

## CLINICAL REVIEW

## Asthma and psychological dysfunction

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**Abstract**

Despite effective treatment, asthma outcomes remain suboptimal. Anxiety and depression occur more commonly in people with asthma than expected, and are associated with poor asthma outcomes. The direction of the relationship and the mechanisms underlying it are uncertain. Whether screening for and treating co-morbid anxiety and depression can improve asthma outcomes is unclear from the current evidence. Primary care clinicians treating asthma should be aware of the possibility of psychological dysfunction in asthmatics, particularly those with poor control. Further research is required to assess the importance of detecting and treating these conditions in community asthma care.

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M Thomas *et al.* *Prim Care Respir J* 2011; 20(3): 250-256<http://dx.doi.org/10.4104/pcrj.2011.00058>**Keywords** asthma, anxiety, depression, psychological dysfunction**Introduction**

Asthma is one of the commonest chronic illnesses treated by primary care clinicians, estimated to affect over 300 million people globally.<sup>1</sup> It is a complex and multifaceted disease that affects health in many ways. Although modern pharmacotherapy is capable of achieving high levels of control for most patients in clinical trials,<sup>2</sup> repeated surveys show that poor control remains common in clinical practice. A recent European survey reported that over half of community-treated patients with asthma had inadequate symptom control.<sup>3</sup> There are many possible reasons for poor control – relating to patients, clinicians, and to the communication between them.<sup>4</sup> Patient-related factors associated with poor outcomes include co-morbidity with a variety of conditions including anxiety and depression,<sup>5</sup> and behavioural factors associated with psychological illnesses such as non-adherence and inadequate self-management skills.<sup>6</sup> Psychological conditions such as anxiety and depression have been reported in surveys to be common in people with asthma<sup>7</sup> and may be associated with poor control.<sup>8</sup> The aim of this paper is to explore this co-morbidity in more detail.

Other long-term illnesses have also been associated with psychological dysfunction. For instance, psychological dysfunction is common in patients with chronic obstructive pulmonary disease (COPD) with an odds ratio for depression in patients with severe COPD of 2.5 times that of matched controls.<sup>9</sup> Psychological dysfunction is often unrecognised in people with COPD, and has been associated with worse COPD outcomes leading to recommendations for systematic screening to be performed as part of a clinical review.<sup>9</sup> Diabetes has also been associated with double the risk of depression in comparison with non-diabetic controls,<sup>10</sup> and co-morbidity is associated with worse outcomes.<sup>11</sup> Similarly, depression is more common in people with epilepsy than in the general population and may be associated with poor outcomes.<sup>12</sup> It is therefore possible that some of the psychological co-morbidities in people with asthma may be common to other long-term conditions, although others may be 'disease-specific'. The surveys described below show that the prevalence of depression in people with asthma is comparable to that found in association with other chronic illnesses that have a negative impact on the sufferer, and that

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the prevalence of anxiety is particularly high in people with asthma.<sup>13</sup>

Asthma has long been linked to psychological dysfunction, with Osler stating in the 19th century that '... in the majority of cases asthma has a strong neurotic element'.<sup>14</sup> Although astute clinicians will often recognise and address psychological needs in their asthma patients during an asthma review, routine assessment of psychological and emotional well-being is not currently a standard part of community-based asthma care. This paper reviews the scientific literature linking asthma and psychological illness. We aim to assess the relevance of psychological co-morbidity in patients with asthma and to answer some practical questions of importance to community-based clinicians treating asthma, such as:

- How common is psychological dysfunction in people with asthma? If there is an association, does asthma result in anxiety and depression or *vice versa*?
- If anxiety or depression is present in people with asthma, is this associated with poor asthma control?
- How do anxiety and depression affect asthma control?
- Can treating anxiety and depression improve asthma control?

To address these issues, Medline searches were performed by pairing the word 'asthma' with the following keywords: anxiety, panic, psychological disorders, and depression. Research based on the bibliographies of the articles located via the MEDLINE search were also identified and reviewed.

## How common is psychological dysfunction in asthma?

Asthma, anxiety, and depression are all common conditions so can occur in the same individual through chance. However, there is now a considerable body of evidence to indicate that psychological dysfunction is more common in people with asthma than would be expected from chance alone. Cross-sectional surveys consistently report higher levels of psychological morbidity (both in terms of average scores on metric scales of anxiety and depression and of the proportion of individuals meeting diagnostic criteria for these conditions) in people with asthma compared with the general population.<sup>7,15-17</sup> These surveys have used a variety of well accepted methods such as structured diagnostic interviews or validated screening questionnaires to diagnose anxiety and depression. Asthma is generally defined by physician diagnosis based on standard clinical diagnostic criteria. A recent international World Health Organization survey of over 85,000 adults in 17 countries<sup>7</sup> used a standardised and detailed structured psychiatric interview with trained interviewers to provide diagnostic information consistent with the internationally accepted Diagnostic and Statistical Manual of Mental Disorders Manual, American Psychiatric Association

(DSM-IV) classification system. This survey reported that the age-adjusted and gender-adjusted odds of mental disorders among people with physician-diagnosed asthma relative to those without was 1.6 (95% CI 1.4 to 1.8) for depressive disorders and 1.5 (95% CI 1.4 to 1.7) for anxiety disorders. This relationship was present within the different countries and ethnic groups surveyed. Similar cross-sectional relationships between asthma and psychological dysfunction have been reported in a paediatric survey using a validated questionnaire, the Spence Children's Anxiety Scale,<sup>17</sup> and in a prospective birth cohort study of over 1,000 children using standard clinical diagnostic criteria for asthma and for psychiatric conditions.<sup>18</sup>

A UK primary care survey published in 2007 using the validated Hospital Anxiety and Depression Scale (HADS) reported higher anxiety and depression scores in adults with physician-diagnosed asthma than in the general community, particularly in patients aged >45 years, and a prevalence of panic disorder of 16% in those with asthma.<sup>19</sup> Anxiety disorders have consistently been reported to be more common than expected in people with asthma, with a reported prevalence of 16–52% in different surveys using different methodologies and screening instruments.<sup>13</sup> These figures indicate that anxiety disorders are up to six times more common in people with asthma than in the general population.<sup>20</sup> The same surveys also report a high prevalence of depressive disorders, occurring in 14–41% of subjects, again being up to six times more common in people with asthma than in the general population.<sup>13</sup> A recent US study of over 180,000 adults with self-reported physician-diagnosed asthma in the National Health Interview Survey found that the prevalence of serious psychological distress (as determined by a structured clinical interview) was 7.5% (95% CI 7.0% to 8.1%) compared with a prevalence of 3.0% in the total surveyed population.<sup>21</sup>

The presence of psychological morbidity is, however, frequently unrecognised by the usual clinicians treating the patient's asthma, so underdiagnosis and undertreatment are common. For instance, in a survey of Canadian adults with physician-diagnosed asthma using a structured psychiatric interview, the Primary Care Evaluation of Mental Disorders,<sup>13</sup> anxiety disorder was found to be present in 12%, depression in 8% and both in a further 11%. However, fewer than 20% of those with significant psychiatric illness were receiving any treatment, and fewer than 15% of all with a psychiatric problem had seen a mental health professional at the time of the survey.

Anxiety and depression are particularly common in people with severe and difficult-to-control asthma, with one survey reporting that the prevalence of significant psychological dysfunction diagnosed by interview with a liaison psychiatrist

was 50%, although again frequently unrecognised and untreated.<sup>22</sup> Patients with severe asthma have been reported to have significantly greater psychological distress – including greater anxiety, impaired cognitive function, and impaired emotional coping mechanisms – than matched patients with less severe disease as assessed by a validated questionnaire instrument, the Millon Behavioral Medicine Diagnostic Inventory, which assesses psychological distress and emotional/behavioral coping factors.<sup>23</sup> Patients who have experienced near-fatal asthma attacks show higher psychological morbidity,<sup>24</sup> reporting greater anxiety as assessed by the Cognitive Depression Inventory and Trait-Anxiety Scale questionnaires, even years after the episode.

There is therefore a wealth of evidence showing a significant association between asthma and psychological dysfunction. Can we say whether this is a causal relationship and, if so, in which direction causality lies? Does having asthma predispose to psychological dysfunction or do psychological problems predispose to asthma, or could the association be explained by other common risk factors, genetic or environmental? Most of the evidence discussed so far is derived from cross-sectional surveys, using diagnostic interviews and/or validated questionnaires to assess the prevalence of these conditions in individuals from different populations at a single moment in time. Such surveys can show associations but cannot confirm a causal relationship or show the direction of any relationship observed.

Longitudinal studies follow the characteristics of a cohort of subjects over time and so provide additional information on the time course of the development of symptoms and diagnoses. Unfortunately there are few such studies in asthma. One prospective Swiss community-based longitudinal cohort study consisted of repeated semi-structured diagnostic interviews conducted by professionals in order to investigate the relationship between asthma and panic disorder in young adults.<sup>25</sup> This study reported that having a diagnosis of asthma at the baseline evaluation was associated with an increased chance of subsequently being diagnosed as having anxiety or panic disorder. After adjusting for potentially confounding variables, active asthma predicted subsequent panic disorder with an odds ratio of 4.5, suggesting that having asthma may result in the subsequent development of panic in some patients. This is perhaps not surprising, given the frightening nature and unpredictability of asthma attacks. However, this study also reported that the presence of panic disorder predicted subsequent asthma with an odds ratio of 6.3, suggesting that psychological dysfunction may precede the development of asthma. Unfortunately, objective testing to confirm the diagnosis of asthma was not undertaken in this study; so, although the psychiatric diagnostic criteria were standardised and robust, there is a possibility that the asthma

diagnosis was mistaken and related to symptoms resulting from anxiety-related hyperventilation.<sup>26</sup> A population-based longitudinal study of over 5,000 American adults without asthma also reported that anxiety and depression at baseline were associated with an increased subsequent risk of asthma, including those without baseline respiratory symptoms and/or abnormal pulmonary function tests.<sup>27</sup> A UK longitudinal birth cohort study that included detailed characterisation of wheezing phenotypes in children<sup>28</sup> found that having childhood asthma was associated with an increased risk of subsequent behavioural problems assessed by the validated Eyberg Child Behavior Inventory, but also that behavioural problems in the child at the age of 3 was a significant risk factor for both a subsequent asthma diagnosis and for late-onset wheezing, again suggesting a bidirectional relationship. Finally, a recent longitudinal study<sup>29</sup> in the USA followed 439 adults with asthma over a 2-year period, reporting that new depression was diagnosed by the usual clinician in 38 individuals with poor asthma control strongly predicting this occurrence.

The available evidence therefore strongly suggests that asthma may precede and predispose to anxiety and depression, but also that psychological and behavioural problems may precede and predispose to asthma.

## **Are anxiety and depression associated with poor asthma outcomes?**

Anxiety and depression are often unrecognised in people with asthma. If there is convincing evidence that they are associated with poor asthma control and worsened outcomes, then their detection would identify at-risk patients and so have a potentially valuable clinical role in asthma management. This section presents a review of the available evidence for any association between psychological problems and poor asthma control.

Consistent evidence from cross-sectional surveys using a variety of validated questionnaire tools suggests that symptomatic asthma control and asthma-related health status are impaired when clinically relevant anxiety or depression are also present.<sup>8,13,15,30,31</sup> This relationship appears to be independent of potentially confounding factors such as age, gender, socioeconomic status, objective asthma severity, and prescribed treatment level. A survey of Canadian adults with asthma<sup>13</sup> found that, after adjustment for age, gender and measures of underlying asthma disease severity, in comparison with those with no psychiatric problem, significantly worse symptomatic asthma control occurred in those with anxiety, depression, and particularly in those with both. In a regression model the presence of psychiatric co-morbidity accounted for 29% of the variance in Asthma Control Questionnaire score.

Anxiety and depression are associated with poor asthma

outcomes across a range of different outcome measures. These include impaired asthma-related quality of life,<sup>32</sup> higher asthma-related health resource utilisation,<sup>32,33</sup> increased asthma-related health costs,<sup>32</sup> less successful emergency treatment,<sup>34</sup> and increased asthma hospitalisation rates.<sup>34</sup> Anxiety is associated with increased use of rescue medication regardless of lung function or objective measures of disease severity.<sup>35</sup> Stress – both acute and chronic – significantly increases the risk of acute asthma attacks,<sup>36</sup> and negative life events are associated with an increased risk of asthma attacks both in the immediate aftermath and in the following 5–7 weeks.<sup>15</sup> Psychological co-morbidity may even be associated with increased asthma mortality risks.<sup>37</sup>

The increased symptoms and worsened asthma-related health status reported by people with psychological dysfunction may relate to a greater perception of symptoms and greater distress associated with them. Asthma symptoms – particularly the perception of breathlessness – are experienced as being more intense in people with co-morbid psychological dysfunction, the association occurring independently of asthma severity and other potentially confounding factors.<sup>38</sup> A similar degree of bronchoconstriction produces greater perceptions of dyspnoea in patients with anxiety and depression. In bronchial provocation testing to measure bronchial hyperreactivity, anxiety was independently associated with an increased intensity of reported breathlessness in response to bronchoconstriction in people with asthma.<sup>39,40</sup> The current evidence therefore suggests that psychological co-morbidity is associated with worse asthma symptoms and worse outcomes across a range of measures.

## How and why do anxiety and depression impact on asthma?

Although there is convincing evidence that psychological dysfunction is common in people with asthma and is associated with poor asthma outcomes, the mechanism(s) underlying this relationship is less clear. There are a number of possible and plausible potential explanations for this association.

Firstly, anxiety and depression may induce behaviours that result in worsened asthma outcomes. Anxiety is a normal and appropriate response to asthma symptoms such as dyspnoea and chest tightness, and may in moderation have beneficial results including appropriate avoidance of triggers, regular use of prophylactic medication, and appropriate contact with health professionals during exacerbations.<sup>40</sup> However, if excessive, anxiety may lead to inappropriate behaviours including poor self-management skills, overuse of bronchodilator medication,<sup>35</sup> poor adherence to controller therapy,<sup>41</sup> poor relationships with health professionals, and indulgence in at-risk behaviour such as non-adherence, poor self-management behaviour and smoking.<sup>42</sup>

Secondly, anxiety is commonly associated with hyperventilation, vocal cord dysfunction, and dysfunctional

breathing. These functional breathing disorders can result in asthma-like symptoms and can act as a trigger for asthma.<sup>43</sup> Abnormal breathing patterns can cause symptoms such as chest tightness and dyspnoea, even in the absence of hypocapnia.<sup>44</sup> Surveys have suggested that symptoms of hyperventilation are common even in people with mild and moderate asthma.<sup>45</sup> Breathing training exercises have been used as a treatment for panic attacks and for asthma. Awareness of the possibility of dysfunctional breathing in association with anxiety may therefore suggest an alternative treatment strategy for some patients with this co-morbidity.<sup>46</sup>

Thirdly, as discussed above, psychological disturbance may be associated with altered symptom perception, with enhanced awareness of breathlessness and bronchoconstriction and so increased distress.<sup>39</sup> Breathlessness is a basic and primitive sensation mediated by areas of the mid-brain associated anatomically and functionally with emotional processing and arousal.<sup>47</sup> It is therefore possible that activation of breathlessness-modulating neural processing circuits can affect the experience of emotion, and that anxiety and emotion can influence the perception of breathlessness.

Fourthly, it is possible that psychological and emotional factors may have biological effects on immunological, hormonal and/or autonomic function that impact on asthma severity and control.<sup>26</sup> Emotion and stress can affect the immune function in ways that are only now beginning to be appreciated and understood.<sup>48</sup> There is some evidence that psychological stress may predispose to the development and severity of atopic conditions including asthma through effects on the immune system.<sup>49</sup> Psychological stress can affect the release of cortisol and the expression of inflammatory mediators in a complex and time-dependent way, with increased airway inflammation associated with stress.<sup>50</sup> Although it is clear that stress can result in measurable neuroimmunological effects that can be associated with asthma morbidity, the precise significance of these biological effects and the ways in which they interact with other stress-related factors such as health beliefs and behaviours is not fully understood.<sup>51</sup>

Finally, it is possible that these conditions may share common and as yet unidentified genetic or environmental risk factors that increase the likelihood of asthma being diagnosed and increase the severity of asthma. Therefore, although there is good evidence for a relationship between asthma and psychological disturbance, there is still much to learn about the mechanisms surrounding this relationship.

## Can treatment of anxiety and depression improve asthma control?

This pivotal question asks whether treatment of co-morbid psychological dysfunction will lead to improved short-term and long-term asthma outcomes. The current evidence is inadequate

to answer this question with any certainty. A Cochrane review of psychological interventions for adults with asthma was published in 2006<sup>52</sup> and considered the effects of interventions targeted on the treatment of anxiety and/or depression – including cognitive behavioural therapy (CBT), relaxation therapy (with or without biofeedback), and counselling – but was unable to draw firm conclusions due to a lack of large and rigorous controlled trials. However, there were some suggestions of improved asthma outcomes associated with a number of interventions targeted on reducing anxiety and depression such as relaxation therapy, CBT, and biofeedback. Recent pilot studies in patients with co-morbid anxiety and depression have reported improved asthma outcomes in patients undergoing panic control programmes<sup>53</sup> or treatment with antidepressant medication.<sup>54</sup> Both these studies were small and preliminary so further research is needed. An observational study in ‘high-risk’ children with asthma suggested potential benefit from co-consultation with a child psychiatrist and a respiratory paediatrician,<sup>55</sup> although a study in adults with difficult asthma showed no benefit from a 6-month nurse-delivered psycho-educational programme.<sup>56</sup> A meta-analysis of psycho-educational interventions in asthma concluded that, although there was some evidence of positive effects, there was not enough evidence to warrant significant changes in current clinical practice at this time<sup>57</sup> and that further studies are needed. Recent studies have reported that completion of an aerobic training exercise programme can improve both anxiety and depression scores, asthma symptom-free days and asthma-related health status in adults with persistent asthma,<sup>58</sup> and that children with poorly controlled asthma showed improvements in health status and in measures of anxiety and depression from an art therapy programme.<sup>59</sup>

In view of how commonly the co-morbidity between psychological problems and asthma occurs, it is perhaps surprising that the evidence base for treatment is so meagre and we consider this an important area for future research.

## Conclusions: messages for practising clinicians

In this review we have attempted to answer a number of questions that are important to primary care clinicians treating asthma. The evidence clearly points to a significant overlap between anxiety, depression and asthma, with a higher prevalence of psychological problems in people with asthma. The evidence also suggests strongly that those with anxiety and depression are more likely to have worse outcomes, so detecting these problems will alert the clinician to patients at risk of poor outcomes. Patients’ adoption of at-risk behaviours such as poor adherence and smoking, which are often a source of frustration and bewilderment to clinicians, may be explained in part by co-existing psychological problems. Whether treatment of anxiety and/or depression will result in improved asthma outcomes, and

which type of treatment is most effective, remains uncertain and should be the focus of further research.

Should we be screening routinely for anxiety and depression in our asthma patients? Simple questionnaire-based screening instruments are widely used in primary care in some parts of the world and in some clinical conditions. This has become accepted practice in other chronic illnesses such as COPD, diabetes, and ischaemic heart disease. We believe that there is a plausible case that this would also be a useful contribution in asthma care. Until further research is completed we cannot be sure whether or not this is a useful investment of time and energy. However, primary care clinicians are used to thinking in ‘holistic’ terms about patients and not looking at illnesses in isolation. We should therefore be more aware of the possibility of anxiety and depression in our asthma patients, particularly those with less than optimal control and in whom poor adherence and risk-taking behaviour is evident. A greater awareness of the possibility that these problems exist, combined with appropriate action when they are detected, should help to achieve better outcomes for asthma patients.

### Conflicts of interest

MT is an Associate Editor of the *PCRJ*, but was not involved in the editorial review of, nor the decision to publish, this article.

### Contributorship

The manuscript was drafted by MT with suggestions and contributions from the other authors.

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## National Review of Asthma Deaths: call for panel assessors

**We are looking to recruit professionals\* to be panel assessors for the National Review of Asthma Deaths (NRAD), being run by the Royal College of Physicians (RCP). Panel assessors must currently be in clinical practice or have retired within the previous five years.**

Every death from asthma in the UK over a 12-month period from the 1 February 2012 will be systematically assessed and will be subject to an in-depth multidisciplinary confidential enquiry. The overriding aim of the confidential enquiry phase of the NRAD is to identify preventable or avoidable factors from individual cases in order to learn lessons for future implementation by healthcare professionals and people who suffer from asthma, in order to prevent deaths in the future. Assessment of cases will be based on a review of case notes against recognised standards of care from national guidelines and a set of quality indicators derived from clinical experts.

**For further information on the project, the role of panel assessors and how you can apply please see our website – [www.rcplondon.ac.uk/nrad](http://www.rcplondon.ac.uk/nrad).**

**Alternatively please email [nrad@rcplondon.ac.uk](mailto:nrad@rcplondon.ac.uk) or phone +44 (0)20 3075 1500**

\*We are looking for:

- consultant respiratory physicians
- consultant paediatricians (preferably with a special interest in respiratory medicine)
- consultants in emergency medicine or consultants in paediatric emergency medicine
- consultants in intensive care
- consultants in paediatric intensive care
- general practitioners (preferably with a special interest in respiratory medicine)
- respiratory nurse specialists (primary, acute or secondary care)
- respiratory nurse specialists with paediatric expertise (primary, acute or secondary care)
- pathologists.