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Exploring the relationship between generalised anxiety/depression scales and asthma-specific quality of life/control questionnaires in a specialist asthma clinic

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ABSTRACT

Introduction: Psychological issues are common in patients with chronic disabling diseases such as asthma. National guidance recommends that specialist asthma clinic attendees should complete questionnaires screening for psychological comorbidities. However, completing these in addition to asthma specific questionnaires can be burdensome. In order to investigate whether anxiety and depression questionnaires can be used in a targeted manner, this study investigates the correlation between the respective scores. We hypothesize that there is correlation between asthma-specific and anxiety/depression questionnaire scores.

Methods: Three-hundred individuals with poorly controlled asthma attending a specialist clinic were asked to complete Asthma Control Questionnaire (ACQ), mini-Asthma Quality of Life Questionnaire (mini-AQLQ), Generalized Anxiety Disorder (GAD-7) and Patient Health Questionnaires (PHQ-9). A Pearson correlation coefficient was generated and area under ROC and confusion matrices were used to assess correlation.

Results: 49% and 47% of patients completing the GAD-7 or PHQ-9 questionnaires, respectively had scores above the screening level for co-morbid anxiety and depression. Additional questionnaires were often incomplete (GAD-7 = 150 and PHQ-9 = 140). GAD-7 and PHQ-9 correlated with ACQ and mini-AQLQ (all $p = < 0.001$, r values 0.53–0.65). Asthma-specific questionnaire scores were predictive of GAD-7 and PHQ-9 scores (AUCs of 0.78 to 0.84). 75% of patients with a mini-AQLQ score of < 3 met the threshold GAD-7 and PHQ-9 score of 10.

Conclusions: ACQ and mini-AQLQ correlate with GAD-7 and PHQ-9 amongst specialist asthma clinic attendees. A mini-AQLQ > 3 suggests patients are unlikely to have anxiety or depression. These findings could be used to identify patients requiring formal screening for psychological co-morbidity.

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Asthma; anxiety; depression; questionnaires; GAD-7; PHQ-9

Introduction

Asthma is estimated to affect more than 300 million people globally and is in the top 20 causes of “years of life lived with disability” (1). Patients with difficult-to-treat asthma (defined as asthma that is uncontrolled despite Global Initiative for Asthma (GINA) step 4 or 5 treatment (regular medium or high dose inhaled corticosteroid (ICS) $\pm$ add on therapy) or that requires such treatment to maintain good symptom control and reduce the risk of exacerbations (2)) are estimated to be some 17% of the total asthma population (3). A subset of those with difficult asthma have severe asthma (defined as asthma that is uncontrolled despite adherence with maximal optimized therapy and treatment of contributory factors, or that worsens when high dose

treatment is decreased (2)). Only 5–10% of those with asthma have severe asthma (4), but this group bears a large proportion of asthma morbidity (5). These individuals have chronic limiting symptoms that restrict both their social and work activities. They also experience relatively abrupt deteriorations in asthma control that are not fully predictable and can lead to frequent unscheduled healthcare use. In a recent large multicentre observational study, 25.8% of patients with severe asthma required hospital assessment, oral corticosteroids or both in the preceding 3 months (6). It is estimated that 50–80% of the total cost of asthma management can be attributed to severe asthma patients (7). A multi-disciplinary team (MDT) approach is often required to differentiate difficult-to-treat from severe asthma.

As per the GINA guidelines, asthma severity is defined by the level of treatment required to control symptoms and exacerbations (8). In order to assess if the current treatment is working, clear, and validated measurements of asthma control are required. Patient completed self-reported measures such as the Asthma Control Questionnaire (ACQ) (9) and the mini-Asthma Quality of Life Questionnaire (mini-AQLQ) (10) are administered as part of routine practice in asthma clinics in accordance with the National Health Service (NHS) England national specialist service specification (11). Other respiratory questionnaires such as the “Sino-Nasal Outcome Test” (SNOT-22) (12), the “Leicester Cough Questionnaire” (13) and “Brompton Breathing Pattern Assessment Tool” (BPAT) (14) are also used to assess specific symptoms in this group.

Patients with asthma are more likely to have anxiety and depression throughout their lifetime (15–17) and those with severe asthma are more likely to report depressive symptoms than those with less severe disease (18). In a recent study 38% of patients with severe asthma reported symptoms of anxiety and 25% reported those of depression (19). Despite this, a recent systematic review reported that psychological health status was only routinely assessed in two thirds of these patients (20). The relationship between asthma, anxiety, and depression is complex and remains poorly understood.

The impact of depression on patients with chronic illness, such as asthma, is well recognized and clear guidance for screening exists (21). Some 20% of patients with chronic physical illness suffer from depression, this is two to three times greater than the burden of depression in the general population. When patients with chronic physical health issues have comorbid depression the functional impairment from their illness is likely to be much greater (21). It is recognized that patients with asthma and psychological ill health have higher healthcare usage (22). The National Institute for Health and Care Excellence (NICE) recommends using validated screening questionnaires for anxiety and depression in patients with chronic illness (21). Two well established examples are the “Generalized Anxiety Disorder-7 item scale” (GAD-7) (23) and the “Patient Health Questionnaire” (PHQ-9) (24). These can be used in specialist asthma clinics to guide the most appropriate use of the limited available support. As access to psychologists is limited (25), it is important to identify those who are most likely to benefit from referral to services.

Participation in questionnaires and surveys can be influenced by personal characteristics such as familiarity with the questions (26), the relationship with the

questionnaire sponsor (27) or personnel (28). Similarly, the intention to participate is also influenced by the perceived importance of the topic, the lack of the intrusiveness of the questionnaires and assurance of confidentiality (29). The addition of psychological screening tools to questionnaires already used in the clinic can add to the administrative burden for both patients and healthcare professionals. Questionnaire fatigue could lead to a lack of patient engagement, reduce the meaningfulness of the scores obtained or result in patients not completing some questionnaires at all.

We aimed to assess the correlation between the commonly used asthma control and asthma specific questionnaires and two anxiety and depression specific screening questionnaires. Significant correlation would allow the use of either anxiety or depression specific questionnaires to be more targeted and therefore reduce the future questionnaire burden in our asthma patient population. We hypothesized that there is correlation between the mini-AQLQ/ACQ questionnaires and GAD-7/PHQ-9 scores.

Methods

We undertook a service evaluation in a tertiary asthma clinic in England. All participants were under the care of a specialist asthma service and, as such met one or more of the following eligibility criteria (11): Symptoms in line with severe asthma and either (1) an episode of acute severe asthma which was considered life threatening within the last 10 years, (2) continuous or frequent oral corticosteroids (defined as 2 or more courses lasting >3 days in the last year), (3) spirometry in keeping with asthma, (4) transition from pediatric asthma services. Inability to complete the questionnaire in English language was the single exclusion criteria.

Over a six-month period in 2018, 300 unique attendees at the clinic were asked to complete four questionnaires on their arrival in the waiting area: ACQ-6, mini-AQLQ, GAD-7, and PHQ-9. These questionnaires were completed on paper and the scores were entered into the electronic clinical notes. At the end of the data collection period, the four scores for each patient (if completed) were collated into a spreadsheet.

Measures

Asthma Control Questionnaire

A 7 item self-reporting questionnaire covering symptoms and rescue inhaler use in the preceding week with one item requiring post-bronchodilator Forced

Expiratory Volume in 1 s as a percentage of predicted (FEV₁%) (completed by clinic staff). A 7-point scale (0 = no impairment, 6 = maximum impairment for symptoms and rescue use) is used. This questionnaire is validated and has test-retest reproducibility with a high intraclass correlation coefficient (0.90). A score of less than one indicates adequately controlled asthma. A change in score of 0.5 is considered the minimally important difference. A higher overall score is indicative of poorer asthma control (30).

Mini-asthma quality of life questionnaire

A 15 item self-reporting quality of life questionnaire that covers both the physical and emotional impact of asthma. It includes symptoms, activities, emotions and environment factors using a 7-point Likert scale. This questionnaire is validated and has test-retest reproducibility. The overall score is the mean across all items. A lower score indicates greater impairment and a change in score of 0.5 is considered clinically important (31).

Generalized Anxiety Disorder -7 questionnaire

A 7 item self-reporting screening tool assessing the frequency of symptoms for generalized anxiety disorder (GAD) in the preceding 2 weeks, measured using a 4-point scale (ranging from 0 = not at all to 3 = nearly every day). A score of 5 is considered mild, 10 is moderate and 15 is severe. Further evaluation is recommended for scores of 10 or higher when used as a screening tool. It has been shown to have good reliability and validity (23).

Patient Health Questionnaire-9

A 9 item self-reporting multipurpose screening tool assessing the frequency of depressive symptoms in the preceding 2 weeks, measured using a 4-point scale (ranging from 0 = not at all to 3 = nearly every day). The overall score is the total for each item. A score of 5 represents “mild” depression, 10 is “moderate,” 15 “moderately severe” and 20 suggests severe depression. A score of 10 has been shown to have a sensitivity and specificity of 88% for major depression (24).

Spirometry

All patients attending the specialist asthma clinic are routinely asked to undertake spirometry. This took place in the hospital Cardiorespiratory department and is performed in line with the Association of Respiratory Technology and Physiology (ARTP) guidance (32), including the requirement to meet repeatability criteria. Patient height and weight were

recorded by spirometry technicians and body mass index (BMI) was calculated.

Procedures

All questionnaires were handed out by clinic staff as patients attended for asthma clinic appointments at the outpatient department (OPD). Both sets of questionnaires are considered part of routine care for those attending a severe asthma service. All four questionnaires were given out together in a bundle. The order of completion by patients was not pre-defined. There was time set aside to complete the questionnaires while awaiting their OPD appointment. Completed forms were collected at the OPD appointment by clinic staff. Patients were not specifically reminded to finish incomplete questionnaires.

Statistical analysis

Analyses were undertaken in SPSS. Descriptive statistics were used to describe the sample population. Two tailed Pearson correlation coefficients were used to assess the level of correlation between questionnaire results in view of the linear relationship between the variables. A correlation matrix was calculated. We also generated receiver operating characteristic (ROC) curves to analyze the sensitivity and specificity of ACQ and mini-AQLQ to predict individuals with PHQ-9 and GAD-7 scores higher than the threshold usually taken to suggest significant psychological dysfunction. The significance test for the area under the ROC curve relates to the null hypothesis that the area = 0.5.

Results

Of the 300 individuals asked to complete the questionnaires, 184 were female (62%) and the mean age was 45.3 years (standard deviation 17.4). Table 1 summarizes the population characteristics. The mean post-bronchodilator FEV₁ as a percentage of predicted was 78.1% (standard deviation 22.1) indicating poorly controlled asthma. The population had a mean BMI in the obese range at 30.1 (standard deviation 7.57). Complete questionnaire results for mini-AQLQ and ACQ were available for 287 and 290 people, respectively. The GAD-7 and PHQ-9 questionnaires were missing or incomplete for 150 and 140 individuals, respectively. The completion rates for the four questionnaires are shown in Table 2. 134 individuals

(45%) completed all questionnaires. The population characteristics for this group are shown in Table 1.

The mean ACQ and mini-AQLQ scores were 2.9 (SD = 1.5) and 3.5 (SD = 1.6), respectively, both in keeping with individuals attending for difficult to treat asthma. The mean GAD-7 score for all respondents was 9.3 (SD = 7.2). 71 individuals (47% of respondents) had a score at or above the threshold of 10 which is usually taken to be consistent with moderate anxiety and indicates that further evaluation is required (33). The mean PHQ-9 score for all respondents was 10.8 (SD = 7.2). Again, a score of 10 indicates that further assessment is recommended (34). Seventy-eight individuals (49% of completed questionnaires) had a score of 10 or more. Table 3 summarizes the results of the questionnaires. Results of the Pearson correlations indicated that there was a significant positive association between ACQ and both PHQ-9 score ($p = <0.0001$, Pearson $r=0.64$) and GAD-7 score ($p = <0.0001$, $r=0.53$). Similarly, results of the Pearson correlation indicated that there

was a significant negative association between mini-AQLQ score and both PHQ-9 ($p = <0.001$, $r = -0.65$) and GAD-7 ($p = <0.001$, $r = -0.59$) scores. A summary correlation matrix is shown in Figure 1. Figure 2 demonstrates the Pearson's correlation matrix in those who completed all four questionnaires.

Figure 3 shows the respective ROC curves for ACQ and inverted mini-AQLQ when compared with a PHQ-9 threshold of 10. The area under the ROC curve for ACQ score against the binary outcome of PHQ-9 being greater or equal to 10 was 0.836 (95% confidence interval (CI) 0.771–0.901, $p = <0.0001$). The area under the ROC curve for ACQ score against the binary outcome of GAD-7 being greater or equal to 10 was 0.783 (95% CI 0.704–0.859, $p = <0.0001$). Similarly, when only those who completed all four questionnaires are analyzed, the area under the ROC curve was 0.785 for ACQ (95% CI 0.768–0.908, $p = <0.0001$) and 0.807 (95% CI 0.745 to 0.889, $p = <0.0001$) for mini-AQLQ. These are shown in Figure 4.

Figure 5 shows the ROC curves for ACQ and inverted mini-AQLQ for a GAD-7 score of 10 or more. The area under the ROC curve for inverted mini-AQLQ score against the binary outcome of PHQ-9 being greater or equal to 10 was 0.813 (95% CI 0.746–0.881, $p = <0.0001$, see Figure 3). The area under the ROC curve for inverted mini-AQLQ score against the binary outcome of GAD-7 being greater or equal to 10 was 0.803 (95% CI 0.730–0.876, $p = <0.0001$, Figure 5). When only those who completed all four questionnaires are selected, the area under the ROC curve was 0.838 for ACQ (95% CI 0.704–0.865, $p = <0.0001$) and 0.817 for Mini-AQLQ (95% CI

Table 1. Study population characteristics.

Study participants	
Total	300
Female	184 (61.3%)
Mean Age (years)	45.3 (SD 22.1)
Mean BMI (kg/m ²)	30.1 (SD 7.57)
Mean post-bronchodilator FEV1 (% predicted)	78.1 (SD 22.1)
Participants who completed all 4 questionnaires	
Total	134
Female	77 (57.5%)
Mean Age (years)	45 (SD 16.9)
Mean BMI (kg/m ²)	31 (SD 6.62)
Mean post-bronchodilator FEV1 (% predicted)	78.4 (SD 21.5)
BMI—Body mass index.	
FEV1—Forced Expiratory Volume in 1 s.	

Table 2. Completion rates for all questionnaires.

	ACQ (% of total sample)	mAQLQ (% of total sample)	PHQ-9 (% of total sample)	GAD-7 (% of total sample)
ACQ (% of total sample)	290(96.6%)	280 (93.3%)	155 (51.7%)	145 (48.3%)
mAQLQ (% of total sample)	280(93.3%)	287 (95.7%)	154 (51.3%)	143 (47.7%)
PHQ-9 (% of total sample)	155(51.7%)	154 (51.3%)	160 (53.3%)	143 (47.7%)
GAD-7 (% of total sample)	145(48.3%)	143 (47.7%)	143 (47.7%)	150 (50%)

PHQ-9—Patient Health Questionnaire-9.

GAD-7—Generalized Anxiety Disorder-7 Questionnaire.

mAQLQ—Mini-Asthma Quality of Life Questionnaire.

ACQ—Asthma Control Questionnaire.

Table 3. Summary of questionnaire results.

Questionnaire	N (%) completed	Mean score	Std. Deviation	N (%) with score of 10 or more
ACQ	290 (97%)	2.89	1.572	NA
m-AQLQ	287 (96%)	3.52	1.630	NA
PHQ-9	160 (53%)	10.79	7.158	78 (49%)
GAD-7	150 (50%)	9.33	7.219	71 (47%)

PHQ-9—Patient Health Questionnaire-9.

GAD-7—Generalized Anxiety Disorder-7 Questionnaire.

mAQLQ—Mini-Asthma Quality of Life Questionnaire.

ACQ—Asthma Control Questionnaire.

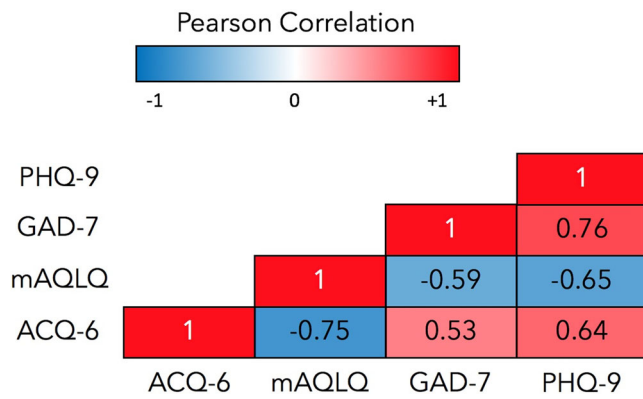


Figure 1. A correlation matrix for PHQ-9, GAD-7, mini-AQLQ, and ACQ-6.

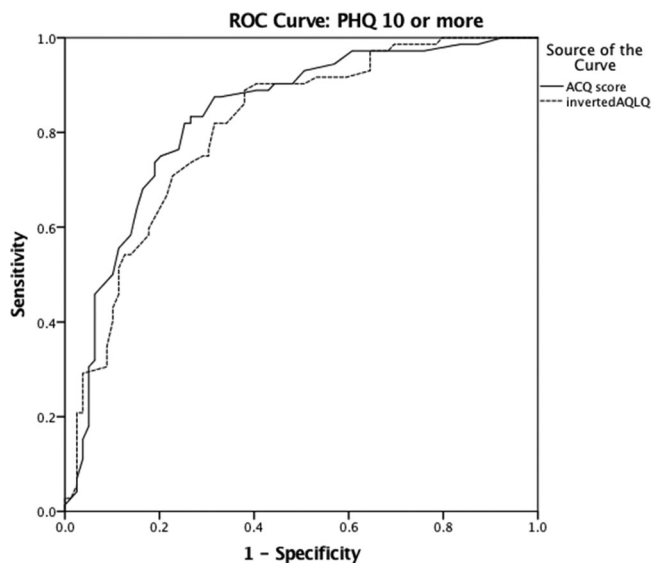


Figure 2. A correlation matrix for patients with all four questionnaires completed (PHQ-9, GAD-7, mini-AQLQ, and ACQ-6).

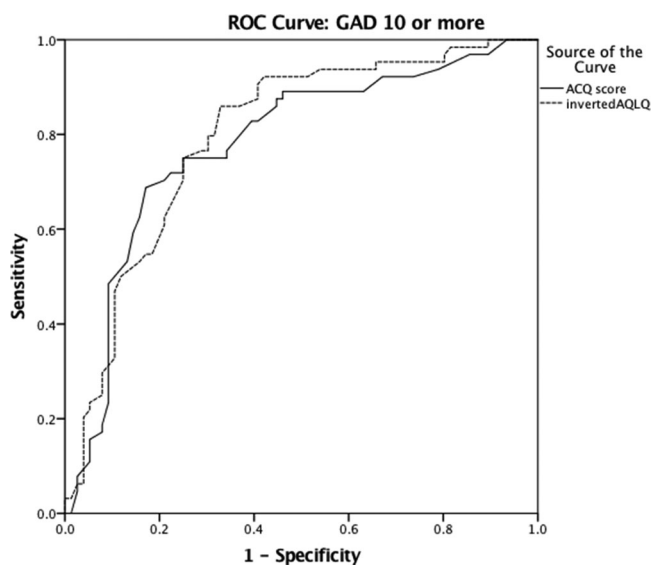


Figure 3: Receiver Operator Curve for ACQ and Mini-AQLQ score for a PHQ-9 threshold of 10.

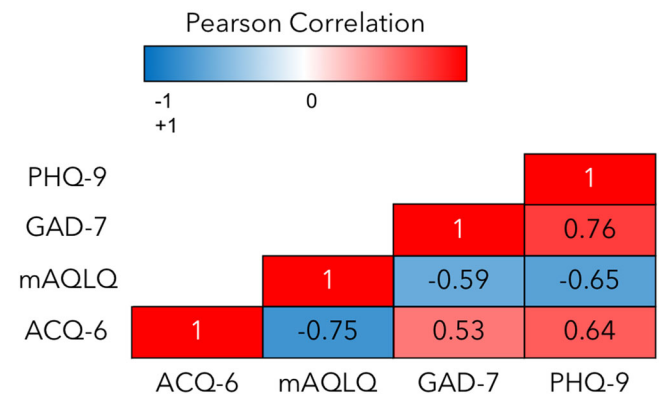


Figure 4. Receiver Operator Curve for ACQ and inverted Mini-AQLQ score for a GAD-7 threshold of 10 respondents who completed all questionnaires.

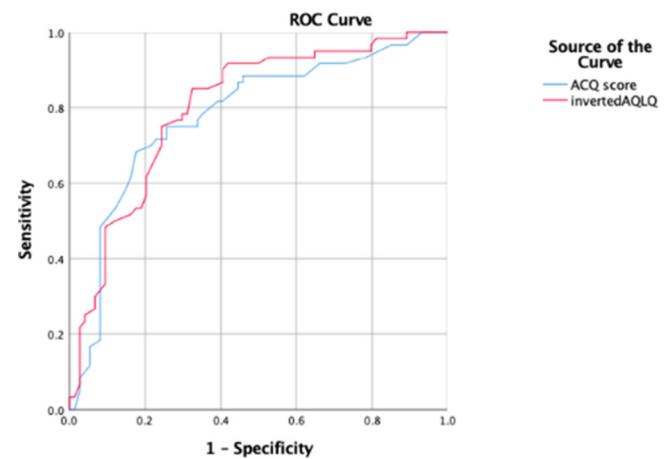


Figure 5. Receiver Operator Curve for ACQ and inverted Mini-AQLQ score for a GAD-7 threshold of 10.

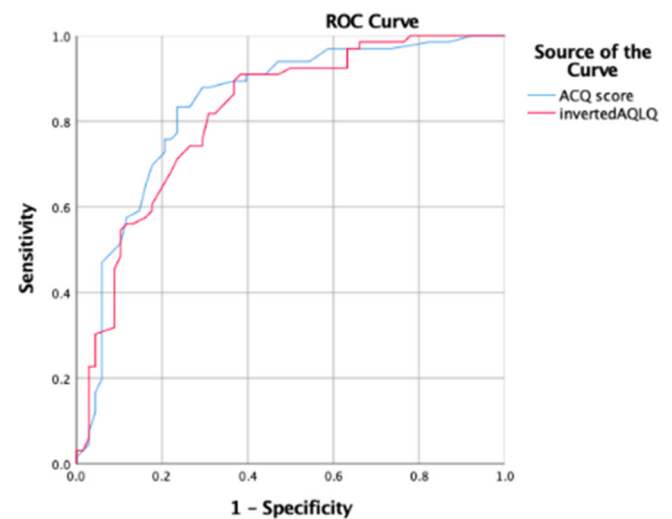


Figure 6. Receiver Operator Curve for ACQ and Mini-AQLQ score for a PHQ-9 threshold of 10 in respondents who completed all questionnaires.

Table 4. Confusion matrix of “gold standard” PHQ-9 score (>10) vs Mini-AQLQ score of < 3.

		“Gold standard” (PHQ-9) of >10		
		Positive	Negative	Total
Mini- AQLQ <3	Positive	52	18	70
	Negative	21	63	84
	Total	73	81	154

Positive Predictive Value = 0.74, Negative Predictive Value = 0.75.

Sensitivity = 0.71, Specificity = 0.78.

Mini-AQLQ—Mini-Asthma Quality of Life Questionnaire.

PHQ-9—Patient Health Questionnaire-9.

Table 5. Confusion matrix of “gold standard” GAD-7 score (>10) vs Mini-AQLQ score of < 3.

		“Gold standard” (GAD-7) of >10		
		Positive	Negative	Total
Mini- AQLQ <3	Positive	49	19	68
	Negative	16	59	75
	Total	65	78	143

Positive Predictive Value = 0.72, Negative Predictive Value = 0.79.

Sensitivity = 0.75, Specificity = 0.76.

GAD-7—Generalized Anxiety Disorder-7 Questionnaire.

mAQLQ—Mini-Asthma Quality of Life Questionnaire.

Table 6. Confusion matrix of “gold standard” PHQ-9 score (>10) vs ACQ score of >5.

		“Gold standard” (PHQ-9) of >10		
		Positive	Negative	Total
ACQ > 5	Positive	21	4	25
	Negative	55	75	130
	Total	76	79	155

Positive Predictive Value = 0.84, Negative Predictive Value = 0.58.

Sensitivity = 0.28, Specificity = 0.95.

PHQ-9—Patient Health Questionnaire-9.

ACQ is—Asthma Control Questionnaire.

0.732 to 0.882, $p = <0.0001$). The curves are shown in Figure 6.

The threshold of a mini-AQLQ of < 3 had both a sensitivity and specificity of greater than 70% for both GAD-7 and PHQ-9 questionnaire results (confusion matrices are shown in Tables 4 and 5). A mini-AQLQ score of <3 would have correctly classified 108 of 143 individuals (75.5%) with a GAD-7 score of > 10 and 115 of 154 individuals (74.6%) with a PHQ-9 score >10. An ACQ score of >5 is strongly predictive of a high PHQ-9 score (positive predictive value = 0.84). A confusion matrix is shown in Table 6. A “positive likelihood ratio” using ACQ for that of a high PHQ-9 score (>10) is 5, a ratio that is similar to other screening tests (35).

Discussion

In a real-world evaluation of individuals attending a specialist asthma clinic, we found that asthma-specific

questionnaires correlate well with the results of additional established anxiety and depression questionnaires. In particular, a mini-AQLQ score of < 3 identifies the majority of individuals with GAD-7 or PHQ-9 scores above the usual threshold of 10 and may represent a useful trigger for more detailed psychological assessment. An ACQ score of >5, indicating poor asthma control, was predictive of co-morbid depression with a similar efficacy to other screening tests in clinical practice. We also found the administration of multiple questionnaires resulted in a substantial proportion being incomplete. The level of asthma control and the asthma quality of life questionnaire scores in this population were similar to those noted in previous studies (36,37). The prevalence of psychological burden in our population, as defined by GAD-7 and PHQ-9 scores above widely used thresholds for anxiety and depression, is high. These findings are consistent with those of previous studies (38–39), and emphasizes the ongoing large unmet need in this population.

The estimated prevalence of difficult-to-treat asthma, as previously noted, is approximately 17% of the asthma population (3). In England, given the prevalence of psychological issues highlighted in this service evaluation and other studies, there are likely to be many thousands of individuals that would benefit from further detailed assessment by a specialist team. Due to the potential volume of patients, some form of further psychological screening tools and triage are required to identify those at greatest need of support to avoid overwhelming the available services.

From a pragmatic perspective, there is a risk of overwhelming patients attending specialist asthma clinics with multiple questionnaires. In our evaluation, 290/600 GAD-7 or PHQ-9 were incomplete suggesting that it is impractical for all patients to complete every questionnaire. The cause of this large deficit is not clear from this service evaluation but may be due to the requirement to complete multiple questionnaires. The ACQ and mini-AQLQ have been validated to provide reliable, objective data on monitoring asthma. Similarly, the GAD-7 and PHQ-9 are also well established and validated questionnaires (23,24) that have been used across a range of diseases. Our results suggest good potential agreement between asthma control and asthma-specific quality of life questionnaires and anxiety and depression questionnaires in a specialist asthma clinic. A targeted strategy, only using questionnaires assessing psychological co-morbidities in those with a mini-AQLQ of <3 could lead to a reduction in the burden of questionnaire administration for

both patients and healthcare professionals in the setting of a specialist asthma clinic.

The nature of the link between asthma and depression/anxiety is not clear. There is evidence that worse asthma control is a risk factor for depression and decreased quality of life (22). There is also speculation that the pro-inflammatory state noted in certain asthma phenotypes is similar to that induced by pro-inflammatory cytokine treatments in humans, long known to be associated with depressive symptoms (40). Hypothalamic-pituitary-adrenal axis dysregulation, noted in major depression (41), may also be present in asthma as a result of the inhaled corticosteroids necessary to treat the condition (42). Irrespective of the underlying etiology, depression and anxiety, as our data suggests, are a significant burden to this patient group.

The main strength of this evaluation is that it investigates practical approaches to guideline-based care delivery for a significant and common clinical condition. In addition, it is novel and provides real world information. The data, although limited by a low GAD-7 and PHQ-9 questionnaire completion rate, are large enough to generate ROC curves with statistical significance.

The key limitation of this service evaluation is the low additional questionnaire return rate. There are a number of possible explanations for this. The order of questionnaire completion was not defined beforehand and therefore patients may have been dissuaded from completing all questionnaires after initially encountering questions of a sensitive nature. Since psychological issues are poorly addressed in asthma services (20) patients may not have viewed this as the role of this service and not completed questionnaires as a result. As the completion time was not defined beforehand, the appointment may have started before they were able to fill all of the questionnaires. The reasons for the low return rate require more detailed qualitative research to be fully established. We acknowledge the limitations of data obtained from a single center, and that these data were not generated through the tight processes of a research study. There is a signal from our data that a mini-AQLQ score of <3 could be a sufficient measure to identify those requiring further investigation for significant psychological co-morbidity. A larger multi-center study is required to further investigate this relationship.

Conclusion

This evaluation represents a real-world sample of individuals attending a specialist asthma clinic. Our

results, in keeping with those of other studies, suggest a high burden of psychological co-morbidity in the specialist asthma service. For the first time our findings indicate that asthma specific questionnaires could potentially be used as a screening tool for significant anxiety and depression when appropriate thresholds are met. In particular, it appears a mini-AQLQ score of <3 could be used to target these questionnaires more effectively. This possibly has the potential to reduce the “questionnaire burden” on patients attending the asthma clinic. However, the generalisability of these findings is unclear given the single-center nature of the analysis. Psychological issues are very common in asthma and have a significant impact on quality of life. We encourage all health care professionals treating patients with a high ACQ or low mini-AQLQ score to consider further screening for comorbid anxiety and depression.

Declaration of interest

The authors report no conflict of interest.

Author contributions

RR, KB, GJ, JB, HB - study co-ordination; RR, KB, JB - data collection and management; RR, KB, GJ, JB, HB - statistical planning and analysis; RR, KB, GJ, JB, HB - manuscript preparation

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