Predictors of relapse after CBT for anxiety disorders in children and adolescents: An Individual Patient Data Meta-analysis

Alexander Lell

Master Thesis - Clinical Psychology

s2352958
September 2022
Department of Psychology
University of Groningen
Examiner/Daily supervisor:
prof. dr. Maaike Nauta
Bas Kooiman, MSc.

A thesis is an aptitude test for students. The approval of the thesis is proof that the student has sufficient research and reporting skills to graduate, but does not guarantee the quality of the research and the results of the research as such, and the thesis is therefore not necessarily suitable to be used as an academic source to refer to. If you would like to know more about the research discussed in this thesis and any publications based on it, to which you could refer, please contact the supervisor mentioned.

Abstract

While cognitive behavior therapy (CBT) is the first-line treatment recommendation for anxiety disorders in children and young people (CYP) in international treatment guidelines, relapse rates remain high and involved factors are poorly understood. The present work aimed to increase understanding by means of an individual patient data meta-analysis (IPDMA) with the primary aim of investigating whether treatment dose, disorder type and/or an interaction thereof can predict relapse rates. To this end, we systematically searched the COCHRANE database, Medline, PsycINFO, Eric, and CINAHL for randomized controlled trials (RCTs) examining CBT for anxiety disorders in CYP, in which diagnostic assessments were conducted at pre-treatment, post-treatment and at a follow-up. Individual patient data was provided by the authors of 47 out of 115 eligible RCTs. Of the data received, 19 RCTs had been synthesized at the time of writing with 663 participants from 14 RCTs contributing to the analyses. Across included RCTs, 20.1% of participants suffered relapse of any anxiety disorder. Relapse rates were the same for social anxiety disorder and for specific phobias (18.2% vs. 18.7%, respectively) but this difference was not statistically significant. Nor did treatment dose or the interaction between treatment dose and disorder type predict relapse rates. The present work found fairly similar relapse rates compared to previous work in the field. The hypothesized moderation was not found. However, statistical power was limited. Results could, therefore, be a consequence of lacking power rather than no effect. Identifying reliable predictors of relapse may ultimately pave the way for tailored approaches to relapse prevention.

Introduction

Anxiety disorders are among the most prevalent mental disorders in children and young people (CYP), with a point prevalence of 7.1% in children aged 3-17 years (Ghandour et al., 2019) and a lifetime prevalence of 31.9% in adolescents aged 13-18 years (Merikangas et al., 2010). While feeling anxious is an integral part of human existence and in many cases an adaptive response to threatening situations, individuals with anxiety disorders suffer from clinically significant levels of anxiety in contexts where objective threat is absent and from a high functional impairment in major life domains as a consequence of their condition (American Psychiatric Association, 2013). Various anxiety disorders exist and while the central object of anxiety differs (e.g., spiders for arachnophobia as an example for specific phobias or the presence and judgments of other people in social anxiety disorder) they share the common denominators of excessive fear, hyperarousal symptoms (e.g., increased heart rate, sweating), avoidance of feared stimuli, and the accompanying functional impairment (American Psychiatric Association, 2013). These symptoms often interact as part of a vicious cycle. Since the feared stimulus evokes strong fear and accompanying hyperarousal symptoms, patients increasingly avoid situations in which a fear response may occur. Avoidance, in turn, is among the main drivers of anxiety disorder maintenance mainly via indirect reinforcement; that is, by decreasing fear and hyperarousal symptoms in the short run while maintaining the problem at hand in the long run (Norton & Paulus, 2017). Due to avoidance, irrational beliefs (e.g., “The spider will bite me.”, “The other people at the counter will see that my hands are shaking and that my face turns red and they will think I’m a fool.”) are maintained rather than corrected. In the long run, avoidance leads to substantial functional impairments in major life domains such as work and social life and often to low self-efficacy beliefs concerning coping with fear (Norton & Paulus, 2017). In the light of their high prevalence in the general population, their potentially chronic course and the high accompanying morbidity, anxiety disorders are among the leading contributors to the global burden of diseases (Xiong, Liu, Liu, & Hall, 2022). Anxiety disorders are highly comorbid across each other (Bandelow, & Michaelis, 2015), with other mental disorders such as major depression or substance use disorders (McLean,

Asnaani, Litz, & Hofmann, 2011), and with physical morbidities such as diabetes type II (Mersha, Tollosa, Bagade, & Eftekhari, 2022), coronary heart disease (Emdin, Odutayo, Wong, Tran, Hsiao, & Hunn, 2016), and obesity (Amiri & Behnezhad, 2019). The COVID-19 pandemic has further increased the global burden of anxiety disorders (Bendau et al., 2021; Huang & Zhao, 2020); and particularly so in young populations (Racine, McArthur, Cooke, Eirich, Zhu, & Madigan, 2021; Śniadach, Szymkowiak, Osip, & Waszkiewicz, 2021). In the light of the high disease burden imposed on affected individuals and society at large, the successful treatment of anxiety disorders remains a global health priority.

Cognitive behavior therapy (CBT) is the first-line treatment recommendation for anxiety disorders (both for adult and pediatric anxiety disorders) in international treatment guidelines and by far the most well-researched psychological intervention for anxiety disorders (Bandelow, Michaelis, & Wedekind, 2017; Clark, 2011; Higa-McMillan, Francis, Rith-Najarian, & Chorpita, 2016; Walter et al., 2020). A comprehensive review summarizing the findings of 111 outcome studies published over the past five decades concluded that CBT for anxiety disorders in CYP is largely effective and an appropriate first-line treatment recommendation (Higa-McMillan et al., 2016). While symptom improvement is an important measure of treatment outcomes to assess the efficacy of a treatment like CBT and to compare the efficacy among various psychological and psychopharmacological interventions, other metrics of treatment success such as remission and relapse are as important. Remission is defined as a lessening of symptoms below a clinical cutoff or the respective clinical diagnostic algorithm (American Psychological Association, 2022b). That is, remitted patients either do not suffer symptoms anymore or they suffer some residual symptoms, which do not meet clinical criteria. As such, remission is a metric that exclusively targets practically significant symptom improvement whereas standardized mean difference, which is perhaps the most common metrics to evaluate the efficacy of interventions, involves pooled (i.e., mean value) comparisons on a group-level (i.e., disregarding that some patients might not have improved in a clinically significant manner). In their meta-analysis of trials examining the efficacy of CBT treatment for CYP, James et al. (2020) defined remission as the absence of a diagnosis, and found a

pooled remission rate of 49.4% for the primary diagnosis at treatment endpoint and a remission rate of 46.8% across anxiety disorders. Since the pooled remission rate was much lower for the wait list control conditions (17.8% for the primary diagnosis), the authors concluded that CBT clearly has an effect beyond symptom improvement caused by time. However, even for the first-line treatment recommendation for the treatment of anxiety disorders for CYP, remission rates are far from being perfect and so are rates of relapse.

Relapse describes the reappearance of a condition after previously having been in remission (American Psychological Association, 2022a). As such, relapse is a central metric for the longevity of treatment success. While standardized mean differences and remission rates at treatment endpoint do inform about the short-term efficacy of a given intervention, they do not speak to long-term effects. Standardized mean differences at follow-up and relapse rate, however, do inform about the longevity of treatment effects. Given that anxiety disorders are potentially chronic conditions, the long-term effects are of particular interest. Ultimately, researchers, clinicians and policy makers do want to disseminate those interventions in clinical practice which have the most favorable treatment profile (e.g., in terms of their benefit- cost ratio) in the long-run, not just the short-run. A meta-analysis by Levy, Stevens and Tolin (2021) examined the overall relapse rate after successful CBT treatment for CYP with an anxiety disorder in randomized controlled trials as well as open trials. Levy et al. defined relapse as having remitted from an anxiety disorder, and meeting criteria for that same anxiety disorder again at a later point in time. Relapse was measured either by meeting diagnostic criteria, scoring below a cutoff on a clinical measure or no longer meeting otherwise specified remission criteria for the specific anxiety disorder. The pooled relapse rate across included samples was 10.5%, and 8% when individuals with a comorbid autism spectrum disorder were excluded. However, the only study in the meta-analysis that defined remission as not meeting criteria for any anxiety disorder, and that defined relapse as meeting criteria for any anxiety disorder at a later time point after having remitted (Ginsburg et al., 2018), found a much higher relapse rate of 48% than the pooled meta-analytic estimate reported by Levy et al. The substantial difference in reported relapse rates between Ginsburg et al.’s study and Levy et al.’s pooled

estimate can most likely be explained by differences in their definitions of relapse. The definition of relapse by Ginsburg et al. was broader and included not just the initial anxiety disorder that a given patient suffered from, but any anxiety disorder that a patient was diagnosed with at follow-up. As such, Ginsburg et al. focused on general relapse in terms of clinically significant anxiety, while most other scholars have focused on relapse of the initial disorder (i.e., irrespective of other anxiety disorder diagnoses). Both approaches have their advantages and disadvantages. One could argue that Ginsburg et al.'s definition does not meet the general definition of relapse, given that it is defined as *reoccurrence* of a condition and thereby excluding first onset. However, one could also argue that the broader definition is more accurate in the realm of anxiety disorders, given the fact that they are highly comorbid (Bandelow, & Michaelis, 2015) and share common denominators in terms of their etiology and maintenance (Norton & Paulus, 2017). The present analysis will use the more general definition applied by Ginsburg et al., which is described in more detail in the method section.

Relapse of anxiety disorders in CYP after successful psychological treatment remains fairly poorly understood. While numerous randomized controlled trials exist that assessed diagnostic status longitudinally including assessment after treatment endpoint (i.e., follow-up assessments), few attempts have been brought forward to summarize these results and to analyze potential predictors of relapse quantitatively. In the present work, an individual patient data meta-analysis (IPDMA) was performed in an effort to analyze potential relapse predictors after successful CBT treatment for anxiety disorders in CYP. IPDMAs bear advantages over ordinary (i.e., pairwise) meta-analyses that analyze summary statistics that are reported in publications. In an IPDMA, the individual patient data (IPD) of all included studies is pooled and then analyzed collectively. From the IPD, custom variables can be designed, which allows studies to be included in an IPDMA that may not have been included in a non-IPD meta-analysis because the relevant data was not reported (in sufficient detail) by the authors of the study of interest. In this way, more participants in total can be included in IPDMAs than in a non-IPD meta-analyses, which increases power. Power is further increased in IPDMAs since within-person heterogeneity can be explained through repeated

measurements per participant. Ordinary meta-analyses cannot account for intra-individual heterogeneity since comparisons are based on aggregated group outcomes rather than individual-level data. As such, IPDMAs may better serve to identify moderators and mediators of wanted or unwanted treatment effects such as moderators of relapse.

A potential factor that may influence CBT treatment outcomes in CYP with anxiety disorders is the dose of CBT received. Glenn et al. (2013) conducted an observational study in which 1,004 individuals with an anxiety disorder were allocated to a treatment condition in which they were allowed to choose between CBT, pharmacotherapy or both. In individuals that opted for CBT, a strong positive relationship between the number of CBT sessions and symptom reduction was found (Rath & Fox, 2018). The authors postulated that the observed positive effect of CBT dose on symptom severity might have been caused by facilitated consolidation processes (i.e., enhanced memory effects). If this is the case, then learning effects might also be detectable for a longer period of time. That is, relapse rates in individuals that received a larger vs. lower treatment dose might be decreased through better consolidation of treatment content. However, the potential effect of treatment dose on relapse rates after successful CBT treatment for CYP with anxiety disorders is not well researched (Levy et al., 2021).

Another factor that may influence treatment effects of CBT for anxiety disorders in CYP is the type of anxiety disorder. For instance, Hudson et al. (2015) found that while 33% of CYP with specific phobia had remitted at treatment endpoint, only 19% of CYP with SoAD had remitted in a large (n = 842) naturalistic CBT study. The observed difference remained stable at follow-up (i.e., 3 to 9 months post-treatment), with a remission rate at follow-up of 44% for CYP with specific phobia and a remission rate of 27.9% for CYP with adiagnosis of SoAD. Similar findings were reported by Waters et al. (2018), who treated 205 children diagnosed with an anxiety disorder with group CBT. The authors found that children with a primary diagnosis of SoAD had lower remission rates post-treatment and at follow-up than children with other primary anxiety disorder diagnoses. These findings suggest that remission rates differ across anxiety disorders with SoAD yielding worse outcomes to other anxiety disorders such as specific phobias. However, Hudson et al. and

Waters et al. both only report the percentage of remitted CYP at follow-up, but not how many of these CYP hadrelapsed at that time point. The question arises whether CYP with SoAD also experience higher relapse rates after successful CBT treatment.

Lastly, both mentioned potential moderators of treatment effects may interact. Levy et al. (2021) postulated that relapse rates after undergoing CBT may depend on an interaction between treatment dose and type of anxiety disorder. The authors hypothesized that specific phobia may exhibit a lower relapse rate than other anxiety disorders because a lower number of sessions is required to achieve remission. On the other hand, Hudson et al. (2015) hypothesize that a CYP with a SoAD may need a larger treatment dose of CBT to achieve remission since SoAD often follows a chronic course. Behavioral inhibition (e.g., habits of avoidance) may have persisted since infancy in many CYP with SoAD, and hence might also require a larger therapy dose (i.e., longer and more sessions) to overcome long held beliefs and behavioral habits.

The present IPDMA aims to answer the following questions: a) How many CYP with a primary anxiety diagnosis relapse after successful CBT treatment? b) Can relapse be predicted by: b1) the dose of treatment? b2) a primary diagnosis of social anxiety disorder vs specific phobia? b3) a combination of treatment dosage and primary anxiety disorder (interaction)?

Methods

Measures

Elegibility Criteria

Studies were included based on the following selection criteria: Main participants of the study were youth (≤18 years) with an anxiety disorder diagnosis where the anxiety disorder is the reason for the referral/presentation and also the main focus of the study (instead of another mental disorder). The anxiety disorder was diagnosed based on DSM criteria, except for selective mutism, including separation anxiety, generalized anxiety, social anxiety, specific phobia, panic, agoraphobia, overanxious disorder, and avoidant disorder. Trials specifically aimed at primary PTSD, OCD and selective mutism were excluded, except if > 50% of the participants met criteria

for an anxiety disorder. In that case, only those participants that had an anxiety disorder were included in analyses. Studies had to be treatment studies aimed at reducing anxiety, and one of the main interventions had to be CBT or components thereof. Studies were excluded that were not randomized controlled trials, that targeted victims of abuse, assault or neglect, or that included medication in the intervention group, and studies that exclusively examined mediators and moderators (instead of treatment effects).

Literature Selection and Data collection

The searched databases and search terms can be found in the appendix. The authors of papers that met the inclusion criteria were contacted and asked to provide the data sets of their study.

Data Extraction and Preparation

The data received from the researchers of included studies was harmonized by several researchers and assistants and collected in a secure storage location. The individuals harmonizing the data followed a code book to create standardized variables for primary and secondary diagnoses at the various time points. For studies that had several follow-up time points, the six months assessment was selected for the analysis if it was present, otherwise the first time point after treatment was used. This was done to maximize comparability, because most studies had a follow-up six months after treatment determination. Nine studies had data available for a six months follow-up, two studies on a three months follow-up and one study on a nine months follow-up. Participants were included that were in a treatment condition that included CBT, and that had a diagnosis for an anxiety disorder pre-treatment and did not have any anxiety disorder diagnoses at post-treatment (*remitted*). To answer research questions b1) - b3), a subset of participants was analyzed that had a diagnosis for either social anxiety disorder or a specific phobia (but not both) at pre-treatment and who had remitted post-treatment.

CBT Treatment Dose

The CBT treatment dose was assessed at study level as the total amount of treatment time in minutes that was prescribed by the treatment program used in the study. The time was calculated from the number and duration of sessions that were prescribed to participants, as indicated in the respective papers. No distinction in the calculation was made between time spent in individual therapy vs time spent in group therapy.

Relapse

Relapse was defined as: *i)* Meeting DSM-5 criteria for an anxiety disorder pre-treatment (primary and/or secondary diagnosis) *ii)* not meeting DSM-5 criteria for any anxiety disorder post-treatment (primary and/or secondary diagnosis) *iii)* meeting DSM-5 criteria for any one anxiety disorder (primary and/or secondary diagnosis) at follow-up.

Diagnoses

Diagnoses considered were specific phobia (any) or SoAD. Diagnoses were determined based on the Anxiety Disorders Interview Schedule (ADIS) (Silverman et al., 2001). The ADIS is a semi-structured interview designed to diagnose current anxiety, mood, obsessive-compulsive, trauma, and related disorders according to DSM-5 criteria. After determining possible diagnoses, the clinician assigns a clinical severity rating (CSR) to each possible diagnosis. The CSR is a rating of severity and/or impairment measured on a scale from zero to eight. A CSR value of four or larger means that the corresponding diagnosis applies to the patient. The primary diagnosis is the one with the highest CSR, all other diagnoses are labeled as secondary. The ADIS has favorable psychometric properties, with an interrater reliability of κ=.92 (Lyneham, Maree & Ronald, 2007), and evidence of responsiveness to treatment effect is available (Kendall et al., 1997). The ADIS is available in a child report version (ADIS-C), a parent report version (ADIS-P) or a child and parent report version (ADIS-CP) (Silverman & Albano, 1996). Of the studies included in this analysis four studies used ADIS-C, three studies the ADIS-P and six studies the ADIS-C/P. The interview schedule per study is listed in table 1.

Statistical analysis

To test the hypotheses that prescribed treatment time, type of disorder, and their interaction may be associated with relapse rates, a multilevel logistic regression model was used with relapse at follow-up being the dichotomous outcome variable (1 = yes, 0 = no). Treatment dose (i.e., length of therapy in minutes) and primary diagnosis (i.e., social anxiety disorder vs. specific phobia) were the investigated independent variables, labeled X_1 and X_2 in the following. X1 was a continuous level-2 variable measured at the study level. X2 was a binary level-1 variable measured at the individual level (1 = social anxiety disorder diagnosis pre-treatment, 0 = specific phobia diagnosis pre-treatment). The interaction term consisted of the product of X1 and X2. Before estimating the model parameters, differences between groups in the dichotomous outcome variable *relapse* were analyzed to see whether a multilevel approach (with the ID of a study at level 2) was warranted. This was done using an intercept-only model and testing the significance of the random intercept. Analyses were run in IBM SPSS 27 for Linux. The level for statistical significance was set conventionally at alpha < .05.

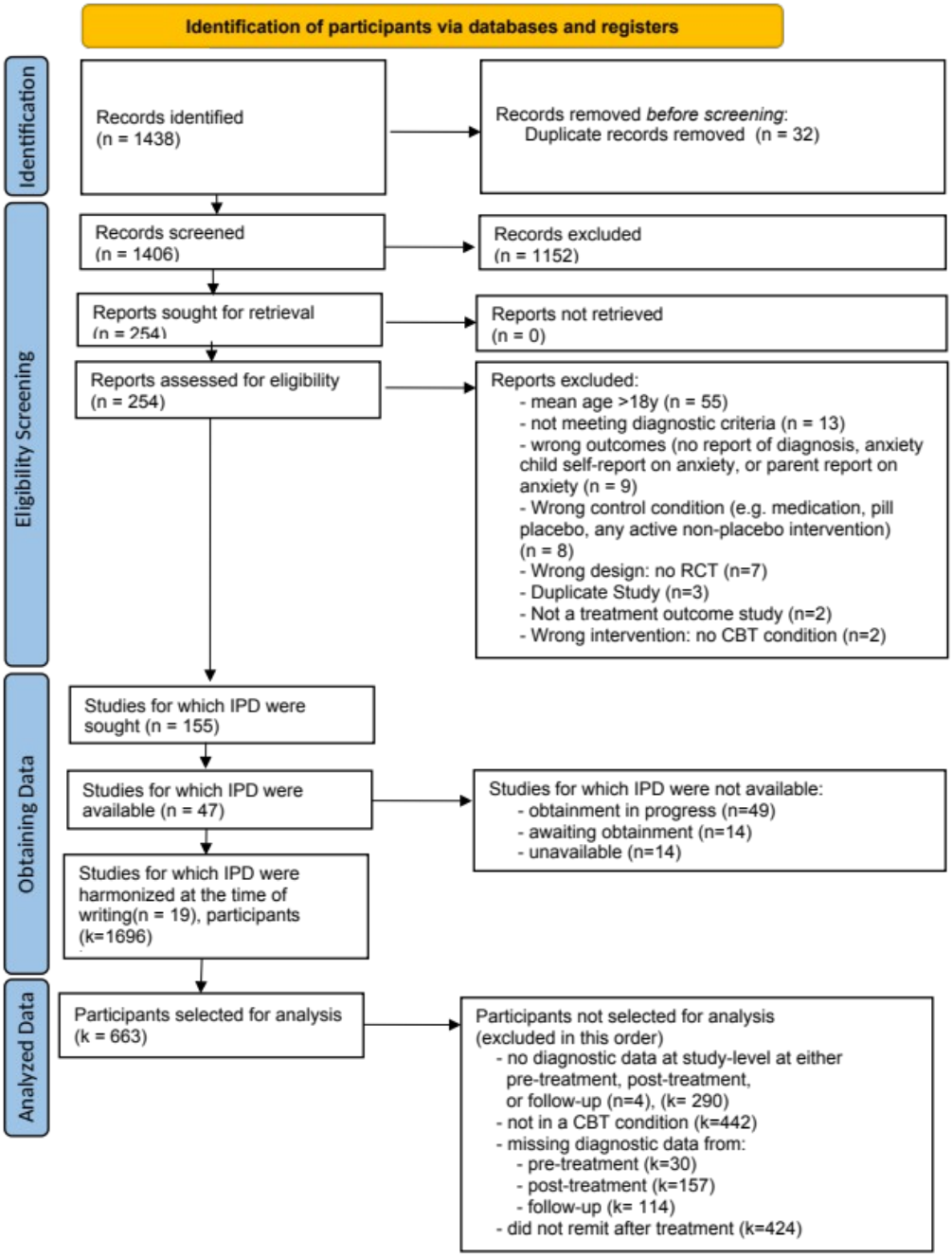

Figure 1
Flow Diagram of Study and Participant Selection

Table 1

Summary Statistics of Included Studies

authors	country	mean age	gender (f / m)	type of CBT	duration of treatment in minutes	fu period in months	diagnostic tool	participants (in treatment conditions)	remitted post-treatment	relapsed (% of remitted)	participants with SoAD	participants with SoAD remitted post-treatment	participants with SoAD relapsed at follow-up (% of remitted)	participants with specific phobia	participants with specific phobia remitted post-treatment	participants with specific phobia relapsed at follow-up (% of remitted)
Beidel et al. 2007	USA	11.9	35% / 65%	social effectiveness therapy for children	2520	3	ADIS-C	31	15 (48.4%)	2 (13.3%)	27 (87.1%)	13 (48.1%)	2 (15.4%)	0 (0.0%)	0 (0.0 %)	-
Bodden et al. 2008	Netherlands	12.4	58% / 42%	family CBT or CBT	962	6	ADIS-C	128	52 (40.6%)	5 (9.6 %)	38 (29.7%)	15 (39.5%)	1 (6.7 %)	28 (21.9%)	15 (53.6%)	1 (6.7 %)
Cobham et al. 1998	Australia	9.5	51% / 49%	CBT or CBT + PAM	600	6	ADIS-P	66	45 (68.2%)	9 (20.0%)	8 (12.1%)	3 (37.5%)	0 (0.0 %)	22 (33.3%)	13 (59.1%)	4 (30.8%)
Dadds et al. 1997	Australia	9.5	73% / 27%	group CBT and PAM	900	6	ADIS-P	57	16 (28.1%)	12 (75.0%)	18 (31.6%)	5 (27.8%)	3 (60.0%)	12 (21.1%)	3 (25.0%)	3 (100.0%
de Groot et al. 2007	Australia	8.8	32% / 68%	CBT or group CBT	600	6	ADIS-P	28	15 (53.6%)	5 (33.3%)	8 (28.6%)	3 (37.5%)	0 (0.0 %)	6 (21.4%)	6 (100.0%)	4 (66.7%)
Flannery-Schroeder 2000	USA	11	48% / 52%	CBT or group CBT	1080	3	ADIS-C	37	16 (43.2%)	5 (31.2%)	9 (24.3%)	2 (22.2%)	1 (50.0%)	12 (32.4%)	7 (58.3%)	2 (28.6%)
Heyne et al. 2002	Australia	11.5	39% / 61%	CBT	400	12	ADIS-C	28	18 (64.3%)	4 (22.2%)	6 (21.4%)	2 (33.3%)	0 (0.0 %)	4 (14.3%)	2 (50.0%)	0 (0.0 %)
Hudson et al. 2009	Australia	10.8	37% / 63%	CBT	1200	3	ADIS-CP	59	0 (0.0 %)	-	17 (28.8%)	0 (0.0 %)	-	8 (13.6%)	0 (0.0 %)	-
Mychailyszyn et al. 2018	USA	9.7	39% / 61%	family CBT	960	12	ADIS-CP	71	3 (4.2 %)	1 (33.3%)	15 (21.1%)	0 (0.0 %)	-	8 (11.3%)	1 (12.5%)	0 (0.0 %)
Rapee et al. 2006	Australia	9	47% / 53%	group CBT	1080	3	ADIS-CP	65	0 (0.0 %)	-	10 (15.4%)	0 (0.0 %)	-	18 (27.7%)	0 (0.0 %)	-
Silverman et al. 1999a	USA	9.6	51% / 49%	Exposure-based cognitive self-control or Exposure-based contingency management	800	6	ADIS-CP	43	31 (72.1%)	0 (0.0 %)	7 (16.3%)	3 (42.9%)	0 (0.0 %)	32 (74.4%)	26 (81.2%)	0 (0.0 %)
Silverman et al. 1999b	USA	9.6	76% / 24%	group CBT	800	6	ADIS-CP	13	5 (38.5%)	1 (20.0%)	2 (15.4%)	1 (50.0%)	0 (0.0 %)	1 (7.7%)	1 (100.0%)	0 (0.0 %)
Silverman et al. 2009	USA	9.9	66% / 34%	CBT or CBT with parental involvement	800	12	ADIS-CP	3	0 (0.0 %)	-	1 (33.3%)	0 (0.0 %)	-	1 (33.3%)	0 (0.0 %)	-
Wood et al. 2006	USA	9.8	35% / 65%	family CBT or CBT	980	12	ADIS-CP	34	23 (67.6%)	4 (17.4%)	16 (47.1%)	8 (50.0%)	3 (37.5%)	1 (2.9%)	1 (100.0%)	0 (0.0 %)
total		10.4	52% / 48%		980 (avg.)	7 (avg.)		663	239 (36.0%)	48 (20.1%)	182 (27.5%)	55 (30.2%)	10 (18.2%)	153(23.1%)	75 (49.0%)	14 (18.7%)

Results

Selection of Included Studies

The search identified 1,438 hits. After removing duplicates and irrelevant hits in the title and abstract screening, 254 records remained for the full-text screening. Of those, 155 studies were deemed potentially relevant to the present research questions and corresponding authors of the given trials were contacted to request the given data. At the time of writing, data from 47 studies had been received. Of those, 19 studies were harmonized at the time of writing, comprising 1696 participants. Of these participants and in this order, 290 were excluded from studies that did not record diagnostic data pre-treatment, post treatment or at follow-up, 442 were excluded because they were not in a CBT treatment condition, 301 were excluded because of missing diagnostic data, and 424 were excluded because they were not in remission post-treatment. A total of 663 was included into the present analysis. To answer research questions b1) to b3), a subset of 130 participants was used who were diagnosed with either SoAD or specific phobia pre-treatment. Of this subset, 75 were diagnosed with SoAD and 55 were diagnosed with specific phobia pre-treatment.

Study Characteristics

Fourteen studies were included in the present analysis. Included studies were conducted in the following countries: USA (k = 7), Australia (k = 6), the Netherlands (k = 1). The average age of participants was 10.4 years (sd = 2.9 years). The follow up periods in months included in the present analysis were three (k = 4), six (k = 6), and twelve (k = 4). Only two studies mentioned explicitly the inclusion of relapse prevention in their interventions, (Bodden et al. 2009; Heyne et al., 2008). The treatment time in minutes ranged from 400 to 2520 minutes, with an average of 980 minutes (s.d. = 535).

Relapse rate

In the current IPDMA study, 36% of CYP (239 of 663) initially remitted from their anxiety disorder after CBT. Of the 239 participants with an anxiety disorder whose anxiety disorder(s) were remitted at post-treatment, relapse was experienced by 48 participants (20.1%). Relapse rates varied considerably and ranged from 75% to 0%. The relapse rate for individuals with an initial diagnosis of SoAD was 18.2% (10 of 55) and the relapse rate for individuals with an initial diagnosis of specific phobia was 18.7% (14 of 75).

Prediction of Relapse

The model fit of the multilevel logistic regression model was AIC = 693.6 and BIC = 699.5. The model had an overall correct classification of 86.2 %, and correctly predicted 96.2 % of non-relapsers, and predicted 41.7% of relapsers correctly. Adding total treatment time as a level-2 predictor did not explain a significant amount of variance in the model (random intercept = $4.709 * 10^{-6}$, s.e. = $3.513 * 10^{-6}$). The simple effect of treatment time on the relapse was not statistically significant (coefficient = -0.003, s.e. = 0.003, p = 0.375, OR = 0.997). Similarly, the simple effect of disorder type (SoAD vs. specific phobia) was not statistically significant (coefficient = -5.581, s.e. = 3.099, p = 0.74, OR = 0.004). Lastly, also the interaction effect of treatment time by disorder type (i.e., SoAD vs specific phobia) was not statistically significant (coefficient = 0.006, s.e. = 0.003, p = 0.1, OR = 0.999).

Discussion

Main Results

The present IPDMA aimed to determine the anxiety disorder relapse rate in CYP after successful CBT treatment as part of randomized controlled trials, and to examine whether the total treatment length, the type of anxiety disorder and/or their interaction may predict relapse rates. Across the included trials, 36% of CYP were remitted after CBT treatment. Of these remitted CYP, 20.1% relapsed (i.e., meeting diagnostic criteria of any anxiety disorder)

during the follow-up period. Neither treatment dose nor anxiety disorder type or their interaction were not found to predict relapse rates in the present IPDMA.

As mentioned before, relapse rates varied considerably and ranged from 75% (Dadds et al., 1997) to 0% (Hudson et al., 2009; Silverman et al., 1999a). Relapse rates may vary for various reasons, one being the initial remission rate. In Hudson et al.'s study, for instance, no participants had remitted from pre- to post-treatment assessment which explains the absence of patients relapsing during follow-up in their trial.

Comparison to the Literature

In the light of lacking IPDMAs in the field, the presented results can only be compared indirectly to results reported in previously published pairwise meta-analyses and to results from primary trials. Overall, results on relapse rates tend to differ in the literature. The relapse rate of 20.1% found in the present analysis is higher than the relapse rate of 10.5% (and 8% excluding individuals with comorbid autism) reported in the meta-analysis by Levy et al. (2021). Differences in relapse rates might be a result of differences in applied definitions. In the present work, remission was defined as not meeting diagnostic criteria for any anxiety disorder and relapse was defined as meeting diagnostic criteria for any anxiety disorder after remission. The definition of relapse in the present work is a broader definition than the one used by Levy et al., who were only looking at the relapse of the primary (i.e., initial) anxiety disorder. The relapse rate found in the present work is similar to that found in adults with anxiety disorders by the same group of authors (i.e., 14%, Levy, O'Bryan, & Tolin, 2021). However, applied definitions differed (i.e., definitions in the present work being broader) as explained above.

The remission rate found in the present analysis (i.e., 36% of patients remitting from pre- to post-treatment) is lower to the remission rate reported in the meta-analysis by Warwick et al. (2017), who used the same definition of remission and reported a remission rate of 42%. Levy et al. (2021) reported an even higher remission rate of 59% in their meta-

analysis. Again, a likely reason for the difference between the remission rate of the current analysis and that found by Levy et al. concerns the respective definitions of remission. Levy et al.'s definition was more lenient than the one applied in the present work (i.e., focusing on the initial anxiety disorder only rather than any anxiety disorder), which could explain the higher remission rates found in Levy et al.'s work compared to the present work. Moreover, the present work included two studies discussed above (Hudson et al., 2009; Mychaslzyn et al. 2018), which had a remission rate of 0% and which were not included in Levy et al.

In the present analysis, no relationship between treatment dose and relapse was found. This is at odds with a previous study. Glenn et al. (2013), as mentioned before, found a positive relationship between dose of CBT received and more favorable outcomes at 12 and 18-months follow-up in CYP with anxiety disorders. However, the present IPDMA is difficult to compare to the RCT by Glenn et al. The present IPDMA included results from randomized controlled trials which applied manual-based treatments and thus standardized the treatment dose. That is, treatment doses varied between studies rather than within studies. The trial by Glenn et al., on the other hand, allowed for more flexible treatment doses within their trial. By introducing more variation in treatment doses while also minimizing the risk of systematic biases (i.e., through random allocation), the study by Glenn et al. might have had a methodological advantage to detect significant effects when compared to the methodology of the present work. However, one study is not a sufficient evidence base to draw firm conclusions. A summary of RCTs, like the present IPDMA, is usually a more powerful approach to answer research questions like the one at hand. However, with 130 included participants (from 14 trials) at the time of writing this thesis, the present IPDMA was likely underpowered. In sum, the evidence concerning a potential effect of treatment dose on CBT outcomes for anxiety disorders in CYP remains inconclusive. Future IPDMAs will involve more data (i.e., statistical power) and be better able to verify or falsify the hypotheses raised.

In the present analysis, relapse rates in CYP with social anxiety and CYP with specific phobia did not differ significantly. This is at odds with findings reported by Hudson et al.

(2015), who found higher relapse rates in CYP with social anxiety disorder relative to CYP with specific phobia. In fact, relapse rates in the present IPDMA were the other way around with slightly higher relapse rates (though not statistically significant) in CYP with specific phobia compared to CYP with social anxiety disorder (18.2% vs. 18.7%, respectively). Again, statistical power might be a potential reason for the differences in findings. The present work involved less than half on the participants included in Hudson et al. (319 vs. 842, respectively). In other words, the present work was likely underpowered to find significant effects. However, lacking power does not explain the opposite results (i.e., higher relapse rates for specific phobias as compared to social anxiety disorder). One possible reason for this difference concerns variation in treatment delivery formats. Hudson et al. examined the effect of group CBT only, while our analysis took into account both group treatments as well as individual treatments. Findings by Ingul et al. (2014), Stangier et al. (2003), and Mörtberg et al. (2007) indicate that individual CBT for social anxiety disorder leads to superior outcomes when compared to group CBT. However, this is a post-hoc explanation based on previous findings and thus speculative. The present work did not conduct sub-analyses on group CBT only and individual CBT only as this would have gone beyond the possible scope of the present work. Therefore, the present work cannot speak to the question whether group CBT (as compared to individual CBT) let to worse outcomes in CYP with social anxiety disorder as observed in the work by Hudson et al. Future IPDMAs with more statistical power and more sophisticated sub-analyses will be better able to answer these questions. For now, results remain inconclusive.

Nevertheless, the present findings have important clinical implications for the treatment of CYP with anxiety disorders. Our analysis reaffirms that CBT is an efficacious treatment for CYP with anxiety, both in terms or remission and protectiveness against relapse. Many patients remit (and even more respond) and most patients do not relapse after remission.

Strengths and Limitations

The present work reports on the first IPDMA in the field of CBT for pediatric anxiety disorders. As stated before, anxiety disorders are prevalent, potentially chronic, and severely disabling conditions and belong to the main contributors to the global burden of diseases. While CBT is the first-line treatment recommendation in international treatment guidelines for anxiety disorders, results are far from being perfect with numerous patients not remitting and a substantial minority relapsing after remission. The present work aimed to increase our understanding of how many CYP relapse after successful CBT treatment and why certain individuals relapse after remission while others do not. In doing so, the present work touches upon a societally relevant issue. An increased understanding of relapse may, for instance, inform tailored approaches to relapse prevention. The present work also applied novel methodologies. The use of IPD in the present analysis allowed to examine relapse, even if relapse was not investigated in the original trial. It also allowed for the use a uniform definition of relapse across trials and thus reducing heterogeneity and increasing internal validity.

A few limitations should be noted. First and foremost, not all data of the eligible studies could be taken into account. Only 19 of the available 47 datasets were harmonized at the time when analyses were conducted. The present work is part of a larger project and the limited scope of the present work did not allow for an inclusion of all eligible data. Consequently, statistical power was relatively low which may explain null findings as mentioned above. When the harmonizing process is finished and all data can be excluded, the raised hypotheses can be answered with more statistical power. Second, the present work operationalized treatment dose as the number of minutes of received therapy. However, other approaches have been used in previous work such as the number of treatment sessions. Both have their advantages and disadvantages. Session length may differ widely from 45 minutes sessions to 90 minutes sessions and beyond. The definition used in the present work may therefore be regarded as the more fine-grained definition as it quantifies the doses more

clearly and thus makes comparisons more valid. Third and last, varying treatment modalities (i.e. group treatment vs. individual treatment) were not accounted for quantitatively, which may or may not have had an effect on the reported results. While these analyses were not the focus of the present work, future research should account for potentially moderating effects of varying treatment delivery formats.

Ideas for Future Research

Despite being the first-line treatment recommendation, CBT produces fairly low remission rates in CYP with anxiety disorders. The remission rate of 44% in the present work certainly is a step up compared to no treatment which is associated with a remission rate of about 18% (James et al., 2020). However, results are far from being perfect and future research should aim towards enhancing treatment outcomes. One approach concerns the usage of readily available resources of patients. Since some patients have been shown to improve by themselves even after the therapy has ended (see Silverman et al, 2009), one idea could be to systematically offer materials to CYP and their parents such as self-help manuals or online resources. Such self-help tools may also include specific information on what to do in case of an emerging relapse, so that the patient (and/or their parents) can immediately act to prevent relapse or alleviate symptoms while waiting for an appointment with a mental health professional.

Further research may further focus on possible predictors of relapse. While in the present work no significant predictions could be observed potentially due to lacking power, future research may find certain patient characteristics (e.g., type of disorder, chronicity of disorder) and/or treatment characteristics (e.g., treatment dose, delivery format) that reliably predict relapse. This would pave the way for research into individualized relapse prevention. Similar approaches have been brought forward for tailoring treatments to maximize efficacy and safety of anxiety disorder treatment though with limited reliable moderators found to this date (Schneider, Arch, & Wolitzky-Taylor, 2015). The ultimate aim (i.e., in the unforeseeable future when reliable predictors of relapse have been established and of clinical utility) is an

increase of the longevity of treatment effects of established treatments such as CBT. Ultimately, clinicians and researchers alike want their patients and participants to be well in the long run not just in the short run.

Conclusions

The present IPDMA analyzed the remission rates, relapse rates and potential predictors of relapse in CYP treated with CBT for their anxiety disorder. More than one third of CYP (36%) remitted between treatment start and endpoint and 20.1% of these remitted CYP had relapsed at follow-up assessment. Treatment dose, type of primary anxiety disorder or their interaction were not significantly related to relapse rates. However, power was limited and results remain inconclusive. Future IPDMAs with more statistical power will be better able to answer the research questions raised. If reliable predictors of relapse are established in future research, these might be utilized in tailored approaches to relapse prevention increasing the longevity of treatment effects.

References

Abbott, M. J., & Rapee, R. M. (2007). Interrater reliability of the Anxiety Disorders Interview Schedule for DSM-IV: Child and parent version. *Journal of the American Academy of Child and Adolescent Psychiatry*, *46*(6), 731–736. https://doi.org/10.1097/chi.0b013e3180465a09

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). https://doi.org/10.1176/appi.books.9780890425596

American Psychological Association. (2022a). *APA Dictionary of Psychology*. https://dictionary.apa.org/relapse

American Psychological Association. (2022b). *APA Dictionary of Psychology*. https://dictionary.apa.org/remission

Amiri, S., & Behnezhad, S. (2019). Obesity and anxiety symptoms: a systematic review and meta-analysis. *Neuropsychiatrie*, *33*(2), 72-89.

Bandelow, B., & Michaelis, S. (2015). Epidemiology of anxiety disorders in the 21st century. *Dialogues in Clinical Neuroscience*, *17*, 327-335.

Bandelow, B., Michaelis, S., & Wedekind, D. (2017). Treatment of anxiety disorders. *Dialogues in Clinical Neuroscience*, *19*(2), 93-107.

Baxter, A. J., Scott, K. M., Vos, T., & Whiteford, H. A. (2013). Global prevalence of anxiety disorders: A systematic review and meta-regression. *Psychological Medicine*, *43*(5), 897–910. https://doi.org/10.1017/S003329171200147X

*Beidel, D. C., Turner, S. M., & Morris, T. L. (2000). Behavioral Treatment of Childhood Social Phobia. *Journal of Consulting and Clinical Psychology*, *68*(6), 1072–1080. https://doi.org/10.1037//0022006X.68.6.1072

Bendau, A., Kunas, S. L., Wyka, S., Petzold, M. B., Plag, J., Asselmann, E., & Ströhle, A. (2021). Longitudinal changes of anxiety and depressive symptoms during the COVID-19 pandemic in Germany: the role of pre-existing anxiety, depressive, and other mental disorders. *Journal of anxiety disorders*, *79*, 102377.

*Bodden, D. H. M., Bögels, S. M., Nauta, M. H., De Haan, E., Ringrose, J., Appelboom, C., Brinkman, A. G., & Appelboom-Geerts, K. C. M. M. J. (2008). Child Versus Family Cognitive-Behavioral Therapy in Clinically Anxious Youth: An Efficacy and Partial

Effectiveness Study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *47*(12), 1384-1394. https://doi.org/10.1097/CHI.0b013e318189148e

Clark, D. M. (2011). Implementing NICE guidelines for the psychological treatment of depression and anxiety disorders: the IAPT experience. *International review of psychiatry*, *23*(4), 318-327.

*Cobham, V. E., Dadds, M. R., & Spence, S. H. (1998). The Role of Parental Anxiety in the Treatment of Childhood Anxiety. *Journal of Consulting and Clinical Psychology*, *66*(6), 893–905.

*Dadds, M. R., Spence, S. H., Holland, D. E., Barrett, P. M., & Laurens, K. R. (1997). Prevention and Intervention for Anxiety Disorders: A Controlled Trial. *Journal of Consulting and Clinical* , *65*(4), 627–635.

*de Groot, J., Cobham, V., Leong, J., & McDermott, B. (2007). Individual Versus Group Family-Focused Cognitive–Behaviour Therapy for Childhood Anxiety: Pilot Randomized Controlled Trial. *Australian & New Zealand Journal of Psychiatry*, *41*(12), 990–997. https://doi.org/10.1080/00048670701689436

Emdin, C. A., Odutayo, A., Wong, C. X., Tran, J., Hsiao, A. J., & Hunn, B. H. (2016). Meta-analysis of anxiety as a risk factor for cardiovascular disease. *The American Journal of Cardiology*, *118*(4), 511-519.

*Flannery-Schroeder, E. C., & Kendall, P. C. (2000). Group and Individual Cognitive-Behavioral Treatments for Youth with Anxiety Disorders: A Randomized Clinical Trial. *Cognitive Therapy and Research*, *24*(3), 251–278.

Ghandour, R. M., Sherman, L. J., Vladutiu, C. J., Ali, M. M., Lynch, S. E., Bitsko, R. H., & Blumberg, S. J. (2019). Prevalence and Treatment of Depression, Anxiety, and Conduct Problems in US Children. *The Journal of Pediatrics*, *206*, 256-267.e3. https://doi.org/10.1016/j.jpeds.2018.09.021

Ginsburg, G. S., Becker-Haimes, E. M., Keeton, C., Kendall, P. C., Iyengar, S., Sakolsky, D., Albano, A. M., Peris, T., Compton, S. N., & Piacentini, J. (2018). Results From the Child/Adolescent Anxiety Multimodal Extended Long-Term Study (CAMELS): Primary Anxiety Outcomes. *Journal of the American Academy of Child & Adolescent Psychiatry*, *57*(7), 471–480. https://doi.org/10.1016/j.jaac.2018.03.017

Glenn, D., Golinelli, D., Rose, R. D., Roy-Byrne, P., Stein, M. B., Sullivan, G., Bystritksy, A., Sherbourne, C., & Craske, M. G. (2013). Who gets the most out of cognitive behavioral therapy for anxiety disorders? The role of treatment dose and patient engagement. *Journal of Consulting and Clinical Psychology*, *81*(4), 639–649. https://doi.org/10.1037/a0033403

*Heyne, D., King, N. J., Tonge, B. J., Rollings, S., Young, D., Pritchard, M., & Ollendick, T. H. (2002). Evaluation of Child Therapy and Caregiver Training in the Treatment of School Refusal. *American Academy of Child and Adolescent Psychiatry*, *41*(6), 687-.

Higa-McMillan, C. K., Francis, S. E., Rith-Najarian, L., & Chorpita, B. F. (2016). Evidence base update: 50 years of research on treatment for child and adolescent anxiety. *Journal of Clinical Child and Adolescent Psychology*, *45*(2), 91–113. https://doi.org/10.1080/15374416.2015.1046177

Huang, Y., & Zhao, N. (2020). Generalized anxiety disorder, depressive symptoms and sleep quality during COVID-19 outbreak in China: a web-based cross-sectional survey. *Psychiatry Research*, *288*, 112954.

Hudson, J. L., Rapee, R. M., Lyneham, H. J., McLellan, L. F., Wuthrich, V. M., & Schniering, C. A. (2015). Comparing outcomes for children with different anxiety disorders following cognitive behavioural therapy. *Behaviour Research and Therapy*, *72*, 30–37. https://doi.org/10.1016/j.brat.2015.06.007

*Hudson, J. L., Rapee, R. M., Deveney, C., Schniering, C. A., Lyneham, H. J., & Bovopoulos, N. (2009). Cognitive-Behavioral Treatment Versus an Active Control for Children and Adolescents With Anxiety Disorders: A Randomized Trial. *American Academy of Child and Adolescent Psychiatry*, *48*(5), 533–544. https://doi.org/10.1097/CHI.0b013e31819c2401

Ingul, J. M., Aune, T., & Nordahl, H. M. (2014). A Randomized Controlled Trial of Individual Cognitive Therapy, Group Cognitive Behaviour Therapy and Attentional Placebo for Adolescent Social Phobia. *Psychotherapy and Psychosomatics*, *83*(1), 54–61. https://doi.org/10.1159/000354672

James, A. C., Reardon, T., Soler, A., James, G., & Creswell, C. (2020). Cognitive behavioural therapy for anxiety disorders in children and adolescents. *The Cochrane Database of Systematic Reviews*, *11*, CD013162. https://doi.org/10.1002/14651858.CD013162.pub2

Kendall, P. C., Flannery-Schroeder, E., Panichelli-Mindel, S. M., Southam-Gerow, M., Henin, A., & Warman, M. (1997). Therapy for youths with anxiety disorders: A second randomized clincal trial. *Journal of Consulting and Clinical Psychology*, *65*(3), 366–380. https://doi.org/10.1037/0022-006X.65.3.366

Lee, P., Zehgeer, A., Ginsburg, G., McCracken, J., Keeton, C. P., Kendall, P., Birmaher, B., Sakolsky, D., Walkup, J., Peris, T., Albano, A., & Compton, S. (2019). Child and Adolescent Adherence With Cognitive Behavioral Therapy for Anxiety: Predictors and Associations With Outcomes. *Journal of Clinical Child and Adolescent Psychology : The Official Journal for the Society of Clinical Child and Adolescent Psychology, American Psychological Association, Division 53*. https://doi.org/10.1080/15374416.2017.1310046

Levy, H. C., O'Bryan, E. M., & Tolin, D. F. (2021). A meta-analysis of relapse rates in cognitive-behavioral therapy for anxiety disorders. *Journal of Anxiety Disorders*, *81*, 102407. https://doi.org/10.1016/j.janxdis.2021.102407

Levy, H. C., Stevens, K. T., & Tolin, D. F. (2021). Research Review: A meta-analysis of relapse rates in cognitive behavioral therapy for anxiety and related disorders in youth. *Journal of Child Psychology and Psychiatry*, jcpp.13486. https://doi.org/10.1111/jcpp.13486

Levy, H. C., Worden, B. L., Davies, C. D., Stevens, K., Katz, B. W., Mammo, L., Diefenbach, G. J., & Tolin, D. F. (2020). The dose-response curve in cognitive-behavioral therapy for anxiety disorders. *Cognitive Behaviour Therapy*, *49*(6), 439–454. https://doi.org/10.1080/16506073.2020.1771413

McLean, C. P., Asnaani, A., Litz, B. T., & Hofmann, S. G. (2011). Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. *Journal of psychiatric research*, *45*(8), 1027-1035.

Merikangas, K. R., He, J., Burstein, M., Swanson, S. A., Avenevoli, S., Cui, L., Benjet, C., Georgiades, K., & Swendsen, J. (2010). Lifetime Prevalence of Mental Disorders in US Adolescents: Results from the National Comorbidity Study-Adolescent Supplement (NCS-A). *Journal of the American Academy of Child and Adolescent Psychiatry*, *49*(10), 980–989. https://doi.org/10.1016/j.jaac.2010.05.017

Mersha, A. G., Tollosa, D. N., Bagade, T., & Eftekhari, P. (2022). A bidirectional relationship between diabetes mellitus and anxiety: A systematic review and meta-analysis. *Journal of Psychosomatic Research*, 110991.

Mörtberg, E., Clark, D. M., Sundin, Ö., & Åberg Wistedt, A. (2007). Intensive group cognitive treatment and individual cognitive therapy vs. treatment as usual in social phobia: A randomized controlled trial. *Acta Psychiatrica Scandinavica*, *115*(2), 142–154. https://doi.org/10.1111/j.1600-0447.2006.00839.

*Mychailyszyn, M. P., Carper, M. M., & Gibby, B. (2018). Exploring the occurrence of sudden gains among anxious youth receiving evidence-based cognitive-behavioral therapy. *Child and Adolescent Mental Health*, *23*(3), 251–257. https://doi.org/10.1111/camh.12254

Norton, P. J., & Paulus, D. J. (2017). Transdiagnostic models of anxiety disorder: Theoretical and empirical underpinnings. *Clinical Psychology Review*, *56*, 122-137.

Racine, N., McArthur, B. A., Cooke, J. E., Eirich, R., Zhu, J., & Madigan, S. (2021). Global prevalence of depressive and anxiety symptoms in children and adolescents during COVID-19: a meta-analysis. *JAMA Pediatrics*, *175*(11), 1142-1150.

*Rapee, R. M., Abbott, M. J., & Lyneham, H. J. (2006). Bibliotherapy for Children With Anxiety Disorders Using Written Materials for Parents: A Randomized Controlled Trial. *Journal of Consulting and Clinical Psychology*, *74*(3), 436–444. https://doi.org/10.1037/0022-006X.74.3.436

Rath, J. F., & Fox, L. M. (2018). Brief Symptom Inventory. In J. S. Kreutzer, J. DeLuca, & B. Caplan (Eds.), *Encyclopedia of Clinical Neuropsychology* (pp. 633–636). Springer International Publishing. https://doi.org/10.1007/978-3-319-57111-9_1977

Schneider, R. L., Arch, J. J., & Wolitzky-Taylor, K. B. (2015). The state of personalized treatment for anxiety disorders: A systematic review of treatment moderators. *Clinical Psychology Review*, *38*, 39-54.

Scholten, W., ten Have, M., van Geel, C., van Balkom, A., de Graaf, R., & Batelaan, N. (2021). Recurrence of anxiety disorders and its predictors in the general population. *Psychological Medicine*.

Silverman, W. K., Albano, A. M., Siebelink, B. M., & Treffers, Ph. D. A. (2001). *ADIS-C: Anxiety Disorders Interview Schedule for DSM-IV - child version*. Swets Test Publ.

Silverman, W. K., & Albano, Anne Marie. (1996). *The Anxiety Disorders Interview Schedule for Children–IV (Child and Parent Versions)*. San Antonio: TX: Psychological Corporation.

*Silverman, W. K., Kurtines, W. M., Ginsburg, G. S., & Weems, C. F. (1999a). *Contingency Management, Self-Control, and Education Support in the Treatment of Childhood Phobic Disorders: A Randomized Clinical Trial*. 13.

*Silverman, W. K., Kurtines, W. M., Ginsburg, G. S., Weems, C. F., Lumpkin, P. W., & Carmichael, D. H. (1999b). Treating anxiety disorders in children with group cognitive-behaviorial therapy: A randomized clinical trial. *Journal of Consulting and Clinical Psychology*, *67*(6), 995–1003. https://doi.org/10.1037//0022-006x.67.6.995

Śniadach, J., Szymkowiak, S., Osip, P., & Waszkiewicz, N. (2021). Increased depression and anxiety disorders during the COVID-19 pandemic in children and adolescents: a literature review. *Life*, *11*(11), 1188.

Stangier, U., Heidenreich, T., Peitz, M., Lauterbach, W., & Clark, D. M. (2003). Cognitive therapy for social phobia: Individual versus group treatment. *Behaviour Research and Therapy*, *41*(9), 991–1007. https://doi.org/10.1016/S0005-7967(02)00176-6

Stewart, L. A., Clarke, M., Rovers, M., Riley, R. D., Simmonds, M., Stewart, G., Tierney, J. F., & for the PRISMA-IPD Development Group. (2015). Preferred Reporting Items for a Systematic Review and Meta-analysis of Individual Participant Data: The PRISMA-IPD Statement. *JAMA*, *313*(16), 1657–1665. https://doi.org/10.1001/jama.2015.3656

Tierney, J. F., Vale, C., Riley, R., Smith, C. T., Stewart, L., Clarke, M., & Rovers, M. (2015). Individual Participant Data (IPD) Meta-analyses of Randomised Controlled Trials: Guidance on Their Use. *PLOS Medicine*, *12*(7), e1001855. https://doi.org/10.1371/journal.pmed.1001855

Warwick, H., Reardon, T., Cooper, P., Murayama, K., Reynolds, S., Wilson, C., & Creswell, C. (2017). Complete recovery from anxiety disorders following Cognitive Behavior Therapy in children and adolescents: A meta-analysis. *Clinical Psychology Review*, *52*, 77–91.

Walter, H. J., Bukstein, O. G., Abright, A. R., Keable, H., Ramtekkar, U., Ripperger-Suhler, J., & Rockhill, C. (2020). Clinical practice guideline for the assessment and treatment of children and adolescents with anxiety disorders. *Journal of the American Academy of Child & Adolescent Psychiatry*, *59*(10), 1107-1124.

Waters, A. M., Groth, T. A., Purkis, H., & Alston-knox, C. (2018). Predicting outcomes for anxious children receiving group cognitive-behavioural therapy: Does the type of anxiety diagnosis make a difference? *Clinical Psychologist*, *22*(3), 344–354. https://doi.org/10.1111/cp.12128

*Wood, J. J., Piacentini, J. C., Southam-Gerow, M., Chu, B. C., & Sigman, M. (2006). Family Cognitive Behavioral Therapy for Child Anxiety Disorders. *Journal of the American Academy of Child & Adolescent Psychiatry*, *45*(3), 314–321. https://doi.org/10.1097/01.chi.0000196425.88341.b0

Xiong, P., Liu, M., Liu, B., & Hall, B. J. (2022). Trends in the incidence and DALYs of anxiety disorders at the global, regional, and national levels: Estimates from the Global Burden of Disease Study 2019. *Journal of Affective Disorders*, *297*, 83-93.

Appendix

Syntax for database search:

```
("anxiety disorder*"
or *phobi*
or "overanxious disorder"
or "avoidant disorder"
or "internali* disorder*")
AND
("parent training"
or "skills training"
or "cognitive therapy"
or "behavio* therapy"
or "cognitive behavio* therapy"
or "cbt"
or "cognitive behavioural therapy" )
AND
(child*
or adol*"
or "teen*"
or "youth"
or "pediatric"
or "paediatric or young"
or "pupil"
or "school-age*")
AND
("randomi*ed controlled trial"
or "controlled clinical trial"
or "random*")
```

Databases Searched

COCHRANE, Medline, PsycInfo, Eric, CINAHL