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Anxiety in asthma: a systematic review and meta-analysis

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Review Article

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Abstract

Background. Background: Growing evidence from observational studies indicates a high prevalence of anxiety in asthma. However, prevalence rates of coexisting anxiety symptoms and comorbid anxiety disorders vary widely across studies. We aimed to evaluate the associations between anxiety and asthma and provide more precise comorbidity estimates.

Methods. We systematically reviewed the literature from case-controlled studies and conducted a meta-analysis to evaluate the pooled prevalence estimates and risks of anxiety symptoms and anxiety disorders in asthma individuals. Screening, data extraction, and quality assessment were undertaken following PRISMA guidelines for preferred reporting of systematic reviews and meta-analysis. A random-effects model was used to calculate pooled prevalence rates. Meta-analysis was conducted using Review Manager 5.3. Multiple databases including PubMed, ScienceDirect, PsychINFO, and PsycARTICLES were searched for publications before 1 December 2019. The review protocol was registered on PROSPERO (ref: CRD42020176028).

Results. In total, 19 studies involving 106813 participants were included. The pooled prevalence of anxiety symptoms and anxiety disorders in individuals with asthma was 0.32 (95% CI 0.22–0.43) and 0.24 (95% CI 0.13–0.41), respectively. The risks of coexisting anxiety symptoms and comorbid anxiety disorders were significantly higher in asthma patients than in non-asthma controls indicated by OR 1.89 (95% CI 1.42–2.52; $Z = 4.37$; $p < 0.001$) and OR 2.08 (95% CI 1.70–2.56; $Z = 6.97$; $p < 0.001$), respectively. Anxiety symptoms and anxiety disorders occur at increased frequency among patients with asthma.

Conclusions. Our findings highlight the need for appropriate assessments for these comorbid conditions, which may help to identify a subgroup of patients who might benefit from interventions designed to reduce anxiety and enhance the quality of life.

Background

Asthma is a major chronic health problem affecting over 300 million worldwide, which causes significant social and financial burdens (Del Giacco *et al.* 2016). It is a complex multifactorial illness involving interactions between neural, endocrine, immune, behavioural and psychological processes (Di Marco, Santus, & Centanni, 2011; Mrazek, 2003). Anxiety is the strongest predictor of breathlessness in asthma (Spinhoven, van Peski-Oosterbaan, Van der Does, Willems, & Sterk, 1997) and has a stronger association with asthma-related health condition than does lung function (Laveneziana *et al.* 2006). Anxiety can enhance symptom perception (Thomas, Bruton, Moffat, & Cleland, 2011; von Leupoldt *et al.* 2009) and negatively impact cognition and coping behaviour (Lavoie *et al.* 2010). Recent reviews have demonstrated that asthma diagnoses significantly increase the risk of psychological conditions (Goodwin *et al.* 2003b; Su *et al.* 2016). Generalized anxiety disorder, panic disorder and agoraphobia, including anxiety related to symptoms, anxiety related to asthma-triggers, and anxiety related to medical treatment (ten Thoren & Petermann, 2000). Observational surveys show the high prevalence of anxiety in asthma patients: up to 30% in children and adolescents and 34% in adults (Katon, Richardson, Lozano, & McCauley, 2004; Weiser, 2007; Wong, Hunter Rowe, Douwes, & Senthilselvan, 2013). Such comorbidity can cause adverse outcomes, such as poor asthma control, symptomatic exacerbation, lower quality of life and increased utilization of emergency services (McCauley, Katon, Russo, Richardson, & Lozano, 2007; Richardson *et al.* 2006).

However, previous research has produced highly disparate findings and little consensus. Most studies did not include a valid control group and used different sample sources and outcome measures (Arif & Korgaonkar, 2016; Han, Forno, Marsland, Miller, & Celedon, 2016; Lehto, Pedersen, Almqvist, Lu, & Brew, 2019; Lu *et al.* 2014; Martinez-Rivera, Vennera, Canete, Bardagi, & Picado, 2011; Ortega, Huertas, Canino, Ramirez, & Rubio-Stipec, 2002). The current study aimed to systematically evaluate current evidence and conduct a meta-analysis to provide more precise estimates of prevalence and risks of this comorbid

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condition. We reviewed and synthesized data from studies reporting anxiety symptoms and anxiety disorders separately.

Methods

The current review and meta-analysis were conducted following PRISMA guidelines for preferred reporting of systematic reviews and meta-analysis (Moher, Liberati, Tetzlaff, Altman, & The PRISMA Group, 2009; Moher *et al.* 2015). The protocol was registered on PROSPERO (Ref: CRD42020176028).

Search strategy

The electronic databases of PubMed, ScienceDirect (Elsevier), PsychINFO and PsycARTICLES were used to select relevant publications before 1 December 2019. The search terms used included 'asthma', intersected with 'anxiety', 'generalized anxiety disorder', 'panic disorder', 'phobias', 'social phobia', 'social anxiety', 'agoraphobia', 'separation anxiety disorder', 'posttraumatic stress disorder' and 'obsessive compulsive disorder'. We also examined reference lists of appropriate articles in order to identify additional relevant studies. Two investigators (GY and RH) independently assessed the literature included in the review. Any discrepancies were discussed and a consensus was reached.

Inclusion and exclusion criteria for study selection

Studies were included if they met the following criteria: (1) published in English in peer-reviewed journals; (2) used a case-controlled study design, which comprised a sample with asthma and a non-asthma control group; (3) included both cross-sectional and prospective studies, with baseline data of prospective studies extracted; (4) fulfilled the diagnostic criteria for anxiety disorders based on the Diagnostic and Statistical Manual of Mental Disorders (DSM) or International Classification of Diseases (ICD); or had symptomatology measures of anxiety; (5) provided sufficient data (including numbers in both groups) allowing the computation of an effect size. Exclusion criteria included: (1) non-English language studies; (2) review papers or full papers not accessible; (3) no valid anxiety diagnosis or anxiety symptom measures. Eligibility criteria were applied during two phases: (a) title and abstract screening and (b) full-text screening. We also scrutinized and hand-searched the reference lists of all the relevant publications identified to check for any additional studies. Disagreements were resolved by discussions between GY and RH to reach a consensus.

Data extraction

Data were extracted using a pre-piloted structured form. In addition to bibliographic information, extraction processes sought the following data: population, study design, sample size, sex (female %), age (Mean or Median or Range), outcome measures, and key results (see details in Table 1).

Quality assessment

After reviewing recommendations for observational studies (Mueller *et al.* 2018), the approach developed by Hawker, Payne, Kerr, Hardey, & Powell (2002) was adopted to assess the methodological quality of individual studies included in this review. Nine components were assessed including the title and abstract, introduction and objectives, method and data, sampling, data analysis, ethical aspects of the research process, the results, transferability or generalizability of the information that emerged, and the implications and usefulness of the study using a four-point Likert scale: from good (4) to very poor (1), thus yielding a maximum score of 36. Overall quality ratings were then assigned as follows: high quality (H), 30–36 points; medium quality (M), 24–29 points; low quality (L), 9–24 points.

Statistical analysis

Random effects meta-analysis was used to synthesize individual study effect sizes and generate an overall effect size due to the clinical and methodological variation across studies. The pooled prevalence of anxiety symptoms and anxiety disorders in patients with asthma was calculated using the random effects model via Comprehensive Meta-Analysis version 2.0. Meta-analysis of odds ratio (OR) was conducted using Review Manager 5.3 software. I^2 test was used to indicate the percentage of variance in a meta-analysis that is attributable to study heterogeneity, with 25, 50, and 75% considered to indicate low, medium, and high heterogeneity, respectively. Funnel plot of standard error by Hedges'g was used to indicate any potential publication bias.

Results

Search results and study characteristics

The PRISMA flow chart (see Fig. 1) illustrates how studies were selected in this review and meta-analysis. Our search strategy yielded an initial total of 19 905 articles. In total, 13 359 potentially relevant articles remained after duplicates were removed. The titles and abstracts of these articles were then screened and 13 121 articles were excluded. A total of 238 full-length articles were then reviewed. Finally, 19 articles which met both inclusion and exclusion criteria were included. Among these, 10 articles reported self-report anxiety symptoms and nine articles reported clinically diagnosed anxiety disorders; all of which had both an asthma group and a non-asthma control group.

Anxiety symptoms and asthma

There were 10 studies involving 52 929 participants (including 6224 asthma patients) reporting anxiety symptoms included in this meta-analysis (Arif & Korgaonkar, 2016; Centanni *et al.* 2000; Cooper *et al.* 2007; Dorhofer & Sigmon, 2002; Ferro *et al.* 2016; Goodwin *et al.* 2003b; Han *et al.* 2016; Lehto *et al.* 2019; Lu *et al.* 2014; Ryu, Chun, Lee, & Chang, 2010). The characteristics of these studies are presented in Table 1. The random effects model was used to calculate the pooled prevalence of anxiety symptoms in asthma patients and in non-asthma controls which were 0.32 (95% CI 0.22–0.43) and 0.21 (95% CI 0.16–0.26), respectively. Meta-analysis using Review Manager 5.3 indicated that the risk of coexisting anxiety symptoms was significantly higher in patients with asthma than that of non-asthma controls (OR 1.89; 95% CI 1.42–2.52; $Z = 4.37$; $p < 0.001$), as shown in the forest plot in Fig. 2.

Anxiety disorders and asthma

There were nine studies involving 53 884 participants (including 24144 asthma patients) reporting anxiety disorders in asthma

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Table 1. Characteristics of studies reporting anxiety symptoms and anxiety disorders in asthma and non-asthma controls

		Asthma group			Non-asthma control group				Anxiety	
Author (Year)	Source of asthma population	Sample size	Female (%)	Age Mean (s.d.)/ median (range)	Sample size	Female (%)	Age Mean (s.d.)/ median (range)	Outcome measures	Asthma group *n* (%)	Non-asthma group *n* (%)
Studies reporting anxiety symptoms										
Lehto *et al.* (2019)	Swedish Twin Registry	2135	57.24	55.03 (7.98)	21 414	52.52	56.11 (7.94)	Self-report questionnaire (anxiety symptoms lasting 1 month or longer)	562 (26.32)	4103 (19.16)
Han *et al.* (2016)	National Health and Nutrition Examination Survey	1635	63.3	47.4 (0.4)	18 637	49.9	47.2 (0.2)	Self-report questionnaire [anxiety symptoms were categorized as binary (at or above the upper quartile (5 days) *v.* the lowest three quartiles (4 days or fewer)] for the number of days feeling anxious in the prior month)	774 (44.1)	5894 (32.7)
Ferro *et al.* (2016)	Population-based study	1258	45.6	13.9 (0.3)	3509	50.0	13.9 (0.3)	YSR (those scoring above 90th percentile were categorized as having clinically relevant symptoms of anxiety)	243 (19.3)	625 (17.8)
Arif & Korgaonkar (2016)	Outpatient clinic	200	–	–	200	–	–	self-report questionnaire (a positive answer to anxiety problems)	158 (79)	43 (21.5)
Lu *et al.* (2014)	Hospital	198	–	–	171	49.1	14.9 (2.43)	Revised Child Anxiety and Depression Scale (T scores of 70 and above indicate clinical threshold of comorbid anxiety)	10 (5.1)	8 (4.7)
Ryu *et al.* (2010)	Outpatient clinic	37	57	56 (45–80)	73	55	66 (51–89)	STAI (scores ⩾50 on the state-anxiety subscale)	6 (16)	12 (16)
Cooper *et al.* (2007)	General practices	455	61.7	42.4 (13.4)	1792	54.6	41.5 (15.9)	HADS (cut-off of 8 + for anxiety)	210 (47.3)	595 (33.2)
Goodwin *et al.* (2003a, 2003b)	Primary care service	176	86.4	18-70	822	72.5	18–70	PRIME-MD PHQ (No cut-off score provided)	46 (26.1)	124 (14.1)
Dorhofer & Sigmon (2002)	University	50	100	–	47	100	–	PAQ (No cut-off score provided)	17 (34)	18 (38.3)
Centanni *et al.* (2000)	Hospital	80	66.3	39.7 (1.64)	40	65	41.6 (1.6)	STAI (cut-off score is 40)	32 (40)	8 (20)

(*Continued*)

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Table 1. (*Continued.*)

Author (Year)	Source of asthma population	Asthma group			Non-asthma control group			Outcome measures	Anxiety	
		Sample size	Female (%)	Age Mean (s.d.)/ median (range)	Sample size	Female (%)	Age Mean (s.d.)/ median (range)		Asthma group *n* (%)	Non-asthma group *n* (%)
Studies reporting anxiety disorders										
Del Giacco *et al.* (2016)	Outpatient clinic	96	75	40.5 (19.0–67.0)	96	75	41.0 (18.0–65.0)	SCID-I; SCID-II	20 (21)	11 (11)
Lee *et al.* (2016)	Taiwan National Health Insurance Research Database	22 797	51.59	–	22 797	51.59	–	ICD-9	1835 (8.05)	957 (4.2)
Sharma *et al.* (2013)	Outpatient clinic	80	–	–	177	–	–	GMHAT/PC	17 (21.2)	23 (13.0)
Martinez-Rivera *et al.* (2011)	Outpatient clinic	264	71.4	48.8 (16)	111	6.2	42 (16)	Clinical diagnosis	92 (35)	6 (5.5)
Ortega *et al.* (2004)	Community	416	–	4–17	1466	–	4-17	Diagnostic Interview DSM-IV	43 (10.3)	81 (5.6)
Goodwin *et al.* (2003a, 2003b)	Community	236	59	41.1 (14)	3945	–	–	DIA-X/M-CIDI	60 (25.4)	596 (15.1)
Caccappolo-van Vliet *et al.* (2002)	Community	19	84.2	42.26 (8.85)	31	87.1	40.68 (7.31)	DIS	5 (26)	2 (6)
Ortega *et al.* (2002)	Community	199	40.7	9–17	1086	37.8	9–17	DISC 2.3	97 (49.2)	410 (37.7)
Bussing *et al.* (1996)	Outpatient clinic	37	32	11 (2.5)	31	39	11.7 (2.4)	K-SADS	16 (43.2)	6 (19.4)

Note: –, data not reported; YSR, Youth Self-Report; STAI, State-Trait Anxiety Inventory; HADS, Hospital Anxiety and Depression Scale; PRIME-MD PHQ, PRIME-MD Patient Health Questionnaire (PHQ) (DSM-IV version); PAQ, Panic Attack Questionnaire; SCID-I, Structured Clinical Interview for DSM-IV diagnosis of Axis I disorders; SCID-II, Structured Clinical Interview for DSM-IV diagnosis of Axis II disorders; ICD-9, International Classification of Disease, Ninth revision; GMHAT/PC, Global Mental Health Assessment Tool-Primary Care and General Health version; DIA-X/M-CIDI, Munich Composite International Diagnostic Interview; DIS, Diagnostic Interview Survey from the Diagnostic and Statistical Manual of the American Psychiatric Association, 3rd Revision (DSM-III); DISC 2.3, Diagnostic Interview Schedule for Children; K-SADS, Schedule for Affective Disorders and Schizophrenia for School-Age Children.

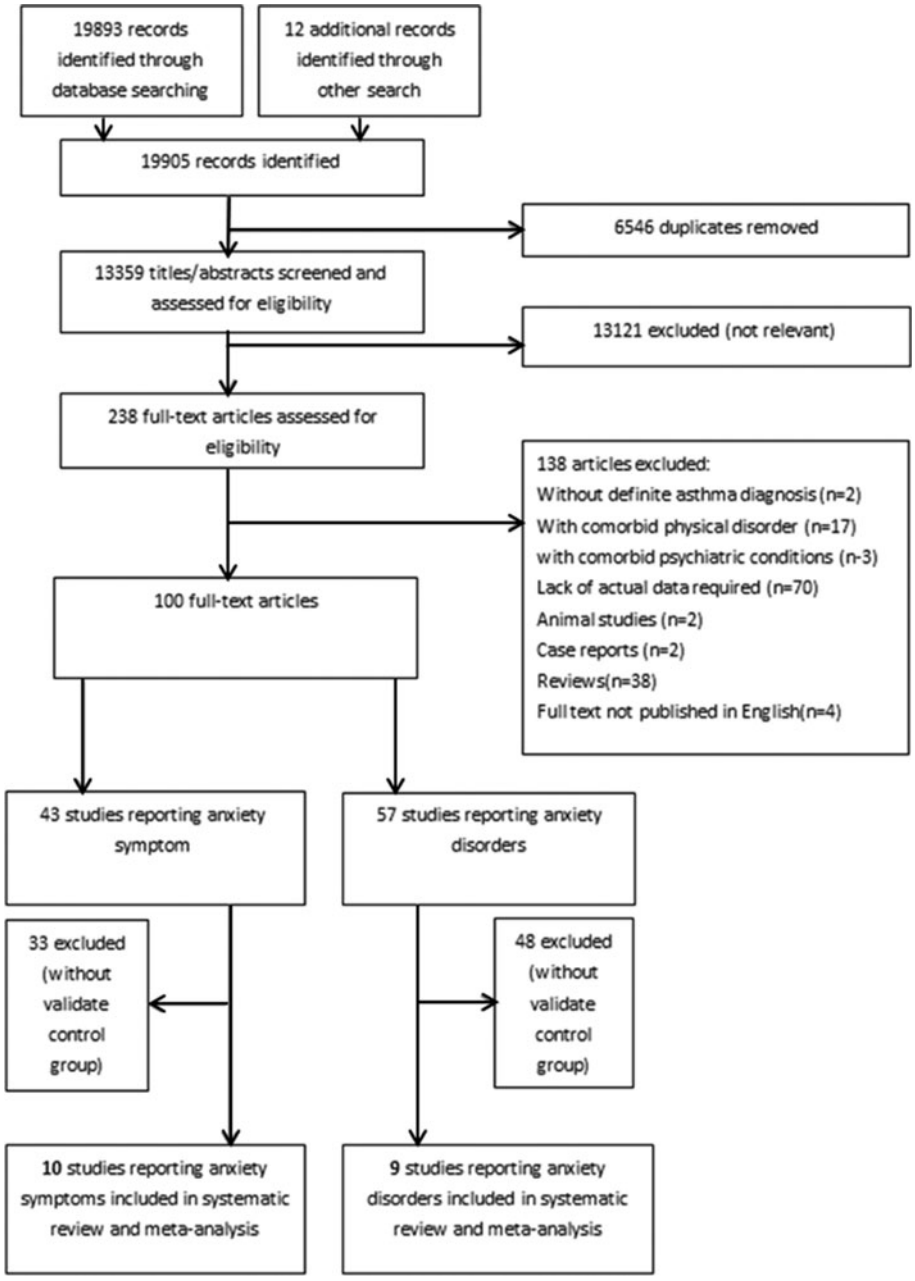


Fig. 1. PRISMA flow chart of study selection.

patients (Bussing, Burket, & Kelleher, 1996; Caccappolo-van Vliet, Kelly-McNeil, Natelson, Kipen, & Fiedler, 2002; Del Giacco *et al.* 2016; Goodwin, Jacobi, & Thefeld, 2003a; Lee, Lee, Lai, Chen, & Stewart, 2016; Martinez-Rivera *et al.* 2011; Ortega *et al.* 2002; Ortega, McQuaid, Canino, Goodwin, & Fritz, 2004; Sharma *et al.* 2013). The characteristics of these studies were extracted and shown in Table 1. The pooled prevalence of anxiety disorders in asthma patients and controls without asthma was 0.24 (95% CI 0.13–0.41) and 0.11 (95% CI 0.05–0.22), respectively. The risk of comorbid anxiety disorders was significantly higher in patients with asthma than those of non-asthma controls (OR 2.08; 95% CI 1.70–2.56; $Z = 6.97$; $p < 0.001$), as shown in the forest plot in Fig. 2.

Assessment of heterogeneity

The meta-analysis revealed significantly different degrees of heterogeneity across studies reporting anxiety symptoms ($\tau^2 = 0.15$, $\chi^2 = 117.34$, df = 9, $p < 0.00001$; $I^2 = 92\%$) and anxiety disorders ($\tau^2 = 0.04$, $\chi^2 = 16.83$, df = 8, $p = 0.03$; $I^2 = 52\%$), respectively. Studies reporting anxiety symptoms had a higher degree of heterogeneity than studies reporting anxiety disorders, possibly due to larger asthma patient populations and higher quality in studies of anxiety disorders. For more details and different weighting of individual study see Table 2 and Fig. 2. Due to the high heterogeneity, random-effects model was used for analysis. The funnel plots (see Fig. 3) indicated a tendency towards reporting positive findings. The underlying causes of the asymmetry include (1) chance due to a relatively small number of studies included; (2) heterogeneity across studies such as differences in methodology including settings, types of outcome measures; and (3) a few smaller studies with higher OR seen in studies conducted by Bussing *et al.* (1996) and Caccappolo-van Vliet *et al.* (2002) known as 'small study effects' also contributing asymmetry in the funnel plot.

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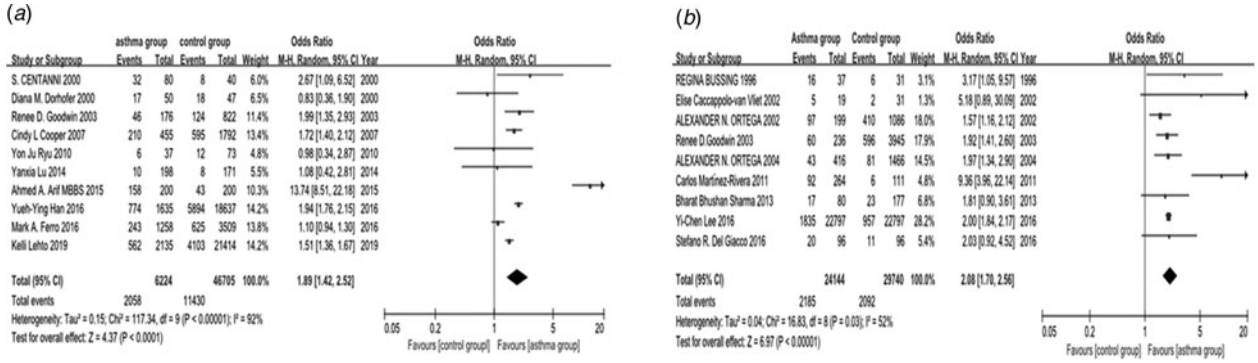


Fig. 2. Forest plot of comparison of anxiety symptoms (2a) and anxiety disorders (2b) in asthma and non-asthma controls. The black diamond at the bottom of the effect size plot represents the overall pooled odds ratio. Odds ratio>1 represents anxiety prevalence higher in the asthma group than in the non-asthma control group.

Table 2. Quality assessment of studies

	A/T	I/A	M/D	S	A	E/B	R	T	I	Total	Grade
Studies reporting anxiety symptoms											
Lehto *et al.* (2019)	3	3	4	3	4	2	4	3	3	29	M
Han *et al.* (2016)	4	3	4	2	3	2	4	3	3	28	M
Ferro *et al.* (2016)	4	3	4	3	4	2	4	3	4	31	H
Arif & Korgaonkar (2016)	4	3	3	3	3	2	4	3	2	27	M
Lu *et al.* (2014)	4	4	3	4	3	2	4	3	3	30	H
Ryu *et al.* (2010)	4	2	3	3	4	1	4	2	3	26	M
Cooper *et al.* (2007)	4	3	4	3	3	2	4	3	3	29	M
Goodwin *et al.* (2003a, 2003b)	3	3	3	3	4	3	4	3	3	29	M
Dorhofer & Sigmon (2002)	3	4	4	3	3	1	3	2	3	26	M
Centanni *et al.* (2000)	3	3	3	3	4	1	4	3	2	26	M
Studies reporting anxiety disorders											
Del Giacco *et al.* (2016)	4	3	4	4	3	2	4	3	3	30	H
Lee *et al.* (2016)	4	4	3	3	3	2	4	3	3	29	M
Sharma *et al.* (2013)	4	3	3	2	3	3	3	3	3	27	M
Martinez-Rivera *et al.* (2011)	4	3	3	3	4	3	4	3	3	30	H
Ortega *et al.* (2004)	3	4	4	3	3	3	4	3	4	31	H
Goodwin *et al.* (2003a, 2003b)	4	3	3	3	3	2	3	3	3	27	M
Caccappolo-van Vliet *et al.* (2002)	3	3	4	3	4	3	4	3	3	30	H
Ortega *et al.* (2002)	3	3	4	3	3	2	3	3	3	27	M
Bussing *et al.* (1996)	3	3	3	4	4	3	3	2	3	28	M

Note: A/T, Abstract and Title; I/A, Introduction and Aims; M/D, Methods and Data; S, Sampling; A, Analysis; E/B, Ethics and Bias; R, Results; T, Transferability; I, Implications. H: high quality, 30–36 points; M: medium quality, 24–29 points; L: low quality, 9–24 points.

Discussion

This up-to-date review of evidence from 19 case-controlled studies involving 106 813 participants includes 30 368 asthma patients and systematically evaluates the association between anxiety and asthma. Prevalence rates of anxiety in asthma varied widely between studies, possibly due to methodological issues including differences in definitions and diagnostic criteria used to define anxiety and in selections of control groups. Meta-analysis provides precise estimates of the prevalence rates and the risks of anxiety symptoms and anxiety disorders, respectively, and indicates significantly elevated comorbidity when compared with the general population.

Anxiety symptoms were reviewed from 10 studies involving 6224 participants, with over one-third of asthma individuals reporting anxiety symptoms measured by psychometric questionnaires. The meta-analysis revealed a significant 1.89 times higher risk of developing anxiety symptoms in asthmatic individuals than in non-asthmatic controls. In contrast, evidence from nine

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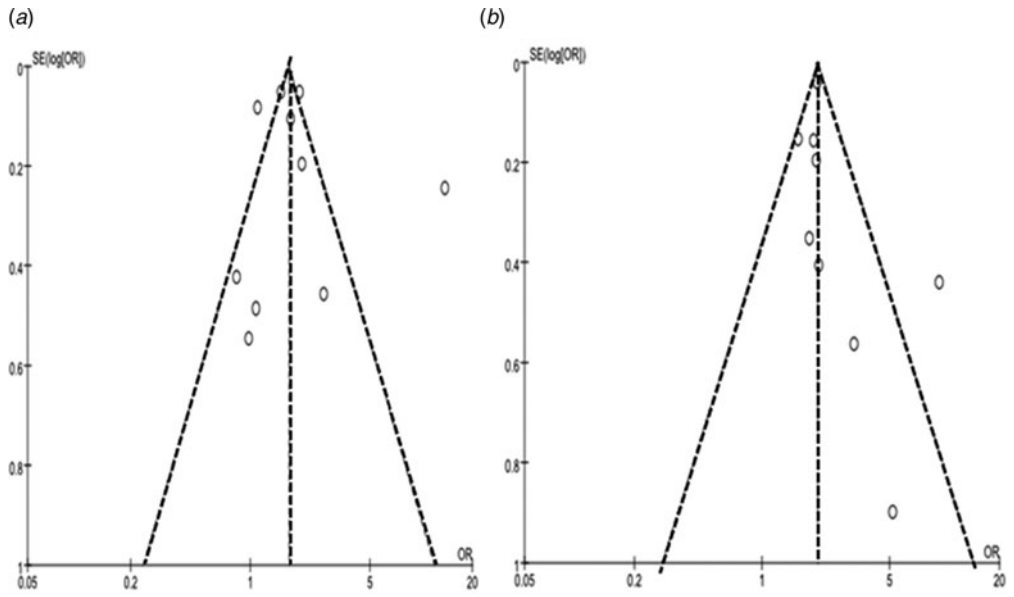


Fig. 3. Funnel plot of standard error by Hedges'g for studies reporting anxiety symptoms (3a) and anxiety disorders (3b). Asymmetry indicates a potential publication bias.

studies involving 24 144 participants revealed that a quarter of asthma individuals developed anxiety disorders, with a significant 2.08 times higher risk than non-asthma controls.

An earlier meta-analysis of 15 studies involving 1494 asthmatic adults suggested that the prevalence of any anxiety disorder was 34% (Weiser, 2007), which is much higher than the figure of 24% reported in our meta-analysis. This is possibly due to the stricter inclusion criteria adopted in our review where only studies with a case-controlled design were selected to remove any confounding factors (most studies included in the earlier review did not include a control group). In addition, most studies in the earlier review examined participants recruited from clinical settings (such as hospitals and outpatient clinics), where comorbidity conditions are usually more burdensome. The inclusion of both clinical and non-clinical populations and matched controls in our review can limit such bias (Berkson, 1946). Another review of evidence across 17 countries suggested the pooled estimate of odds ratio for anxiety disorders was 1.5 (95% CI 1.4–1.7) (Scott *et al.* 2007) which is lower than the figure of 2.08 (95% CI 1.70–2.56) indicated in our meta-analysis: possibly because the earlier review examined only community populations.

It is important to consider to what extent the results of the studies are consistent. I^2 test results derived from our meta-analyses revealed substantial heterogeneity across the 10 studies reporting anxiety symptoms in asthma, and moderate heterogeneity across the nine studies reporting anxiety disorders in asthma. Reasons for heterogeneity, other than characteristics and size of study populations, include different methodological issues such as recruitment pathways, measurement tools and diagnostic criteria, asthma severity and duration, other comorbid physical conditions, settings and countries where each study was carried out, as well as publication bias as indicated in the funnel plots. It should be noted that the effects of these potential sources of heterogeneity were not examined, due to the relatively small numbers of studies included in this review, however, sub-group analysis and meta-regression should be conducted when there are adequate numbers of studies in future meta-analysis. Although the consideration of risk and protective factors linked to comorbid anxiety in asthma is not within the scope of our review, factors like gender, marital status, educational years, urbanization levels, residential areas, levels of care, other comorbid physical conditions (such as cardiovascular disease and diabetes), childhood trauma and negative life events have all been found to be associated with anxiety in asthma (Goodwin, Fergusson, & Horwood, 2004; Grigsby, Anderson, Freedland, Clouse, & Lustman, 2002; Lu, Feng, Lim, & Ng, 2013; Roy-Byrne *et al.* 2008; Scott *et al.* 2008), whereas socio-economic advantage, younger age and oral prednisolone usage may be protective factors (Protsiuk *et al.* 2019; Tzeng *et al.* 2018).

The mechanisms underlying comorbid anxiety in asthma remain unclear. One biological theory suggests that repetitive experiences with hypoxia and hypercapnia due to asthma may sensitize neural circuits that control fear responses, such as neurons in the amygdala and locus coeruleus, to overreact and to enhance fearful perceptions of conditioned stimuli such as the sensation of breathlessness (Katon *et al.* 2004). Evidence from adults and adolescents support this theory (Goodwin *et al.* 2003b; Perna, Ieva, Caldirola, Bertani, & Bellodi, 2002; Pine *et al.* 2000). Another potential biological mechanism is linked to complex psycho-neuro-immunological pathways involving mainly pro-inflammatory cytokines and imbalance towards the Th2 T-cell response (Del Giacco *et al.* 2016). Castillo and colleagues (Castillo, Zheng, & Yang, 2018) found that pro-inflammatory cytokines played an important role in the pathogenesis of allergy-related diseases, such as asthma. Studies have shown that cytokines such as interleukin (IL)-6, tumour necrosis factor-alpha, IL-10, and monocyte chemoattractant protein-1/CCL2 might be associated with emotional disorders, including anxiety disorders (Kohler *et al.* 2018; Rosenblat & McIntyre, 2017). Another recent study showed that pro-inflammatory cytokines, salivary cortisol and alpha-amylase were potentially implicated in the development of generalized anxiety disorder in asthma patients (Yang, Liu, Xu, Shi, & Du, 2017). Genetic studies suggest shared genes and potential causal links between asthma

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and anxiety disorders (Zhu *et al.* 2019). A locus is significantly associated with both asthma and anxiety disorders (sentinel SNP: rs1709393) and the NR3C1 gene substantially modifies the level of trait anxiety in asthma sufferers (Panek, Pietras, Szemraj, & Kuna, 2014). Cognitive theory can be used to explain the psychosocial mechanisms underlying the comorbidity of anxiety with asthma (Katon *et al.* 2004): it suggests that long periods and unpredictable experiences with asthma may generate fearful or uncontrollable beliefs about respiratory symptoms which can provoke panic attacks (Carr, Lehrer, Rausch, & Hochron, 1994; Roy-Byrne & Stein, 2001). Some individuals may misinterpret normal occurrences of breathlessness as indicative of an asthma attack and if they then respond to these normal bodily sensations in the same way as if they were asthma symptoms, anxiety may increase. Subsequently, avoidance or escape behaviours may appear, which would lead to long-term anxiety (Dudeney, Sharpe, Jaffe, Jones, & Hunt, 2017).

A high prevalence of anxiety also occurs in a range of other physical illnesses including gastrointestinal disease, pulmonary disease, cardiovascular disease, and chronic pain (Bordoni, Marelli, Morabito, & Sacconi, 2017; Celano, Daunis, Lokko, Campbell, & Huffman, 2016; Meuret, Tunnell, & Roque, 2020; Neuendorf, Harding, Stello, Hanes, & Wahbeh, 2016; Ortego *et al.* 2016). While a medical condition can be sufficient enough to be a stressor for an individual to develop anxiety, some shared underlying biological mechanism may also contribute to anxiety and comorbid physical illness. Growing evidence also suggests neurotransmitter disturbances, hypothalamic-pituitaryadrenal axis dysfunction, and neuroplasticity may also contribute to these comorbid conditions. Future work is warranted to identify potential shared underlying pathological mechanisms between anxiety and asthma as this could offer novel intervention targets and optimize clinical outcome.

Conclusions

The current study provides precise comorbidity and risk estimates of coexisting anxiety symptoms and comorbid anxiety disorders in individuals with asthma. It highlights the need for early and appropriate assessment for anxiety symptoms and disorders in individuals with asthma. This could help to stratify a subgroup of patients who may benefit from interventions targeted at anxiety which might lead to better overall health and quality of life. Further research is warranted to examine underlying mechanisms and identify modifiable risk factors which may offer new intervention approaches to benefit asthma patients with comorbid anxiety.

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Conflicts of interest. None.

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