

1 **Patient Perceived Barriers to Exercise and their Clinical Associations**
2 **in Difficult Asthma**

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27 Abstract

28 **Background:**

29 Exercise is recommended in guidelines for asthma management and has beneficial effects on
30 symptom control, inflammation and lung function in patients with sub-optimally controlled
31 asthma. Despite this, physical activity levels in patients with difficult asthma are often
32 impaired. Understanding the barriers to exercise in people with difficult asthma is crucial for
33 increasing their activity, and in implementing successful, disease modifying, and holistic
34 approaches to improve their health.

35 **Methods:**

36 62 Patients within the WATCH Difficult Asthma Cohort (Southampton, UK) completed an
37 Exercise Therapy Burden Questionnaire (ETBQ). The results were analyzed with
38 contemporaneous asthma-related data to determine relationships between perceived
39 exercise barriers and asthma and comorbidity characteristics.

40 **Results:**

41 Patients were reflective of a difficult asthma cohort, 66% were female, and 63% were atopic.
42 They had a high BMI (median [Inter-quartile range]) of 29.3 [25.5-36.2], age of 53.5 [38.75,
43 65.25], impaired spirometry with FEV1 73% predicted [59.5, 86.6%] and FEV/FVC ratio of 72
44 [56.5, 78.0] and poor symptom control, as defined by an Asthma Control Questionnaire
45 (ACQ6) result of 2.4 [1.28, 3.2]. A high perceived barriers to exercise score was significantly
46 correlated with increased asthma symptoms ($r=0.452$, $p<0.0001$), anxiety ($r=0.375$, $p=0.005$)
47 and depression ($r=0.363$, $p=0.008$), poor quality of life ($r=0.345$, $p=0.015$) and number of
48 rescue oral steroid courses in the past 12 months ($r=0.257$, $p=0.048$). Lung function, blood

49 eosinophil count, FeNO, Nijmegen and SNOT22 scores, BMI and hospitalisations in the
50 previous year were not related to exercise perceptions.

51 **Conclusion:**

52 In difficult asthma, perceived barriers to exercise are related to symptom burden and
53 psychological morbidity. Therefore, exercise interventions combined with psychological input
54 such as CBT to restructure thought processes around these perceived barriers may be useful
55 in facilitating adoption of exercise.

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57 **Key Words:** Asthma, exercise, barriers, psychology

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77 Background

78 Exercise is recommended in national and international guidelines for asthma management^{1,2,3}
79 and appears to have beneficial effects on symptom control, inflammation and lung function
80 in patients with sub-optimally controlled asthma.⁴ Despite this, physical activity levels in
81 patients with severe asthma have been demonstrated to be impaired.⁵ Patients with difficult
82 and severe asthma comprise only 5-10% of all patients with asthma. ^{6,7} However, they are
83 disproportionately more likely to demonstrate poorly controlled symptoms and inflammation
84 on optimised treatment regimens. This drives a significant proportion of healthcare costs,
85 reported to consist of near to 50% of total asthma therapy costs.^{6,8} In related disease areas,
86 exercise interventions are being offered at scale using novel technologies such as healthcare
87 apps to increase patient centred management in COPD which could be harnessed for
88 prevalent diseases such as difficult asthma.⁹⁻¹² Understanding of the barriers to exercise is
89 crucial in increasing activity in patients with difficult asthma, and in implementing a successful
90 exercise training programme to improve their health outcomes.^{13,14}

91 In the general population, reasons for physical inactivity are due to a combination of
92 insufficient leisure time and increased mechanization of occupational and domestic
93 activities.¹⁵ In patients with asthma there may be additional disease related barriers to
94 exercise such as fear of provoking respiratory symptoms and exacerbation, and
95 misinterpretation of physiological shortness of breath in response to increased aerobic
96 activity. Understanding these may facilitate design of exercise interventions.

97 Alongside patients with severe asthma, patients with relatively mild disease have been shown
98 to avoid physical activity because they are concerned about triggering symptoms.¹⁶ However,
99 asthma severity, as assessed by FEV₁ and methacholine challenge, were not predictive of VO₂

100 (maximal oxygen uptake) peak as a marker of aerobic fitness, and the relationship between
101 asthma severity and VO2 max has been detailed in athletic individuals previously. These
102 findings suggest that disease severity does not determine fitness in asthma patients who
103 manage to overcome perceived barriers to exercise and undertake regular physical
104 activity.^{16,17} Relatively few studies have investigated the barriers and facilitators to exercise
105 and physical activity in asthma. However, those which have focus predominantly on
106 adolescents. This is partly because asthma tends to affect younger populations in childhood
107 and adolescence at a time when they should be establishing healthy lifestyles. This is
108 therefore a critical point for intervention to encourage long-term adoption of physical
109 activity.¹⁸ Whilst qualitative studies suggest healthy participants and asthma patients
110 consider that exercise is beneficial,¹⁹ a study of elementary school teachers demonstrated
111 few were aware that students with asthma need not avoid exercise.²⁰ Other barriers have
112 also been identified that prevent this group of patients engaging with physical activity. For
113 example, lack of time is more likely to be reported as a barrier in younger patients.¹⁹ Fear of
114 exacerbating symptoms is also a common theme amongst adolescents²¹ and adults,¹⁹ with
115 patients with more severe disease more likely to view exercise as detrimental. Intensity of
116 physical activity undertaken by asthma patients has been shown to be positively correlated
117 with peak expiratory flow.²² Although causation could not be determined in this cross-
118 sectional study, it raises the question as to whether those with less severe disease are able to
119 undertake more activity or whether those who undertake more activity are able to modulate
120 their disease burden, as supported by findings in a recent review.²³ Obesity and
121 musculoskeletal problems are conditions that are common in asthma and exacerbated by oral
122 steroid therapy. These are also reasons for this patient population not exercising, as were
123 extreme weather conditions.¹⁹ Facilitators included the desire to be healthy and

124 encouragement from a motivated companion or physician. Lifestyle activities have been
125 shown to be more acceptable to patients as a way to increase their physical activity levels.¹⁹
126 In terms of intrinsic characteristics, patients with less asthma knowledge, lower self-efficacy
127 and more negative attitudes towards asthma were more likely to view exercise negatively.¹⁹
128 Similar themes were noted in a group of middle aged African American women with poorly
129 controlled asthma who participated in focus groups to determine barriers to walking.
130 Domains identified in this group included limited physical capability, lack of knowledge, lack
131 of self-monitoring skills, lack of areas to walk, lack of social support and beliefs about
132 consequences and capability.²⁴
133 In this paper we present the perceived barriers to exercise in patients with difficult asthma in
134 a group recruited from the Wessex Asthma Cohort of Difficult Asthma (WATCH). Furthermore,
135 we assess their relationships to aspects of asthma severity and control.

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137 **Methods**

138 **WATCH Data Collection**

139 WATCH is a longitudinal clinical cohort of patients with Difficult Asthma (n = 501) based at
140 University Hospitals Southampton NHS Foundation Trust (UHSFT), Southampton, United
141 Kingdom (UK). All patients managed with British Thoracic Society Step “high dose therapies”
142 and/or “continuous or frequent use of oral steroids”¹ in the Adult or Transitional Regional
143 Asthma Clinic at UHSFT were invited to participate. Briefly, research data capture was aligned
144 with the extensive clinical characterisation required of a commissioned National Health
145 Service (NHS) Specialist Centre for Severe Asthma.²⁵ Data acquisition at enrolment included

146 detailed clinical, health and disease-related questionnaires (Asthma Control Questionnaire
147 (ACQ6), St George's Respiratory Questionnaire (SGRQ) and EQ-5D-5L, Nijmegen
148 questionnaire for dysfunctional breathing, Sinonasal Outcome Test (SNOT22) for sinonasal
149 symptom burden and Hospital Anxiety and Depression score (HADS) for anxiety and
150 depression), anthropometry, allergy skin prick testing (SPT), lung function testing, radiological
151 imaging (in a subset of those who were clinically indicated) and collection of biological
152 samples (blood, and urine). Brief longitudinal updates of data were obtained annually. A
153 detailed outline of study protocol and methodology has previously been published.²⁵ The
154 Exercise Therapy Burden Questionnaire (ETBQ) has been validated in French and Spanish for
155 the assessment of barriers to physical activity in chronic illness and consists of 10 questions
156 graded from 0-10; a higher score indicates higher perceived barriers to exercise^{10,26,27} (see
157 supplement for questionnaire). Ninety patients were approached to complete an ETBQ,
158 either as part of their WATCH enrolment, or whilst they were attending a routine clinic follow-
159 up visit between January 2019 and February 2020. Those patients who did not attend clinic
160 during this time or were not due a WATCH follow up visit during this period may not have
161 been approached. A total of 62 patients fully completed the questionnaire. Data were then
162 extracted for the clinical correlates which most temporally associated with the ETBQ
163 completion. The primary outcome was to identify whether a higher asthma disease burden
164 was related to greater perceived barriers to exercise. Secondary outcomes focused on
165 relationship between barriers to exercise and specific areas of asthma disease burden.

166 Data Analysis

167 Statistical analysis was performed using SPSS 24 (NY, USA), and GraphPad Prism 8 (La Jolla,
168 California, USA). Non-parametric tests were used due to some of the data being non-Normally

169 distributed. Quantitative variables are presented as median and inter-quartile range (IQR).
170 Mann-Whitney and Fisher's exact tests were used to compare the WATCH cohort as a whole
171 with the ETBQ cohort. Results for these variables were compared using an independent
172 samples Mann Whitney test, Kruskal Wallis and Independent Samples Median tests were
173 used to look for differences between groups. Associations between variables were tested
174 using a Spearman's Rho test. A p value of <0.05 was considered statistically significant.

175

176 Results

177 Demographic data

178 The sub cohort of patients who completed the ETBQ were comparable in most core
179 characteristics to the wider WATCH cohort (table 1). The only significant differences between
180 the ETBQ group and the overall WATCH cohort were that the cohort as a whole had a higher
181 mean [95% confidence interval] use of rescue oral corticosteroids (OCS) (3.60 [3.24, 3.96] vs
182 1.93 [1.24, 2.62], $p < 0.0001$), a higher rate of hospitalisation in the previous 12 months (0.76
183 [0.59, 0.93] vs 0.24 [0.01, 0.47], $p = 0.0025$), a lower FeNO (31.1 [27.5, 34.8] vs 48.55 [16.5,
184 80.6], $p = 0.03$) and a higher HADS-D score (5.4 [5.0, 5.8] vs 4 [0.1, 5.0], $p = 0.04$). Biologic use
185 was higher in the ETBQ group than the WATCH cohort overall (39% vs 18%, $p = 0.0016$),
186 demographic and disease-related characteristics of the ETBQ group are given in table 1.

187 Barriers to exercise results

188 There were no significant differences between those patients who completed the
189 questionnaire and the overall group of patients who were approached to complete the
190 questionnaire in terms of median BMI (30.00 vs 29.65, $p = 0.9$), FEV1 (73.43 vs 73.43, $p = 0.83$,

191 ACQ 6 score (2.4 vs 2.5, $p=0.45$), OCS courses (1 vs 1, $p=0.77$), hospitalisations (0 vs 0, $p=0.24$),
192 blood eosinophils (0.2 vs 0.2, $p=0.7$) or FeNO (21 vs 20, $p=0.55$). Verbal feedback from patients
193 who were approached but did not complete the questionnaire suggested reasons for not
194 doing so which included time and uncertainty regarding the relevance of the questionnaire if
195 they had not been specifically prescribed an activity. 49 (79%) of the patients who fully
196 completed the questionnaire took part in some focussed physical activity, with 18 (29%)
197 stating that they played sports, 11 (17.7%) attending physiotherapy sessions and 20 (32.3%)
198 undertaking a home-based exercise programme. There was a median (IQR) total score of 25.5
199 [11.25, 42.75] out of a possible total score of 100.

200 Median [range] results for the specific questions within the ETBQ are shown in table 2.
201 Motivation (3 [0-10]), pain or discomfort (4 [0-10]), fatigue (5 [0-10]) and being reminded of
202 their asthma (5 [0-10]) were the most limiting factors to exercise programmes within this
203 group. There were no significant differences for individual questions or overall score when
204 grouped by gender ($p=1$). There were no significant differences in total scores when grouped
205 across age range ($p=0.479$) or body mass index ($p=0.671$). However, when the individual
206 question scores were analysed by body mass index, there was a significant difference in scores
207 for question 1 (The exercise causes me pain) for patients when group by BMI ($p=0.017$) (figure
208 1). However, post-hoc pairwise comparisons were not significant once adjusted for multiple
209 testing.

210 When individual question scores were analysed for differences across the age range, there
211 were significant differences in scores for question 6 (exercising reminds me of my condition),
212 with those in the diagnosed at the age of 6-11 group scoring significantly higher than those in
213 the 5 years and under group ($p<0.05$) (figure 2).

214 Relationships between ETBQ score and asthma related assessments

215 We then looked at relationships between a high total ETBQ score and markers of asthma
216 severity and symptom burden. High perceived barriers to exercise scores were significantly
217 correlated with increased asthma symptoms, as measured by the Asthma Control
218 Questionnaire (ACQ6) ($r=0.452$, $p<.0001$), and number of rescue OCS uses in the past 12
219 months ($r=0.257$, $p=0.048$) (figure 3). Psychological co-morbidities in the form of anxiety and
220 depression were assessed by the Hospital Anxiety and Depression Score (HADS). There was
221 significant correlation between high perceived barriers to exercise therapy and high HADS
222 scores, both for anxiety ($r=0.363$, $p=0.008$) and depression ($r=0.375$, $p=0.002$), independently
223 and as a total score ($R=0.389$, $P=0.004$) (figure 4). Low perceived quality of life scores were
224 assessed by the EQ-5D-5L and the St George's Respiratory Questionnaire (SGRQ) and
225 correlated with a higher perceived barriers to exercise (figure 5). Lung function (pre BD FEV1;
226 $r=-0.087$, $p=0.522$), eosinophil count ($r=0.154$, $p=0.235$), FeNO, Nijmegen ($r=0.213$, $p=0.151$)
227 and SNOT22 scores ($r=-0.078$, $p=0.151$), BMI ($r=0.180$, $p=0.168$) and hospitalisations ($r=-0.78$,
228 $p=0.548$) in the previous year were not significantly correlated with ETBQ score. There were
229 no statistically significant differences in total ETBQ score or individual question scores when
230 participants were divided by biologic use in the last 12 months. No significant differences in
231 lung function results, eosinophil counts and FeNO were seen for those on and not on
232 biological treatments.

233

234 Discussion

235 Perceived barriers to exercise in patients

236 We assessed the perceived barriers to exercise in patients with difficult asthma under the
237 care of a tertiary clinical service to create a better real-life understanding of relevant limiting
238 factors. To the best of our knowledge, this is the first study to explore this in patients with
239 difficult asthma. Although differences were seen in OCS and rates of hospitalisation, our
240 patient group was generally comparable to the WATCH Cohort as a whole, and representative
241 of a typical group of patients with difficult asthma. Patient perceptions of barriers to exercise
242 in difficult asthma were high. The median score within our cohort were comparable to those
243 found in patients with cardiovascular disease and much higher than those seen in patients
244 with cancer.²⁸ The distribution of scores was wide throughout the cohort, suggesting that
245 perceived barriers to exercise are patient specific, possibly reflecting the heterogeneity of
246 difficult asthma. Identification of values of low, medium and high scores for the ETBQ have
247 not been identified, but may be useful to identify in the future. There did not appear to be
248 significant differences between sex of the patient and perceived barriers to exercise. This
249 contrasts with a previous study which investigated perceived barriers to exercise in a cohort
250 of university students with disabilities. This study demonstrated that the most significant
251 barriers to exercise were interpersonal in nature and that females were more likely to
252 experience higher interpersonal barriers.²⁹ It may be that within our difficult asthma patient
253 group, the disease related barriers to exercise were great enough to balance out any sex
254 specific barriers. The lack of correlation with frequency of hospitalisations is interesting,
255 suggesting that exacerbations on a background of reasonable day to day control may impact
256 less on perceptions of barriers to exercise than a constant level of poor control with few

257 exacerbations. This may be of relevance to prescribing criteria for biological treatments,
258 which, at present focus on exacerbation frequency.³⁰

259 BMI impacts perceived barriers to exercise

260 There was a significant difference for Q1 score in BMI categories, as identified by the overall
261 Kruskal Wallis test. The post-hoc pairwise comparisons were not significant. However, this
262 was probably due to a lack of statistical power due to small group sizes. This effect of BMI on
263 perceived barriers to exercise is noteworthy, but not a wholly unexpected finding as
264 differences between BMI and barriers to physical activity have previously been demonstrated
265 in young Australian males.³¹ Patients with asthma who are obese have a greater symptom
266 burden and lose more days to illness than non-obese asthma patients.³² This population are
267 more likely to benefit from exercise interventions to address both obesity and asthma driven
268 inflammation.^{33,34} It is therefore important to adapt current exercise interventions to make
269 them more accessible to this group of patients, potentially with classes available for this group
270 of patients specifically to help alleviate concerns around others' perceptions, and
271 psychological and dietician support alongside this. Understanding that perceived barriers to
272 exercise differ for obese patients with asthma is the essential first step in doing this. Further
273 work investigating the specific causes of pain in these patients is now important. The lack of
274 correlation between BMI and overall perceived barriers to exercise is interesting. It may be
275 that the majority of the perceived barriers to exercise in obese patients is related to pain, but
276 overall the perception of barriers to exercise was not increased by a BMI. BMI is a gross
277 measure of obesity, and noted to be overestimated in those with high muscle mass. This may
278 add further ambiguity to results, and investigation of bioimpedance data would perhaps give
279 further clarification.

280 Differentially perceived barriers to exercise dependent on age of diagnosis

281 In this present study, significantly different perceptions on the effect of asthma to barriers to
282 exercise were demonstrated between groups based on age of diagnosis. Those whose disease
283 started between the ages of 6-11 were more likely to see their disease as a barrier to exercise
284 than those diagnosed under 5 years old. This appears to be a key stage for engagement in
285 sport in later life, with a report from The Women in Sport Research group showing that if
286 children start to drop out of sporting activities at this age then they tend not to re-engage as
287 adults.³⁵ Comparatively, exercise levels in children at age 7 are not reduced in those with a
288 diagnosis of asthma.³⁶ It may be that diagnosis at this age compounds the effects of this
289 transition point. Diagnosis at this age may result in a higher dropout rate from physical activity
290 which continues into adulthood. This could partly explain some of the lower levels of activity
291 seen in patients with asthma compared to the general population. Targeted interventions in
292 this age group may go some way to ameliorating this effect.⁵

293 Perceived symptom burden impacts perceived barriers to exercise

294 A high perceived symptom burden as assessed through the symptom scores (ACQ6) and
295 number of rescue courses of OCS were found to significantly correlate with an increased
296 perceived barrier to exercise. Correlations between a perceived high barrier to exercise
297 therapy and disease specific assessments are reflective of the literature. Those with more
298 severe disease have previously been shown to view exercise as more likely to be
299 detrimental.¹⁹ Both these measures of symptom burden are partially subjective. ACQ scores
300 reflect patient interpretation of their symptoms over the preceding week. Furthermore,
301 rescue courses of OCS are often started by patients as part of a rescue pack on the basis of
302 deteriorating symptoms. However, in this present research, objective asthma specific

303 markers of severity such as lung function and markers of Type 2 high disease did not correlate
304 with perceived barriers to exercise. Similarly, a cross-sectional analysis of physical activity in
305 the UK millennium cohort demonstrated that activity levels in children with asthma were not
306 affected by the severity of their disease.³⁶ This is a clinically relevant finding which suggests
307 that severity of disease is not necessarily a barrier to exercise. This has been supported by
308 our pilot work,³⁷ and that of others,³³ investigating exercise intervention in asthma patients.
309 This suggests that high levels of biological disease are not necessarily a barrier to adoption of
310 exercise for some patients. This data is of use for reassuring both patients and clinicians that
311 exercise intervention is safe in asthma regardless of disease severity.

312 Psychological co-morbidity in the form of a high HADS Anxiety, depression and total scores
313 also correlated significantly with a higher perceived barriers to exercise score. A meta-analysis
314 has previously identified low mood and stress as two of the most significant barriers to
315 exercise in mental illness.³⁸ However, exercise has also been demonstrated to improve mood
316 associated with reduction in depression-associated inflammation in COPD³⁹ and in health.⁴⁰
317 A similar pattern has been seen with QoL where exercise specific self-efficacy has been shown
318 to correlate with health related QoL in COPD.⁴¹ Therefore, our results which show that a
319 higher barrier to exercise correlates with a lower QoL score are not unexpected. Exercise is,
320 however, known to improve health related QoL in asthma^{4,23} and therefore interventions to
321 address this paradox need investigating.

322 Challenges and considerations

323 There are limitations to this study. Firstly, the strength of correlations throughout were low-
324 moderate, this was likely a result of the numbers who completed the questionnaire. Secondly,
325 a questionnaire format will not provide as detailed or accurate information as a qualitative

326 interview format. However, there are advantages to a questionnaire format, in that
327 participants may be more honest with regards to barriers to exercise than they would be with
328 a face-face interviewer. Furthermore, a questionnaire format reduces time demands on
329 patients and clinical staff both in a research and clinical context, whilst still providing
330 noteworthy findings, which could then potentially be expanded on in a qualitative way. The
331 ETBQ was the most specific questionnaire available at the time of conception of this study to
332 address the question of perceived barriers to exercise within the context of a chronic disease,
333 thus this questionnaire was chosen to be used.

334 With regards to other limitations, asthma symptoms can fluctuate and the clinical data was
335 not necessarily collected at the same time as the ETBQ. However, the clinical data which most
336 closely aligned temporally with the ETBQ data was extracted from the database to reduce any
337 inaccuracies. Also, questionnaires were completed at different stages of enrolment in the
338 WATCH study; some at baseline, and others at follow up visits. Similarly, perceived patient
339 barriers to exercise may change depending on the day of the exercise, this may not be
340 captured by a single time point questionnaire. There were a few significant differences
341 between the WATCH cohort and the ETBQ sub-cohort, including number of rescue courses of
342 OCS in the last 12 months, which was higher in the WATCH cohort as a whole. This may partly
343 explain the only borderline significance of the correlation between ETBQ total score and OCS
344 rescue courses. Besides this, the ETBQ cohort was representative of the wider WATCH
345 population and there was no difference between those who completed the questionnaire
346 compared to those who did not, suggesting this was not a bias to taking part in the ETBQ
347 study. The ETBQ focuses on a prescribed activity and yet some patients within the cohort
348 were not prescribed any activity. If this were the case, then they were asked to complete the
349 questionnaire from the perspective of what prevents them from exercising rather than the

350 burden of any prescribed exercise. However, misunderstanding of this may explain why only
351 62 of the 90 participants invited to complete the ETBQ fully completed the questionnaire.
352 With any self-reported questionnaire-based research, there is always the concern of
353 responder bias. However, patients were asked to complete the questionnaire regardless of
354 whether they undertook regular exercise. This removed any expectation that they should be
355 taking part in exercise.

356

357 Conclusion

358 Patient perceived barriers to exercise are more related to symptom burden and psychological
359 morbidity than to specific disease severity indicators. Therefore, exercise interventions
360 combined with psychological input such as CBT to restructure thought processes around
361 these perceived barriers may be useful in facilitating adoption of exercise.

362

363 List of Abbreviations

364 ACQ Asthma Control Questionnaire

365 BD Bronchodilator

366 BMI Body Mass Index

367 ETBQ Exercise Therapy Burden Questionnaire

368 FeNO Fractional Exhaled Nitrogen Oxide

369 FEV1 Forced Expiratory Volume in 1 second

370 FVC Forced Vital Capacity

371 HADS Hospital Anxiety and Depression Score

- 372 ICU Intensive Care Unit
- 373 OCS Oral corticosteroids
- 374 SGRQ St George's Respiratory Questionnaire
- 375 SNOT 22 Sinonasal Outcome Test

376 **Declarations**

377 **Ethics approval and consent to participate**

378 Written informed consent has been obtained from each study participant. The study design,
379 protocol and paperwork were IRB approved by West Midlands – Solihull Research Ethics
380 Committee (REC reference: 14/WM/1226).

381 **Consent for publication**

382 Not applicable

383 **Availability of data and materials**

384 All data generated or analysed during this study are included in this published article [and its
385 supplementary information files]

386 **Competing interests**

387 K.S reports grants from AstraZeneca, grants from Asthma UK, outside the submitted work.
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399 Authors' contributions

400 Anna Freeman, Tom M.A. Wilkinson: conceptualization. Colin Newell and Deborah Knight:
401 data curation. Anna Freeman and Helen Moyses: formal analysis. David Hill, Adnan Azim,
402 Anna Freeman: investigation and methodology. Laura Presland, Deborah Knight, Ramesh J.
403 Kurukulaaratchy, Hans Michael Haitchi: project administration and resources. Tom M.A.
404 Wilkinson, Ramesh J. Kurukulaaratchy, Karl J Staples: supervision. Anna Freeman: original
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406 Staples: review & editing.

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527 Figure Legends

528 **Figure 1:** Q1 (The exercise causes me pain): results for comparison using Kruskal Wallis Test
529 to compare ETBQ scores for question 1 when grouped by BMI category (mdn and IQR), with
530 significantly higher scores noticed in those overweight ($p=0.017$)

531 **Figure 2:** Q6 (Exercising reminds me of my condition)- : Independent samples Median Test
532 results for comparison of ETBQ scores for question 6 when grouped by age at diagnosis (mdn
533 and IQR), with significant differences in the age 6-11 group ($p=0.03$)

534 **Figure 3:** Correlation between symptom scores (ACQ6, figure 4A) and rescue OCS (figure 4B)
535 as assessed by Spearman Rank Correlation with r and p values

536 **Figure 4:** ETBQ and psychological comorbidity for anxiety and depression (HADS total, figure
537 5A), anxiety (HADSA, figure 5B), depression (HADSD, figure 5C), as assessed by Spearman Rank
538 Correlation with r and p values

539 **Figure 5:** ETBQ and Quality of Life Scores for SGRQ total (6A), impacts (6B) and symptoms
540 (6C), and EQ-5D5L health today 6D, and EQ-5D-5L Index (6E as assessed by Spearman
541 correlation, with r and p value

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544 Tables

545 Table 1: Demographic and disease related data

	<i>WATCH Cohort as a whole (n)</i>	Median [IQR]	<i>N (%)</i>	<i>EBTQ Cohort Baseline Data (n)</i>	Median (IQR)	<i>N (%)</i>	<i>P value</i>
Demographics							
Female	501		65.3%	62		69.4%	ns
Age at Study Enrolment (years)	501	52 [38.5, 63.0]		62	53.5 [35.75, 65.25]		ns
Age at asthma diagnosis	479	19 [4, 40]		62	23 [3.0, 40.35]		ns
BMI	495	29.7 [25.6, 35.3]		60	29.25 [25.5, 36.23]		ns
Obese	495		48.3%	62		48.3%	ns
Current or Ex Smokers	500		47.6%	62		31.1%	ns
Co-Morbidities							
Rhinitis	446		67.5%	62		58.1%	ns
Eczema	495		26.1%	62		25.8%	ns
Bronchiectasis	493		6.9%	62		16.1%	ns
GORD	495		14.1%	61		50%	ns
Depression	486		64.8%	62		17.7%	ns
Anxiety	454		36.8%	62		19.4%	ns

Dysfunctional Breathing	451		48.7%	61		41%	ns
Intermittent Laryngeal Dysfunction	476		14.5%	59		10.2%	ns
Sulphite Sensitivity	447		7.7%	62		4.8%	ns
Salicylate Sensitivity	493		25.1%	62		21%	ns
Sleep Apnoea			7.2%	62		6.5%	ns
Healthcare Utilisation							
≥1 Asthma Related ICU Visits ever	500		28.2%	60		1.7%	ns
≥1 Asthma Hospital Admission (last 12 months)	497		29.0%	62		11.3%	P=0.0025
≥3 Rescue Oral Corticosteroids (last 12 months)	448		43.6%	60		31.7%	ns
Maintenance oral corticosteroids	479		29.9%				P<.0001
Biological treatment in last 12 months	495		17.6%			39%	P=.0016
Blood Test Results							

Eosinophil Count					0.2 [0.1, 0.4]		ns
Lung Function Test Results							ns
FeNO50 (ppb)	329	19.7 [10.0, 38.7]		62	22[14, 45.5]		P=.03
Post BD FEV1 (%)	341	75 [59.3, 92.1]		57	73.4 [59.5, 86.6]		ns
Post BD FEV1/FVC (ratio)	340	68 [58, 78]		57	72 [56.5, 78]		ns
Skin Prick Tests							
Positive to any Aeroallergen	391		68.0%	52		75%	ns
Positive to Aspergillus	355		15.8%	47		17%	ns
Questionnaires							
ACQ6 Score	467	2.5 [1.5, 3.5]		62	2.4 [1.28, 3.2]		ns
Epworth Score	424	8 [4, 12.75]		55	8 [3, 11]		ns
HADS Total Score	418	10.5 [6, 18]		53	8 [4.0, 15.5]		ns
HADS A Score	425	6 [3, 10]		55	5 [3, 9]		ns
HADS D Score	426	4 [2, 8]		53	3 [1, 6]		P=.04
Hull Cough Score	378	25 [14, 36]		48	30 [14.25, 41.75]		ns
Nijmegen Score	373	21 [12, 31]		47	21 [13, 26]		ns
SNOT22 Score	324	31.5 [20, 50]		40	36.5 [23.25, 48.75]		ns

EQ_5D_5L Index value	170	0.72 [0.53, 0.83]		62	0.72 [0.54, 1.00]		ns
SGRQ Total Score	381	51.1 [35.25, 67.34]		49	59.6 [37.1, 63.4]		ns
SGRQ Symptoms Score	411	67.73 [50.72, 81.31]		53	68 [53, 81.7]		ns
SGRQ Activity Score	389	66.1 [43.7, 85.7]		50	66.2 [41.8, 73.8]		ns
SGRQ Impacts Score	396	38.71 [22.76, 55.74]		52	36 [25.4, 54.1]		ns

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547 **Table 2: ETBQ question results for total cohort**

Question	Median	Range
Q1 (Pain or discomfort)	4	0-10
Q2 (Fatigue)	5	0-10
Q3 (Boredom)	1	0-10
Q4 (Too Difficult)	2	0-9
Q5 (Wastes Time)	0	0-9
Q6 (Reminds of Condition)	5	0-10
Q7 (Lacks Support)	0	0-10
Q8 (Lacks Motivation)	3	0-10
Q9 (Inappropriate)	0	0-9
Q10 (Not Efficient)	0.5	0-10

548 *Median (and min-max) results for each of the ten questions comprising the ETBQ for the*
549 *total cohort are shown (n=62).*

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