



# *Recent developments in the treatment of anxiety disorders in children and adolescents*

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Recent developments in the treatment of anxiety disorders in children and adolescents

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## Abstract

Anxiety disorders are among the most common emotional difficulties experienced by children and young people. They cause significant disturbance to the lives of young people and their families and present a risk for lifelong psychological disturbance. Effective psychological (i.e. Cognitive Behaviour Therapy (CBT)) and pharmacological interventions (e.g. selective serotonin reuptake inhibitors (SSRIs)) have been established. However the risk of adverse effects and unknown long term effects of using SSRIs has led to recommendations that CBT is delivered as a first line intervention. Recent innovations have included the development of low intensity CBT programmes, delivered briefly via parents or online. These hold promise to increase access to psychological therapies for children and young people with these common and severe difficulties.

## **Introduction**

Anxiety disorders are among the most common mental health difficulties across the lifespan, with a lifetime prevalence of 28.8%.<sup>1</sup> They commonly have their onset during childhood or adolescence, with approximately 50% of those affected in adulthood first experiencing difficulties before the age of 11 years.<sup>1</sup> Indeed the prevalence of anxiety disorders in childhood and adolescence is high, with worldwide prevalence rates estimated at 6.5%.<sup>2</sup> This high prevalence is of serious concern given that childhood anxiety disorders often run a chronic course, are associated with substantial interference in young peoples' social, educational and family lives, and are a risk for the development of other mental health problems in later life, such as depression.<sup>3-5</sup> Effective psychological and pharmacological interventions for childhood anxiety disorders have been established, and early treatment has been found to be associated with lasting benefits, including reduced suicide ideation in adulthood.<sup>6</sup> However, relatively few children and adolescents in need access these treatments<sup>7</sup>, and of those that do, a significant minority do not benefit.<sup>8</sup> This paper will give an overview of recent developments in the treatment of anxiety disorders in children and young people, with a particular focus on how to increase the number of children affected by these common difficulties who are able to access and benefit from evidence-based interventions. The pertinent literature was identified using PubMed and Google Scholar until March 31<sup>st</sup> 2015 and the reference lists of identified reports.

### **What do anxiety disorders look like in children and adolescents?**

Anxiety is a normal emotion that everyone experiences at times. The content of normative fears, anxieties, and worries in childhood typically follows a developmental course, characterized by early fears relating to separation from a caregiver to more complex concerns, such as being

negatively socially evaluated during adolescence.<sup>9 10</sup> As can be seen in Table 1, the onset of particular types of anxiety disorders often mirrors the normative development of these sorts of fears and worries, with, for example, separation anxiety disorder typically having a relatively early onset and social anxiety disorder having a later onset. Furthermore, the sorts of fears and worries that children and young people with an anxiety disorder experience may not differ substantially in content from the normative fears and worries of their peers.<sup>11</sup> Instead an anxiety disorder is distinguished from the usual fears and worries that children and young people experience based on (i) the frequency that the fears/worries occur, (ii) the interference caused (for example, due to avoidance, distress, and/or associated physical symptoms), and (iii) the duration of the problem.<sup>12</sup> The most common anxiety disorders experienced by children and young people in both clinic and community populations are separation anxiety disorder, social anxiety disorder, generalized anxiety disorder, and specific phobias.<sup>13 14</sup> However, young people may also experience the remaining DSM-5 anxiety disorders of selective mutism, panic disorder and agoraphobia, either on their own or alongside other anxiety disorders. A summary of the clinical characteristics for each of the DSM-5 anxiety disorders are given in Table 1.

### **What treatments are effective for anxiety disorders in children and adolescents?**

#### **(i) Psychological Interventions**

Cognitive Behaviour Therapy (CBT) has been far more extensively evaluated than any other intervention for anxiety disorders in children and adolescents. CBT for anxiety disorders focusses on identifying and challenging thoughts and behaviours that contribute to the maintenance of a disorder, counteracting avoidance through exposure to the feared situations or objects, and developing alternative responses that break the maintaining cycle.<sup>15</sup> The most recent

Cochrane review of CBT for childhood anxiety disorders identified 41 studies<sup>8</sup> with young people aged 4-18 years (although those under the age of 7 years were relatively under-represented). The majority of studies used a generic treatment approach rather than being designed for treatment of a specific anxiety disorder. Based on the 26 studies included in the analyses, 59.4% of those who received CBT remitted from their anxiety disorder compared to 17.5% of the waitlist controls, as defined by absence of an anxiety disorder, as diagnosed by a reliable and valid structured interview. The Number Needed to Treat (NNT) was 3, meaning that for one additional participant to attain remission, three participants would have needed to receive treatment. Notably there was a moderate degree of inconsistency between study findings, but this was not accounted for by the delivery format of CBT, i.e. group, individual, or family formats. Only three studies looked at the comparative remission rates of CBT versus a waitlist control beyond the post-treatment assessment. Overall 77% of those who received CBT and 52% of those in the waitlist conditions no longer had an anxiety disorder at the long-term follow-up (6 – 24 months), which fell short of significance (and the same was true for symptom reduction). In the three studies compared longer-term remission in CBT to an active control (e.g. psychoeducation and support), remission rates were 60% and 42% respectively which did not reflect a significant difference (and again the same was true on the basis of symptom reduction). However the ‘active treatment control’ did include a CBT programme delivered in a low intensity form (e.g. brief parent-led CBT approaches, see below). To date no trials have compared CBT to a non-CBT based active treatment condition that is actually used within therapeutic contexts (with most trials using control interventions that simply control for spending time talking to a therapist), so we have no evidence on which to conclude that CBT is *more* effective than another psychological therapy that might be used in child and adolescent mental

health settings. In the absence of robust evidence that any other psychological treatment approach is effective, CBT remains the first choice treatment approach.

While CBT has been established as being better than no treatment, a significant minority of children (approximately 40%) continue to experience significant disturbance at the end of a course of treatment. One of the major challenges now is to establish who CBT does and does not work for and to identify what is required in order to improve outcomes. Although recent reviews of studies that have examined predictors of treatment outcome for children and adolescents with anxiety disorders have concluded that there is no clear and consistent pattern in terms of demographic and clinical factors that are associated with treatment outcomes (e.g. Knight, McLellan, Jones, & Hudson, 2014)<sup>16</sup>, the majority of studies included in these reviews have been vastly underpowered. A recent collaboration, the Genes for Treatment (GxT) Study, has addressed this problem by collating CBT treatment outcome data from a number of sites internationally. Participants were 1,519 children (aged 5-18 years, although the majority were pre-adolescent) who had a primary anxiety disorder. The most consistent finding was that individuals with social anxiety disorder, comorbid mood or externalising disorders had poorer outcomes both immediately after CBT and at longer term follow-up.<sup>17</sup> Ongoing work is now required to establish how to improve treatment outcomes in these contexts.

While the GxT study failed to find a significant independent association between parental anxiety, depression and stress *symptoms* and child/adolescent CBT outcomes, significant associations have typically been found where studies have examined the presence of parental anxiety *disorder* status (at least in pre-adolescent children), with roughly half as many children



recovering following CBT where one or more of their parents also has an anxiety disorder (e.g. Bodden et al., 2008<sup>18</sup>; Hudson et al., 2013).<sup>19</sup> This is of potential importance, given the high degree to which anxiety disorders run in families (e.g. Cooper et al., 2006).<sup>20</sup> However, in a recent trial of 210 families in which both the child (aged 7-12 years) and their mother met diagnostic criteria for a current anxiety disorder, we found relatively good outcomes (with 60-75% recovered by the 12 month follow-up) for children following CBT regardless of the nature of parental support (which included treatment of the mother's anxiety disorder, an intervention focused on mother-child interactions, or active control conditions).<sup>21</sup> Of particular note, improvements in maternal mental health were found across all treatment conditions, highlighting the reciprocal nature of child and parental anxiety. In other words, children with anxiety disorders can achieve good outcomes in the context of parental anxiety disorders and these positive effects are likely to generalize to bring benefits to the wider family.

(ii) Pharmacological and combined interventions

The most recent Cochrane review of the efficacy of pharmacotherapy for anxiety disorders in children and young people identified 22 trials of short-term selective serotonin/norepinephrine reuptake inhibitors (SSRI/SNRI) administration, of which 14 studies included 'treatment response' as an outcome.<sup>22</sup> Pharmacotherapy was found to be effective (58% responders) compared to placebo (31.5% responders; NNT = 4). There was significant variation in trial outcomes, however this was not accounted for by the type of medication (SSRI/SNRI). Of note, the majority of included studies focused on paediatric Obsessive Compulsive Disorder (OCD) which is no longer categorized as an 'anxiety disorder' in the widely used diagnostic manual, the DSM-5 (DSM-5 reference- APA)- leaving few studies to inform practice about the common

anxiety disorders which are the focus of this paper. However, a significant development in this field is the Child/Adolescent Anxiety Multimodal Study (CAMS) which assigned 488 children (aged 7-17 years) with a primary diagnosis of separation anxiety disorder, generalized anxiety disorder, or social anxiety disorder to (a) 14 sessions of CBT, (b) sertraline (up to 200 mg per day), (c) a combination of CBT and sertraline, or (d) a placebo drug for 12 weeks. All therapies were superior to placebo in terms of treatment response, with 80.7% ‘much/very much improved’ for the combination treatment, 59.7% for CBT, and 54.9% for sertraline.<sup>23</sup>

As the largest single trial conducted within this field, CAMS has presented opportunities to explore questions that individual studies have previously been underpowered to address, in particular relating to who does and does not benefit from intervention. In CAMS, and partially consistent with the GxT findings reported above, poorer outcomes were found (across all treatment conditions) for those with higher initial anxiety severity, adolescents (versus children), participants of minority status, those with higher levels of caregiver strain and those with social anxiety disorder (although these associations varied somewhat depending on the study outcome used).<sup>24, 25</sup> Few factors were associated with differential responses between treatment conditions, although there was some suggestion that the participant’s principal diagnosis may moderate outcomes- with individuals with separation anxiety disorder appearing to respond best to the combination treatment, those with social anxiety disorder responding best to either of the condition that included sertraline, and those with GAD responding best to either condition that included CBT.<sup>25</sup> These secondary analyses should be considered as preliminary, however may offer some interesting directions for future research, and, ultimately practice.

A recent analysis of adverse events in CAMS concluded that sertraline was generally tolerable and safe as an acute treatment, however there was an increased rate of psychiatric adverse events (specifically disinhibition and increased motor activity) in the treatment groups containing sertraline compared to CBT (reported in 15.7% of the CBT + sertraline group, 7.5% of the sertraline group and 2.1% of the CBT group).<sup>26</sup> Although the figure for the CBT group is extremely low, it still serves to remind us that any treatment has the potential to cause negative effects and harm; however, this is an area that has been under-researched in studies of psychological therapy for children and young people to date. When children (7-12 years) and adolescents (13-17 years) were compared, children in the sertraline arm showed more adverse events overall than the adolescents. Notably, the majority of participants in this study were children, with only 25.6% of participants aged 13 years or older, so caution is needed in drawing conclusions and recommendations for the adolescent group. Furthermore there remains limited evidence related to the optimum dosage of SSRIs, their long-term positive and/or adverse effects, and the effects of treatment discontinuation. On the basis of their findings, the authors highlight ‘the need for careful assessment and monitoring of adverse events’ (Rynn et al., 2015; p 186) with SSRI treatments for children and adolescents with anxiety disorders, and suggest that ‘it may be prudent, especially for children less than 12 years of age, to consider treatment with CBT first’ (p186). This suggestion is consistent with the recent NICE guideline for social anxiety disorder<sup>27</sup> which include specific guidelines relating to children and young people. It recommends that affected children and young people should be offered individual or group CBT focused on social anxiety disorder using routine sessional outcome measures to monitor progress, and that pharmacological approaches should not ‘routinely’ be offered (NICE guideline). There is an absence of data on the treatment preferences of children and young people

with anxiety disorders, however parents of anxious children, prefer CBT to pharmacological interventions for their children, believing it to be more acceptable, believable, and effective in the short- and long-term.<sup>28</sup> In line with the NICE recommendations and parental preferences, the remainder of this review will focus predominantly on CBT approaches to the treatment of anxiety disorders in children and adolescents.

### **How can we increase access to evidence-based interventions for children and young people with anxiety disorders?**

Studies in various countries, including the UK, USA and Australia, have identified that only a minority of children experiencing emotional or behavioural problems access professional support (e.g. Green et al., 2005<sup>29</sup>; Sawyer et al., 2001<sup>30</sup>) and this problem appears to be particularly acute for anxiety disorders.<sup>31</sup> One reason for the lack of access to evidence based treatments is no doubt that CBT is costly to deliver. For example, the U.K. Improving Access to Psychological Treatments Children and Young People's initiative (CYP-IAPT) recommends the 'Coping Cat' programme<sup>32</sup> which involves 16 weekly 50 minute sessions. Furthermore CBT involves specialist training and supervision for therapists which only a minority (about 20%) of professionals in UK child and adolescent mental health services (CAMHS) have received<sup>33</sup> with two-thirds of CAMHS professionals reporting that they lack key CBT skills.

In line with guidance for increasing access to treatment in adult populations (e.g., NICE, 2011), recent therapeutic innovations have focused on brief or low-intensity versions of CBT that can be delivered by non-specialists, with the ultimate aim of delivering treatment within a stepped-care framework. The logic here is to deliver brief, relatively simple, first-line treatments routinely to

service users with a relatively good prognosis, reserving more intensive treatments for those who do not respond to the first-line treatment and those whose prognostic profile indicates that they require more input (e.g., Bower & Gilbody, 2005).<sup>34</sup> In recent years 'low intensity' approaches to the treatment of childhood anxiety disorders have been developed and evaluated, in particular (a) brief interventions in which parents are guided by a therapist in the application of a book to help their child overcome their difficulties with anxiety, and (b) interventions that are predominantly delivered electronically (i.e. online or similar) with therapist support.

(a) Brief parent-led guided CBT for child anxiety disorders

In this approach parents are provided with written resources that guide them in how to help their child apply CBT principles within their day to day life, and typically a therapist supports the parent in putting these principles in to place with their child. This approach has been evaluated predominantly with pre-adolescent children and found to be effective in Australian rural and urban populations<sup>35-37</sup> and recently in a UK CAMHS population.<sup>38</sup> Typically these studies have found outcomes that are similar to those found in trials of more intensive CBT (e.g. 76% 'much/very much improved' following only 5.5 hours of therapist support, compared with 25% in the waitlist condition; NNT= 2).<sup>38</sup> Notably this approach has been found to be effective even when delivered by non-specialists<sup>38</sup> and feasible within UK and US primary care services<sup>39 40</sup> suggesting that this may be a cost-effective means to improve access to evidence based treatments for children with anxiety disorders.

(b) E-therapies

Over the last five years there has been enormous growth in the use and popularity of ‘e-therapies’, no doubt due to the rapid rate of adoption of technology in to peoples’ everyday lives, and the potential that this approach brings to deliver interventions efficiently. Despite this growth and enthusiasm there remains a lack of robust evaluation of e-therapies for anxiety disorders in children and adolescents, although some promising findings have emerged. A recent systematic review identified seven CBT-based programs that have been systematically evaluated with children or adolescents with mixed anxiety disorders, mixed anxiety and depression, or social anxiety disorder specifically.<sup>41</sup> In all cases, the programs were supported with therapist input, but to varying extents. Overall, anxiety improved, with medium effect sizes, however there was less data for children than for adolescents and the data with children was considered to be weaker. Taken together, these studies suggest that e-therapies may be a promising low-intensity approach for the treatment of anxiety disorders in children and, perhaps particularly, adolescents.

### **Implications for clinical practice**

The substantial societal burden associated with anxiety disorders in childhood and adolescence highlights the need for effective identification and intervention. Effective psychological and pharmacological interventions do exist, yet psychological interventions can be difficult to access and pharmacological interventions bring greater risk of adverse effects and may be less popular. As such, there is a need for services to develop stepped care models of treatment in which low intensity treatments are delivered as a first step, with more intensive treatments reserved for those who do not or who are unlikely to benefit from the low intensity approach (see Figure 1). Indeed, a number of studies have now demonstrated the feasibility and effectiveness of low intensity approaches, in particular brief parent-led guided CBT for children with anxiety

disorders, and online CBT for adolescents with anxiety disorders. As an example, the UK Improving Access to Psychological Therapies (IAPT) programme has embedded a stepped care model in to adult mental health services, with low intensity psychological interventions now readily available in many regions of the UK and a rapid uplift in the number of adults with common mental health disorders who have accessed evidence based psychological therapies (e.g. Department of Health, 2012).<sup>42</sup> A similar model of service delivery is now required for children and adolescents with common mental health disorders, such as anxiety disorders, where effective low intensity interventions exist in order to help many children and young people overcome problems before they become so severe as to require specialist, high intensity interventions.

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**Table 1.** The characteristics and age of onset for DSM-5 anxiety disorders.

Anxiety disorder	Clinical characteristics	Age of onset (in years) <sup>a</sup>	
		Median	Inter-quartile range
Separation anxiety disorder	Developmentally inappropriate and excessive fear/anxiety concerning separation from those to whom the child is attached, which has been present for at least 4 weeks.	7	6-10
Specific phobia	Marked fear/anxiety about a specific object or situation that is out of proportion to the actual danger posed and the sociocultural context and is persistent, typically lasting 6 months or more. The object or situation almost always provokes immediate fear/anxiety and is actively avoided or endured with intense fear/anxiety.	7	5-12
Selective mutism	Consistent failure to speak in specific social situations in which there is an expectation for speaking despite speaking in other situations, for at least 1 month (not limited to the first month of school).	-	-

Social anxiety disorder	Marked fear/anxiety about one or more social situations in which the individual is exposed to possible scrutiny by others, occurring in peer settings and not just in interactions with adults. Situations are avoided or endured with intense fear/anxiety and the fear/anxiety is out of proportion to the actual threat posed and sociocultural context, typically lasting for 6 months or more.	13	8-15
Agoraphobia	Marked fear/anxiety about 2 or more of the following situations: using public transport, being in open or enclosed spaces, standing in line or being in a crowd or being outside of the home alone. The situations almost always provoke fear/anxiety due to thoughts that escape might be difficult, help might not be available or other incapacitating/embarrassing symptoms and situations are actively avoided, require the presence of a companion or are endured with intense fear/anxiety, lasting 6 months or more.	20	13-33
Panic disorder	Recurrent unexpected panic attacks, consisting of an abrupt surge of intense fear/discomfort that peaks within minutes and includes 4	24	16-40

symptoms such as palpitations, sweating, trembling, sensations of shortness of breath, chest pain, nausea, dizziness). At least 1 attack has been followed by at least 1 month of persistent worry about additional attacks or their consequences, or a significant maladaptive change in behaviour related to the attacks.

Generalized anxiety disorder	Excessive anxiety and worry that is difficult to control, associated with at least one physical symptom (e.g., restlessness, difficulty concentrating, sleep disturbance), occurs more days than not for at least 6 months.	31	20-47
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*Note.* <sup>a</sup> Reported in Kessler et al. (2005). The inter-quartile range is the number of years between the 25th and 75th percentiles of the age-of-onset distributions. All anxiety disorders (except panic disorder) require that the disturbance causes clinically significant distress or impairment in areas such as academic or social functioning.



