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ORIGINAL ARTICLE

An Observational Investigation of Dysfunctional Breathing and Breathing Control Therapy in a Problem Asthma Clinic

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Objectives. Dysfunctional breathing (DB) is recognized as an associated problem in patients with asthma and may be identified by the Nijmegen questionnaire. We conducted an observational study to determine if breathing control therapy (BCT) improved Nijmegen scores or asthma-related quality of life in patients attending a problem asthma clinic. **Methods.** Nijmegen and Mini Asthma Quality of Life (Mini-AQLQ) questionnaires were completed. Patients with a positive Nijmegen (≥ 23 , DB) were referred for BCT and progressive exercise testing (PET) to seek confirmation of dysfunctional breathing. Follow-up questionnaire data were collected at 6 months. **Results.** A total of 102 patients were studied. The total mean Nijmegen score was 26.4 (range 1–61). Those with a score ≥ 23 (DB group, $n = 65$, 64%) had significantly lower Mini-AQLQ (mean 2.83) than the non-DB group ($n = 37$, mean 4.12, 95% CI for difference 0.87, 1.87, $p < 0.0001$). There was a strong relationship between Nijmegen score and Mini-AQLQ ($r = -0.63$, $p < 0.001$) at baseline; 10 of 17 DB patients who completed PET showed inappropriate hyperventilation. Follow-up data, available for Nijmegen and Mini-AQLQ in 44 and 46 patients respectively, showed no significant change in either of these parameters. **Conclusions.** The strong relationship between Mini-AQLQ and Nijmegen scores and poor relationship between Nijmegen scores and PET-identified inappropriate hyperventilation suggest that a positive Nijmegen score overestimates the presence of dysfunctional breathing in patients with moderate to severe asthma. We found no evidence that a moderate intensity breathing control intervention had any impact on Nijmegen scores or asthma-related quality of life in this patient group.

Keywords asthma, dysfunctional breathing, quality of life, breathing control therapy

INTRODUCTION

It is increasingly recognized that dysfunctional breathing (or hyperventilation syndrome) can be an important co-existing factor in patients with asthma (1, 2). Potential diagnostic tests such as the hyperventilation provocation test (3, 4) and Nijmegen questionnaire (5) have not been extensively validated in patients with asthma. After identification of dysfunctional breathing, patients are usually managed with relaxation techniques or breathing control therapy. Thomas (6) found breathing retraining reduced Nijmegen scores and produced a non-sustained improvement in asthma-related quality of life among patients with mild to moderate asthma in primary care, but whether this can be extrapolated to cohorts in secondary care with more severe disease has not been investigated. A further more recent study, again based in primary care, found improvements in respiratory symptoms (measured by St George's Respiratory Symptoms Questionnaire) with the Papworth method of breathing and relaxation technique compared with no additional treatment, although this was not targeted at patients felt to have dysfunctional breathing (7). We have investigated the relationships between asthma quality of life and Nijmegen scores, while monitoring the effect of breathing retraining, undertaken as part of our protocolized assessment and management of patients attending a problem asthma clinic.

Hyperventilation is defined as breathing in excess of the body's metabolic requirements and results in a reduction

in arterial $p\text{CO}_2$, respiratory alkalosis, and wide ranging symptoms (8). The term "hyperventilation syndrome (HVS)," coined over 60 years ago, described patients with hypocapnic symptoms and those of anxiety (9). Despite this, however, there remains no clear consensus on the gold standard for diagnosis of HVS. Demonstration of a respiratory alkalosis by measurement of arterial blood gases will be of value during the attack but will not always be helpful when assessing a patient in between episodes. The fact that a degree of hyperventilation may be or is commonly seen with symptomatic asthma further complicates the issue. It is also clear that some patients who may not necessarily be hyperventilating may have other breathing pattern abnormalities such as frequent sighing or irregularity of breathing (10) that may manifest themselves as intermittent breathlessness or sensation of over-breathing, which is perhaps best brought under the term "dysfunctional breathing" (11).

We sought to identify dysfunctional breathing in a cohort of patients with moderate to severe asthma, measuring Nijmegen and mini AQLQ scores, undertaking progressive exercise tests, where possible to confirm inappropriate hyperventilation and monitoring the effect of breathing control therapy on these scores.

METHODS

All patients attending the Problem Asthma Clinic at Glasgow Royal Infirmary over a 5.5-month period were assessed using a standard protocol, which is based on previous experience and the reported literature (12, 13). Baseline data on current treatment and current symptoms of asthma morbidity were recorded using the Royal College of Physicians

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(RCP) 3-symptom score (days and nights affected by asthma symptoms, and days of limited activity due to asthma over the previous 7 days) (14). Case notes were reviewed to determine the basis for patients' diagnosis of asthma. Patients completed the Nijmegen Questionnaire and the Mini Asthma Quality of Life Questionnaire (Mini-AQLQ) (15). Maximum Nijmegen score is 64, with a score ≥ 23 defining hyperventilation in non-asthma patients. The minimal clinically important change for Mini-AQLQ is ± 0.5 (16) but such information is not known for the Nijmegen questionnaire. The study group was separated into two groups, on the basis of a Nijmegen score less than 23 (described as having no evidence of dysfunctional breathing syndrome [No DB]) or ≥ 23 (those with evidence of dysfunctional breathing [DB]). Patients in the DB group were reviewed by a Respiratory Physiotherapy Specialist (PV) with experience in breathing control and assessed for their individual requirement for breathing control therapy (BCT). This group of patients were referred for progressive exercise testing (PET) to confirm the presence of inappropriate hyperventilation. This was defined by a decrease of transcutaneous pCO_2 to less than 35 mm Hg or by more than 10% from baseline. It was felt to be out of the scope of our standard clinic protocol to perform PET in the non-DB group. There were some occasions where the physiotherapy specialist was not present at the outpatient clinic, and in these circumstances, a separate out-patient review was arranged.

Assessment of Breathing Pattern and Breathing Control Therapy (BCT) – DB Group

Breathing pattern, including rate, depth and location, and end inspiratory and expiratory breath holding times were assessed. Data on inspiratory breath hold time (in seconds) at end of inspiration at initial visit and subsequent follow-up visits were collected.

The possible relationship between asthma and over-breathing was discussed with the patient, followed by re-education of any specific components of the patient's breathing pattern, which were identified as being dysfunctional (tidal volume, flow rate, or respiratory rate). The breathing cycle was broken into three phases: relaxed tidal inspiration, passive expiration to tidal volume, and active effort to reach expiratory reserve with encouragement for a natural pause of a few seconds before the next inspiratory phase. Forced inspiratory or expiratory movements were discouraged as these were thought likely to reinforce or precipitate dysfunctional breathing pattern and therefore symptoms. Nasal breathing, to maximize conditioning of air reaching the lungs, was encouraged. Patients were encouraged to practice the new breathing pattern 6 to 8 times per day for 10 minutes at a time initially. Once learned, the new breathing pattern was advised during sitting, standing, walking, and activities that would provoke breathlessness. This approach represents standard physiotherapy practice.

After the initial assessment, patients who required further intensive input were identified. These patients tended to be those who were unable to establish good abdominal breathing patterns or were unable to sustain an expiratory pause for more than three consecutive breaths. They were offered weekly outpatient review for 4 weeks followed by physiotherapy review coinciding with subsequent asthma clinic appoint-

ments. All patients were therefore followed-up at subsequent clinic appointments.

Progressive Exercise Testing

Symptom-limited exercise tests were performed using an electrically braked bicycle ergometer (SECA Cardiotest 100; Salford, England). The patients were initially monitored for 2 minutes while seated at rest, to obtain baseline values, then asked to exercise for as long as possible until symptomatic limitation. During the first 2 minutes of exercise, no additional load was applied. Thereafter, the work load was increased by 10 to 25 watts, depending on the individual patient, every minute until symptomatic limitation. Throughout each test, minute ventilation ($V'E$), oxygen consumption ($V'O_2$), and carbon dioxide ($V'CO_2$) were measured breath by breath by on-line ventilation and expired gas analysis (MedGraphics CPX-D). An ECG recording was made throughout the test. The ventilatory anaerobic threshold on exertion was calculated by the curve fitting method using a plot of $V'O_2$ against $V'CO_2$. (17) The dead space to tidal volume ratio (V_D/V_T) and alveolar-arterial oxygen gradient ($A-aO_2$) was computed from mixed expired gas concentrations and blood gas analysis (Chiron Diagnostics Rapid Lab 855) using an arterialized ear lobe capillary sample. The blood samples were obtained at rest and at peak exercise with the gas exchange values calculated using standard equations. (18) Transcutaneous pCO_2 was also measured throughout the procedure.

Follow-Up

Nijmegen and Mini-AQLQ responses, in addition to breathing pattern parameters, were collected on review of all patients attending the clinic at approximately 6 months follow-up in the clinic where available. Some patients had been discharged by this time point, and others defaulted. We were looking for a long-term effect from this intervention and judged this to be an appropriate time to collect outcome data.

Statistical Analysis

Spearman's rank correlations were used to examine relationships between parameters when one or both were non-normally distributed. Pearson's correlations were used to examine relationship between normally distributed parameters. Baseline questionnaire data in groups divided according to Nijmegen scores were compared using Mann-Whitney U tests. Follow-up questionnaire data were compared to baseline with Mann-Whitney U tests. All data was analyzed using Minitab (version 14) statistical software.

RESULTS

Baseline Data

A total of 111 patients were assessed over a 5.5-month period; 9 had previously been examined by the Physiotherapy Specialist for BCT and so were excluded from analysis. There were 72 women (71%) and 30 men. The average age (range) was 48 (13.5–83) years. Case notes were reviewed to determine best objective evidence of asthma available for each patient (Table 1).

The range of asthma treatment of the study group at baseline is shown in Figure 1.

TABLE 1.—Basis of asthma diagnosis in study population ($n = 102$).

Best objective evidence available	Number of patients
Bronchodilator reversibility $> 12\%$	52
Bronchial Hyper-reactivity (BHR)	8
PEFR variability	19
Steroid trial	1
Good clinical history only	11
No objective evidence	11

A total of 28 patients were taking long-term oral corticosteroids (range 5 mg – 30 mg per day, median 10 mg).

Patients reported the full range of RCP asthma morbidity scores (0 – 21, with a higher score indicating more severe symptoms) with a median score of 14 (IQR 3.8 – 21). There were eight patients who did not have complete RCP symptom score data at baseline.

Baseline Nijmegen and mini-AQLQ scores for the whole study population are shown in Table 2. The mean (range) overall Mini-AQLQ score for the cohort was 3.30 (1.07 – 6.93) and mean (range) Nijmegen score for the cohort was 26.4 (1 – 61). All parameters were normally distributed. The overall Mini-AQLQ score and each domain (symptoms, environment, emotional, and activities data not shown) correlated well with the Nijmegen scores, as shown in Figure 2.

Nijmegen scores varied widely across the range of RCP symptom scores (Figure 3), although a statistically significant correlation was observed (Spearman's Rank $r = 0.43$, $p < 0.001$). There was a better relationship between RCP symptom score and Mini-AQLQ (Spearman's Rank $r = -0.69$, $p < 0.001$, Figure 4).

There were significant differences between groups for total Mini-AQLQ scores (Table 2) and all Mini-AQLQ domains (Appendix 1)

Progressive exercise testing (PET). Of the 65 patients with positive Nijmegen scores, 21 (33%) had a co-morbidity that made progressive exercise testing impossible. Of those able to undertake PET (42), 24 (57%) attended for this investigation; 7 patients were unable to complete this investigation because of wheeze (4) or locomotor problems (3); 17 PETs were therefore undertaken.

Mean (SD) VO_2 max attained was 11.5 (4.6) mL/kg/min, representing mean (SD) 44.4 (14.9) % predicted values. All

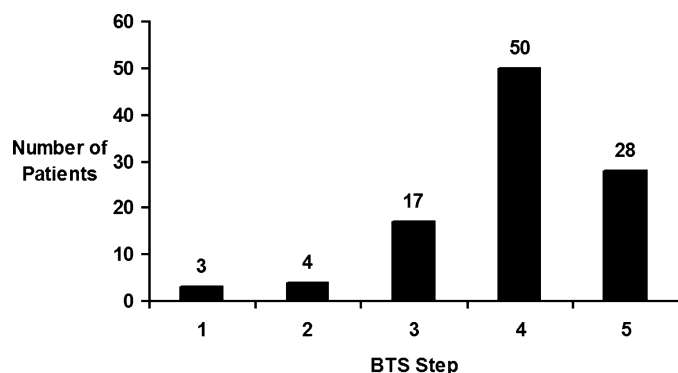


FIGURE 1.—Level of asthma treatment of study group.

TABLE 2.—Baseline Questionnaire Data: Nijmegen and Mini-AQLQ scores (DB = dysfunctional breathing).

Variable	Range	Mean (SD)	95% CI for difference between No-DB and DB, p value
Mini-AQLQ (total)			
All patients ($n = 102$)	1.07–6.93	3.30 (1.36)	0.87, 1.87, $p < 0.0001$
No DB ($n = 37$)	1.27–6.93	4.12 (1.43)	
DB ($n = 65$)	1.07–5.47	2.83 (1.07)	
Nijmegen			
All patients ($n = 102$)	1–61	26.4 (11.5)	*****
No DB ($n = 37$)	1–22	14.5 (5.4)	*****
DB ($n = 65$)	23–61	33.2 (7.9)	*****

patients had a VE/VCO_2 more than 30 (range 34–73), mean (SD) 47.6 (9.1) indicating an elevated ventilatory response. This was deemed inappropriate and indicative of hyperventilation/DB (decrease of transcutaneous pCO_2 to < 35 mmHg or by $> 10\%$ from baseline) in 10 of 17 patients (59%).

There was no difference in Nijmegen scores of those patients with and without evidence of inappropriate dysfunctional breathing on PET. This data are shown with the scatter of Nijmegen scores in Figure 5.

Physiotherapy assessment and attendance for Breathing Control Therapy (BCT) – DB Group. A total of 9 of 65 patients did not attend BCT at any given time with the remaining 56 patients being reviewed on a median (range) of 3 (1–15) occasions; 8 patients were seen once only.

Follow-Up Data

Follow-up questionnaire data were available for mini-AQLQ in 46 patients (17 No DB, 29 DB) and Nijmegen scores in 44 (15 No DB, 29 DB), at an average (SD) of 186 (23) days; 1 patient with a positive baseline Nijmegen score completed follow-up questionnaires but had not attended BCT and therefore was excluded from analysis. The most frequent reasons for missing data were prior discharge from the clinic or failure to attend around the desired follow-up of 6 months after baseline data collection.

The results are grouped according to the baseline Nijmegen score (Table 3), with only those having baseline and follow-up scores included. 95% confidence intervals were calculated

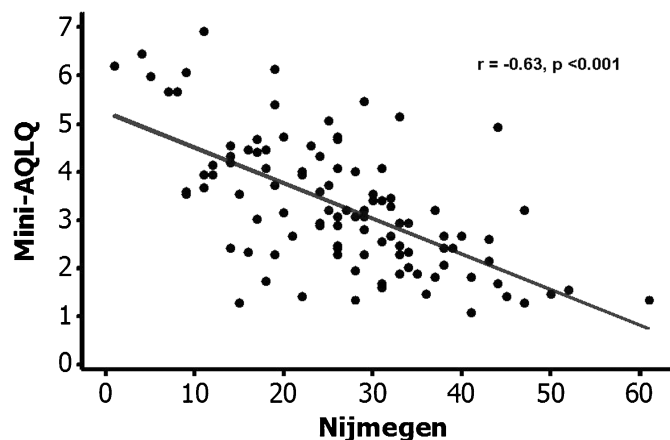


FIGURE 2.—Relationship between Nijmegen and Mini-AQLQ (total score).

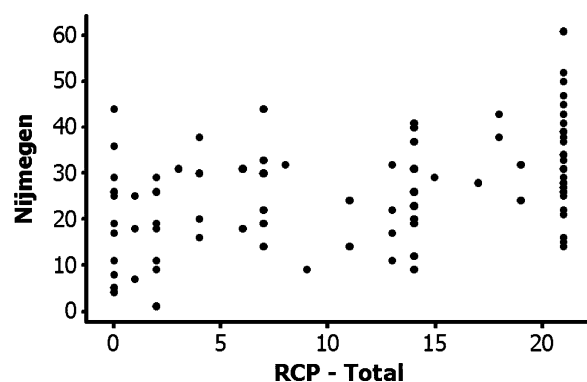


FIGURE 3.—Relationship between level of asthma symptoms and Nijmegen score.

(Mann-Whitney U tests) for the difference between baseline and follow-up scores (also shown in Table 3) and demonstrate no significant difference in either overall Mini-AQLQ (or any separate domain, data not shown) or Nijmegen scores in either No DB or DB groups.

Although there were no significant differences between baseline and follow-up Nijmegen scores in either group, there were 8 of 29, 28% of patients in the DB group whose Nijmegen scores fell into the normal range following BCT. There was no significant difference in level of asthma symptoms following BCT compared with baseline in this subgroup of patients (RCP score, 95% CI for difference $-9, 12$ (Mann-Whitney U-test).

There were 9 of 29 (31%) of the patients who received BCT and completed follow-up data who had a clinically significant improvements in Mini-AQLQ and this was observed in 6 of 17 (35%) of those without evidence of DB.

In the 17 patients who completed PET, follow-up Nijmegen and Mini-AQLQ were available in 5 of the 10 patients shown to have inappropriate hyperventilation on PET and 3 of the 7 not shown to have inappropriate hyperventilation. At follow-up there was no difference seen in either parameter (Appendix 2).

Global physiotherapy assessment of efficacy of BCT. Inspiratory breath hold times (BHT) were improved in all patients after BCT from median (IQR) of 10 (7–15) seconds

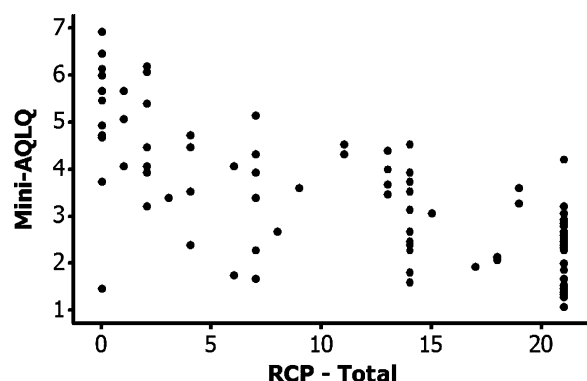


FIGURE 4.—Relationship between level of asthma symptoms and Mini-AQLQ.

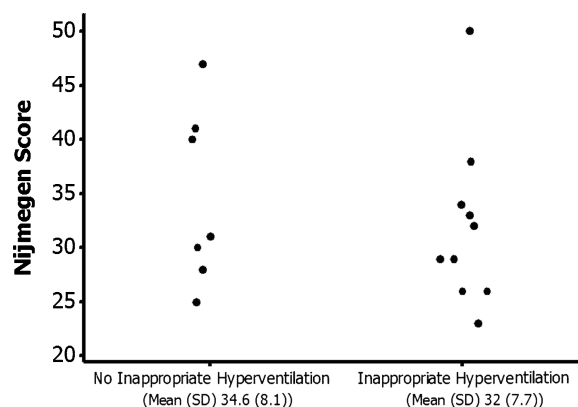


FIGURE 5.—Nijmegen scores for patients completing PET ($n = 17$), subdivided by the finding of no inappropriate hyperventilation ($n = 7$) and inappropriate hyperventilation ($n = 10$).

at baseline to 20 (15–22) seconds at follow-up (95% CI $-10, -5$, $p < 0.001$ by the Mann-Whitney U-test, Figure 6, $n = 55$). BHT did not correlate with Nijmegen ($r = -0.24$, $p = 0.071$) but did show a statistically significant correlation with Mini-AQLQ ($r = 0.38$, $p = 0.005$, Figure 7).

After BCT, global assessment of compliance and benefit was made by PV. This was done with the knowledge of all objective measurements, including breath hold times and Nijmegen scores beforehand and afterwards. Seven of 29 patients who attended and had follow-up data were felt to have complied well and benefited from BCT. These patients had a mean (SD) decrease in Nijmegen score of 5.1 (7.5).

There were 8 patients whose Nijmegen score decreased to less than 23. Only 3 were included in the subgroup identified above as having complied well and benefited from BCT. Median BHT improved from 15 to 21 seconds in this subgroup (95% CI for difference $-13.01, 0.0$, $p = 0.049$). All but 1 also had an improvement in Mini-AQLQ (range $-0.27, 2.93$, mean [SD] $0.96 [0.99]$), and 5 had more than 0.5 improvement in total Mini-AQLQ score with improvements in all four AQLQ domains and no significant difference in level of asthma symptoms (median RCP score of 8 at baseline and follow-up).

DISCUSSION

In collating and analysing these data from as complete as possible a cohort of patients attending a problem asthma clinic, we have described the range of symptoms, quality of life, and Nijmegen scores in a group, most of whom (78%)

TABLE 3.—Follow-up Mini-AQLQ and Nijmegen scores (DB = dysfunctional breathing).

Variable	Range	Mean (SD)	95% CI for Difference FROM Baseline
Nijmegen			
DB ($n = 29$)	14–49	29.7 (9.3)	$-1, 9$
No DB ($n = 15$)	6–32	18.5 (7.3)	$-9, 2$
Mini-AQLQ (Overall)			
DB ($n = 29$)	1.20–5.33	3.04 (1.07)	$-0.87, 0.33$
No DB ($n = 17$)	1.27–6.27	4.22 (1.47)	$-1.33, 1.00$

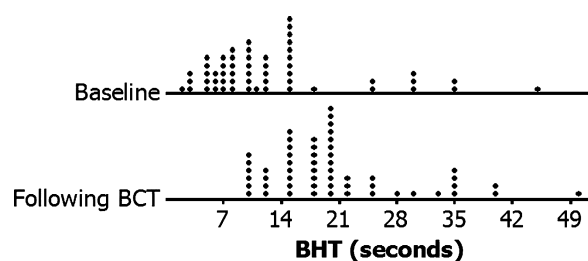


FIGURE 6.—Inspiratory Breath Hold Time (BHT) at baseline and follow up.

have objective evidence of asthma and most (76%) were on BTS step 4 or 5 asthma therapy. This analysis shows the impact on quality of life and the distribution of Nijmegen scores, which in a normal population would suggest dysfunctional breathing. Analysis of the inter-relationships between symptoms and quality-of-life measures shows that Nijmegen responses and RCP symptom scores relate closely to Mini-AQLQ, although Nijmegen scores correlated less well with RCP symptom scores, raising the possibility that Nijmegen questions are assessing quality of life more generally in patients with asthma.

We defined dysfunctional breathing by Nijmegen score but sought to confirm the presence of inappropriate hyperventilation by progressive exercise testing. The Nijmegen score is a 16-item questionnaire designed to identify patients with dysfunctional breathing on the basis of frequency of symptoms such as “feeling tense,” “short of breath,” and “tingling fingers.” This questionnaire had a sensitivity of 91% and specificity of 95% in the diagnosis of DB in a non-asthma population (5) (using clinical diagnosis as the gold standard) but has not been extensively validated in patients with asthma. Some of the questions relate to typical asthma symptoms with the possibility that dysfunctional breathing would thereby be over-estimated in this group.

Recently a useful role for Nijmegen scoring in diagnosing DB in patients with asthma was suggested when Thomas (19) used this questionnaire to estimate the prevalence of dysfunctional breathing in a primary care sample of patients with asthma. In this study, 63 of 219 (29%) scored positively. Objective evidence of asthma was not detailed for this study cohort, with patients selected on the basis of a clinical diagnosis

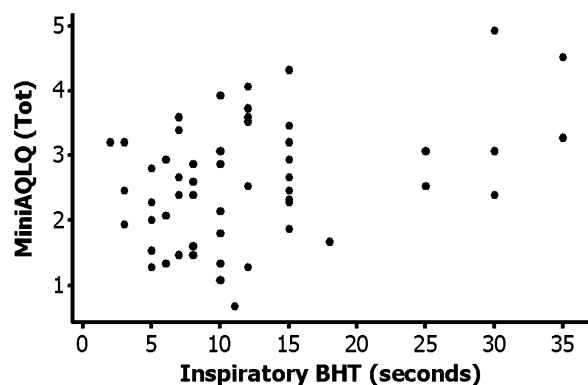


FIGURE 7.—Relationship between inspiratory Breath Hold Time (BHT) and mini-AQLQ.

and who had received a prescription for bronchodilator therapy. In the subsequent randomized controlled trial of BCT, however, most patients (28 of 33) had objective evidence of asthma (6).

Other tools have been studied for the identification of hyperventilation, such as the Hyperventilation Provocation Test (HVPT) (20), but again this has not been validated in patients with asthma. In clinical practice, progressive exercise testing detects inappropriate hyperventilation on exertion, but there is no data on sensitivity or specificity in its detection of DB, especially in patients with asthma. The lack of a gold standard makes objective study of this phenomenon difficult and highlights the importance of global assessment by a specialist therapist as a further method of assessment.

Using the standard definition, based on Nijmegen score, to identify DB, our baseline data show a high prevalence of this (65 of 102, 64%) in this cohort of patients with asthma. This is a higher frequency than in Thomas's cohort quoted above, which may reflect a higher prevalence of DB in patients with more severe disease (77 of 101 patients were on BTS step 4 treatment or above) but may also be due to the Nijmegen questionnaire overestimating the prevalence of DB, by wrongly attributing symptoms of poor asthma control to dysfunctional breathing. In keeping with this interpretation, we found a significant relationship between level of asthma symptoms, using a numerical version of the RCP symptom score, with symptoms rated over the previous week, and Nijmegen scores ($r = 0.43$, $p < 0.001$). We found a stronger relationship between Nijmegen and Mini-AQLQ than between symptom score and mini-AQLQ, raising the possibility that Nijmegen is measuring the perceived impact of symptoms, and thus, some aspect of asthma-related quality of life. We are currently undertaking further analysis of individual question responses in patients having Nijmegen, Mini-AQLQ, and Hospital Anxiety and Depression scores to test whether Nijmegen responses overlap entirely with responses to items previously considered to be measuring quality of life and psychological adjustment (26).

We sought to confirm the presence of inappropriate hyperventilation by PET, seen in 10 of the 17 patients (59%) in whom we had these data. Given that neither Nijmegen nor PET can be regarded as a gold standard, is not clear whether the lack of agreement between Nijmegen-identified DB and PET-identified inappropriate hyperventilation is explained by poor specificity of the Nijmegen or poor sensitivity of PET. From the scatterplot of Nijmegen scores in those with and without inappropriate hyperventilation on PET (Figure 5) it is clear that increasing the threshold Nijmegen score, in patients with asthma would not affect this if PET is considered the gold standard. Clearly it would have been interesting to look at PET findings in those with negative Nijmegen scores, but this would have been out of the scope of our normal clinic protocol. Finally, it is important to note that the low attendance rate for PET limits the generalizability of these findings.

The second part of this observational study involved assessing the effect of breathing control therapy on Nijmegen and mini-AQLQ scores. We observed no significant differences in Nijmegen or mini-AQLQ scores (either total or separate domain scores) after BCT in either group, with Nijmegen scores in particular showing evidence of regression to the mean.

There was a subgroup of eight patients with a clinically coherent pattern of changes, whose Nijmegen scores fell into the normal range. In this subgroup, breathing control may have had a positive impact because parallel changes in pharmacotherapy are unlikely to have had this effect. However, it is also possible that parallel and unrelated change in these patients' psychological state had an impact on both breath hold times and quality of life.

The possibility that Nijmegen is measuring aspects of quality of life is suggested by the seven patients who were felt to have complied well and benefited from BCT on subjective assessment, without any improvement in Nijmegen scores. Perhaps we are as busy clinicians in the early 21st century identifying an abnormal breathing pattern as a physical symptom, rather than as part of a syndrome of psychological distress.

Thomas's data can be interpreted as showing a nonspecific effect of breathing retraining that had a greater impact on asthma-related quality of life than Nijmegen scores (6). In this study, 9 of the 16 patients randomized to receive breathing retraining benefited in terms of clinically relevant changes in asthma related quality-of-life scores 1 month after breathing retraining exercises compared to 2 of 15 in the control group. Only overall change in the activities domain of the AQLQ remained significantly greater compared to controls after 6 months. The Nijmegen score of the study patients decreased but the difference was only statistically significant at 6 months. There was very little change in asthma therapy in either group in this study during follow-up.

The Mini-AQLQ is increasingly being used in clinical trials of asthma treatment to measure quality of life outcome (28, 29). We found similar proportions of patients with and without DB who had significantly improved (≥ 0.5) Mini-AQLQ scores (9/29, 31% and 6/17, 35%). Our study design makes it difficult to draw firm conclusions from this but certainly it does not suggest a definite treatment effect.

Clearly there are different methods of delivering breathing retraining. We judged the intervention we used to be applicable to normal clinic practice and likely to be sufficiently intensive to produce benefits, but this has not been confirmed by these observational results. Patient compliance may have limited our ability to influence deeply ingrained patterns of behavior. There are no comparative data on the most effective form of breathing retraining nor which health care professional should administer it, although one study of the Buteyko breathing technique which addresses asthma symptoms rather than dysfunctional breathing, found that asthma symptoms and bronchodilator use improved compared with placebo in symptomatic asthma patients with ongoing airflow obstruction (30). A recent review (31) identified a general trend of improvement in quality-of-life measurements with the Buteyko method used as a treatment for asthma. Our data show no evidence that this strategy was successful and suggest that any formal RCT assessment of breathing control in the setting of patients with moderate to severe asthma would need to be highly specific in terms of identification of patients likely to benefit and more intensive in nature and in the measurement of outcomes, since it is illogical to expect long-term benefit if no short-term advantage is identifiable. In such an RCT, it would also be important to compare a psychological intervention with breathing retraining, as well as

having a control group to test the specificity of any observed effect.

In summary this observational study has increased our understanding of two aspects of patients with moderate to severe asthma, as judged by having persistent symptoms despite high levels of treatment. First we have a better understanding of the range of Nijmegen, RCP symptom, and mini-AQLQ scores and the strong relationships that exist between these scores, suggesting that they are measuring related phenomena. We have also observed a poor relationship between BHT and Nijmegen. We have shown only a loose relationship between Nijmegen score and inappropriate hyperventilation measured by PET. Our second observation is that a moderate intensity breathing retraining program, undertaken in parallel with patients' normal clinic attendance had no benefit overall, with the pattern of benefit seen in subgroups raising the possibility that this intervention may not have had a specific physiotherapeutic effect. This will be useful in planning an RCT to address this issue, although we have also identified the problem caused by the lack of a gold standard method of identifying dysfunctional breathing in patients with asthma, which is likely to hamper its further study, until this issue is definitively addressed.

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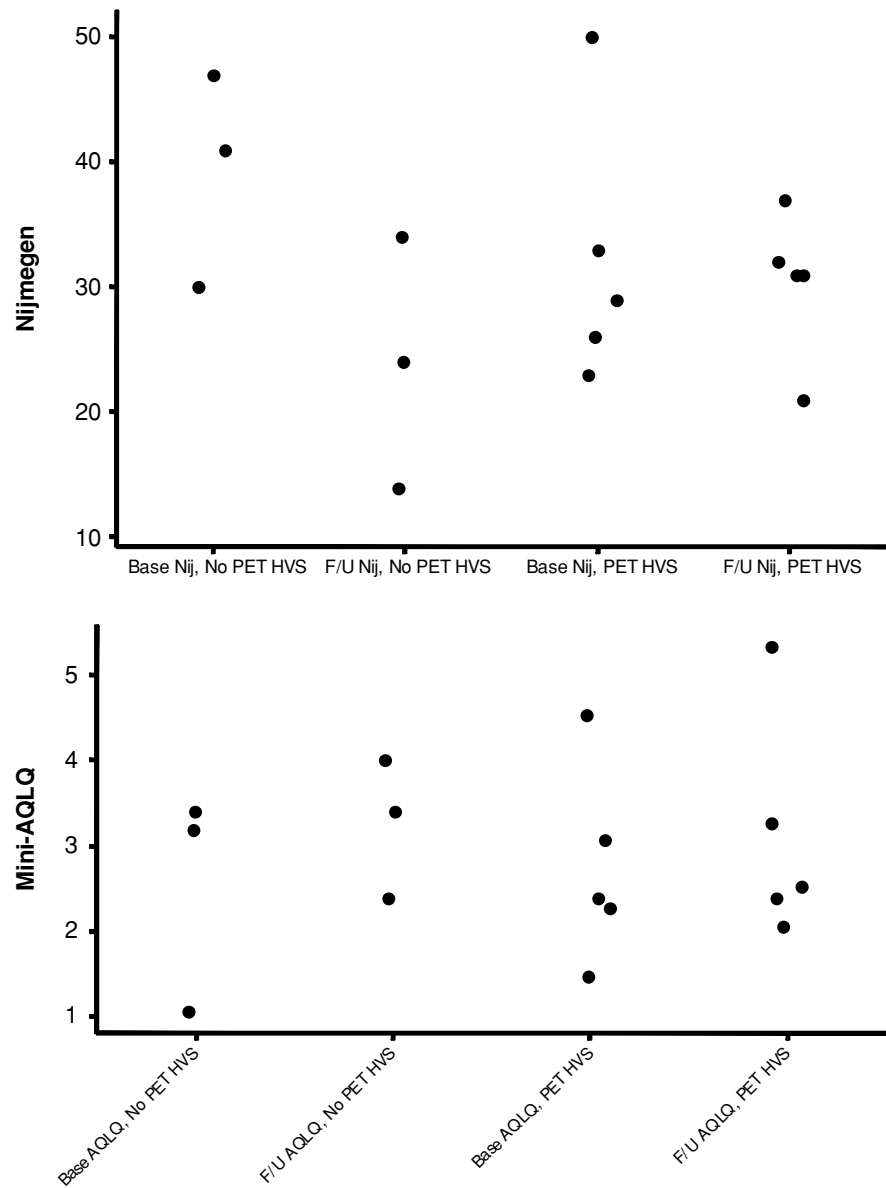
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APPENDIX 1.—(Supplemental data): Baseline Questionnaire Data: Nijmegen and Mini-AQLQ scores (DB = dysfunctional breathing).

Variable	Range	Mean (SD)	95% CI for difference between No-DB and DB, <i>p</i> -value)
Mini-AQLQ (Overall)			
All patients (<i>n</i> = 102)	1.07–6.93	3.30 (1.36)	0.87, 1.87, <i>p</i> < 0.0001
No DB (<i>n</i> = 37)	1.27–6.93	4.12 (1.43)	
DB (<i>n</i> = 65)	1.07–5.47	2.83 (1.07)	
Mini-AQLQ (Symptom Domain)			
All Patients (<i>n</i> = 102)	1.00–6.80	3.11 (1.40)	0.8, 2.00, <i>p</i> < 0.0001
No DB (<i>n</i> = 37)	1.00–6.80	4.01 (1.53)	
DB (<i>n</i> = 65)	1.00–5.40	2.60 (1.03)	
Mini-AQLQ (Environment Domain)			
All Patients (<i>n</i> = 102)	1.00–7.00	3.43 (1.64)	0.33, 2.00, <i>p</i> = 0.004
No DB (<i>n</i> = 37)	1.33–7.00	4.12 (1.82)	
DB (<i>n</i> = 65)	1.00–6.67	3.03 (1.40)	
Mini-AQLQ (Emotional Domain)			
All Patients (<i>n</i> = 102)	1.00–7.00	3.27 (1.56)	0.33, 1.67, <i>p</i> = 0.01
No DB (<i>n</i> = 37)	1.00–7.00	3.84 (1.66)	
DB (<i>n</i> = 65)	1.00–6.00	2.94 (1.42)	
Mini-AQLQ (Activities Domain)			
All Patients (<i>n</i> = 102)	1.00–7.00	3.44 (1.63)	1.00, 2.25, <i>p</i> < 0.0001
No DB (<i>n</i> = 37)	1.25–7.00	4.45 (1.64)	
DB (<i>n</i> = 65)	1.00–6.75	2.87 (1.33)	
Nijmegen			
All Patients (<i>n</i> = 102)	1–61	26.4 (11.5)	*****
No DB (<i>n</i> = 37)	1–22	14.5 (5.4)	*****
DB (<i>n</i> = 65)	23–61	33.2 (7.9)	*****



APPENDIX 2.—Available baseline and follow-up Questionnaire data for patients who had PETs ($n = 8$, 3 no inappropriate ventilation [labeled No PET HVS], 5 inappropriate ventilation [labeled PET HVS]). Mann-Whitney U-tests show no significant differences in any group.