



Anxiety disorders in children and adolescents: A summary and overview of the literature

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ABSTRACT

Considerable work has advanced understanding of the nature, causes, management, and prevention of anxiety disorders in children and adolescents over the past 30 years. Prior to this time the primary focus was on school refusal and specific phobias. It is now recognised that children and adolescents experience the full gamut of anxiety disorders in very similar ways to adults and that anxiety disorders in the paediatric years can predict a lifelong mental-health struggle. Given the vast array of specific studies in this field, the current review summarises current knowledge about these high prevalence disorders, points to overarching limitations, and suggests potentially important future directions. Following a brief historical overview, the review summarises knowledge about demographic and epidemiological characteristics, distal and proximal risk factors, current treatment directions, and prevention. There is still a great deal to learn about the causes and treatments of child and adolescent anxiety disorders. By amalgamating our current knowledge, this review provides a window to the research directions that are likely to lead to future advances.

1. Introduction and historical overview

Like much research in applied psychology, the history of treating anxiety in young people¹ can be traced back over a century. For the most part, the history of evaluating treatment for anxiety disorders in young people can be described as rigorous, highly informative, and an exemplar of incremental science. In short, much has been learned (HigamcMillan et al, 2015; Southam-Gerow & Prinstein, 2014) and reasonable confidence can be ascribed to the findings, given the overall methodological quality of the work.

The Diagnostic and Statistical Manual of Mental Disorders (DSM) exemplifies such progress, and across the several editions and even within versions of the DSM, the labels for the anxiety disorders in young people have evolved. For example, overanxious disorder was described in the third edition of the DSM reflecting excessive worry, concerns about personal competence, need for reassurance, and self-consciousness. This specific disorder was later eliminated partly due to its overlap with social phobia. Thus, most young people who would have met criteria for this diagnosis would now be diagnosed with the more clearly delineated generalised anxiety disorder, reflecting persistent and excessive worry, with excessive concern about routine matters and

difficulty managing worry. Social phobia has been renamed social anxiety disorder, the persistent fear of social/performance situations involving potential scrutiny by others. In contrast, the label separation anxiety disorder, referring to young people who have an unusual-for-their-level-of-development severity of intense anxiety tied to separating from a caregiver, has remained over time. The more recent iterations of DSM, to its credit, provide detailed diagnostic criteria that are useful, though not without limitations, for making differential diagnoses. For example, selective mutism has appropriately now been moved into the anxiety disorders (American Psychiatric Association, 2013) from its previous placement among a broad range of disorders first evident in childhood. However, strong overlap with social anxiety disorder (Milic, Carl, & Rapee, 2020), raises serious questions about whether these disorders really require separate diagnostic labels. On the other hand, obsessive compulsive disorder has been moved out of the group of anxiety disorders with the publication of the DSM-5. However, the marked overlap between obsessive compulsive disorder and anxiety disorders (Stein et al., 2010), its similar response to treatment (Hudson, Rapee, et al., 2015), and its historical conceptualisation as an anxiety disorder, raise questions about this decision. Similar concerns exist for post-traumatic stress disorder, which was also moved outside of the

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¹ We use the terms “young people” and “paediatric” to broadly refer to children and adolescents.

anxiety disorder category in DSM-5.

The essential features of paediatric anxiety disorders – avoidant behaviour and catastrophic thinking – have been consistent criteria for their categorisation over time. The names change, the specific nature of the avoidance varies, the details of the maladaptive thinking fluctuate, but the unwanted emotional distress and misguided avoidant behaviour persist. Experience and data indicate that those young people who met the bygone anxiety disorder criteria would also qualify for the DSM criteria that followed (e.g., Kendall & Warman, 1996).

Aside from nosological considerations, paediatric anxiety researchers have built a growing knowledge base concerning factors that underpin and maintain the disorders. Early research focused heavily on self-statements and similar verbal cognitive processes (Kendall & Chansky, 1991) before the more recent move to less conscious information processing mechanisms. In terms of external environmental influences, there was an early realisation of the importance of peer relationships to anxious young people (La Greca & Lopez, 1998), a focus that has been extended more recently into more sophisticated longitudinal modelling. So too, an early interest in the role of parents suggested that normative responses might inadvertently contribute to maintenance of child anxiety and that they could be included in treatment (Barrett, Dadds, & Rapee, 1996; Rapee, 1997).

Although there have been minor variations, the history of research on treating paediatric anxiety has been impressively incremental. The vast majority of empirical work focused on cognitive behavioural therapy (CBT). Although the core principles of CBT are relevant across ages, clinical researchers working with young people recognised the need to apply developmental science to treatment to ensure that clinical methods were compatible with children's cognitive and socio-emotional competencies (Kendall, 1984). Following case studies and small evaluations of anxiety-related problems, initial RCTs (Barrett et al., 1996; Kendall, 1994) compared comprehensive CBT packages to wait-list, showing good success. As part of a progressive and cumulative science, the next needed evaluation required evaluation of treatment versus an alternate treatment of similar duration and comparable credibility. Perhaps surprisingly, some of the earliest examinations of this issue failed to show marked differences between CBT and education placebo for child anxiety (Last, Hansen, & Franco, 1998; Silverman, Kurtines, Ginsburg, Weems, & Rabian, 1999). However, further improvements led to CBT packages that were more efficacious than either education placebo (Hudson et al., 2009) or client-centred treatment (Silk et al., 2018).

Advancements were also evident in studies of the potential mediators of outcome: the variables that changed within the treatment and were meaningfully responsible for the observed improvements. For example, some data indicate that changes in physical symptoms mediated medication treatment (Hale et al., 2018) whereas changes in coping self-talk mediated gains in CBT (Kendall, Cummings, et al., 2016a, b). This work on mediators as well as moderators of treatments for paediatric anxiety brings us to the cutting edge of current work. Other cutting-edge work began to capitalise on technology and the potential to deliver treatment electronically (Cunningham et al., 2009; Khanna & Kendall, 2010). More recently, this delivery has moved to online websites, apps, and even attempts at gameification (Bry, Chou, Miguel, & Comer, 2017; Cervin & Lundgren, 2022).

The primary aim of this review is to provide an overarching summary of core components of what is a vast and rapidly increasing literature. We do not attempt to provide a comprehensive or quantitative review (which would require an entire book) but rather rely on our combined experience in the field to summarise the primary current knowledge and highlight selected current limitations and future directions of likely importance. Following the information on prevalence, comorbidity, age of onset, impact, and demographics, we address distal risk factors (e.g., genetics, temperament, environment, life events, school, peers, parenting, neurophysiology) as well as more proximal risk factors (e.g., threat responding, fear conditioning, safety learning). The treatment of

paediatric anxiety is reviewed with a focus on the effectiveness of CBT and information regarding how to improve its outcomes and increase its access by those in need. Medications and novel treatments are also discussed. Our review closes with consideration of prevention programs, such as those implemented in schools and by parents.

2. Characteristics of anxiety disorders

2.1. Prevalence

Collectively, anxiety disorders are the most common form of mental disorder in young people with a world-wide prevalence, collapsed across time frames, of 6.5% (Polanczyk, Salum, Sugaya, Caye, & Rohde, 2015). Estimates from different studies show some variation likely due to differences in measures, methods, included disorders, and time frames. However, most population estimates based on diagnostic interviews indicate that around 5–10% of young people (aged 6–18 years) meet diagnostic criteria for an anxiety disorder within a 12-month period (Canino et al., 2004; Farbstein et al., 2010; Lawrence et al., 2015; Vicente et al., 2012). Although estimates of lifetime prevalence are far less common, average lifetime prevalence up to 18 years (i.e., the prevalence of any anxiety disorder across the child/adolescent period) has been estimated at around 15–20% (Beesdo, Knappe, & Pine, 2009).

Prevalence estimates for specific anxiety disorders tend to be less reliable and show considerable variation among studies. This variation is partly influenced by age of the samples. Separation anxiety disorder typically shows the greatest prevalence among child samples (Canino et al., 2004; Ford, Goodman, & Meltzer, 2003; La Maison et al., 2018; Lawrence et al., 2015; Vicente et al., 2012), although estimates vary between 1 and 6% among those under 13 years. In contrast, social anxiety disorder is more prevalent within adolescent samples (Benjet, Borges, Medina-Mora, Zambrano, & Aguilar-Gaxiola, 2009; Kessler et al., 2012; Lawrence et al., 2015; Vicente et al., 2012), although actual estimates for this disorder are also quite variable (3–11%). Generalised anxiety disorder shows surprisingly low prevalence (0.5–4%) and its estimate in population studies does not appear to match clinical experience, where it is one of the most frequent disorders among treatment-seeking populations (Kendall et al., 2010; Waite & Creswell, 2014). When assessed, specific phobias are the most prevalent form of anxiety disorder and often inflate overall prevalence estimates (Benjet et al., 2009; Farbstein et al., 2010; Kessler et al., 2012; La Maison et al., 2018). However, they are most likely to show “mild” impact (Benjet et al., 2009), consistent with their lack of clinical presentation.

2.2. Comorbidity

Consistent with a hierarchical structure approach to psychopathology (Murray, Eisner, & Ribeaud, 2016), and the forced categorical approach of DSM, paediatric anxiety disorders show high levels of comorbidity, both homotypic (within the anxiety disorders) and heterotypic (between groups of disorders). Clinical presentation with only a single anxiety disorder is rare and young people with one anxiety disorder commonly meet criteria for one or more additional anxiety disorders (Kendall et al., 2010; Rapee et al., 2013). Heterotypically, anxiety disorders show strongest comorbidity with depression, especially by adolescence (Costello, Mustillo, Erkanli, Keeler, & Angold, 2003; Cummings, Caporino, & Kendall, 2014; Khanal et al., 2022). Around 10–15% of clinically anxious young people will meet diagnostic criteria for a mood disorder (Cummings et al., 2014). Anxiety disorders are also comorbid with externalising disorders, including both attention deficit hyperactivity disorder and oppositional defiant disorder (Costello et al., 2003; Khanal et al., 2022; Ollendick, Jarrett, Grills-Taquechel, Hovey, & Wolff, 2008), especially among younger samples. Compared to young people with no comorbidity or homotypic comorbidity, those with heterotypic comorbidity are more disordered, showing both more severe anxiety symptoms and greater functional impairment (Cummings et al.,

2014; Rapee et al., 2013). Recent research has focused on comorbidity with autism spectrum disorder and has shown high rates of anxiety disorders among young people with autism spectrum disorder (Lai et al., 2019; van Steensel, Bogels, & Perrin, 2011). Reasons for the comorbidity are not yet clearly identified. Some possibilities include overlap in symptoms between the two distinct disorders (Lau et al., 2020; Tyson & Cruess, 2012), anxiety developing as a consequence of autism spectrum disorder (Shephard et al., 2019; Wood & Gadow, 2010), or shared risk factors including overlap in early temperamental markers (Shephard et al., 2019).

Anxiety disorders in young people also predict a range of future mental disorders. A history of anxiety disorder is a strong predictor of future anxiety and mood disorders (Costello et al., 2003; Magson et al., 2022; Pine, Cohen, Gurley, Brook, & Ma, 1998). Young people with anxiety disorders are also at increased risk for concurrent and future eating disorders (Convertino & Blashill, 2022; Hughes, 2012). Interestingly, anxiety disorders during the adolescent years appear to protect against substance use disorders but significantly increase the risk for future (adult) substance use disorders (Costello et al., 2003; King et al., 2020).

2.3. Age of onset

Anxiety disorders begin early in life and are one of the earliest types of disorders to emerge (Merikangas et al., 2010; Solmi et al., 2022). However, this global statement disregards marked differences in onset between the anxiety disorders. Separation anxiety disorder and specific phobias of animals and the environment are typically the first anxiety disorders to emerge with onset mostly before age 10 (Beesdo et al., 2009; Copeland, Angold, Shanahan, & Costello, 2014; Solmi et al., 2022). Although social anxiety disorder can be diagnosed early in life, its most common age of onset is in early adolescence (Beesdo-Baum & Knappe, 2012; Lijster et al., 2017; Rapee et al., 2019). In contrast, data on the age of onset of generalised anxiety disorder is more variable with some retrospective evidence that its onset is in the adult years (Kessler et al., 2007; Solmi et al., 2022). However, prospective research shows a much earlier onset in later adolescence (Beesdo, Pine, Lieb, & Wittchen, 2010; Rhebergen et al., 2017). Divergent from these paediatric forms of anxiety, the mean age of onset for panic disorder is in early adulthood (Copeland et al., 2014; Lijster et al., 2017).

2.4. Impact

Avoidance is the hallmark of anxiety and therefore paediatric anxiety disorders are associated with a wide variety of life impairment (Swan & Kendall, 2016). Anxious young people show impairments in peer relationships – they are less liked than their non-anxious peers, display poorer social performance, are more commonly victimised, and have fewer friendships (Christina, Kakar, Magson, & Rapee, 2021; Kingery, Erdley, Marshall, Whitaker, & Reuter, 2010; Verduin & Kendall, 2008). Academic performance is also strongly impacted by anxiety. Young people with anxiety disorders attend fewer days of school, report less school engagement, show poorer academic performance, and ultimately terminate their schooling earlier than non-anxious young people (Goodsell et al., 2017; Lawrence et al., 2015; Lee et al., 2009). An Australian population survey showed that young people with anxiety disorders fell increasingly further behind their peers in core academic skills from grade 3 to grade 9 (Goodsell et al., 2017). By grade 9 anxious adolescents were performing on average two years behind their cohort on numeracy and literacy.

2.5. Demographic correlates

Relative to externalising or mood disorders, paediatric anxiety disorders are associated with relatively few demographic predictors. In contrast to most forms of mental disorder, socioeconomic status and

family income are not consistently associated with anxiety disorders. Although some research has shown significant associations between anxiety disorder and family socioeconomic status (Khanal et al., 2022; Lawrence et al., 2015; Vicente et al., 2012), other studies have failed to demonstrate such an association (Benjet et al., 2009; La Maison et al., 2018; Merikangas et al., 2010). Similarly, parent education and marital status are inconsistently related to child anxiety disorder, although when associations are found they typically show that anxiety disorders are more likely in the context of lower parent education and in single parent families (Khanal et al., 2022; La Maison et al., 2018; Lawrence et al., 2015; Merikangas et al., 2010; Vicente et al., 2012).

The most consistent demographic correlate for paediatric anxiety is sex, with females being at markedly higher risk (Benjet et al., 2009; Merikangas et al., 2010; Vicente et al., 2012). Interestingly the sex difference is far smaller during childhood and appears to increase from the early stages of puberty (Khanal et al., 2022; Vicente et al., 2012). It is also interesting that the sex differences in most treatment-seeking samples are minor or non-existent (e.g., Jónsson, Thastum, Arendt, & Juul-Sørensen, 2015; Swan et al., 2018), perhaps suggesting that the functional impairment that commonly brings people to treatment (Dickson, Kuhnert, Lavell, & Rapee, 2022; Reardon, Harvey, & Creswell, 2020), is perceived as larger for boys than girls in many societies.

3. Risk for the development of anxiety disorders

3.1. Genetics

Work on genetics and neurophysiology provides important clues about mechanistic factors operating within the brain that shape risk for anxiety disorders. These clues provide novel ideas about prevention and intervention. Research on genetic risk includes studies using behavioural and molecular approaches. Behavioural genetics research estimates the overall magnitude of genetic effects, while molecular genetics research identifies only a subset of such effects (Smoller et al., 2019). Nevertheless, unlike behavioural genetics studies, molecular genetics research links particular molecules to risk for anxiety disorders (Purves et al., 2020).

3.2. Behavioural genetics

Family studies consistently find higher risk for anxiety disorders in children who have relatives with either mood or anxiety disorders as compared to children who have relatives without psychopathology (Penninx, Pine, Holmes, & Reif, 2021). Many studies find high rates of anxiety disorders in children born to parents with a range of individual disorders, including various types of anxiety disorders as well as mood disorders, with an approximate two-fold increase in risk (Lawrence, Murayama, & Creswell, 2019; Lee, Feng, & Smoller, 2021; Zeytinoglu et al., 2021). Such findings highlight the large proportion of variance accounted for by risk that is common across internalizing distress (Waldman, Poore, van Hulle, Rathouz, & Lahey, 2016). Twin studies parse this familial risk into genetic and environmental components. Most twin studies find sizable genetic components underlying risk for virtually all mental disorders. Compared to other mental disorders, genetic risk for anxiety disorders generally involves smaller influences leaving greater impact from environmental than genetic factors (Smoller et al., 2019). Nevertheless, genetic influences still account for a sizable proportion of risk, approximately 30–40% of the overall liability for anxiety diagnoses or for high scores on symptom scales (Lewis & Plomin, 2015). Two major sets of questions arise from existing behavioural genetics research.

One set of questions concerns specificity in genetic risk, which appears to cross nosology boundaries. Thus, some individual anxiety disorders, such as social anxiety disorder and panic disorder, share genetic risk that does not correlate as strongly with genetic risk for other anxiety disorders, such as generalised anxiety disorder (Waszczuk, Zavos,

Gregory, & Eley, 2014). Similarly, mood disorders, particularly major depressive disorder, share as strong a genetic risk with some anxiety disorders as individual anxiety disorders share with each other (Penninx et al., 2021). This suggests that current nosology fails to accurately map onto genetic risk for anxiety and other mental disorders and raises significant questions about finding approaches to classification that correspond to genetic understandings of mental disorders (e.g., Waldman et al., 2016).

A second set of questions concerns developmental expressions of genetic risk. Cross-sectional studies generally find comparable levels of genetic risk in paediatric and adult anxiety disorders. However, studies in adults typically utilise only one informant, unlike studies in young people, which utilise multiple informants that generate only partly overlapping risk estimates (Lewis & Plomin, 2015; Purves et al., 2020; Waszczuk et al., 2014). Thus, questions arise on methods for integrating these cross-informant data. Longitudinal work raises additional questions by suggesting that genetic factors identified in cross-sectional studies of young people encompass at least three components of risk (Lewis & Plomin, 2015; Waszczuk et al., 2014). One component operates primarily in childhood; another first arises in adolescence; a final component manifests stably across development. More work is needed to clarify the precise relation between changing genetic and clinical features of anxiety across development.

3.3. Molecular genetics

Molecular genetics research has passed through various phases, leading to the current approach that relies heavily on genome-wide association studies (GWAS). This approach typically requires studies with many thousands of patients, and no such GWAS studies implicate particular genes in paediatric anxiety disorders (Jami et al., 2022). Moreover, molecular genetic studies generally have made more progress in research on disorders such as autism and schizophrenia, with strong genetic components, as compared to anxiety disorders (Smoller et al., 2019). However, available studies on anxiety in adults generally extend findings from behavioural genetics research by identifying individual genes with very small effects. This means that variations in particular genes identified on individuals' chromosomes do predict variation in anxiety levels among these individuals, although, the small effects of individual genes means that this variation must involve many genes before it can approach clinical utility. However, some initial work suggests that the contribution of individual genes to overall heritability is higher in anxiety disorders than in conditions such as major depressive disorder (Purves et al., 2020). This raises hope that progress will begin to accelerate in future research on the genetics of paediatric anxiety. Importantly, genetic research holds the hope of identifying risk factors that operate before clinical expressions of anxiety manifest. However, current research remains many years away from producing clinically actionable results.

3.4. Neurophysiology

Notable neurophysiology research includes studies that acquire peripheral measures as indirect indicators of brain function and studies that more directly assess the brain through imaging. Studies of peripheral markers generate consistent associations with clinical indicators in relatively large samples. However, it remains unclear precisely how the brain contributes to these associations between peripheral markers and anxiety disorders. Imaging more directly implicates the brain in anxiety disorders, but sample sizes remain small, and few replicable associations exist.

3.5. Peripheral neurophysiology

Measures of attention, threat-related learning, and psychophysiology represent the peripheral measures most consistently related to risk for

anxiety disorders. Research identifies peripheral neurophysiology markers by examining the effects that threats produce on the brain in ways that also impact peripheral physiology. While other studies examine baseline physiology, such studies often are based in laboratories, which might influence physiology based on features of the laboratory. Much of this work is described in detail in the later section on psychological factors and hence the overall findings will only be briefly overviewed here.

One set of studies extends research in rodents and non-human primates showing the capacity of threats to influence attention through effects on amygdala function (Abend et al., 2018; Pagliaccio et al., 2019; Pine & Fox, 2015). This includes data from studies in patients showing threats have greater impact on children with anxiety disorders as compared to healthy children (Abend et al., 2018; Pine & Fox, 2015). A second set of studies extends research on threat learning expressed through conditioning and extinction (Duits et al., 2015). This work generally finds elevated responding on measures of heart rate, skin conductance, and startle potentiation, which are known to correlate with changes in threat responsive neural circuitry. A final set of studies extends research on threats' capacities to impact various psychophysiological parameters (Abend et al., 2020; Kujawa, Glenn, Hajcak, & Klein, 2015; Nelson et al., 2022; Penninx et al., 2021). This includes diverse immunological, respiratory, endocrinologic, and cardiovascular factors, which might account for relations between mental and physical health markers among patients with anxiety disorders. As with studies of attention and threat learning, this research finds that children with anxiety disorders manifest physiologic profiles suggestive of enhanced sensitivity to threats (Abend et al., 2020).

3.6. Brain imaging

Imaging studies quantify brain structure and function in a more direct manner than studies of peripheral physiology. However, immaturity in methods leads imaging studies to generate less consistent findings than studies of the peripheral physiology of paediatric anxiety disorders (Marek et al., 2022). Such immaturity plagues many sectors of brain imaging research, where few findings replicate for many psychiatric conditions (Linke et al., 2021). At least for mood and anxiety disorders, the most recent findings from structural brain imaging studies suggest that initial findings reflect Type I errors (Bas-Hoogendam et al., 2020). Large scale studies generally fail to detect replicable structural correlates of paediatric anxiety disorders (Marek et al., 2022). Moreover, while findings from functional imaging appear more promising (A. L. Gold et al., 2020a, 2020b), as with studies of genetics, the available research suggests that brain function relates more consistently to overall levels of psychopathology as opposed to specific disorders. For example, functional brain imaging studies find that both anxiety disorders and other conditions manifest similar-appearing signs of threat hypersensitivity (McTeague et al., 2020).

Studies examining neural correlates of cognitive control may represent the most promising area for imaging research on paediatric anxiety (Penninx et al., 2021). Cognitive control occurs when children must suppress inappropriate habitual actions so that they can correctly make difficult choices, as indicated by relatively high error rates or response times on a task. Most imaging research examines one of two cognitive control indicators. Considerable work links paediatric anxiety to difficulty responding to task rules in high-conflict scenarios, a finding linked to functioning in dorsal regions of frontal and parietal cortex (Cardinale et al., 2022). As with threat-responsiveness, this pattern occurs in many disorders besides paediatric anxiety disorders (McTeague et al., 2017). A more specific pattern arises for studies of error sensitivity, where anxiety disorders appear relatively unique in showing neural hyper-sensitivity to errors. The most consistent findings arise for a measure known as the error-related negativity (ERN), which manifests in the electroencephalographic response to errors (Penninx et al., 2021). In one especially intriguing study, ERN at age 6 predicted the onset of new anxiety

disorders three years later, even after controlling for baseline child and maternal anxiety (Meyer, Hajcak, Torpey-Newman, Kujawa, & Klein, 2015).

In summary, studies examining genetic and neurophysiologic risk factors generate interest due to the hope that such work might provide clues about mechanistic factors operating within the brain that shape risk for anxiety disorders. While consistent, replicable, and specific results remain to be demonstrated, these clues provide potentially novel ideas about prevention and intervention. For example, novel approaches might select subgroups of patients based on underlying biomarkers. This could include either measures of attention or error processing, as has been done in preliminary work (Amir et al., 2023; White, Sequeira, et al., 2017a). Using these biomarkers, this approach could attempt to select from currently available treatments, as has been done in adults with major depressive disorder, where biomarker profiles predict likelihood to respond to established treatments (Dunlop et al., 2023). Alternatively, this approach could attempt to use novel treatments, specifically designed to change the underlying biomarkers (Amir et al., 2023; White, Sequeira, et al., 2017a). This could include either novel treatments as stand-alone therapies (Amir et al., 2023) or novel treatments added to established ones (White, Sequeira, et al., 2017b).

3.7. Temperament

The strong evidence for a heritable basis to anxiety along with its trait-like presentation lends itself to the hypothesis that anxiety disorders are preceded by a core temperamental style (Filippi, Valadez, Fox, & Pine, 2022; Liu & Bell, 2020; Rapee, Schniering, & Hudson, 2009). Consistent with this proposal, most temperament nosologies identify an “anxious” temperament – variously referred to as inhibition, withdrawal, shyness, or fearfulness (Liu & Bell, 2020; Rapee et al., 2009). Kagan’s conceptualisation of behavioural inhibition has received the greatest research attention. According to Kagan (2022; Kagan, Snidman, Arcus, & Reznick, 1994), a reactive temperament characterised by excessive motor activity and negative emotional reactivity to novel stimuli can be identified as early as 3 months (Fox, Snidman, Haas, Degnan, & Kagan, 2015; Kagan, Snidman, & Arcus, 1998). In turn, this temperament increases risk for behavioural inhibition in the toddler years, which is characterised by avoidance of novel, unfamiliar events. Ultimately, behavioural inhibition is argued to be a major risk factor for the development of anxiety disorders, especially when combined with relevant environmental conditions (see below). A major complication of this theory is the potential tautology relating to the extent that temperamental inhibition and anxiety reflect the same underlying construct. Nonetheless, reviews of the literature suggest that although they are highly related, these variables do reflect distinct constructs (Rapee & Coplan, 2010). In addition to an inhibited style of temperament, some theory has pointed to other forms of temperament that may provide additional risk for anxiety disorders. Primary among these is work suggesting the role of processes related to the ability to regulate and control internal processes, variously referred to as effortful control, regulation, or reactivity (Liu & Bell, 2020; Lonigan, Vasey, Phillips, & Hazen, 2004).

Longitudinal research has supported the prediction that early inhibition leads to later anxiety disorders. Toddler or preschool children showing high levels of withdrawal, inhibition, or shyness are at significant increased risk for anxiety disorders in childhood to adolescence (Chronis-Tuscano et al., 2009; Edwards, Rapee, & Kennedy, 2010; Rapee, 2014; Schwartz, Snidman, & Kagan, 1999). A recent review of the longitudinal literature concluded that early inhibition provided a three-fold increase in the odds of developing later anxiety disorder (Sandstrom, Uher, & Pavlova, 2020). Interestingly, although there is some prospective association between inhibition and all anxiety disorders (Sandstrom et al., 2020), the strongest and most consistent prediction is for social anxiety disorder (Clauss & Blackford, 2012; Sandstrom et al., 2020). This evidence may suggest that social anxiety

disorder is the most “personality-like” of the anxiety disorders, which in turn, may link to its slightly poorer treatment responsivity (see later section).

Of course, not all highly inhibited children develop mental health concerns, and it is therefore commonly assumed that inhibited temperament interacts with additional variables, both internal and external, to trigger anxiety disorders (Degnan, Almas, & Fox, 2010; Hudson & Rapee, 2004). Evidence for this prediction is limited and inconsistent. One theory is that anxiety disorders are triggered by a combination of inhibition and attentional control (perhaps underpinned by poor effortful control) (Liu & Bell, 2020; White, McDermott, Degnan, Henderson, & Fox, 2011). Only a few studies have supported this prediction. For example, White and colleagues (White et al., 2011) showed that inhibition at two years of age interacted with the child’s ability to control their attentional focus at four years of age to predict anxiety symptoms at preschool age.

A logical prediction is that inhibited temperament will interact with negative life events to predict anxiety disorders. This prediction has received surprisingly little evaluation (see later section). However, in one study (N = 332), children who were higher on fearful temperament at age three showed greater increases in symptoms of anxiety in response to a hurricane experienced at age 9 (Kopala-Sibley et al., 2016).

Finally, theory has consistently argued that a child’s interaction with their parents, in particular an overprotective style of parenting, should moderate the relationship between temperamental inhibition and later anxiety disorder (Hudson & Rapee, 2004). Evidence for this prediction, however, has been inconsistent (Hudson, Dodd, Lyneham, & Bovopoulos, 2011; Vreeke, Muris, Mayer, Huijding, & Rapee, 2013) (see below).

In summary, although it is almost a truism to say that anxiety disorders are preceded by temperamental risk, there remain many unanswered questions. Most critically, the relation between anxiety and inhibition and whether these constructs are even distinct (Rapee & Coplan, 2010), remains far from determined. In addition, interactions and mediations between inhibited temperament and environmental risk factors require far more exploration.

3.8. Social/environmental factors

In addition to their focus on genetic factors, twin studies have also highlighted the substantial environmental influence on the development of anxiety, estimated at between 40 and 60% of the variance (Lewis & Plomin, 2015). To date much of the research on identifying environmental influences has focused on parental responses, driven by robust findings that the risk of anxiety disorders is elevated among offspring of parents with anxiety disorders (Lawrence et al., 2019) and that intergenerational transmission of anxiety symptoms is largely independent of genetic effects (at least for parent-adolescent offspring associations; Eley et al., 2015). However, it is critical to keep in mind that while the risk of anxiety disorders is elevated among offspring of parents with anxiety disorders, approximately half of children with anxiety disorders do not have a parent with an anxiety disorder (e.g., 49%; Lawrence et al., 2019), and equally the majority of offspring of parents with an anxiety disorder do not have an anxiety disorder (e.g., 65%; Lawrence et al., 2019). Furthermore, past reviews have suggested that parenting accounts for only 4% of the variance in child anxiety (McLeod, Weisz, & Wood, 2007; Rapee, 1997). As such, while it is important to understand the potential role of parental and family factors in the development of anxiety disorders, it is clearly critical that we also look beyond these factors to children’s wider environmental experiences.

Studies that have sought to identify environmental risks for anxiety disorders in children have focused on circumstances and experiences that might promote a sense of threat in the environment and/or diminish confidence in one’s own ability to cope in the face of challenge. These risks are consistent with internal, psychological processes that are hypothesised to maintain anxiety disorders (see below) and include negative life events, as well as experiences in particular contexts (e.g. at

school) and through interactions with others (e.g. peers). To rebalance the focus of the literature somewhat, these areas will be briefly considered first, before considering what is known about the role of parents and critically how different risk factors might interact.

3.9. Negative life events

A number of studies has suggested that children with anxiety disorders experience more negative life events than non-anxious children (e.g., Allen, Rapee, & Sandberg, 2008; Grover, Ginsburg, & Jalongo, 2005) and that this relationship remains even after controlling for other (non-anxiety) disorders (Allen & Rapee, 2009; Dunn et al., 2011; Phillips, Hammen, Brennan, Najman, & Bor, 2005). For example, Dunn et al (2011) found that experiencing a “severe” cluster of childhood adversities was associated with a 70% increase in the risk of anxiety disorders, however this was a modest increase in risk when compared to the contribution that adversities made to conduct disorders, depression, and self-harm. While childhood adversities (including negative life events) commonly cluster, it has been hypothesised that particular types of events (i.e. threat-related) may pose particular risks for anxiety disorders (whereas loss related events may be a risk for mood disorders) (Eley & Stevenson, 2000). Others have considered whether even more specific events pose particular risks for child anxiety disorder, (e.g. living in a dangerous neighbourhood and parental drug use) (Shanahan, Copeland, Jane Costello, & Angold, 2008) or for subtypes of anxiety disorder (Tiet et al., 2001).

A major challenge associated with this life events research is that it has predominantly involved cross-sectional designs and retrospective measures meaning it is difficult to tease apart the direction of the relationship between negative life events and child anxiety disorders. This is important to consider as bidirectional relationships are perfectly plausible. For example, Tiet et al (2001) found a significant association between a parent changing their job and child separation anxiety disorder, but this could equally reflect a precipitant of or a response to child separation anxiety disorder. Consistent with this suggestion, research has shown that young people with anxiety disorders reported significantly more negative events that were “dependent” on the child’s actions than nonanxious/depressed controls (although not as many as depressed young people) (Allen et al., 2008; Connolly, Eberhart, Hammen, & Brennan, 2010). A small number of longitudinal studies have evaluated reciprocal relationships between life events and anxiety and suggest that particular life events may create a risk for the emergence of anxiety disorders, which may then create risks for further negative life events. For example, Edwards et al (2010) showed that anxiety symptoms among preschool children at mean age 4 predicted negative life events over the following 12 months, which in turn predicted their anxiety at mean age 5 years.

3.10. School environment

School-related worries are among the most frequently reported concerns of children and young people with anxiety disorders (Weems, Silverman, & La Greca, 2000) so the distinct lack of research that has addressed school factors as risks for the development of anxiety disorders is striking. Many features of the school environment bring potential risks, including, negative social evaluation by peers and teachers, extended absence from caregivers, and academic pressure. There is emerging evidence that more authoritarian, punitive teaching styles may be associated with increased levels of child anxiety (Manley, Tu, Reardon, & Creswell, 2022) and it is plausible that these may be heightened among children with unmet educational needs. For some young people, these pressures can lead to difficulties regularly attending school (Goodsell et al., 2017), with approximately half of the adolescents referred for treatment for school nonattendance meeting criteria for one or more anxiety disorders (McShane, Walter, & Rey, 2001). The potential role of the school environment as a risk for the development of

anxiety disorders has clear implications for large-scale prevention and treatment, highlighting the urgent need for future research in this area.

3.11. Peer relationships

Research has focused on associations between both positive (friendships) and negative (victimisation) peer relationships and child anxiety with most work focusing on social anxiety, limiting some conclusions that can be drawn. Most evidence suggests that socially anxious and withdrawn young people have fewer close and supportive friendships than more confident children (Kingery et al., 2010; Rubin, Wojslawowicz, Rose-Krasnor, Booth-LaForce, & Burgess, 2006). Here we again run into problems with distinguishing direction of effects given that when children present in an anxious manner they are less liked by peers than when acting in a non-anxious manner (Baker, Hudson, & Taylor, 2014; Luchetti & Rapee, 2014; Verduin & Kendall, 2008). The limited longitudinal research has been mixed, with one study showing that negative peer relationships predict social anxiety at a later time point (Tillfors, Persson, Willén, & Burk, 2012), while another showed that social anxiety predicted negative peer relationships, but not the reverse (Rapee, Magson, et al., 2022a). Combining diverse interactions such as peer disinterest, rejection, support, and hierarchies, into a single, overall “peer relationship” construct likely contributes to the conflicting results and future research should provide more nuanced evaluations.

In addition to a lack of general positive peer relationships, there is evidence that young people with anxiety disorders are more likely than their peers to experience peer victimisation (Cohen & Kendall, 2015; Hunt et al., 2022). There has been considerable longitudinal research to explore this association, with elevated anxiety symptoms found to be both a risk for and outcome of peer victimisation (e.g., Forbes, Fitzpatrick, Magson, & Rapee, 2019; Kljakovic & Hunt, 2016). In a meta-analysis of longitudinal studies, Christina et al. (2021) showed a small effect of anxiety on later victimisation ($r = 0.21$) and a slightly larger effect for victimisation predicting later anxiety ($r = 0.31$). Interestingly, some research has shown that anxious adolescents are more likely to interpret ambiguous peer comments as an indication of bullying (Calleja & Rapee, 2020). Hence, there is likely to be a vicious cycle wherein anxiety increases both real and perceived experiences with peer victimisation which, in turn, lead to greater anxiety.

Additional research has also shown that the ways in which young people interact socially when they are experiencing high levels of anxiety may lead to further increases in anxiety. For example, a recent longitudinal study showed that social anxiety in adolescence was predicted by the degree to which young people engaged in upward appearance comparisons (Rapee, Magson, et al., 2022b). The authors suggested that helping young people to avoid making upward and negative social comparisons may help reduce the incidence of social anxiety disorder. These findings are particularly intriguing given the increasingly central place of social media in the lives of both children and adolescents bringing enhanced opportunities for upward social comparisons (Fardouly, Magson, Rapee, Johnco, & Oar, 2020) and other positive and negative social interactions.

3.12. Parental behaviours

Theories of the development of paediatric anxiety disorders highlight the potential role of parental behaviours (especially modelling, information transfer, overcontrol, and rejection/lack of warmth) that may increase the child’s sense of threat and limit opportunities to develop confidence in coping (Murray, Creswell, & Cooper, 2009; Spence & Rapee, 2016; Waters & Craske, 2016; Wei & Kendall, 2014). Meta-analyses have shown emerging evidence for associations between child anxiety and parental autonomy granting, modelling, over-involvement, aversiveness and conflict among pre-adolescents (Yap & Jorm, 2015), whereas among (nonclinical) adolescents the most robust associations were for aversive parenting and lack of warmth, although

effect sizes were in the small to medium range (Yap, Pilkington, Ryan, & Jorm, 2014). Notably some of the research included in these reviews was limited by reliance on retrospective reports of parental behaviours and this has no doubt distorted the pattern of results. For example, a systematic review focused on adolescents, which did not include retrospective reports, found a somewhat different pattern of results with small to medium associations between adolescent anxiety and perceived parental control, anxious rearing, and parental rejection/lack of warmth (Waite, Whittington, & Creswell, 2014). Nonetheless the majority of this research remains questionnaire-based and cross-sectional, and few studies have used longitudinal or experimental designs - we have focused on those that have in the sections that follow.

In terms of parental modelling of fearful behaviours, experimental approaches have demonstrated that an increase in toddler fear and avoidance is precipitated when mothers express more fear in the presence of threat cues, such as toy snakes and spiders (Gerull & Rapee, 2002) or strangers (de Rosnay, Cooper, Tsigaras, & Murray, 2006). Naturalistic longitudinal studies have yielded similar results, with higher maternal and paternal expressed social anxiety being associated with later infant avoidance of a stranger (Aktar, Majdandžić, de Vente, & Bögels, 2014; Murray et al., 2008). Interestingly, early parental anxious modelling (at child age 12 months) continued to predict child anxious responding at 30 months, although concurrent parental behaviour did not, suggesting that there may be sensitive periods for the impact of parental modelling.

Experimental studies have also provided support for a causal effect of parental overcontrol on child anxiety, in 4–5 year olds (Thirlwall & Creswell, 2010) and 7–13 year olds (de Wilde & Rapee, 2008). In both studies, children showed higher levels of observed anxiety when their parents had acted in a controlling manner, although in Thirlwall and Creswell (2010) this was only the case for children with higher trait anxiety. Longitudinally, observed maternal overprotective behaviour in early childhood has predicted the child's anxious symptoms one to five years later (Buss, Zhou, & Trainer, 2021; Hudson & Dodd, 2012). In contrast, no such prediction was shown in early adolescence (Johnco et al., 2021) which may again suggest that particular parental responses have a greater impact at certain stages of development. Importantly, there is also increasing evidence to support the reverse relationship between child anxiety and parental responses. For example, adolescent anxiety has been found to predict later controlling parenting (Wijsbroek, Hale, Raaijmakers, & Meeus, 2011) and parental criticism (Nelemans, Hale, Branje, Hawk, & Meeus, 2014) - and in both of these studies there was no evidence of parenting to child effects. However, one study reported interesting differences based on the source of reporter among a sample of early adolescents and their mothers (Rapee, 2009). When mothers provided the source of information, adolescent anxiety predicted perceived maternal anxious responding 12 months later. However, when information was provided by the adolescent, perceived maternal anxious parenting predicted the adolescent's anxiety a year later. Finally, at least one study has demonstrated reciprocal effects between maternal overprotective behaviours and child anxiety based on maternal report across a one-year period at preschool age (Edwards et al., 2010). In contrast, paternal reports showed only that overprotective behaviours predicted later child anxiety.

Together these studies suggest that particular parental responses, such as higher parental control and protection, may be a normative response to children's anxious and inhibited behaviours but that these same behaviours may lead to increases in child anxiety in some circumstances at particular stages in their development. At the same time, the complex interplay between age of the young person, parent sex, and informant source, means that far more sophisticated work is needed before the potential impact of parent behaviours on paediatric anxiety can be fully elucidated.

3.13. Environmental factors: reasons for caution and promising directions

The reviewed literature highlights some potential environmental risk factors for the development of anxiety disorders in children and young people, but what is also striking is the amount that remains unknown. A major limitation across the research includes the lack of diversity in studied populations (despite evidence of cross-cultural differences in for example, associations between parental responses and child anxiety; (Oh, Shin, Moon, Hudson, & Rapee, 2002; Raudino et al., 2013). Parenting studies have also predominantly included mothers (for notable exceptions see Möller, Nikolić, Majdandžić, & Bögels, 2016) and there has typically been a lack of systematic consideration of child age. Indeed, many studies include children and adolescents from broad age ranges, despite theoretical reasons and empirical evidence that demonstrates different associations between key risk factors and age (Möller et al., 2016; Waite & Creswell, 2015). Other limitations that run across this literature include an insufficient focus on what causes anxiety disorders (as opposed to elevated symptoms) and a general lack of consideration of specificity of effects, both in comparison with other mental disorders and between different anxiety subtypes.

Of critical importance, studies have also largely failed to take into account the potential interactive nature of environmental and other risks. For example, the effects of life events (Broeren, Newall, Dodd, Locker, & Hudson, 2014), parental modelling (de Rosnay et al., 2006) and overcontrol (Thirlwall & Creswell, 2010) have all both been found to be moderated by child temperament and many of these factors also appear to be more likely to occur when children have inhibited temperament, elevated anxiety symptoms, or anxiety disorders (e.g., Edwards et al., 2010; Wijsbroek et al., 2011). Some recent exceptions have highlighted the complex bidirectional, dynamic, and interactive nature of risk and protective factors for child anxiety symptoms and disorders. For example, in a multi-method longitudinal study that followed children from 36 months to 15 years of age, Lorenzo et al. (2022) found that the interaction between child temperament and parenting at 36 months predicted changes in social anxiety symptoms from 9 to 15 years of age, with the steepest decrease in social anxiety symptoms over adolescence occurring for temperamentally fearful children who experienced highly supportive parenting at 36 months. Ultimately, going forwards we need research that uses robust methods and research designs that can help us determine which factors interact to increase risks for anxiety disorders, when, and for whom.

3.14. Psychological factors

The preceding sections have described distal risk for paediatric anxiety, yet 'proximal' precursory psychological factors, are also thought to play a role in the transfer of risks into symptoms, possibly mediating the effects of distal risk factors on symptom expression (see Fig. 1). A wealth of experimental research, focusing on attention, interpretation, memory biases, and fear conditioning in anxious young people has pointed to potential proximal psychological factors that underpin elevated anxiety. Broadly, these studies suggest that anxious young people demonstrate (a) elevated *threat responding*, (b) enhanced *threat generalisation*, and (c) impaired *threat maintenance*.

3.15. Threat responding

3.15.1. Attention bias studies

Studies examining threat responding, as indexed by threat attention biases, have produced mixed results among young people. A meta-analysis focused largely on reaction time methods concluded that anxious young people exhibit attention biases toward threat, although to a lesser degree than adults (Dudenev, Sharpe, & Hunt, 2015). In contrast, a later meta-analysis that included only studies using eye-tracking methods, failed to show an initial visual attention bias towards threat but did find that anxious young people were more avoidant

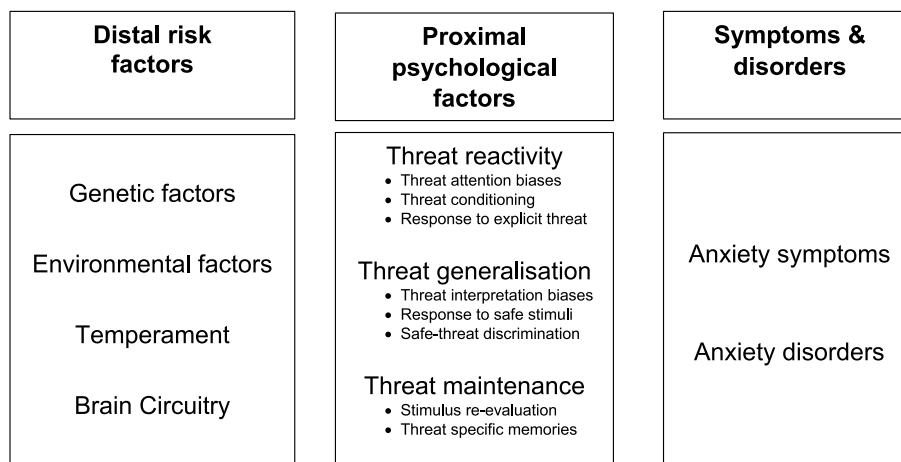


Fig. 1. Conceptual model illustrating distal risk factors, proximal psychological factors, and anxiety symptoms and disorders.

of threat across the time course of viewing than non-anxious young people (Lisk, Vaswani, Linetzky, Bar-Haim, & Lau, 2020). This research is supported by evidence that all young people, through until at least early adolescence, show a common attention bias toward threat, regardless of their level of anxiety (Burris, Barry-Anwar, & Rivera, 2017; Oar et al., 2022; Waters, Lipp, & Spence, 2004). Hence, preferential attention to threat may reflect a normal developmental process that preserves safety, which may eventually decline, allowing differences in threat attention between anxious and non-anxious young people to emerge (Kindt & Van den Hout, 2001). The precise developmental stage at which this change occurs is not yet clear, however, some research has demonstrated that biased attention to threat stimuli is associated with greater symptoms of anxiety (and depression) in older adolescents and young adults (Jenness et al., 2021). Longitudinally, threat attention biases have not been found to predict child anxiety symptoms, however, such studies have tended to focus on unselected samples of children up to 12–13 years of age (Henricks et al., 2022).

The attention bias literature is also complicated by mixed evidence related to the direction of bias – toward or away from threat. At least some evidence suggests that young people with distress disorders (e.g., generalised anxiety disorder) exhibit biases towards threat, whereas young people with fear disorders (e.g., specific phobias) exhibit attention biases away from threat (Salum et al., 2013; Waters, Bradley, & Mogg, 2014).

Stronger associations between threat attention bias and anxiety have been observed when links between threat attention bias and anxiety symptoms have been examined in the context of other risk factors, although a wide variety of factors has been examined and there are few consistently replicated effects (Gibb et al., 2011; Jenness, Hankin, Young, & Smolen, 2016; Pérez-Edgar et al., 2010). Several studies have documented concurrent links between attention biases towards threat and anxiety in children with high levels of behavioural inhibition (BI) (Morales, Taber-Thomas, & Pérez-Edgar, 2017; Pérez-Edgar et al., 2010; White, Degnan, et al., 2017b) and irritability (Elvin, Waters, & Modecki, 2022), and between greater activation in the ventro-lateral prefrontal cortex (VLPFC), the anterior cingulate cortex (ACC) and the amygdala in clinically anxious young people (Monk et al., 2008; Swartz et al., 2014) and those with high levels of BI (Auday, Taber-Thomas, & Pérez-Edgar, 2018; Fu, Taber-Thomas, & Pérez-Edgar, 2017).

Taken together, threat attention biases may be common to children and become more pronounced in anxious young people later in development, with the expression of the bias towards or away from threat among clinically anxious children influenced by different combinations of risk factors. However, there is currently little indication of whether threat attention biases might be a cause or a consequence of anxiety disorders in young people. One way to look at this issue is to manipulate

attention and look at its effects on anxiety. This has been done in the context of novel interventions referred to as attention bias modification (ABM) (MacLeod & Clarke, 2015). Most research has found similar symptom and threat attention bias reductions in ABM and control conditions (Linetzky, Pettit, Silverman, Pine, & Bar-Haim, 2020; Ollendick et al., 2019; Pettit et al., 2020) suggesting that factors unrelated to threat contingency, such as practice effects or non-emotional learning mechanisms, may influence treatment outcomes (Mogg, Waters, & Bradley, 2017). Indeed, Pettit et al. (2020) found that general attention control, but not attentional bias to threat, was significantly improved at post-treatment in anxious young people completing ABM and a control condition.

3.15.2. Fear conditioning studies

Fear conditioning studies also suggest associations between elevated threat responding and anxiety in young people. Studies have reported greater fear responses to the aversive unconditioned stimulus (US) on trials of the conditioned stimulus (CS) that are paired with an aversive event (CS+) as well as conditioned fear responses to the CS + itself in anxious young people relative to non-anxious peers, although there are some inconsistencies across measures (Britton et al., 2013; Craske et al., 2008; Lau et al., 2008; Waters, Henry, & Neumann, 2009). In a recent meta-analysis of children and adolescents, Dvir, Horovitz, Aderka, and Shechner (2019) found that anxious young people exhibited elevated responses to both the CS+ and CS- during conditioning relative to healthy peers.

In terms of links with risk factors, several studies have found that larger responding to the US on CS + trials during conditioning differentiated offspring of parents with anxiety disorders compared to offspring of healthy parents (Craske et al., 2008; Waters, Peters, Forrest, & Zimmer-Gembeck, 2014) and predicted higher anxiety symptoms 12 months later in healthy offspring of mothers with emotional disorders, but not healthy low-risk comparisons (Waters, 2017). Similarly, more fearful children with poorer parent-child relationship security exhibit greater reactivity to the CS+ (Bilodeau et al., 2020; Gilissen, Koolstra, van Ijzendoorn, Bakermans-Kranenburg, & van der Veer, 2007).

3.16. Threat generalisation

3.16.1. Interpretation studies

Young people with elevated anxiety symptoms and disorders endorse threatening interpretations of benign/neutral situations more than non-anxious peers (Stuijffzand, Creswell, Field, Pearcey, & Dodd, 2018), with some suggestion of content-specificity effects (Klein et al., 2019; Mobach, Rinck, Becker, Hudson, & Klein, 2019). Similarly, using the homophone/homograph tasks, anxious young people, relative to

non-anxious peers, more often select threatening meanings of words (Eley et al., 2008; Taghavi, Moradi, Neshat-Doost, Yule, & Dalgleish, 2000). In studies employing ambiguous faces, anxiety-associated effects have been found in the mis-categorisation (but not fear ratings) of various negative faces (Lau et al., 2012; Waters, Craske, Bergman, & Treanor, 2008). One meta-analysis concluded that the link between threat interpretation bias and anxiety increases in strength from childhood to adolescence (Stuijzand et al., 2018). Prospective studies have mostly failed to show that interpretation biases precede changes in anxiety symptoms (Blöte, Miers, Van den Bos, & Westenberg, 2019; Creswell & O'Connor, 2011; Lester, Lisk, Carr, Patrick, & Eley, 2019), perhaps suggesting that they are a consequence rather than a cause of anxiety disorder.

Similarly, studies that have experimentally manipulated interpretations (cognitive bias modification of interpretations; CBM-I) have produced mixed findings in relation to both changes in threat interpretations and anxiety symptoms in anxious young people (de Voogd et al., 2017; Lau, 2013; Telman, Holmes, & Lau, 2013). It has been suggested that anxiety symptoms may be more likely to change following CBM-I for highly anxious and clinical populations (e.g., Cristea, Kok, & Cuijpers, 2015). However, subsequent studies with clinically anxious children still found minimal impact of CBM-I training on either negative interpretations or anxiety symptoms (Klein et al., 2015; Orchard, Apetroaia, Clarke, & Creswell, 2016).

Children's threat interpretation biases have been found to be associated with parental overcontrol, parental anxiety and parents' threat attention biases (Affrunti & Ginsburg, 2012; Micco & Ehrenreich, 2008) both cross-sectionally (Creswell, Schniering, & Rapee, 2005; Schneider, Unnewehr, Florin, & Margraf, 2002) and over time (Creswell, Cooper, & Murray, 2010). However, offspring at-risk due to parent anxiety have been found not to differ in their extent of threat interpretation from offspring of healthy parents (Waters et al., 2008) or to do so only for some parent anxiety disorders e.g., panic disorder, but not others, e.g., animal phobia (Schneider et al., 2002).

3.16.2. Fear conditioning studies

Consistent with interpretation bias studies, fear conditioning studies suggest that anxious young people excessively generalise threat to safe stimuli. Overall responses to the CS during conditioning are larger in anxious compared to non-anxious young people (Britton et al., 2013; Craske et al., 2008; Haddad, Bilderbeck, James, & Lau, 2015; Waters et al., 2009) and a recent meta-analysis found persistent elevated responding to the CS- as well as the CS+ during conditioning in anxious relative to non-anxious young people (Dvir et al., 2019). One study indicated that the perceptual discrimination between safety and threat stimuli may improve with age, an improvement that is paralleled by reduced overgeneralisation of threat in older adolescents (Reinhard et al., 2022). Thus, the possibility that poor safe-threat discrimination underlies persistent threat overgeneralisation and heightened anxiety into adolescence warrants further research. One innovative application of this work has involved enhancing perceptual threat-safety discrimination, with implications for novel intervention. Among 9- to 14-year-old children, Ginat-Frolich, Gendler, Marzan, Tsuk, and Shechner (2019) found that a discrimination training group showed better threat-safe discrimination than a placebo training group and less threat overgeneralization to other stimuli as indicated by physiological but not cognitive measures than did placebo and no training conditions. This effect was moderated by age, with the training found to be more effective in older youths.

A few studies have examined associations between environmental risks, threat generalisation and anxiety. Reactivity to a CS- during conditioning has been found to characterise offspring of mothers with trauma exposure and PTSD or anxiety disorders compared to offspring of healthy mothers (Craske et al., 2008; Stenson et al., 2021; Waters, Peters, et al., 2014). However, this same reactivity to the CS- has been found to predict higher anxiety symptoms in children 12-months later

irrespective of their mothers' diagnostic status and thus, may be more strongly influenced by child-related factors (Waters, 2017). Notably, high levels of neuroticism in adolescents have been found to predict elevated reactivity during safe phases of explicit threat cue tasks (Craske et al., 2009) and in turn, elevated reactivity during safe phases predicted the onset of anxiety disorders four years later (Craske et al., 2012).

3.17. Threat maintenance

Threat maintenance refers to the persistence of elevated reactivity and fear following new information that threat stimuli are now safe. Threat maintenance can be examined via differences in the extinction of conditioned fear responses with new information that the CS+ is now safe via the repeated absence of the aversive US. Several studies reported larger SCRs to the CS+ during extinction in anxious compared to non-anxious young people (Craske et al., 2008; Jovanovic et al., 2014; Waters et al., 2009) and that only anxious young people continued to display differential responses to the CS+ versus the CS- during extinction (Liberman, Lipp, Spence, & March, 2006). Associations between severity of anxiety and both SCRs and unpleasantness ratings of CS+ and CS- persist throughout extinction among anxious young people and also during extinction recall several days later (Dvir et al., 2019; Klein, Abend, Shmuel, & Shechner, 2022). This suggests that a failure to re-evaluate stimuli when faced with new safety information may be a critical characteristic of anxious young people (Waters & Pine, 2016) and holds important implications for treatment.

Psychological processes underlying threat maintenance may be influenced by different combinations of risk factors and symptom expression. Numerous studies have shown that children of parents with anxiety disorders exhibit larger SCRs to the CS+ and the CS- relative to low-risk comparisons during extinction and extinction retest phases of fear learning tasks (in addition to the acquisition phase as noted earlier) (Craske et al., 2008; Waters, Peters, et al., 2014). However, anxious young people may exhibit greater amygdala activation to both CSs compared to healthy offspring of parents both with and without anxiety disorders (Chauret et al., 2019). Furthermore, larger SCRs to the CS- during extinction have been associated with higher PTSD, internalizing, and externalising symptoms 2 years later (Susman, Weissman, Sheridan, & McLaughlin, 2021), suggesting a lack of specificity.

In sum, elevated reactivity to threat cues, generalising reactivity to safe cues, and difficulty reducing generalised threat reactivity when situations are no longer threatening, are candidate proximal psychological mechanisms that mediate between distal risk factors (including child temperament, parental psychopathology, and parenting style) and anxiety symptoms and disorders. Variation in methodology, age ranges of young people assessed and the severity and type of anxiety disorders across studies to date have contributed to mixed findings. Nevertheless, some psychological processes, such as elevated threat responding, may be more stimulus, context and developmentally dependent whereas others, such as threat generalisation, may be more stable and become further pronounced with increasing age. Greater precision is required in documenting the conditions under which anxiety-related psychological processes have (and have not) been observed and utilising associated measures and methods in future studies employing longitudinal designs. Additionally, greater focus on adapting measures and methods to be able to identify psychological risk markers on a case-by-case basis to personalise treatments to patient risk profiles could improve treatment outcomes (Waters & Pine, 2016). Furthermore, some of the mixed findings and new directions to date suggest the roles of broader cognitive control and specific memory processes that might contribute to and underpin sustained threat reactivity and threat maintenance (Andrea L. Gold et al., 2020a, 2020b; Songco, Booth, Spiegler, Parsons, & Fox, 2020). Such findings illuminate the need for ongoing innovation in experimental research on psychological factors and integrative theory development (Waters & Craske, 2016).

4. Treatment and prevention of paediatric anxiety disorders

4.1. Psychological treatments for paediatric anxiety disorders

Cognitive Behavioural Therapy (CBT) is the most extensively evaluated psychological intervention for paediatric anxiety disorders (e.g., Dickson et al., 2022) and to date there have been limited evaluations of non-CBT approaches. Exceptions include supportive child-centred therapy (Silk et al., 2018), mindfulness-based interventions (Odgers, Dargue, Creswell, Jones, & Hudson, 2020) and acceptance and commitment therapy (Hancock et al., 2018) but due to the modest available literature on these non-CBT approaches, our focus will be on CBT. It is also important to point out from the start that, with some notable exceptions, treatment research has typically grouped young people from broad age ranges and has predominantly included Western populations. Although neither age nor ethnicity have been found to consistently moderate treatment outcomes (Norris & Kendall, 2021) and positive outcomes from CBT for child anxiety disorders have been found across diverse cultures (Arendt, Thastum, & Hougaard, 2015; Ishikawa et al., 2019; Pina, Silverman, Fuentes, Kurtines, & Weems, 2003), going forward it will be important that we better understand how treatments need to be adapted to be most accessible and effective across development and cultures (Chavira, Bustos, Garcia, Ng, & Camacho, 2017).

4.2. Treatment outcomes

The most recent Cochrane review of CBT for child anxiety disorders (James, Reardon, Soler, James, & Creswell, 2020) identified 88 eligible RCTs and concluded that there was moderate quality evidence that CBT leads to greater remission of primary and all anxiety disorders than passive controls in the short term, with an average of 49% of participants being free of their primary anxiety disorder following CBT compared to 18% in the waitlist/no treatment control arms. Despite the large and growing number of studies, few studies include 'active' controls, so while CBT generally outperforms treatment as usual or alternative treatments, the evidence can be said to remain tentative. Other limitations of the available literature include a relative lack of studies to evaluate treatments among younger children (with less than 6% of studies focusing on children under 8 years of age) and for children with additional needs, for example, those associated with neurodiversities or intellectual disabilities. Further, there is a serious lack of studies that evaluate "hard data" on functional improvements (e.g., school absenteeism) (Dickson et al., 2022), which are arguably the most important outcomes for families (Creswell et al., 2021).

Another limitation of current treatment studies highlighted by James et al (2020) is the lack of controlled data on long term outcomes. Cautionary findings come from the long-term follow-up of the large Child/Adolescent Anxiety Multi-modal (CAM) trial, which compared CBT, SSRI, CBT + SSRI, and pill placebo for the treatment of anxiety disorders in 7–17 year olds (Walkup et al., 2008). Initial results from CAM showed similar outcomes for CBT and SSRI (46% remission from anxiety disorders) and an advantage from the combined treatment (68%; compared to 24% in the placebo arm). However, in a rigorous examination of longer-term outcomes, which assessed outcomes annually over a four-year period (between 4 and 12 years after randomisation), only 22% of participants (with similar patterns across arms) were found to be in stable remission, with 30% having a chronic course of anxiety disorders and 48% relapsing at some point (Ginsburg et al., 2018). Among those who showed initial remission, positive functional outcomes were maintained for 3–12 years (Swan et al., 2018). Together the available literature highlights that while CBT is effective and currently has the most robust evidence base of any psychological therapy for the treatment of paediatric anxiety disorders, there remains substantial room for improvement.

4.3. Improving outcomes from CBT

To identify how to improve outcomes from CBT for paediatric anxiety disorders, answers to the following interlinked questions will be critical.

4.3.1. Who does CBT (not) work for?

As highlighted by a recent review (Norris & Kendall, 2021), research findings are extremely inconsistent when it comes to predictors (and moderators) of treatment outcomes, with mixed findings for a range of variables including child age, gender, race/ethnicity, socio-economic status, anxiety severity and comorbidity. Many studies lack sufficient power or variance to address these questions, however the one particular predictor that has emerged consistently is the presence of social anxiety disorder (Hudson, Keers, et al., 2015; Lundkvist-Houndoumadi & Thastum, 2015; Taylor et al., 2018). Indeed a recent systematic review found a post CBT recovery rate of only 35% when participants had a primary diagnosis of social anxiety disorder, compared to 54% for other anxiety disorders (Evans, Clark, & Leigh, 2021). As highlighted by Norris and Kendall (2021), there is a need for examination of theory-driven predictors of treatment outcome, with sufficiently powered studies to examine their effects in isolation and combination. In the meantime, a clear take away message is that, while outcomes could be better, the evidence does not justify withholding CBT from children with anxiety disorders based on any particular characteristics.

4.3.2. What is maintaining the problem?

Unlike models of anxiety disorders in adults, which have focused on identifying *maintaining* factors underlying the problem (e.g., Clark & Wells, 1995; Rapee & Heimberg, 1997), models of anxiety disorders in children and adolescents have typically focused on developmental risk factors (e.g., Spence & Rapee, 2016). These models are helpful in guiding prevention, but they provide limited information on which to base treatments. Recent reviews that have focused on the applicability of adult maintenance models, for social anxiety disorder in particular, have provided encouraging evidence for adolescents (Leigh & Clark, 2018); although less so for children (Halldorsson & Creswell, 2017). These reviews also highlight the need for maintenance models to incorporate developmental considerations, including the potential for different mechanisms to be influential at different stages of development (e.g., Rapee et al., 2019) and the changing role of environmental influences through childhood and adolescence, including interactions with family and peers.

One novel intervention, positive search training, aims to target several potential maintaining processes, including enhanced attention control on goal-directed stimuli and the inhibition of threat distractors, while also encouraging stimulus re-evaluation and memory rehearsal of strategies to enhance the generalisation of new learning. Several studies have found promising effects of positive search training on clinically anxious children's anxiety symptoms relative to waitlist control conditions (Waters et al., 2015; Waters et al., 2016) and as a classroom-based intervention relative to CBT (Waters et al., 2019). Notably, children who showed greater consolidation of the memory strategies during treatment achieved greater improvement in global functioning at post-treatment (Waters et al., 2015). Taken together, greater understanding of processes that maintain anxiety in young people along with strategies that can reliably modify these underlying mechanisms, should be a clear focus of future research.

4.3.3. What are the active ingredients and enhancers of treatment?

Surprisingly little research has addressed the relative impact of specific therapeutic procedures in the treatment of paediatric anxiety disorders (Higa-McMillan, Francis, Rith-Najarian, & Chorpita, 2016). The strongest evidence has highlighted the critical role of exposure in positive treatment change (e.g., Higa-McMillan et al., 2016; Peris et al., 2015; Teunisse et al., 2022). However, it remains unclear how to

optimise outcomes from exposure in children and young people, which is not helped by a lack of consistency in approaches and findings (Plaisted, Waite, Gordon, & Creswell, 2021; Teunisse et al., 2022). There is some evidence, for example, that introducing anxiety management strategies prior to exposure (as is often done in CBT for child anxiety disorders) may not be necessary (Ale, McCarthy, Rothschild, & Whiteside, 2015) and, in the case of relaxation, may be detrimental (Whiteside et al., 2020).

One novel attempt to enhance learning from exposure has combined exposure with attention bias modification (ABM) to target elevated threat responding and improve safety learning. Waters, Farrell, et al. (2014) combined dot-probe ABM or a control condition with a single session of exposure therapy for young people with specific phobias. Although greater reductions in children's danger expectancies and attention bias were found using ABM, there were no significant differences between conditions in clinical outcomes. However, in a study comparing ABM or control plus a full course of CBT relative to CBT alone, Shechner et al. (2014) found that only the active ABM plus CBT group showed significant reduction in child- and parent-rated anxiety symptoms (although there were no differences from the CBT + control arm based on clinician reports).

A potential enhancer of paediatric anxiety treatment that has received particular attention is parental involvement. Logically, a critical difference between treatment for adults and children should be the potential for beneficial impact of incorporating parents into treatment for paediatric anxiety. Yet, reviews and meta-analyses have consistently failed to find overall differences in child outcomes whether including or not including parents (James et al., 2020; Reynolds, Wilson, Austin, & Hooper, 2012). However, as highlighted by Lawrence, Parkinson, Jasper, Creswell, and Halligan (2021), wide variability in the focus and extent of parental involvement across studies precludes clarity about what works and for whom (Manassis et al., 2014). Indeed, it is likely that the way in which parents should optimally be involved will vary in line with children's cognitive abilities and the degree to which they can bring about changes in the child's wider environment. Some interesting hints come from an analysis of a large, combined dataset, which showed that actively training parents in anxiety management practices resulted in significantly greater maintenance of treatment gains than either no parental involvement or simply logistic involvement (Manassis et al., 2014).

Some recent studies of social anxiety disorder have begun to highlight key mechanisms to enhance outcomes from CBT for this specific disorder. Firstly, recent experimental studies have demonstrated benefits of dropping safety behaviours and shifting focus of attention (Leigh, Chiu, & Clark, 2021) and modifying mental imagery (Leigh, Chiu, & Clark, 2020) during social challenge tasks for the reduction of symptoms of social anxiety in adolescents. Second, recent evaluations of disorder-specific cognitive therapy have either found that (strong) outcomes were mediated by changes in safety behaviours and negative cognitions (Leigh & Clark, 2022) or that there was at least a tendency for greater changes in measures of attentional focus, safety behaviours and negative cognitions following a modified disorder-specific form of CBT compared to standard CBT (Rapee, McLellan, et al., 2022a). As such, Rapee and colleagues (2022a, b) suggested that 'we are on the right track' by specifically targeting the psychological processes believed to maintain social anxiety disorder. Indeed, it is likely that a similar approach of careful identification and targeting of maintaining mechanisms can help us improve outcomes for a wider range of anxiety disorders in young people.

4.4. Increasing access to CBT

Despite the evidence for the effectiveness of CBT for paediatric anxiety disorders, few anxious young people access empirically-validated treatments. First, few diagnostically anxious young people seek help (Lawrence et al., 2015; Merikangas et al., 2011). Second,

among those who do seek help, only a small proportion receive empirically-validated treatment. In a study conducted across England in 2017, despite 65% of families having sought help, only 2% of children identified as having an anxiety disorder had received CBT (Reardon et al., 2020). Elsewhere a similar picture is seen; a recent Australian study found higher rates of access to CBT among children with elevated symptoms of anxiety (19.5%), however the majority of children whose families had sought help for anxiety (66.3%) had not received CBT (Gandhi, Ogradev-Lee, Jones, & Hudson, 2022). To address this major problem, the following will be required:

4.4.1. Efficient modes of treatment delivery

A major barrier to the implementation of CBT in routine practice is the limited availability of trained practitioners within often highly stretched clinical services. Notably, in the most recent Cochrane review, there was no evidence of differences in remission from primary anxiety disorders for treatments involving above or below 10 h of therapist contact time (James et al., 2020), highlighting the potential to increase access to effective treatments through briefer interventions. Indeed, there is now good clinical, and emerging economic, evidence for a range of efficient modes of delivering CBT for children with anxiety disorders, including single session interventions for specific phobias (e.g., Oar, Farrell, Conlon, Waters, & Ollendick, 2017) and therapist-guided brief interventions (Bennett et al., 2019), including in online forms (Pennant et al., 2015).

4.4.2. Efficient and accessible service delivery models

There is emerging evidence that incorporating brief, therapist-guided interventions into a stepped care model of treatment delivery (Kendall, Makover, et al., 2016b), brings potential for good clinical outcomes and cost-efficiencies. For example, in a randomised controlled trial to directly test this model with young people with anxiety disorders, Rapee et al. (2017) found similar outcomes following a stepped care approach to treatment (incorporating (i) brief therapist-guided CBT, (ii) standard face to face CBT, and (iii) individually tailored CBT) compared to standard face to face CBT only, but with significantly lower intervention costs from a societal perspective (though not significantly so from a combined health and societal perspective) (Chatterton et al., 2017). As such, stepped care appears to be a promising approach, although Rapee et al.'s (2017) finding that the third step appeared to add little in terms of further recovery, highlights the need for future research to identify the optimal number and composition of steps required to optimise the clinical and cost-effectiveness of this approach.

As well as considering *how* we deliver interventions, we also need to consider *where* we deliver them to maximise reach and accessibility. While it won't be a suitable setting for all, schools are increasingly being recognised as being well placed for the identification of and early intervention for common mental health problems and there is now a growing number of examples of efficient and effective intervention delivery for children and young people with anxiety disorders identified via schools (Haugland et al., 2020; Leigh & Clark, 2022). Furthermore, the increasing application of codesign methodologies will help to ensure that school-based approaches are delivered in ways that are most likely to overcome barriers to access and engagement (Burns & Rapee, 2022; Waters et al., 2022; Williamson et al., 2022).

4.4.3. Implementation of evidence-based practice in routine care

Ultimately the impact of our growing knowledge about treatment for child anxiety disorders will depend on implementation of this learning in practice (Kendall et al., in press). There are a number of reasons to be concerned about the extent to which this happens currently. For example, in a randomised controlled trial of CBT vs treatment as usual delivered by novice school-based clinicians, Ginsburg, Pella, Pikulski, Tein, and Drake (2020) noted wide disparities in both the implementation of CBT and in clinical outcomes (41% free of their primary anxiety disorder), compared to those typically reported in research

trials. Furthermore, in a survey of clinicians providing treatment to children with anxiety disorders in the USA, despite 80% endorsing CBT as their therapeutic orientation and exposure having been identified as a key therapeutic ingredient (see above), only 5% endorsed providing exposure-focused treatment (Whiteside, Deacon, Benito, & Stewart, 2016). Encouragingly however, there are some notable exceptions with several studies indicating that routine service providers in community health centres are able to achieve comparable outcomes to those reported in efficacy trials when provided with structured, evidence-based programs (e.g., Creswell et al., 2017; Djurhuus & Bikic, 2019; Jónsson et al., 2015; Villabø, Narayanan, Compton, Kendall, & Neumer, 2018). Going forward it is critical that researchers, families, clinicians, and other stakeholders work closely together to ensure the latest evidence is implemented in practice to achieve the best outcomes possible for anxious young people.

4.5. Medication therapies

Clinical trials have examined the efficacy of various medications for paediatric anxiety disorders. The strongest data exist for the SSRIs, where at least four trials, each in more than 50 young people with anxiety disorders, demonstrate efficacy (Locher et al., 2017; Strawn et al., 2020). The effect sizes over placebo reported in these studies are large and at least as good as studies of CBT for paediatric anxiety disorders. Nevertheless, as discussed below, several factors influence views on whether or not SSRIs or CBT should be considered first line treatments. The serotonin-norepinephrine reuptake inhibitors (SNRIs) represent the only other established medication (Locher et al., 2017), where duloxetine has Food and Drug Administration (FDA) approval for the treatment of paediatric generalised anxiety disorders in the USA. Other medications used to treat paediatric anxiety disorders include additional antidepressant medications, benzodiazepine medications, and some anticonvulsant medications (Klein & Slomkowski, 1993; Penninx et al., 2021; Strawn, Lu, Peris, Levine, & Walkup, 2021). However, none of these treatments are as well established as even SNRIs, let alone SSRIs.

Patients typically ingest SSRIs, SNRIs, or other medications on a daily basis in an attempt to alleviate anxiety. Novel medications might provide benefits when used in a more limited and synergistic fashion, taken only at the time of a CBT exposure-therapy session, to increase learning or enhance retention of extinction during the therapy. The most-studied example of such a synergistic treatment concerns the partial glutamatergic agonist, d-cycloserine, which facilitates extinction in rodents, an effect that could be relevant to an enhancement of the response to CBT. However, evidence to support clinical use remains inconsistent (Rapee et al., 2016; Rosenfield et al., 2019; Smits et al., 2020). Other medications and somatic therapies, such as brain stimulation, also could synergize learning during CBT, but concerns about the tolerability of such treatments limits their use with young people (Pine, Wise, & Murray, 2021).

4.5.1. SSRI treatment

Despite their established efficacy, three key questions remain concerning SSRI treatment. One question concerns the relative efficacy of SSRIs and CBT. While the effect size may appear larger in SSRI than CBT trials, effects are heavily influenced by source of informant and measurement instruments, which often differ between trials. Therefore, the most relevant data directly contrast the two treatments. Only one such large-scale trial has directly compared efficacy in paediatric anxiety disorders (Walkup et al., 2008). The findings from this trial suggest that, although there were significantly more dropouts from the medication condition than CBT, the two treatments are roughly equivalent in their efficacy. The second question concerns the comparative tolerability of the two treatments, which both generally are well tolerated. However, SSRIs could possibly induce long-term changes in brain function with unclear clinical impact when given early in development (Shrestha

et al., 2014). Hence, when combined with data demonstrating comparable efficacy, concern about long-term changes in brain function leads some clinicians to recommend CBT as a first-line treatment before SSRIs (e.g., Andrews et al., 2018). Moreover, caregivers commonly view pharmacotherapy for paediatric anxiety disorders as less acceptable than psychotherapy (Brown, Deacon, Abramowitz, Dammann, & Whiteside, 2007; Lazaratou, Anagnostopoulos, Alevizos, Haviara, & Ploumpidis, 2007). Finally, questions remain about the added benefit of SSRI therapy when combined with CBT. One trial suggested a benefit to such combined therapy when compared with either SSRI or CBT monotherapy (Walkup et al., 2008). However, in this trial, combined therapy was delivered in an open fashion, which could have led expectancy to create greater efficacy in the group receiving combined therapy as compared to the two mono-therapy groups. Indeed, a recent study that used procedures to match expectancy across groups suggested that SSRI therapy provided no additional benefit beyond CBT combined with placebo in the treatment of paediatric anxiety disorders (Hudson et al., 2021). In brief, there is good evidence for the efficacy of medications in reducing paediatric anxiety disorders and their efficacy appears at least as strong as CBT. However, concerns about potential impacts on the developing brain and potentially negative attitudes to medication for young people in at least some communities, means that medications likely have their strongest role as a second-line intervention.

4.6. Prevention of paediatric anxiety disorders

The possibility that anxiety disorders could be prevented before they begin to cause major life impairment has started to receive increasing attention over the past two decades (Rapee, 2002). Empirical evaluation of programs to prevent the development of anxiety disorders has now been conducted at the level of universal (everyone), indicated (those with high symptoms), and selective (those high on risk factors) interventions. The majority of research has addressed universal programs delivered within schools and the least evidence has addressed selective interventions, perhaps due to our relatively limited knowledge of risk and causal factors for anxiety. One of the primary limitations of the research into prevention is the relatively small proportion of studies that include long-term follow-up and diagnostic assessment. To conclude that anxiety disorders are prevented, it is imperative to assess actual disorder and to demonstrate that new onset (incidence) has been reduced, which may not occur for years following the intervention. Unfortunately, the majority of research relies on symptomatic assessment and is limited to post-intervention outcomes or at best, short-term follow-up.

The majority of preventive interventions for anxiety disorders has been delivered through schools, either to whole classes, grades, or the entire school. Most interventions deliver cognitive and/or behavioural strategies, most commonly in a universal format, over approximately 8–12 weeks, and target either anxiety specifically or anxiety and depression more generally. Overall, school-based preventive interventions for anxiety have shown small post-intervention effects on symptoms of anxiety (around 0.1 to 0.2) (Fisak, B, Richard, & Mann, 2011; Johnstone, Kemp, & Chen, 2018; Stockings et al., 2016; Werner-Seidler et al., 2021). Follow-up outcomes have largely been maintained in the shorter term but show some deterioration in the longer-term (Johnstone et al., 2018; Mychailyszyn, Brodman, Read, & Kendall, 2012; Stockings et al., 2016; Werner-Seidler et al., 2021). An additional caveat that needs to be mentioned is the possibility for iatrogenic effects, a possibility that has been observed in some universal work (Wigelsworth et al., 2018). A few trials have demonstrated significant (although small) long-term effects (Waldron, Stallard, Grist, & Hamilton-Giachritsis, 2018; Werner-Seidler et al., 2021) and it would be interesting for future research to identify specific characteristics of interventions that may facilitate long-term benefits. However, even these studies have mostly interpreted “long-term” as 12–24 months (Werner-Seidler et al., 2021). Follow-up of school-based prevention of

anxiety into adulthood, or even right across the years of schooling, are non-existent. Among the considerably smaller number of studies that have evaluated the impact of school-based prevention on clinical anxiety disorder, some significant reduction in risk has been demonstrated immediately post intervention that was not maintained by 12 months following program delivery (Stockings et al., 2016). It is noteworthy that most universal programs have simply used standard CBT treatment methods and few, if any, have directly addressed risk factors for anxiety as described in our earlier section.

A considerably smaller literature has evaluated prevention programs delivered outside of the school setting and these have more commonly followed a selective or indicated format (Lawrence, Rooke, & Creswell, 2017). Most indicated programs have targeted children scoring high on temperamental inhibition (e.g., Bayer et al., 2022; Chronis-Tuscano et al., 2021; Rapee, 2013), given its strong risk for anxiety disorder (see above). Only a handful have addressed other risk factors such as high parent anxiety (e.g., Ginsburg, Drake, Tein, Teetsel, & Riddle, 2015). Additionally, based on theories pointing to the potential role of parents in the onset of anxiety disorders (see above), and the potential for parents to apply prevention principles in their children's day to day lives, a significant body of research has evaluated anxiety prevention programs that directly address parents. These programs typically attempt to alter parenting skills or the parent-child relationship, or alternately, use the parent to deliver skills-training to their child (Yap et al., 2016). One meta-analysis that evaluated parent-oriented studies where the target was any aged offspring (preschool to adolescence) showed small, significant effects on anxiety symptoms ($d = -.27$) (Yap et al., 2016). In contrast, a review that focused on prevention programs targeted only to parents of preschool aged children (aged 2–5 years), showed large reductions in anxiety symptoms ($SMD = -.72$) (Howes Vallis, Zwicker, Uher, & Pavlova, 2020). It is perhaps not surprising that larger effects are seen in younger children from programs targeting parents given the greater influence that parents maintain at this stage of life.

Several moderators of outcomes have been evaluated but the wide variation in measurement and the limited sample sizes mean that few consistent moderators have been identified (Moreno-Peral et al., 2020). One of the most addressed questions is whether the intervention type (universal, indicated, selective) impacts outcomes. Unfortunately, the limited number of selective and indicated programs has meant that most reviews have collapsed them into a single "targeted" category. In general, few significant differences have been shown between these types of intervention for anxiety, although the size of effect typically slightly favours targeted programs (Feiss et al., 2019; Fisak et al., 2011; Werner-Seidler et al., 2021). Over time, targeted programs appear to maintain effects better than universal interventions (Werner-Seidler et al., 2021). Among programs focused on parents, those that teach the parent to help their child (parent as coach) appear to show considerably larger effects than those addressing the parent/child relationship or parenting skills (Yap et al., 2016).

5. Conclusion

Scientific research into paediatric anxiety disorders has increased dramatically over the past 30 years. As a result, we now have far greater knowledge about key characteristics, risk and maintaining factors, treatments, and prevention of these highly prevalent disorders. Nonetheless, the field has a long way to go. As an example, although we now have very well-established programs for the treatment of anxiety disorders in young people, less than half are free of all anxiety disorders immediately following treatment (James et al., 2020). This proportion typically increases over the following months (Hudson et al., 2009; Rapee, Abbott, Baillie, & Gaston, 2007), but the fact remains that a significant proportion of young people with anxiety disorders continue to meet criteria for their disorder even following our current best efforts at treatment. This, combined with the very low proportion of anxious young people in the community who receives empirically-validated

treatment (Gandhi et al., 2022; Reardon et al., 2020) makes paediatric anxiety disorders a serious risk for long-term disability (King et al., 2020; Swan et al., 2018). By summarising the current state of the literature into paediatric anxiety disorders, we have highlighted key gaps in our knowledge and potentially important directions for future research. Among the many remaining important issues, a few in particular, stand out.

First, more researchers need to listen to relevant stakeholders – including not only the young people experiencing chronic anxiety, but also their caregivers, teachers, and mental health providers (e.g., Lawrence et al., 2021). Codesigned interventions may increase reach and contributions from stakeholders can help to improve acceptability of services.

Similarly, research needs to incorporate far stronger representation from the entire population. The majority of current research is conducted with highly educated, motivated, and Caucasian samples recruited through university clinics. These samples are quite different to the populations found in typical community services (Ehrenreich-May et al., 2011; Southam-Gerow, Chorpita, Miller, & Gleacher, 2008).

Not only does the representativeness of research need to improve, but overall sample sizes are commonly far too small to draw reliable conclusions. It is likely that the best way to move research forward is to compile consortia of researchers in a similar manner to that used in the genetics field (e.g., Lester et al., 2016). It is only in this way that the large samples required to fully address many questions, especially related to causes and moderators, can be recruited.

Finally, applied work needs to be underpinned by strong theory, good understanding of causal and maintaining factors, and reliable and valid measures. In all these areas, there is still a lot to learn with relevance to paediatric anxiety disorders. Continued investment in strong, basic science that aims to increase our understanding of the factors that cause and maintain anxiety disorders in young people along with measures that reliably and validly assess factors of greatest relevance to stakeholders, will unleash the greatest opportunities to improve the lives of young people experiencing debilitating anxiety.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

No data was used for the research described in the article.

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