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Anxiety is more common in children with asthma

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ABSTRACT

Objective There are a variety of reasons why there may be an association between asthma and anxiety in children. Research into the relation between asthma and anxiety has been limited by the sole use of parent-reported or self-reported asthma symptoms to define asthma status. The objective of this study was to determine if children with physician-defined asthma are more likely to suffer anxiety than children without asthma.

Design A population-based, cross-sectional assessment, of self-reported anxiety symptoms.

Setting and participants Children aged 5–13 years from Barwon region of Victoria, Australia. Asthma status was determined by review with a paediatrician. Controls were a sample of children without asthma symptoms (matched for age, gender and school).

Outcome measure The Spence Children's Anxiety Scale (SCAS) written questionnaire. The authors compared the mean SCAS score, and the proportion of children with an SCAS score in the clinical range, between the groups.

Results Questionnaires were issued to 205 children with asthma (158 returned, response rate 77%), and 410 controls (319 returned, response rate 78%). The SCAS scores were higher in asthmatics than controls ($p < 0.001$); and were more likely to be in the clinical range (OR=2.5, 95% CI 1.1 to 5.8, $p=0.036$). There was no evidence that these associations could be explained by known confounding factors.

Conclusions Children with asthma are substantially more likely to suffer anxiety than children without asthma. Future studies are required to determine the sequence of events that leads to this comorbidity, and to test strategies to prevent and treat anxiety among children with asthma.

INTRODUCTION

There are several reasons why there may be a relation between asthma and anxiety. Asthma is an unpredictable and frightening illness that may lead to dyspnoea-induced fear conditioning and alteration of the respiratory receptor set point.¹ In concert, anxiety may predispose to asthma by stimulating airway inflammation and hyper-responsiveness.^{2,3} Anxiety may also increase the use of asthma medications⁴ and, in turn, asthma medications may induce anxiety.⁵ Asthma and anxiety also share a number of risk factors, such as parental cigarette smoking^{6,7} and stress during childhood.^{8,9}

Comorbid anxiety is likely to have¹⁰ significant detrimental effects among children with asthma. Anxiety has been shown to result in an increase in the number of asthma-related urgent medical reviews.¹¹ Anxiety also results in increased use

What is already known on this topic

- ▶ Both asthma and anxiety are common conditions that pose a major health burden.
- ▶ There are sound theoretical reasons why there may be a relation between asthma and anxiety in children.
- ▶ Previous studies regarding the relation between asthma and anxiety in children have been limited by the use of questionnaire-derived parent-reported wheeze to define asthma status.

What this study adds

- ▶ Children with asthma are at substantially higher risk of anxiety than their non-asthmatic peers.
- ▶ Children with asthma who are missing a lot of school may be at particular risk.
- ▶ The use of a screening instrument, such as the SCAS, may also be a useful strategy.

of asthma medications⁴ which may be associated with a range of potential adverse effects. Most notably, at higher doses, inhaled steroids may affect growth, bone mineralisation and adrenal function¹²; and inhaled long-acting β_2 adrenoreceptor agonists may induce tachyphylaxis.¹³

Cross-sectional studies have found a consistent association between anxiety and asthma, where asthma has been measured by parent/self-report^{14,15} or review of medical records.¹⁶ However, the findings from longitudinal studies are conflicting.^{17,18} Hasler *et al* followed a community sample of 591 young adults between the ages of 19 and 40 years and found an independent, bidirectional longitudinal association between self-reported asthma and panic symptoms.¹⁷ By contrast, Goodwin *et al* prospectively recorded parent/self-reported anxiety, depression and asthma symptoms/diagnosis in a cohort ($n=1000$) from birth until the age of 21 years.¹⁸ There was an association between asthma and anxiety in the unadjusted data, but this was no longer apparent after fitting a fixed logistic regression model to adjust for fixed unobserved confounding factors.

The sole use of parent or self-reported asthma symptoms/diagnosis, or review of medical

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records, to define asthma status is an important limitation in the majority of studies. This is because parent/self-report is an inaccurate method of defining asthma status,¹⁹ and episodes of anxiety/panic resulting in a medical review may be difficult to distinguish from acute asthma. Only one study (involving adults) has been undertaken regarding anxiety and asthma in which the definition of asthma included physician review.²⁰ The findings suggest that anxiety disorders are associated with both 'non-severe' (OR=1.51; 95% CI 1.00 to 2.32) and 'severe' asthma (OR=2.09; 95% CI 1.30 to 3.36). As far as we are aware, no similar studies have been conducted among children. The aim of this project was to determine, using a large, population-derived sample, whether anxiety is more common among children with a diagnosis of asthma confirmed by a paediatric physician in comparison to children without asthma.

METHODS

We conducted a cross-sectional survey of anxiety symptoms among primary school children with and without asthma.

Population

This study was part of a larger investigation of childhood asthma conducted in the Barwon region of Victoria, Australia.²¹ We used the protocol of the International Study of Asthma and Allergies in Childhood (ISAAC) to survey asthma symptoms among primary school children in the region. The questionnaire included a request for respondents to volunteer their contact details. We attempted to contact and interview parents who reported within the ISAAC questionnaire that their child had suffered four or more episodes of wheeze in the preceding 12 months. The telephone interview was designed to identify children who had suffered four or more episodes of asthma, each associated with (1) wheeze, (2) increased work of breathing and (3) requiring at least 24 hours of treatment with reliever medication and (4) at least one of which resulted in an urgent medical review. Children who met these criteria then underwent a clinical review with a paediatrician to determine whether the diagnosis of asthma was in accordance with the major international asthma guidelines.^{22 23} In particular, we required a history of (1) recurrent episodes of wheeze and respiratory distress which improved with the use of bronchodilator medication and (2) that the presence of wheeze had been confirmed on one or more occasions by a physician conducting chest auscultation. For each participant with asthma we enrolled two non-asthmatic controls. We identified all survey respondents without asthma symptoms who were the same age (in years), gender and attended the same school as the participant with asthma. These names were then placed in a random sequence. We spent two weeks attempting to contact the parents of the top two children in the sequence before progressing to the next name. A telephone interview was conducted to confirm the absence of asthma symptoms. We did not determine other aspects of health in the control children.

Approval for the study was obtained from local ethics committees and all participants signed an informed consent form.

Study measurements

Anxiety symptoms were assessed using the Spence Children's Anxiety Scale (SCAS).²⁴ The SCAS consists of 44 items (38 assessing symptoms of anxiety, and six relate to positive, filler items to reduce negative response bias). Each item is

scored 0–3, and therefore, the total possible anxiety score is 114. The subscales include panic/agoraphobia, social anxiety, separation anxiety, generalised anxiety, obsessions/compulsions and fear of physical injury. The SCAS comes in a form designed for children to self-report (the SCAS-child) and a form designed for parental report (the SCAS-parent). Both the SCAS-child and SCAS-parent have good test-retest reliability and internal consistency.²⁵ The SCAS-child and SCAS-parent were posted out to families. We asked that the parent who spends the most time with the child complete the SCAS-parent. We defined satisfactory completion as having completed 36 or more of the 38 anxiety-related SCAS items. We defined a SCAS score (child or parent) as being within the clinical range if it was greater than 2 SDs above the mean score among the non-asthmatic children in this study. This definition was stratified by gender.

A supplementary questionnaire contained items relating to the following potentially confounding factors: age, sex, socio-economic status, care giver's level of education, household crowding, care giver's cigarette smoking practices and history of clinical anxiety in a first degree relative.

Among children with asthma, atopic status was determined via skin prick testing. Glycerinated allergen extracts (HollisterStier, Spokane, WA, USA) and histamine (10 mg/ml positive control.) were introduced to the forearm using metal lancets (Stallergenes, Antony, France) according to standard guidelines.²⁶ We tested using house dust mite (*Dermatophagoides pteronyssinus* 1), dog, cat and grass antigens. A positive skin prick test was defined as a weal with a diameter at least 3 mm greater than that produced by a negative control solution at 15 minutes.²⁶

Statistical analysis

A two-sided t test was used to compare mean SCAS scores between children with and without asthma, for both the child and parent versions of the scale. ORs comparing the likelihood of a SCAS score in the clinical range between children with and without asthma were estimated using conditional logistic regression. Potential confounding was investigated using regression techniques. We planned to include variables in the regression models that were (1) associated with the score ($p < 0.05$) in univariable analysis and (2) made greater than a 10% difference in the effect estimate. Categorical outcomes were compared between asthmatic children with and without 'clinical' anxiety using the standard χ^2 test. We checked for effect modification by gender using interaction tests. Analyses were performed with Stata, version 10.

RESULTS

A total of 158 children with asthma and 319 non-asthmatic children adequately completed the questionnaire. In each case, the SCAS-child was completed by the child's mother. The participant flow is shown (figure 1). Overall, approximately 60% of the eligible children with asthma within the Barwon region participated. Response rates were similar among children with and without asthma. The mean age of respondents was 9.0 years (range 5.8–13.5 years), and 319 (67%) were male. Among the participants with asthma, 125 (79%) demonstrated atopic sensitisation, 103 (65%) had a history of eczema, 74 (47%) had suffered greater than eight asthma exacerbations in the preceding year, 71 (45%) reported asthma interval symptoms and 101 (64%) were regularly using an asthma preventive medication.

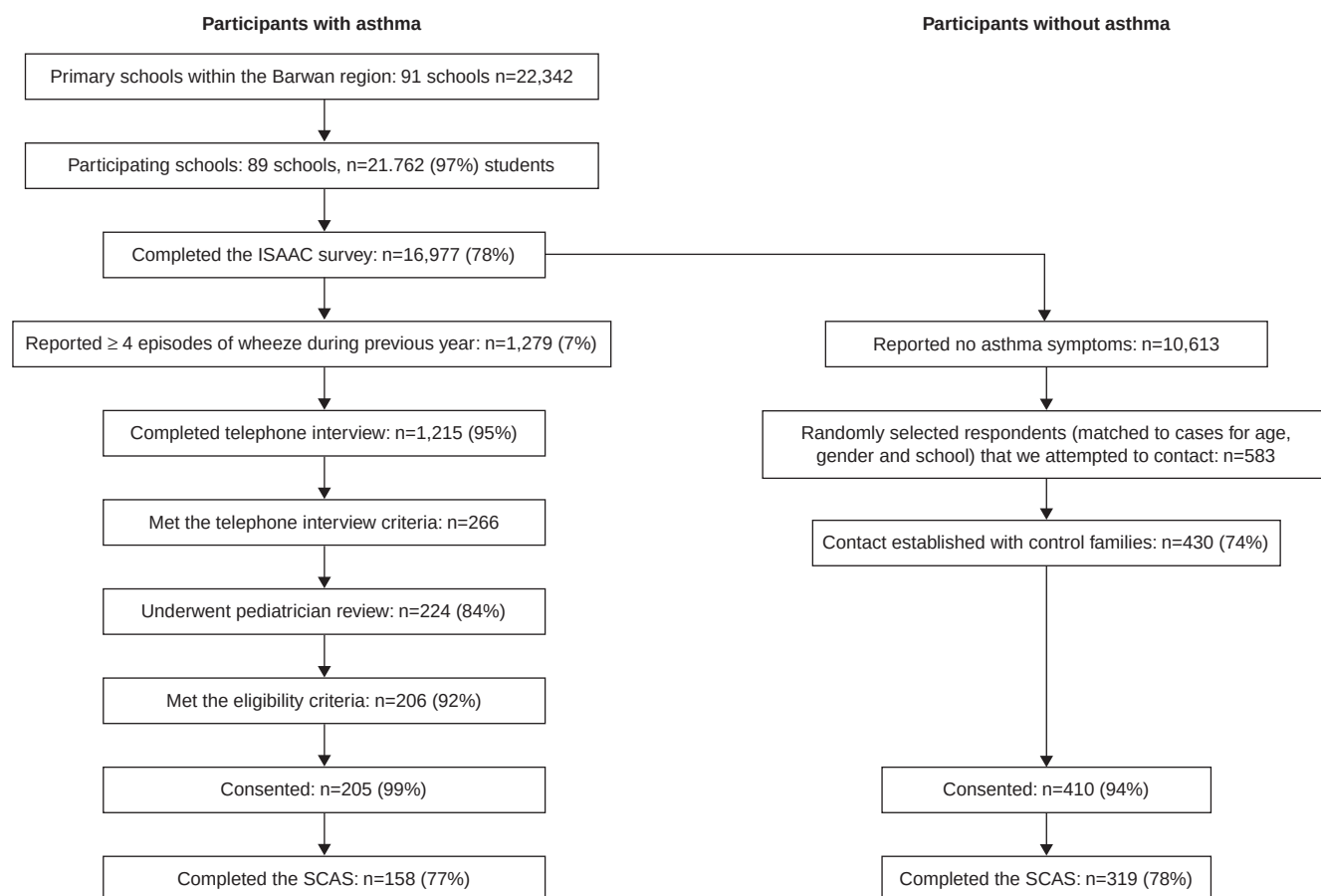


Figure 1 Participant flow.

The correlation between the SCAS-child and SCAS-parent scores was 0.74 (95% CI 0.68 to 0.80). The SCAS-child scores were higher than the SCAS-parent scores (19.9 vs 16.7; mean difference=3.2, 95% CI 1.7 to 4.7, $p<0.001$). The difference between the SCAS-child and SCAS-parent scores was not related to the child's asthma status ($p=0.86$). The SCAS-child scores were higher in girls than boys (21.9 vs 18.8; mean difference=3.1, 95% CI 0.7 to 5.5, $p=0.012$). Similarly, the SCAS-parent scores were higher in girls than boys (18.2 vs 15.8; mean difference=2.4, 95% CI 0.3 to 4.4, $p=0.027$).

The SCAS-child and SCAS-parent scores were higher among asthmatic than non-asthmatic children (table 1). Similarly, the proportion of children with a SCAS-child and SCAS-parent score in the clinical range was higher among asthmatic than non-asthmatic children. Parental cigarette smoking was retained in the regression model investigating the SCAS-parent scores. No other potentially confounding variables met the retention criteria. There was no evidence that the difference in the mean SCAS-child score (figure 2), or odds of having a SCAS-child score in the clinical range (figure 3), were greater among subgroups defined by various markers of asthma severity. Similar results were seen for the SCAS-parent.

With regard to the SCAS-child subscales panic/agoraphobia ($p<0.001$), separation anxiety ($p=0.003$), generalised anxiety ($p<0.001$) and obsessions/compulsions ($p<0.001$) scores were

all higher among children with asthma. There was no difference in social anxiety ($p=0.181$) or fear of physical injury ($p=0.138$) scores in relation to asthma status. There was no evidence that gender modified the relation between asthma and the SCAS-child score or any of the subscales ($p>0.1$ for each interaction test). A similar pattern was seen among the SCAS-parent subscales (data not shown).

Among children with asthma, those with a SCAS score in the clinical range had a similar pattern of health resource utilisation to those with a score in the non-clinical range (table 2). However, there was some evidence that those with a score in the clinical range were more likely to be regularly using an asthma preventive medication, and were more likely to be missing a substantial amount of school (table 2).

DISCUSSION

This study demonstrates that primary school-aged children with asthma are at substantially higher risk of anxiety than their non-asthmatic peers. The estimated difference was 4.8 points (95% CI 2.4 to 7.2) on the SCAS-child scale, which was 41% of the SD in the non-asthmatic group. Concordantly, children with asthma were more likely to have a SCAS score in the clinical range (OR=2.5, 95% CI 1.1 to 5.8, $p=0.036$). As far as we are aware, this is the first time that this association has been demonstrated using a sample of children with paediatrician-defined asthma in comparison to an appropriate control series.

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Table 1 SCAS-child and SCAS-parent scores among children with and without asthma

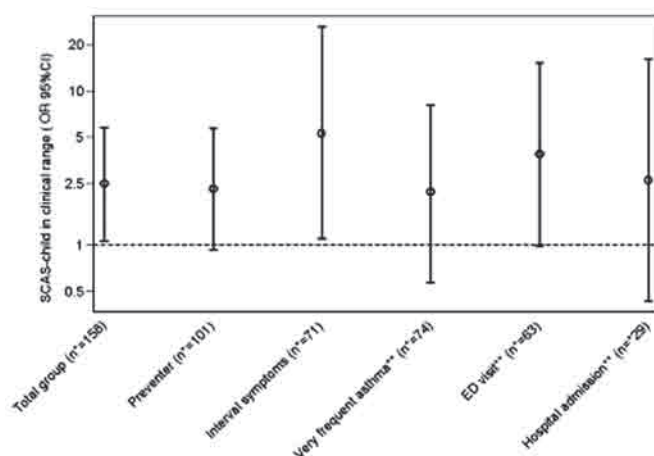
	Asthma (n=158)	No asthma (n=319)	Difference (95% CI)	p Value
SCAS-child score* (mean (SD))	23.1 (14.2)	18.3 (11.6)	4.8 (2.4 to 7.2)	<0.001
SCAS-parent score* (mean (SD))	20.9 (12.8)	14.6 (9.5)	6.3 (4.2 to 8.3)	<0.001
			OR† (95% CI)	p Value
SCAS-child in clinical range	16/142 (11%)	12/307 (4%)	2.5 (1.1 to 5.8)	0.036
SCAS-parent in clinical range	26/132 (17%)	13/306 (4%)	4.9 (2.2 to 10.9)	<0.001
			5.4 (2.0 to 14.5)‡	0.001

*Total score possible=114.

†OR calculated using conditional logistic regression to allow for matching between cases and controls.

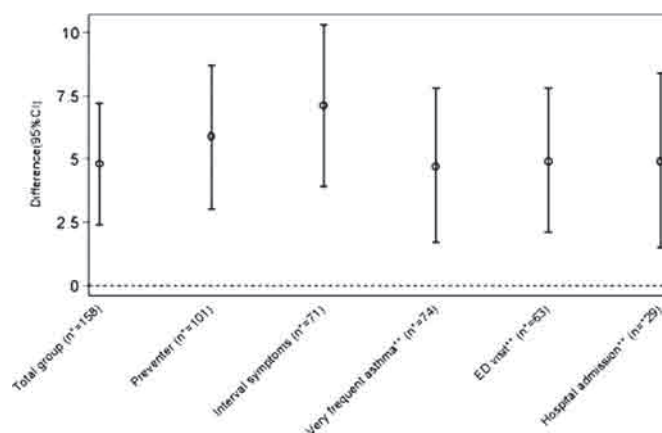
‡OR adjusted for parental cigarette smoking.

SCAS, Spence Children's Anxiety Scale.

**Figure 3** The odds of an SCAS-child score in the clinical range among participants with asthma compared to participants without asthma. The ORs are shown for the total group, and for subgroups defined by various markers of asthma severity. In each case the asthmatics were compared to all non-asthmatic participants. *The number of asthmatic participants included in the analysis. **During the preceding year. ED visit, emergency department visit; hospital admission, hospital admission for asthma; interval symptoms, asthma symptoms on more than two occasions each week; preventer, regularly using an asthma preventive medication; very frequent asthma, greater than eight episodes per year.

The strengths of this study include a population-based sampling strategy, high participation and response rates, a large number of participants, the use of a paediatric clinical assessment to define asthma status and the use of two separate measurements of anxiety symptoms. However, there are several limitations. We have relied solely on parent and child report to measure anxiety. We used a validated instrument, and it is encouraging that there was high parent-child correlation on the SCAS scores. Assessment by a psychologist or psychiatrist would be helpful to identify those children with a DSM IV diagnosis of an anxiety disorder, but this was beyond the scope of the project. It is also possible that, as the questionnaires were sent home, the parent supervising the process may have influenced their child's responses.

It is also plausible that parental anxiety may be influential in interacting with comorbid asthma and anxiety in the child at a number of levels. For instance, parental anxiety may foster

**Figure 2** The mean difference in SCAS-child scores among participants with and without asthma. The differences are shown for the total group, and for subgroups defined by various markers of asthma severity. In each case the asthmatics were compared to all non-asthmatic participants. *The number of asthmatic participants included in the analysis. **During the preceding year. ED visit, emergency department visit; hospital admission, hospital admission for asthma; interval symptoms, asthma symptoms on more than two occasions each week; preventer, regularly using an asthma preventive medication; very frequent asthma, greater than eight episodes per year.**Table 2** Health resource utilisation, regular use of asthma preventive, and school absenteeism among asthmatic children (n=158) with and without clinical anxiety

	SCAS-child scores			SCAS-parent scores		
	Non-clinical (n=142)	Clinical (n=16)	p Value	Non-clinical (n=132)	Clinical (n=26)	p Value
ED visit*	56 (47%)	7 (47%)	0.977	53 (47%)	10 (43%)	0.709
Hospital admission*	26 (22%)	3 (20%)	0.870	25 (22%)	4 (18%)	0.666
Regular asthma preventer	87 (61%)	14 (88%)	0.038	83 (62%)	18 (69%)	0.538
School absenteeism†	15 (11%)	4 (25%)	0.092	10 (8%)	9 (35%)	<0.001

*During the last year.

†Defined as missing more than 1 month of school during the past 6 months.

ED, emergency department; SCAS, Spence Children's Anxiety Scale.

a heightened awareness of dyspnoea in the child, a tendency to administer excessive amounts of asthma medications, and an increased tendency to miss school. A more complete understanding of the pathway leading to comorbid asthma and anxiety in the child requires an understanding of the role of the parent.

It should also be noted that our definition of clinical anxiety (2 SDs above the mean SCAS scores among non-asthmatic children) is relatively arbitrary. Non-asthmatic children are not an unselected population, as by definition, children with asthma have been excluded. Given that asthma and anxiety share a number of risk factors, such as parental smoking and anxiety, it is reasonably likely that the prevalence of anxiety among our non-asthmatic controls is lower than it would be among an unselected population. While we can be confident that the risk ratio for clinical anxiety is significantly elevated among children with asthma in comparison to children without asthma, the prevalence of DSM IV anxiety disorders within each group is uncertain.

Our findings extend previous cross-sectional studies that have found an independent association between anxiety and asthma, where asthma has been measured by parent/self-report,^{14 15} or review of medical records¹⁶; and corroborate a study that demonstrated an independent relation between anxiety and physician-diagnosed asthma in adults.²⁰ Thus it is unlikely that the association between anxiety and asthma is simply due to anxiety symptoms being misinterpreted as asthma. Previous studies suggest that panic disorder and generalised anxiety disorder are the patterns of anxiety most strongly associated with asthma.^{17 20} Our data are in keeping with these findings. A recent study also found a strong relation between social anxiety and self-reported asthma among adolescents.¹⁵ The authors suggested that this might relate to concerns about exhibiting symptoms or taking medications in front of peers. There was little evidence of an association between scores on the social anxiety subscale of the SCAS and asthma among the primary school children in our study. However, it is possible that an association between social anxiety and asthma evolves as children move from the primary school years into adolescence. Longitudinal data from adults suggest there is a bidirectional longitudinal association between anxiety and asthma¹⁷—that is, that anxiety may be a risk factor for developing asthma, and vice versa. It is not clear whether this bi-directional longitudinal association is also apparent among children¹⁸ although, interestingly, it has been demonstrated that behavioural difficulties in pre-school children may antecede the development of wheezing disorders.²⁷

The relation between asthma and anxiety has important clinical implications. Internalising disorders such as anxiety are relatively easy to overlook during a medical consultation, particularly when the focus is another problem, such as asthma. Therefore, the clinician must actively consider whether anxiety may be contributing to the child's asthma symptom complex. Children with asthma who are missing a substantial amount of school may be at particular risk of comorbid anxiety. The use of a screening instrument, such as the SCAS, can be a useful strategy. Importantly, once relevant children are identified, anxiety is amenable to treatment.²⁸

This study has implications for future research. Studies incorporating a standardised assessment of anxiety by a mental health professional(s) among children with and without physician-defined asthma would provide more rigour than the current study. Follow-up data from cohorts such as those described here are needed to quantify the longer-term issues associated with comorbid asthma and anxiety. Longitudinal data are required in order to understand the sequence of events, and developmental context, that lead to comorbid asthma and anxiety. It may be useful to identify critical ages and events (eg, hospital admission). Studies are required to evaluate whether parental anxiety is involved in the relation between childhood asthma and anxiety. Perhaps most importantly, interventional studies are needed to evaluate strategies for the prevention and treatment of anxiety among children with asthma.

In conclusion, we have found that children with asthma are at substantially higher risk of anxiety than their non-asthmatic peers. Clinicians should actively seek evidence of anxiety among children with asthma, and should be aware that children who are missing a substantial amount of school may be at particular risk. The use of anxiety screening tools may assist in this process. Future studies are required to

evaluate whether parental anxiety is involved in the pathogenesis of comorbid asthma and anxiety, to determine the sequence of events and developmental context that leads to an association between asthma and anxiety, to document the longer-term sequelae of this comorbidity and to evaluate strategies to prevent and treat anxiety among children with asthma.

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Competing interests This project was funded by the Jack Brockhoff Foundation, the Murdoch Childrens Research Institute and the National Health and Medical Research Council of Australia.

Ethics approval This study was conducted with the approval of the Barwon Health, Geelong, Victoria, Australia.

Provenance and peer review Not commissioned; externally peer reviewed.

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