

ORIGINAL ARTICLE: ASTHMA

Anxiety in youth with asthma: A meta-analysis

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Abstract

OBJECTIVES: Anxiety often presents comorbidly with asthma in youth under 18; however, prevalence rates are unclear. The aim of this review was to provide an up-to-date analysis of the literature investigating the prevalence of anxiety disorders, and comparisons of anxiety disorders and symptomatology in youth with asthma, compared to those without.

METHODS: A systematic search was conducted using the databases PsycINFO, MEDLINE, EMBASE, and CINAHL.

RESULTS: The search process produced 15 studies ($n = 7443$) reporting data on youth with asthma and anxiety disorders, 11 studies ($n = 10\,332$) reporting data on youth with and without asthma and anxiety disorders, and 28 studies ($n = 5848$) reporting data on youth with and without asthma and anxiety symptomatology. Youth with asthma had an anxiety disorder prevalence rate of 22.7%. Youth with asthma also had a greater number of anxiety disorders, compared to those without asthma ($d = 0.37$, 95%CI: 0.24-0.50, $P < 0.001$), and higher levels of anxiety symptomatology than youth without asthma ($d = 0.29$, 95%CI: 0.19-0.39, $P < 0.001$).

CONCLUSIONS: Youth with asthma display a prevalence rate for anxiety disorders that is more than three times higher than the prevalence in healthy youth. For the specific anxiety disorders investigated, elevated prevalence rates for youth with asthma were also found. Future research needs to focus on the factors that mediate or predict the development and maintenance of anxiety in youth with asthma and the development of clinically efficacious treatments.

KEYWORDS

adolescent, anxiety, asthma, child, youth

1 | INTRODUCTION

Asthma is the leading chronic illness for children and adolescents (youth), with point prevalence rates of approximately 9.5%.¹⁻³ Medically, a diagnosis of asthma carries with it a risk of further morbidity and, although rare, increased mortality.⁴ Psychosocially, asthma in youth has been associated with increased educational difficulties,⁵ behavioral and social difficulties,⁶⁻⁸ and psychological impairment.⁹

Research into the comorbidity between psychological disorders and pediatric asthma shows evidence of the presence of internalizing

disorders such as anxiety, at higher rates than what has been shown in youth without asthma.¹⁰⁻¹² However, with reports of prevalence ranging from 14%¹³ to 49%,¹⁴ there is discrepancy regarding the exact rate of anxiety disorders in youth with asthma. This discrepancy appears the result of methodological differences in the empirical literature such as sample age, geographical location, or socioeconomic status, the type of anxiety disorder measured or the measurement method used. It is also unclear why youth with asthma have high rates of anxiety and what types of anxiety disorders youth with asthma are likely to experience.

Only one model has been developed to explain the relationship between asthma and anxiety development in youth. Park et al¹⁵ proposed that following the onset of asthma symptoms, the source of anxiety may be the symptoms of asthma itself. Their model was

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adapted from a model explaining panic disorder. In panic disorder, people misinterpret normal bodily sensations (eg, shortness of breath) as catastrophic or life threatening. This misinterpretation leads to an increase in anxiety. People then engage in avoidance, escape, or other behaviors in order to feel safe. However, these behaviors ultimately work to maintain the anxiety. Park et al proposed that anxious youth with asthma may misinterpret normal occurrences of breathlessness (eg, those caused by physical exertion) as indicative of an asthma attack, in a similar way to that which has been proposed in other respiratory diseases such as chronic obstructive pulmonary disease.¹⁶ If youth respond to these normal bodily sensations in the same way as they would if they were asthma symptoms (ie, take rescue medication such as short acting β -agonists), the symptoms are unlikely to subside. This is expected to further increase anxiety for someone with asthma. Subsequently, they would attempt to engage in avoidance or escape behaviors similar to those of people with panic, which would maintain anxiety in the long term.

If Park et al's¹⁵ model is correct, we would expect panic disorder to be particularly inflated in youth with asthma, compared to other anxiety disorders. Such a specific relationship between panic disorder and asthma has been noted in adults^{10,17} but whether this is also true for pediatric asthma is unknown. In the two prior meta-analyses of anxiety in youth with asthma, neither examined specific anxiety disorders. Piquart and Shen¹⁸ investigated anxiety in youth with chronic illness generally and found that youth with all chronic illnesses, including asthma, displayed higher levels of anxiety (as indicated by a disorder or symptoms), compared to controls, with a small effect size for asthma of $d = 0.13$. Piquart and Shen¹⁸ compared data for youth with asthma to normative data if no control group was reported. While this led to an increase in the number of studies in their meta-analysis, it is unlikely the normative samples included a completely asthma-free population; thus there is a risk that children with asthma were over-represented in the control groups. Lu et al¹⁹ found an anxiety prevalence rate of 33% in adolescents. While this study did not include normative data in a control group, the findings were limited by sample size as the meta-analysis included only five studies, one of which included a sample of participants aged 16-21 years, thus not an exclusively youth, or adolescent, sample. Further, neither review investigated specific anxiety disorders, nor did either examine differences in youth with and without asthma in regard to anxiety as indicated by a diagnosis of a disorder, versus high anxiety symptomatology.

The current paper aimed to fill these gaps and provide an updated meta-analytic review of research published since Lu et al.¹⁹ Specifically, we attempted to investigate general and specific anxiety disorder prevalence rates in a sample of youth ranging from 0 to 18, and look individually at levels of anxiety disorders and anxiety symptomatology in youth with asthma, compared to a sample without asthma. We aimed to determine (1) how common anxiety disorders are in youth with asthma; (2) the rates of specific anxiety disorders for this population; and (3) the difference in anxiety disorders and symptomatology between youth with and without asthma.

2 | METHOD

This meta-analysis followed standard PRISMA criteria for systematic reviews.²⁰

2.1 | Search strategy

We conducted a systematic search of electronic databases PsycINFO, MEDLINE, EMBASE, and CINAHL to 01 July 2015. MESH search terms included *asthma*, intersected with *paediatric/pediatric*, *child*, *adolescen**, *youth*, intersected with *anx**, *panic*, *GAD*, "*generalised anxiety disorder*," "*separation anxiety disorder*," "*anxiety symptoms*," "*psychological distress*," *depression*, "*depressive symptoms*." Due to known comorbidity between depression and anxiety in youth,²¹ search terms relating to depression were included so as to not exclude any studies on depression that included a measure of anxiety. A search of reference lists of relevant articles²² was also conducted.

2.2 | Selection criteria

The inclusion criteria were that the study:

- Included a sample of youth under 18 with a diagnosis of asthma.
- Included a measure of anxiety, either a clinical diagnosis according to the Diagnostic and Statistical Manual of Mental Disorders,²³ or a self/parent/teacher-reported measure of anxiety symptomatology.
- Provided data allowing the computation of an effect size or such data was available from the authors.

Studies included in the analyses comparing the presence of anxiety disorders and symptomatology between youth with and without asthma were required to include a control group to meet inclusion criteria. Studies included in the anxiety disorder prevalence analysis did not require the presence of a control group. Exclusion criteria included non-English studies, studies that reported on anxiety symptomatology without a control group, studies that reported on "internalizing disorders" or "psychological disorders" in general where anxiety could not be discerned from other disorders, and studies where asthma could not be discerned from other illnesses.

2.3 | Data extraction

Methodological and outcome data were extracted into a Microsoft Excel spreadsheet by the reviewer (JD), with 20% of the data extracted independently by another reviewer (EJ). Correlations between the raters for double extracted data were ≥ 0.99 ($P < 0.05$).

The following methodological information was extracted: authors, year of publication, geographical location of study (continent), sample size, sample type (medical or community), % male, mean age, youth anxiety measures (diagnostic interview, questionnaires etc.), youth asthma information (severity, medication), informant of youth anxiety, and informant of youth asthma.

The following decisions were made prior to data extraction:

- In studies with more than one assessment point, we included only the baseline scores.

- b. If a clinical diagnostic interview and self/parent-report measures were included, we extracted both data points and included them in the separate disorder and symptomatology analyses, respectively.
- c. Where studies compared multiple groups of youth with asthma (ie, mild and severe) to a single control group, the number of controls was divided by the number of asthma groups to avoid inflating the control n .
- d. Where studies reported results for independent samples (eg, separate results for males and females, or mild and moderate asthma severity), we combined these into one sample per study for the analysis.
- e. Anxiety disorder studies were included if they reported on a sample of youth with asthma, regardless of whether there was a control condition. These studies contributed to the prevalence analysis only.
- f. When participant data were reported in more than one study, we selected the study with the largest n .

2.4 | Statistical analysis

We conducted the meta-analysis using Comprehensive Meta Analysis version 3. The first analysis calculated the overall event rate to determine the prevalence of anxiety disorders among youth with asthma. In the subsequent analyses, Cohen's d was used to calculate whether youth with asthma had greater anxiety disorders and symptomatology than youth without asthma. A positive d indicates that the asthma group had higher anxiety than the control group.

To determine heterogeneity of the overall effects, Cochrane's Q tests for heterogeneity were performed, and I^2 was reported. Publication bias was evaluated by Rosenthal's fail-safe N^{24} and Duval and Tweedie's trim and fill method.²⁵

3 | RESULTS

3.1 | Search process

Overall the search yielded 3552 articles, of which 1645 were duplicates (Fig. 1 shows the flowchart of the search). In step 1 of the search, two reviewers (JD, EJ) read the titles and abstracts of the 1907 articles for potential inclusion. Interrater reliability was substantial (Kappa = 0.72). Articles were excluded on the basis of title and abstract if they were not deemed to report data on anxiety in youth with asthma ($n = 1431$). Step 2 of the search process was a full-text review of the remaining 476 articles by the same two reviewers. Interrater reliability remained substantial (Kappa = 0.78). Four hundred and thirty-three articles were excluded, as they did not meet full inclusion criteria (as outlined in the method). After exclusion, there were 43 articles that met the study criteria (see supplementary data for the reference list of included studies). Of the 43 articles, 15 reported on anxiety disorders and could be included in the prevalence analysis, 11 reported on anxiety disorders and also included a control group and were included in the anxiety disorder comparison analysis and 28 reported on anxiety symptoms and included a control group, thus could be included in the anxiety symptomatology analysis.

3.2 | Prevalence of anxiety disorders

Fifteen studies ($n = 7443$) were included that allowed for the calculation of the overall prevalence of anxiety disorders (see Table 1). The average prevalence of anxiety disorders in young people with asthma was 22.7%. The prevalence rate of individual anxiety disorders was also calculated where possible. The average prevalence of generalized anxiety disorder (GAD; $k = 6$) was 6.4%, separation anxiety

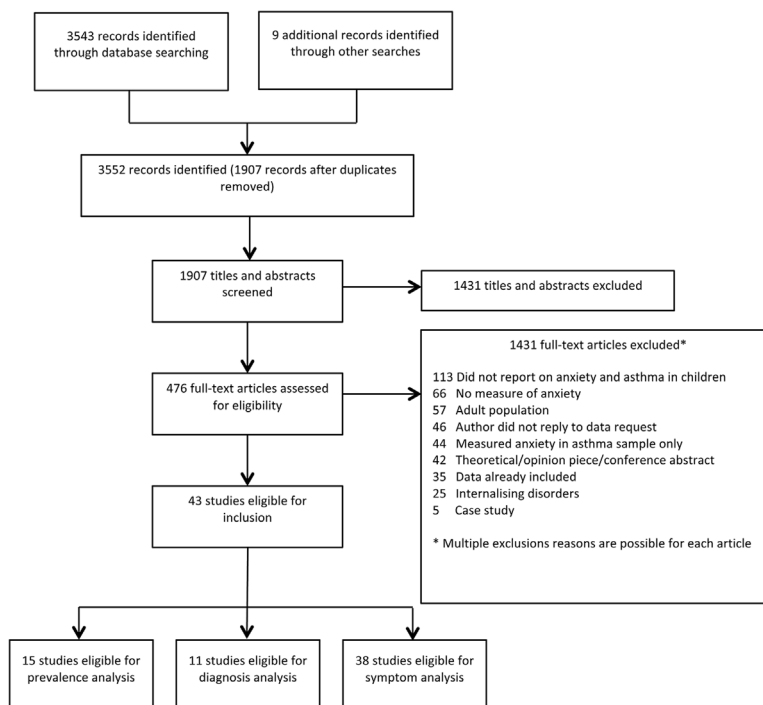


FIGURE 1 Flowchart of the study inclusion process

TABLE 1 Studies included in anxiety disorder prevalence analysis

Authors	Year	Location	Asthma			Control						
			n	Age	% Male	Sample	Informant	n	Age	Method	Informant	ER
Ali et al	2015	North America	1920	-	-	Community	Physician	-	-	Archival	Other	13.1
Bush et al	2007	North America	769	14	53.4	Community	Parent	-	-	I: DISC	Child	13.5
Bussing and Burket	1993	North America	37	11.1	67.6	Community	Physician	31	11.7	I: K-SADS	Child/parent	43.2
Garg and Silverberg	2014	North America	1256	-	-	Community	Parent	-	-	I: phone	Parent	3.7
Goodwin et al	2004	Oceania	183	18	-	Community	Physician	842	18	I: CIDI	Child	23
Goodwin et al	2005	North America	74	-	-	Medical	Physician	-	-	I: DISC	Child/parent	18.9
Goodwin et al	2014	North America	375	13	58.9	Community	Parent	1846	13.1	I: DISC	Child	30.9
Katon et al	2007	North America	769	14	53.4	Community	Physician	582	14.1	I: DISC	Child	9.1
Ortega et al	2002	North America	199	-	59.3	Community	Parent	-	-	I: DISC	Child/parent	48.7
Ortega et al	2003	North America	612	-	-	Community	-	1279	-	I: DISC	Child/parent	9.2
Pine et al	1994	North America	15	9.7	53	Community	-	211	-	I: DISC	Parent	46.7
Ross et al	2007	North America	53	14.7	50.9	Medical	Physician	-	-	I: ADIS	Child/parent	39.6
Tegethoff et al	2015	North America	1044	-	-	Community	Self-report	-	-	I: CIDI	Child	35.5
Turkoglu and Kerimoglu	2012	Europe	33	11.8	51.5	Medical	Physician	32	13	I: K-SADS	Child	18.2
Vila et al	1998	Europe	92	11.7	68.5	Medical	Physician	-	-	I: K-SADS	Child	31.5

ADIS, Anxiety Disorder Interview Schedule; DISC, Diagnostic Interview Schedule for Children; CIDI, Composite International Diagnostic Interview; ER, event rate; n, number of participants; ADIS, Anxiety Disorder Interview Schedule; DISC, Diagnostic Interview Schedule for Children; CIDI, Composite International Diagnostic Interview; K-SADS, Kiddie-Schedule for Affective Disorders and Schizophrenia.

disorder ($k = 7$) was 9.5%, social phobia ($k = 5$) was 7.3%, panic disorder ($k = 6$) was 4.5%, and agoraphobia ($k = 4$), was 5.4%.

3.3 | Anxiety disorders

There were 11 between-group comparisons (from 11 articles; $n = 10\,332$) included in the anxiety disorder analysis, published between the years 1993 and 2014 (Table 2). All were cross-sectional. The location of the studies included Oceania ($k = 1$), Europe ($k = 1$), and North America ($k = 9$). Studies mainly reflected a community sample ($k = 10$).

Asthma disorders were informed through physician report ($k = 4$), parent-report ($k = 4$), and self-report ($k = 1$). Two studies did not report information on asthma disorder informant. Three studies reported data on medication usage for youth with asthma, and three on asthma severity.

Ten studies diagnosed anxiety via a clinical interview (DISC $k = 6$; CIDI $k = 2$; K-SADS $k = 2$). The remaining study captured diagnostic data via a phone interview. Informants of anxiety were youth ($k = 5$), parents ($k = 3$), and both youth and parents ($k = 3$). The total number of asthma participants was 5493 with sample sizes ranging from 15 to 1256. Of the studies that included data on age ($k = 6$) and gender ($k = 6$), the mean age of asthma participants ranged from 9.7 to 18 years and the % males ranged from 51.5% to 67.6%. The total number of control participants was 4839, with sample sizes ranging from 31 to 1846. The mean age of control participants ranged from 13 to 18 years and the % males ranged from 48.3% to 61.3%.

Results from the 11 studies were analyzed to investigate between-group differences in anxiety disorders for youth with and without asthma. The combined effect size between the two groups was $d = 0.37$ (95%CI: 0.24-0.50, $z = 5.58$, $P < 0.001$), indicating a small-to-medium effect. This indicates that youth with asthma exhibit a greater number of anxiety disorders, compared to youth without asthma. There was a large amount of variability within the effect size $Q_w = 32.79$, $P < 0.001$; however, a medium to large proportion of the variability reflected real differences $I^2 = 69.50$.

Tests for heterogeneity were significant ($P < 0.001$), thus results are presented in the context of random effects models. Publication bias analysis showed that the failsafe N for the overall effect for anxiety disorders was 274. According to the trim and fill analysis, one study may have been missing. When this study was added to the meta-analysis, the effect size attenuated toward the null but remained significant ($d = 0.30$, 95%CI: 0.17-0.44).

3.4 | Anxiety symptomatology

There were 38 independent comparisons, from 28 studies ($n = 5848$), included in the anxiety symptom analysis, published between the years 1979 and 2015 (Table 3). All were cross-sectional. The location of the studies included Oceania ($k = 2$), Asia ($k = 3$), Europe ($k = 10$), and North America ($k = 13$). Sample type was split between medical ($k = 12$), community ($k = 15$), and other ($k = 1$).

Of the 28 studies, 18 reported information on informant of asthma diagnosis. Asthma diagnosis was informed through physician report ($k = 11$), parent-report ($k = 4$), and self-report ($k = 3$). Medication usage was reported by seven studies. Six studies reported that the

TABLE 2 Studies included in the analysis on anxiety diagnoses between youth with and without asthma

Authors	Year	Location	Asthma			Control			Method	Informant	d
			n	Age	% Male	Sample	Informant	n	Age		
Bussing and Burket	1993	North America	37	11.1	67.6	Community	Physician	31	11.7	Child/parent	0.64*
Feldman et al	2010	North America	958	-	-	Community	Parent	-	-	Parent	0.49*
Garg and Silverberg	2014	North America	1256	-	-	Community	Parent	-	-	Parent	1.09*
Goodwin et al	2004	Oceania	183	18	-	Community	Physician	842	18	Child	0.26*
Goodwin et al	2014	North America	375	13	58.9	Community	Parent	1846	13.1	Child	0.25*
Katon et al	2007	North America	769	14	53.4	Community	Physician	582	14.1	Child	0.46*
Ortega et al	2002	North America	199	-	59.3	Community	Parent	-	-	Child/parent	0.26*
Ortega et al	2003	North America	612	-	-	Community	-	1279	-	Child/parent	0.27*
Pine et al	1994	North America	15	9.7	53	Community	-	211	-	Parent	0.69*
Tegethoff et al	2015	North America	1044	-	-	Community	Self-report	-	-	Child	0.09
Turkoglu and Kerimoglu	2012	Europe	33	11.8	51.5	Medical	Physician	32	13	Child	0.94*

-, data not reported; d , standardized mean difference; n , number of participants; DISC, Diagnostic Interview Schedule for Children; CIDI, Composite International Diagnostic Interview; I, Diagnostic Clinical Interview K-SADS, Kiddie-Schedule for Affective Disorders and Schizophrenia.

* $P < 0.05$.

sample used one or more medications and one study reported PRN medication. For asthma severity, 13 samples in 10 studies had data on asthma severity. Six samples included youth with mild-severe asthma, two studies included a sample with mild asthma, two with mild-moderate asthma, one with moderate, one with moderate-severe, and one with severe asthma.

Anxiety symptoms were measured through questionnaires ($k = 26$), interviews ($k = 1$), and a phone survey ($k = 1$). There were a range of questionnaires used, with the State-Trait Anxiety Inventory being the most common ($k = 7$). Anxiety informants included self-report ($k = 20$), parent-report ($k = 6$), and other-report ($k = 1$), with one study not reporting anxiety informant. The total number of asthma participants was 1308 with sample sizes ranging from 18 to 158. Of the studies that included data on age ($k = 20$) and gender ($k = 25$), the mean age of asthma participants ranged from 8.7 to 17.2 years, and the % males ranged from 44% to 74%. The total number of control participants was 4540, with sample sizes ranging from 5 to 692. The mean age of control participants ($k = 20$) ranged from 8.7 to 17 years and the % males ($k = 25$) ranged from 43.2% to 82.8%.

The 28 studies were analyzed to investigate between-group differences in anxiety symptomatology for youth with and without asthma. The combined effect size was $d = 0.29$ (95%CI: 0.19-0.39, $z = 5.39$, $P < 0.001$), indicating a small effect. This suggests that youth with asthma are reported to have higher levels of anxious symptoms, compared to youth without asthma. There was a large amount of variability within the effect size $Q_w = 82.01$, $P < 0.001$; however, a medium proportion of the variability reflected real differences $I^2 = 54.88$.

Tests for heterogeneity were significant ($P < 0.001$) and results are presented in the context of random effects models. The failsafe N for anxiety the effect of anxiety symptomatology was 510. The trim and fill analysis indicated that three studies may have been missing. When these were added to the analysis the effect size attenuated away from the null and remained significant ($d = 0.30$, 95%CI: 0.20-0.40). A comparison between the effect sizes for anxiety disorders and anxiety symptomatology was non-significant ($Q = 0.761$, $P = 0.38$).

4 | DISCUSSION

This meta-analysis provides a comprehensive review of anxiety disorders and symptomatology in youth with asthma. Our aims were to determine the prevalence rates of anxiety disorders for youth with asthma, both in general and for specific anxiety disorders, and the difference in anxiety disorders and symptomatology between youth with and without asthma.

Results indicated that youth with asthma had greater levels of both anxiety disorders and symptomatology, than youth without asthma. In addition, we found that the pooled prevalence of clinically diagnosed anxiety in youth with asthma was 22.7%. This finding suggests that over one in five youth with asthma have anxiety. At over three times higher than the prevalence rate of anxiety in healthy youth,²⁶ these results unequivocally confirm that youth with asthma are more likely to experience anxiety disorders. Results also showed the prevalence of specific anxiety disorders is inflated in youth with

asthma compared to healthy youth. We found prevalence rates of 9.5% for separation anxiety disorder, 7.3% for social phobia, 6.4% for GAD, 5.4% for agoraphobia, and 4.5% for panic disorder. The prevalence rates of GAD and social phobia were three times higher in our analysis than what has been reported for youth generally and the prevalence rates for separation anxiety, panic disorder, and agoraphobia in youth with asthma were twice as high.^{26,27}

Based on the model proposed by Park et al,¹⁵ and the relationship between panic disorder and anxiety shown in adults with asthma,^{10,17} panic disorder was expected to be particularly inflated in youth with asthma. This was not the case, suggesting that perhaps the model may only partially explain the development and maintenance of anxiety in this population. Of note, is that the lower rate of panic disorder, compared to other anxiety disorders, is not dissimilar to what is seen in healthy youth, where prevalence is quite low during childhood and increases during adolescence and early adulthood.²⁸ This increase is potentially due to differences in how youth and adults understand the cognitive component of panic. Young people may have difficulty interpreting symptoms or sensations relating to panic attacks as being particularly life threatening as it is thought that their understanding of their own mortality does not develop until late childhood/early adolescence.²⁹ Therefore, it is possible that only through conceptualizing one's own mortality does the interpretation of panic symptoms and implication of panic attacks become anxiety provoking and panic disorder ensues.³⁰

Instead of a higher prevalence of panic disorder, there was a spread of anxiety disorders experienced by youth with asthma. Again, this is not dissimilar to what is seen in a healthy youth population. Establishing that youth with asthma present with a range of anxiety disorders is an addition to the research field in this area and should be used to inform the development of psychological treatment for this population. In adults with asthma, psychological treatment approaches tend to focus on treating panic disorder or symptoms of panic,³¹⁻³² which is understandable given the higher prevalence rate. In children, our results indicate that a more transdiagnostic treatment approach may need to be established. Indeed, the benefit of transdiagnostic treatments has been indicated in other pediatric populations such as those with pain³³ and somatic complaints³⁴

The spread of anxiety disorders in youth with asthma and, thus, lack of evidence confirming Park et al's¹⁵ model does not necessarily mean that the asthma is not a major contributor to anxiety development and maintenance. It is highly likely that anxiety in youth with asthma is related in some way to the asthma itself, or the consequences of asthma. However, a third variable could also be influencing the anxiety, such as parental psychopathology. In healthy youth, research has shown that parental psychopathology is associated with an increase in childhood anxiety,³⁵ and parents of youth with asthma have higher levels of anxiety than parents of those without.³⁶ Further, there is evidence indicating that mothers who were stressed during pregnancy were more likely to have young children who developed asthma.³⁷ It is possible that parental anxiety may be moderating the relationship between asthma and anxiety in youth.

Although there is a larger proportion of youth with asthma who experience anxiety compared to healthy youth, the ratio of anxiety to no anxiety is just over 1:5, signifying that the majority of youth with asthma are able to manage the illness without developing an anxiety

TABLE 3 Studies included in the analysis on anxiety symptomatology between youth with and without asthma

Authors	Year	Location	Asthma			Control			Method	Informant	d
			n	Age	% Male	Sample	Informant	n	Age		
Alcakaya et al	2003	Europe	37 55	10.2	67	Community	Physician	25	10.2	Q: STAI	0.14
Arif	2010	North America	35	-	54	Community	Parent	371	-	I	0.30
Austin et al	1994	North America	134	10.2	64.9	Community	Physician	136	10.5	Q: CSCI	0.48*
Bender Benz et al	2005	North America	27	10.6	44	Community	Physician	21	10.3	Q: BASC	0.41
Bender et al	1991	North America	44	11.4	-	Community	Physician	24	11.7	Q: CMAS	0.23
Brook	1995	Asia	25	14.92	52	Community	-	54	15.94	Q: STAI	0.06
Bruzzese et al	2009	North America	142	-	-	Community	Youth	622	-	Q: SAS-A & SPAL-C	-0.01
Caffrey-Craig	2005	Europe	80	11.22	63	Community	Physician	30	11.32	Q: RCMAS	0.08
Halterman et al	2006	North America	112 123	-	63 59	Community	Parent	1384	-	S: PACE	0.31*
Kashani et al	1988	North America	56	-	64.3	Medical	Physician	56	-	I: DICA-P	0.42*
Lau et al	2014	Europe	18	12	66.7	Medical	Parent	38	11	Q: SCARED	0.04
Letitre et al	2014	Europe	70	11.3	61.4	Medical	Physician	70	11.3	Q: STAI	0.12
Lu et al	2014	Asia	61 137	15.1 14.9	59 59.9	Medical	Physician	171	14.9	Q: RCADS	0.03
Markson and Fiese	2000	North America	43	8.7	56	Community	Parent	43	8.7	Q: RCMAS	0.31
Meijer	1979	North America	30	-	50	Community	Parent	29	-	Q: MCQ	0.18
Olson et al	1993	North America	39	9.9	74	Other	Other	145	13.5	Q: RCMAS	0.37*
Padur et al	1995	North America	25	11.7	72	Medical	-	25	11.4	Q: CSCI	0.52
Rietveld	2000	Europe	25	-	60	Medical	Physician	25	-	Q: STAI	0.19
Rietveld et al	2000	Europe	36	17.2	50	Medical	Physician	36	17	Q: STAI	0.16
Rietveld et al	2002	Europe	42	13.4	45.2	Community	Youth	25	13.44	Q: NASSQ	1.21*
Rietveld et al	2005	Europe	32	13.7	53.1	Community	Youth	29	14.3	Q: STAI	1.59*
Röder et al	2003	Europe	79	10.1	50.6	Medical	Physician	359	9.8	Q: SCQC	-0.04
Silverglade et al	1994	North America	41 34 54	-	61 47.1 63	Medical	Physician	74	-	Q: MAACL	0.61*
Singh et al	2012	Asia	50	9.62	62	Medical	Physician	50	11.36	Q: CPMS	0.21
Turkoglu and Kerimoglu	2012	Europe	33	11.8	51.5	Medical	Physician	32	13	I	0.30
Vuillermin et al	2010	Oceania	158	9	67	Community	Physician	319	9	Q: SCAS	0.49*
Weston et al	1989	Oceania	65	-	-	Community	Youth	343	-	Q: SCA	0.38*
Wolf et al	2008	North America	50	13.3	74	Community	Physician	33	13.5	Q: RCMAS	-0.02

-, data not reported; d, standardized difference between the means; BASC, Behavior Assessment System for Children; CMAS, Children's Manifest Anxiety Scale; CPMS, Childhood Psychopathology Measurement Scale; CSCI, Piers-Harris Children's Self-Concept Scale; DICA-P, Diagnostic Interview for Children and Adolescents - Parent version; I, interview; MAACL, Multiple Affect Adjective Checklist; MCQ, Mother-Child Questionnaire; NASSQ, Negative Affectivity Self-Statement Questionnaire; PACE, Parent's Appraisal of Children's Experiences; Q, questionnaire; RCADS, Revised Children's Anxiety and Depression Scale; RCMAS, Revised Children's Manifest Anxiety Scale; S, survey; SAS-A, Social Anxiety Scale for Adolescents; SCA, Sport Competition Anxiety Test; SCARED, Screen for Child Anxiety-Related Emotional Disorders; SCAS, Spence Child Anxiety Scale; SCQC, Stress Coping Questionnaire for Children; SPAL-C, Social Phobia and Anxiety Inventory for Children; STAI, State-Trait Anxiety Inventory for Children; STAI-C, State-Trait Anxiety Inventory for Children.

*P < 0.05.

disorder. Nonetheless, for those who do have comorbid anxiety, research shows their outcomes are worse in terms of both psychological functioning and asthma.^{11,38} Therefore, it is important that health practitioners working with a pediatric asthma population identify this substantial minority. Psychologically, this could be through the use of anxiety symptom measures, such as the State-Trait Anxiety Inventory for Children,³⁹ and the Youth Asthma-related Anxiety Scale,⁴⁰ both of which have been validated in youth with asthma. Biologically, there has been recent evidence indicating that the presence of dampened Neuropeptide Y (NPY) could mediate the association between stress and an enhanced inflammatory response in youth with asthma.⁴¹ Thus, assessing for levels of NPY could provide an indication of those youth with asthma who experience chronic stress and may be at risk of anxiety development and poorer asthma outcomes. The identification of youth with comorbid asthma and anxiety then allows health professionals to direct them to services providing treatment. For example, appropriate treatment options include cognitive behavior interventions, which have been shown to be effective in reducing anxiety in youth when delivered both in-person^{42,43} and remotely through online or smartphone mediums.^{44,45}

A strength of the meta-analytic procedure is being able to pool results from a large number of comparable studies to increase statistical power and improve estimates of anxiety in youth with asthma. However, the paper is not without limitations. First, the inclusion of cross-sectional studies did not allow for causal relationships to be determined. In adults, there is evidence of bi-directionality between asthma and anxiety¹⁷ and it would be informative to see whether this is also present in youth. Further, the articles did not provide data on whether the onset of anxiety disorders preceded the diagnosis of asthma or vice versa. As such, it remained unclear whether the asthma condition exacerbates underlying anxiety sensitivity, whether anxiety emerges as a response to the asthma, or whether anxiety predates the asthma diagnosis. Second, compared to the review by Pinquet and Shen,¹⁸ we had fewer studies that met inclusion criteria as we included only studies that had a reported control group in our between-group analyses. However, our effect size for anxiety symptomatology was double that reported by Pinquet and Shen¹⁸, perhaps indicative of the difference of using an asthma-free control sample. Third, a number of studies that appeared to meet our main inclusion criteria were unable to be included due to inadequate data to compute an effect size and lack of author reply. Given our publication bias analyses, these studies were unlikely to have affected the overall results, and little divergence appeared between the results of the studies included and not included in the meta-analysis. However, their inclusion would have strengthened the analysis by allowing for a more comprehensive review. Finally, we were unable to identify potential moderators of anxiety in youth with asthma. It is possible that there are some individual factors that increase the rate of anxiety in youth with asthma such as parental anxiety,³⁶ smoking status of the parent of child,⁴⁶ obesity,⁴⁷ or asthma control.⁴⁸ Unfortunately, these factors were not measured with sufficient frequency to allow their use as moderator variables, but future research investigating asthma and anxiety should also measure these factors to try and understand the associations more clearly.

The above limitations, notwithstanding the results of this meta-analysis, provide important insights into anxiety in youth with asthma. It is the first review to determine a pooled anxiety disorder prevalence rate and confirm the increased rate of both diagnosed anxiety and anxiety symptomatology in a sample of youth with asthma, under the age of 18. Moreover, we confirmed the prevalence of a range of specific anxiety disorders, thus expanding our understanding of anxiety in this population. Future research needs to focus on the gaps that still exist, such as the factors that mediate or predict the development and maintenance of anxiety in youth with asthma, the causal relationship between the comorbidity, and the development of clinically efficacious treatments.

CONFLICT OF INTEREST

All authors declare no conflicts of interest.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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