0.26 (-1.06, 0.54)	N/A				
ABM/CBM-I for social or test anxiety in young people	Sportel 2013	Insufficient sample size	Moderate	1	156	-0.05 (-0.36, 0.27)	N/A				
CBM-I for anxiety in young people	Fu 2013 Salemink 2011	Insufficient sample size	Moderate	2	176	0.17 (-0.13, 0.46)	0%				
CBM-I for depression in young people	Micco 2013	Insufficient sample size	Low	1	45	-0.10 (-0.69, 0.48)	N/A				
CBM-I for phobia in young people	Teachman 2008	Insufficient sample size	Low	1	40	-0.14 (-0.76, 0.48)	N/A				
CBM-I for OCD in young people	Clerkin 2011	Insufficient sample size, indirect intervention (immediate	Low	1	100	-0.23 (-0.63, 0.16)	N/A				

		assessment after single treatment)									
cPST in adolescents	Hoek 2012	Insufficient sample size, ROB (high	Low	1	45	Anxiety: 0.12 (-0.46, 0.71)	N/A	_			
and young people		attrition), indirect comparator (waitlist control)				Depression: -0.04 (-0.63, 0.54)					
Mobile phone application for	Kauer 2012	Insufficient sample size, ROB (potential	Low	1	83	Anxiety: 0.08 (-0.36, 0.52)	N/A	_			
young people		assessment bias)				Depression: 0.11 (-0.33, 0.55)	N/A				
Computerised exposure for spider phobia in children and young people	Muris 1998	Insufficient sample size, ROB (high attrition), indirect intervention (immediate assessment after single treatment)	Very low	1	17	-0.01 (-0.96, 0.94)	N/A	1	17	0.47 (-0.50, 1.44)	N/A
Website for PTSD in children and young people	Cox 2010	Insufficient sample size, ROB (high attrition)	Low	1	56	-0.21 (-0.73, 0.32)	N/A				

¹Important heterogeneity for self-rated, but not for clinician-rated outcome

Note. ABM=Attention bias modification; CBM-I=Cognitive bias modification of interpretation; cCBT=Computerised cognitive behavioural therapy; PTSD=Post-traumaitc stress disorder; cPST=Computerised problem solving therapy; I²=Measure of inconsistency (proportion of total variability explained by heterogeneity); k=Number of studies; N=Number of participants in the analysis; N/A=not applicable; OCD=Obsessive compulsive disorder; PTSD=Post traumatic stress disorder; ROB=Risk of bias; SMD=Standardised mean difference.

Table 3 Evidence summary for interventions versus an active intervention

Intervention and comparator	Study	Reason for downgrading	GRADE evidence quality	Se	lf-rate	ed outcome		C	linicia	n-rated outcome	
•				k	N	SMD (95% CI)	I^2	k	N	SMD (95% CI)	\mathbf{I}^2
cCBT versus face-to-face CBT for anxiety in children	Khanna 2010	Insufficient sample size, indirect intervention (high therapist input)	Low	1	33	-0.05 (-0.73, 0.64)	N/A	1	33	-0.15 (-0.83, 0.54)	N/A
cCBT versus face-to-face CBT for anxiety in young people	Sethi 2010 Sethi 2013 Spence 2011	Insufficient sample size, indirect intervention (therapist input in all studies), important inconsistency ¹	Low	3	151	-0.04 (-0.36, 0.28)	0%	1	88	-0.13 (-0.55, 0.29)	N/A
cCBT versus face-to-face CBT for depression in young people	Sethi 2010 Sethi 2013	Insufficient sample size, indirect intervention (therapist input in all studies), important inconsistency	Low	2	63	1.65 (0.88, 2.41)	30%				
cCBT versus face-to-face counselling for depression in young people	Merry 2012	Insufficient sample size, indirect control (not all participants received counselling)	Low	1	187	-0.23 (-0.51, 0.06)	N/A	1	187	-0.11 (-0.40, 0.18)	N/A
ABM/CBM-I versus group CBT for social or test anxiety in	Sportel 2013	Insufficient sample size	Moderate	1	170	-0.20 (-0.50, 0.11)	N/A				

young people	3.5 1 1000	T 221 1 1				1.1.1.(0.00.0.1.0)	/-			0.01./0.10	
Computerised	Muris 1998	Insufficient sample	Very low	1	17	1.14 (0.09, 2.18)	N/A	1	17	0.91 (-0.10,	N.A
versus in vivo		size, ROB (high								1.93)	
exposure for		attrition), indirect								,	
		* *									
spider phobia in		intervention									
children and		(immediate									
young people		assessment after									
		single treatment)									

¹Important heterogeneity for self-rated, but not for clinician-rated outcome

Note. ABM=Attention bias modification; CBM-I=Cognitive bias modification of interpretation; cCBT=Computerised cognitive behavioural therapy; I²=Measure of inconsistency (proportion of total variability explained by heterogeneity); k=Number of studies; N=Number of participants in the analysis; N/A=not applicable; ROB=Risk of bias; SMD=Standardised mean difference