

Factors Associated With Quality of Life in Children With Asthma Living in Scotland

Vaida Taminskiene, MPH,^{1,2} Somnath Mukhopadhyay, PhD,³ Colin Palmer, PhD,⁴ Anil Mehta, PhD,⁵ Jon Ayres, MD,⁶ Arunas Valiulis, PhD,^{2,7} and Steve W. Turner, MD^{1*}

Summary. Introduction: Asthma affects children's quality of life (QoL) but factors associated with QoL are not well understood. Our hypothesis was that there are factors linked to QoL which are amenable to treatment or environmental modification. Methods: QoL was ascertained in a study designed to link environmental exposures to asthma outcomes. Univariate and multivariate analysis were used to determine which factors are associated with QoL. Results: There were 553 children with asthma where QoL was determined, mean age 10.3 and 312 (58%) were boys. The median QoL score was 5.9 (interquartile range 4.6, 6.8). In the multivariate model, asthma severity (as evidenced by British Thoracic Society, BTS, treatment step), smoking exposure, socioeconomic status and rhinitis were associated with the QoL score. QoL score was reduced by (i) 30% [95% confidence interval 20, 39] for those on BTS step 4 compared to BTS step 1 treatment (ii) 11% [2, 19] for children with $\geq$ two resident smokers with reference to no resident smokers (iii) 3% [1, 5] for each quintile difference in deprivation compared to the most affluent and (iv) 9% [4, 14] for children with rhinitis compared to no rhinitis. Conclusions: The QoL for children with asthma in the UK is generally good. Clinicians caring children with asthma should consider routinely asking about smoke exposure and hayfever symptoms in addition to assessing asthma control. *Pediatr Pulmonol.* 2016;51:484–490. © 2015 Wiley Periodicals, Inc.

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INTRODUCTION

Asthma is a common chronic condition which affects all age groups and its prevalence is high in many countries, especially among children.¹ The prevalence of asthma and its symptoms in children varies between countries.² In Scotland, approximately 25% of children have a lifetime history of asthma.³

Asthma costs the UK National Health Service £1 billion per annum and the cost of inhaler prescribing to children is approximately £5 per child in the whole population.⁴ In addition to the financial cost, asthma has an impact on the quality of life of children^{5–7} and can disrupt the life of the wider family.^{1,5,6} Surprisingly little is known about what factors are associated with QoL in childhood asthma but family dynamics and asthma severity have been identified as being relevant. One study from the USA reported that the level of control and transitions within the family (e.g., a family member married, left home, began college, or moved back home) were important to QoL.⁸ Another study from the US found that asthma control in 8–17 year olds was directly linked to parental factors, such as satisfaction with shared decision making.⁹ Poor asthma control has been linked to reduced QoL,^{7,9,10} but this might be expected given the common indices used to assess both, i.e. frequency of

¹Child Health, University of Aberdeen, Aberdeen, United Kingdom.

²Institute of Public Health, Faculty of Medicine, Vilnius University, Vilnius, Lithuania.

³Department of Paediatrics, University of Brighton, Brighton, United Kingdom.

⁴Department of Pharmacogenetics, University of Dundee, Dundee, United Kingdom.

⁵Division of Cardiovascular and Diabetes Medicine, University of Dundee, Dundee, United Kingdom.

⁶Department of Occupational Health, University of Birmingham, Birmingham, United Kingdom.

⁷Clinic of Children's Diseases, Faculty of Medicine, Vilnius University, Vilnius, Lithuania.

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*Correspondence to: Steve Turner, MD, Child Health, Royal Aberdeen Children's Hospital, Aberdeen, AB25 2ZG, UK.
E-mail: s.w.turner@abdn.ac.uk

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symptoms. A study from Greece has also shown that health related QoL is related to loss of asthma control with an interaction with severity.⁷ In the general population, exposure to second hand smoke and co-morbidities associated with asthma such as eczema and hay fever are associated with poor QoL in the general population^{11–13} but this has not been explored within a population of children with asthma.

Our research question was what factors were associated with QoL in children with asthma? We focused on associations between QoL and environmental factors some of which have been identified as leading to asthma exacerbations.¹⁴ We also explored associations between QoL and comorbidities associated with increased asthma symptoms such as obesity, eczema and hayfever.^{15–17} Our hypothesis was that there are factors linked to QoL which are amenable to treatment or environmental modification.

METHODS

Study Design

The Paediatric Asthma Gene Environment Study (PAGES) is a cross-sectional study of asthmatic children in Scotland designed to study gene-environment interactions for asthma outcomes (<http://www.asthma-pages.com/>) Children were recruited from primary and secondary care, the upper age was 16 years and lower age was 2 years for secondary care and the lower age was 5 years for primary care (the higher inclusion age for primary care was to reduce the chance of misdiagnosis). Asthma and QoL questionnaires were completed. Age appropriate versions of the Children's Asthma Control Test (CACT) were completed; the maximum scores from the 4–11 and >11 years CACT are 27 and 25, respectively and no adjustment was made for this minor difference. A subset participated in a clinical assessment which included spirometry, bronchodilator response, exhaled nitric oxide (ENO) measurement, skin prick test, saliva cotinine measurement, and weight and height. Exposure to second hand smoke in this population was validated by salivary cotinine measurement within a subset.¹⁸ Quality of life scores were related to indices of asthma severity, comorbidities and environmental exposures (including socioeconomic status). The study received ethical approval, written parental consent and verbal assent from participants was obtained.

Questionnaires

The respiratory questionnaire provided details of asthma treatment (categorised by British Thoracic Society/Scottish Intercollegiate Guidelines Network treatment step)¹⁹ and included questions from Biobank (<http://www.ukbiobank.ac.uk/>) which captured environmental exposures. Parents of all children were given the

Paediatric Asthma Quality of Life Questionnaire²⁰ to complete. Parents were asked to complete the questionnaires on their child's behalf if aged under five years and in collaboration with older children, that is, the parent asked the child the question and the child answered from the list of responses for that question. The range of scores for this questionnaire is 0 to 7 and the minimally clinically useful difference in score is 0.5 or approximately 9% assuming a median score of 5.5.²¹ The QoL tool was designed for children ≥ 7 years old, and we therefore compared the QoL scores between children ≥ 7 years old and those <7 years to determine whether QoL scores were different in the young age group; if there was a difference then it would not be valid to combine data for older and younger children. The following variables were compared in older and younger children in the lowest and highest quartiles of QoL: asthma severity, CACT, history of exacerbation in previous six months.

Physiological Measurements

Height and weight were measured using standard apparatus in each centre by qualified and trained paediatric nurses using standard methodology. The apparatus were regularly calibrated. Body mass index was calculated and expressed as a centile adjusted for sex and age²²; overweight was defined as BMI > 85th centile and ≤ 95 th centile and obesity as BMI > 95th centile. Spirometry was determined using a portable device (ML3500, MicroLab) in accordance with standard guidelines²³ and bronchodilator response was determined to 200 micrograms salbutamol delivered from metered dose inhaler via large volume spacer device. Exhaled nitric oxide (ENO) was measured using a NIOX MINO[®] analyser following the internationally agreed methodology.²⁴ The skin prick reactivity was determined using the standard methodology²⁵ to the following common environmental allergens: egg, grass, house dust mite, cat dander, dog dander, peanut, *Aspergillus fumigatus* and *Alternaria Alternans*. Saliva was collected using a Salivette[®] (Sarstedt Ltd, Leicester, UK) and cotinine analysed by ELISA at ABS Laboratories (Welwyn Garden City, UK).

Statistical Analysis

The results were expressed as the number of observations and percentages for categorical variables and as mean ($\pm$ SD) values for continuous variables and median (interquartile range) for variables without normal distributions. The main variable (QoL) was not normally distributed and was natural log transformed prior to multivariate analysis. Spearman correlation, Mann–Whitney and Kruskal–Wallis tests were used to study univariate associations between QoL and continuous variables dichotomous variable and categorical variables

respectively. Variables which we considered were plausibly associated with QoL were comorbidities (obesity, rhinitis, and eczema) and environmental exposures (exposures to second hand smoke (SHS), mould, cat and dog). Confounders were gender, age, socioeconomic status and severity (BTS/SIGN treatment step, there were only 5 cases receiving step 5 treatment and composite of treatment groups 4 and 5 was created). Environmental exposures, comorbidities or covariates which were associated with QoL where $P < 0.1$ in the univariate models were included in a multivariate model where natural log transformed QoL was the outcome. Significance was assumed at $P < 0.05$ in the multivariate model. Associations with QoL were reported as a percentage by anti logging the regression coefficient. The results were analyzed by SPSS version 22.0 and R package version 3.0.3.

RESULTS

Characteristics of Study Population

There were 977 children recruited in whom QoL results were available in 553 children (Fig. 1), mean age 10.3 years (± 3.5), 58% male. The median overall QoL score (IQR) was 5.9 (4.6, 6.8) and for activity, symptom and emotion domains were 3.4 (2.8, 4.6), 5.9 (4.6, 6.7) and 6.4 (5.1, 7.0), respectively. Where salivary cotinine data were available, the median (IQR) concentration for the 105 children with no resident smokers was 0.05 ng/ml (0.05; 0.75), for 32 children living with one resident smoker was 0.44 ng/ml (0.2; 1.52) and for 21 children living with two resident smokers was 1.98 (0.69; 6.63), Kruskal Wallance test $P < 0.001$. Table 1 compares details of the children where QoL was determined with the whole study population. Children where QoL data were available were from more affluent communities and more likely to be recruited from primary care and exposed to cats and dogs. The overall QoL score was similar for children aged less than seven years and older and also for symptom and emotion domains but not for activity domain (see online

supplement Table E-1). The median asthma control test score was highest (21) for children in BTS/SIGN treatment step 1 and lowest for those on step 4 or 5 (13), Kruskal–Wallis test $P \leq 0.001$ (see online supplement table E-2). Poor QoL scores were associated with poor asthma control, increased recent exacerbations and increased ENO, see on line supplement Table E3.

Univariate and Multivariate Analyses

In univariate analyses, overall QoL was significantly ($P < 0.05$) and positively associated with affluence and inversely with asthma severity (as evidence by BTS/SIGN treatment step) and also reduced in association with obesity and rhinitis and exposure to smoking, Table 2. Associations between reduced QoL and exposures to visible mould and dog were of borderline significance (i.e., P between 0.05 and 0.10), Table 2. QoL was not related to sex, exposure to cats or the presence of eczema.

QoL was positively related to asthma control (Rho = 0.63, $P < 0.001$, $n = 298$). In the multivariate model where weight category was included ($n = 261$) overall QoL was only significantly associated with BTS/SIGN treatment step. When weight category was not included in the model ($n = 497$) BTS/SIGN step, socioeconomic status, number of smokers at home and current rhinitis were associated with QoL, Table 3. QoL within the symptom and emotion domains was also related to number of smokers, rhinitis, socioeconomic status and asthma severity (see online supplement Tables 4 and 5). QoL within the activity domain was only related to socioeconomic status and severity (see online supplement Tables 4 and 5). Since the QoL questionnaire was developed for children aged ≥ 7 years, all multivariate analyses were repeated including only children aged ≥ 7 years and the results were essentially unchanged.

DISCUSSION

The quality of life of children with asthma is important to the children themselves and also their parents and healthcare professionals but little is understood about what determines QoL. This paucity of evidence was the rationale for undertaking the present analysis. The main finding was that clinically significant reductions in QoL were associated with avoidable exposures (i.e., ≥ 1 smoker at home) or treatable co-morbidities (i.e., current rhinitis), as well as asthma severity and socioeconomic status. Whilst there is little a clinician can do to address disease severity and socioeconomic status, they can encourage parents who smoker to quit (or create a smoke free home) and also enquire about and treat rhinitis symptoms in their patients.

The aim of our study was to describe associations between potentially modifiable factors and QoL and not to study the relationship between QoL and asthma control,

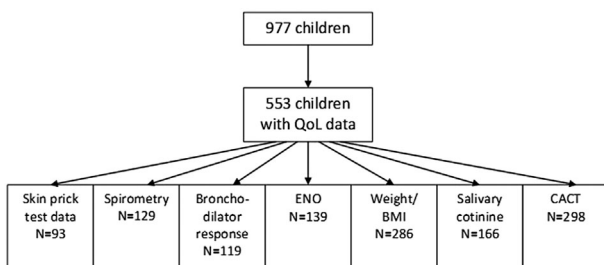


Fig. 1. A Consort style diagram showing the number of individuals where data were available. QoL, quality of life; ENO, exhaled nitric oxide; BMI, body mass index; CACT, children's asthma control test.

TABLE 1—Comparison of Details of All Children in the PAGES Study and the Subset Where Quality of Life (QoL) Details Were Determined

	Whole PAGES study population	Details of those where QoL were obtained
% Male sex (n)	59% (519/886)	58% (312/541)
Mean age (SD), years	9.5 (3.8)	10.3 (3.5)
Median SIMD (IQR), 5=most affluent	3 (1, 5)	4 (1, 5)*
% Recruited from secondary care	74% (693/937)	58% (322/553)*
% Exposed to smoking		
Not exposed	69% (598/871)	72% (386/537)
One smoker	23% (199/871)	20% (105/537)
More than one smoker	9% (74/871)	9% (46/537)
% Exposed to visible damp	13% (112/895)	11% (61/551)
% Exposed to cats	30% (266/895)	34% (186/551)*
% Exposed to dogs	43% (387/895)	47% (256/551)*
% Obese	21% (103/483)	19% (53/277)
% with any exacerbation during the last 6 months	49% (423/863)	43% (237/547)
% with current rhinitis	37% (330/895)	38% (211/551)
% with current eczema	39% (348/895)	39% (215/551)
% with positive skin prick test	82% (100/122)	85% (79/93)
Median CACT score (IQR)	18 (13, 21)	18 (14, 22)
BTS step		
1	10% (89/889)	9% (47/548)*
2	35% (308/889)	40 (219/548)
3	46% (412/889)	44% (239/548)
4 and 5	9% (80/889)	8% (43/548)
Mean % Predicted FEV ₁ (SD)	94 (16) n = 176	94 (17) n = 129
Median bronchodilator response (IQR), % change in FEV ₁	4.3 (1.8, 8.5)	2.1 (1.6, 2.7)
Median Exhaled Nitric Oxide (IQR), parts per billion	21 (12, 50)	22 (13, 53)

SIMD, scottish index of multiple deprivations. * $P < 0.05$ for comparison with whole population.

which is apparent in our population and others,^{7,9,10} and by not including asthma control in our final model we achieved our aim. The relationship between QoL and asthma control is complex with asthma control either being on the causal pathway between factors such as second hand smoke exposure and rhinitis and QoL, or being consequential to these factors but highly correlated with QoL. We demonstrate that reduced asthma control is associated with almost all of the factors associated with reduced QoL (Table 2) and for this reason did not include asthma control in the main model (Table 3). When asthma control was added to the multivariate model, the magnitude of the relationship the relationships between QoL and rhinitis and number of smokers was diminished and non-significant, and this might be explained by co linearity between QoL and asthma control as well as the smaller sample size.

The only study with a design similar to ours was undertaken in a Greek population and concluded that the main determinant of QoL was lack of asthma control.⁷ In univariate analyses, that is, not considering lack of control, QoL was associated paternal smoking, pet ownership, living in an “asthma unfriendly” house and having a “friendly environment” at school⁷ but these associations were subsumed when loss of control was considered. Some of the univariate associations in the

earlier study⁷ are consistent with univariate observations made here, for example, QoL may be related to parental smoking. In addition to different approaches to considering asthma control, differences in severity between the populations studied in Scotland and Greece and the differences in QoL tool used may explain the apparent different findings between populations.

There are studies confirming that QoL is lower in adults and children with severe and moderate asthma,^{26,27} and we also observed a relationship between poor QoL and increasing asthma severity. There is evidence that QoL is impaired by additional determinants of QoL in asthma include psychological factors, dyspnea during exercise or other allergic conditions.^{28,29}

The health related QoL used in our study was applied in a different setting to that initially intended by Juniper and colleagues, that is, we applied to some children aged under seven years and the questionnaire was completed at home by children and their parents and was not researcher-administered. Parental assessment of their child's QoL may be different than the child's (particularly in mothers compared to fathers⁷) with some tools of health related QoL assessment, but the agreement between children and parents evaluation is moderate.³⁰ Despite these methodological issues, the mean score of overall QoL, and also the three domains,

TABLE 2—Results of Univariate Analyses Comparing Overall Quality of Life With Variables Which Were Plausibly Associated With or Confounders for Quality of Life and Asthma Control

	PAQLQ		Asthma control	
	Median PAQLQ score for category or Rho value	<i>P</i> value	Median score for category or Rho value	<i>P</i> value
Environmental exposure				
Number of smokers	None 6.1 (n=386) One 5.5 (n = 105) >One 5.1 (n = 46)	<0.001	None 18 (n = 291) One 16 (n = 107) > One 17 (n = 37)	0.012
Visible damp	Yes 5.6 (n = 61) No 6.0 (n = 490)	0.099	Yes 18 (n = 58) No 18 (n = 388)	0.883
Exposure to dog	Yes 5.8 (n = 256) No 6.0 (n = 295)	0.053	Yes 17 (n = 214) No 18 (n = 232)	0.051
Exposure to cat	Yes 6.0 (n = 186) No 5.9 (n = 365)	0.955	Yes 18 (n = 135) No 18 (n = 311)	0.226
Co morbidity				
Weight category	Healthy 5.8 (n = 188) Overweight 5.1 (n = 36) Obese 4.8 (n = 53)	0.024	Healthy 18 (n = 161) Overweight 18 (n = 41) Obese 15 (n = 58)	0.094
Current rhinitis	Yes 5.7 (n = 211) No 6.1 (n = 340)	<0.001	Yes 16 (n = 187) No 19 (n = 259)	0.001
Current eczema	Yes 5.8 (n = 215) No 6.0 (n = 336)	0.129	Yes 17 (n = 187) No 18 (n = 259)	0.022
Confounders				
Socioeconomic status	Rho 0.146 (n = 553)	0.001	Rho 0.103 (n = 423)	0.035
BTS treatment step	1 6.2 (n = 47) 2 6.4 (n = 219) 3 5.5 (n = 239) 4 and 5 3.6 (n = 43)	<0.001	1 21(n = 31) 2 19(n = 134) 3 17(n = 232) 4 and 5 13(n = 45)	0.001
Sex	Male 6.0 (n = 312) Female 5.8 (n = 229)	0.171	Male 18 (n = 240) Female 16(n = 173)	0.019
Age	Rho -0.068 (n = 553)	0.109	Rho -0.231 (n = 446)	<0.001

was consistent with previously published values.^{31,32} Furthermore, increased symptoms, severity, recent exacerbation and ENO were all correlated with lower QoL scores in the older and the younger age group (with the exception of ENO which was not measured in the latter). This association and consistency with external populations assures us that the outcome reported in our study is robust.

Asthma severity and its control are known to be determinants of QoL in children⁷ and our study confirmed this, but also demonstrated novel associations between QoL and number of smokers in the house and rhinitis. Whilst asthma severity is probably determined in early life, along with lung function, and may not be easily modified, reducing exposure to SHS at home and treatment of rhinitis symptoms are considerably easier. Given the overlap between QoL and CACT, avoiding SHS and managing rhinitis might be expected to improve asthma control as well as QoL. SHS is well known to exacerbate asthma symptoms and lead to poorer control^{14,19,33} but this is the first study to observe an association between SHS exposure and poor QoL in children with asthma. Many parents who smoke find it hard to quit, but parents are prepared to change their

smoking habits and create smoke free homes³⁴ and this could be discussed in routine asthma consultations.

Rhinitis is a common comorbidity for children with asthma^{19,35} and although not perceived to be as “serious” as asthma, our results indicate that the child’s QoL is adversely affected by rhinitis symptoms. The management of rhinitis is well described^{36,37} and consideration should be given to rhinitis symptoms in asthma consultations. In our study eczema, a condition with underlying allergic mechanisms like rhinitis, was not linked to QoL in univariate analyses although there are studies showing that eczema reduces QoL in children without asthma.^{11–13} This is the first study to have related eczema to QoL within an asthma population and it is possible that results from eczema populations are not transferrable to children with asthma who also have eczema.

Our study has a number of strengths and weaknesses. A strength is that this was the first study to focus on how modifiable exposures and treatable comorbidities are associated with QoL in children with asthma. A second strength is that we have recruited a heterogeneous population from across Scotland in primary and secondary care so our results are likely to be generalisable.

TABLE 3—Factors Associated With Overall Quality of Life in Multivariate Analysis

	% reduction in QoL [95% CI] not including asthma control*	P value	% reduction in PAQLQ [95% CI]†	P value
Number of resident smokers				
0	0 n = 376		0 n = 188	
1	6 [−1, 14] n = 100	0.095	5 [−3, 13] n = 56	0.226
2	11 [2, 19] n = 46	0.019	2 [−9, 13] n = 26	0.714
Current rhinitis				
No	0 n = 321		0 n = 160	
Yes	9 [4, 14] n = 201	0.001	7 [0, 13] n = 110	0.080
BTS treatment step				
1	0 n = 47		0 n = 21	
2	−6 [−18, 4] n = 210	0.237	−13 [−28, 1] n = 99	0.059
3	7 [−4, 16] n = 222	0.212	−3 [−17, 9] n = 125	0.603
4 and 5	30 [20, 39] n = 43	<0.001	6 [−10, 20] n = 25	0.425
Socioeconomic status				
Per quartile change relative to most affluent quartile	3 [1, 5]	0.011	2 [0, 5]	0.045
Log transformed asthma control scoreRelative to log transformed QoL score	—	—	0.40 [0.30, 0.50]	<0.001

The effect size is presented as a percentage relative to the reference. PAQLQ, paediatric asthma quality of life questionnaire. Age and sex were included in the models.

*n = 497; Adjusted R-square 0.203; †n = 270; Adjusted R-square 0.348.

Methodological strengths include our validation of second hand smoke exposure by salivary cotinine in a subset of participants and the fact that QoL is reproducible over at least one month, suggesting that our results are representative of a meaningful period of time.³⁸ One weakness of the study is that physiological measurements were not obtained in all children and with more data we might have been able to relate the QoL scores to spirometry, bronchodilator response and skin prick test in addition to ENO which we were able to relate to QoL. A further weakness is that details of compliance and attitude to health and disease were not captured in this study but may be important factors affecting QoL.³⁹ Finally, exposure to pets was defined only as current exposure, but previous exposures in early childhood were not assessed which can have impact on asthma severity as well as QoL in later life.⁴⁰

In summary, the QoL in children with asthma is an important health outcome which is determined by a number of factors of which some are amenable to intervention. Although the associations described herein do not prove causation, it is plausible that preventing exposure to SHS and treating rhinitis symptoms can contribute to the improvement of QoL children with asthma.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article at the publisher's web-site.

Factors associated with quality of life in children with asthma living in Scotland

V. Taminskiene^{1, 2}, S.Mukhopadhyay³, C.Palmer⁴, A Mehta⁵, J Ayres⁶, A. Valiulis^{2,7}, S Turner¹

¹Child Health, University of Aberdeen

²Institute of Public Health, Faculty of Medicine, Vilnius University

³Department of Paediatrics, University of Brighton

⁴Department of Pharmacogenetics, University of Dundee

⁵ Division of Cardiovascular and Diabetes Medicine, University of Dundee

⁶Department of Occupational Health, University of Birmingham

⁷ Clinic of Children's Diseases, Faculty of Medicine, Vilnius University

Online supplement

E-Table 1. Comparison of overall Quality of Life (QoL) scores and within the three QoL domains between children aged <seven years and older.

	Younger children	Older children
Median overall score (range)	5.9 (1.4, 7.0)	5.9 (1.5, 7.0)
Median activity score (range)	2.9 (0, 7.0)	3.4 (0.6, 7.0)*
Median symptoms score (range)	5.9 (1.6, 7.0)	5.9 (1.3, 7.0)
Median emotions score (range)	6.1 (1.4, 7.0)	6.4 (1.1, 7.0)

*Mann Whitney U test $p=0.038$ for difference with younger children.

E-table 2. Comparison of Children's Asthma Control Test (CACT) scores across groups stratified by British Thoracic Society/Scottish Intercollegiate Guidelines Network (BTS/SIGN) guidelines. Kruskal Wallis test $p < 0.001$ for differences across the groups

BTS/SIGN treatment step	Median CACT score (range)
1	21 (8-25) n=31
2	19 (5-27) n=134
3	17 (3-27) n=232
4 and 5 combined	13 (4-27) n=45

E-Table 3. Comparison of indices of asthma severity and asthma control for groups stratified by quartile of Overall Quality of Life score and by age <7 years or ≥7 years.

	Children aged <7 years		p	Children aged ≥7 years		p
	Lowest QoL quartile	Highest QoL quartile		Lowest QoL quartile	Highest QoL quartile	
Median CACT score (IQR)	17.0 (14.0, 20.0) N=9	24.0 (23.0, 25.0) N=9	<0.001	14.0 (11.0, 16.0) N=68	24.0 (20.0, 25.0) N=62	<0.001
Proportion with recent exacerbation	21 (20.4%) N=27	11 (10.7%) N=27	0.021	70 (15.8%) N=110	28 (6.3%) N=112	<0.001
Median BTS treatment step (IQR)	3 (2, 3) N=27	2 (2, 3) N=28	0.0218	3 (3, 3) N=110	3 (2, 3) N=112	<0.001
Mean % Predicted FEV ₁ (SD)				93 (15) n=44	94 (14) n=24	p>0.05
Mean % Predicted FEV ₁ /FVC (SD)				91 (10) n=42	91 (11) n=24	p>0.05
Mean % Predicted FEF ₂₅₋₇₅ (SD)				76 (27) n=42	79 (27) n=24	p>0.05
Median bronchodilator response (IQR)				3.9 (1.2, 8.1) n=38	3.7 (2.0, 6.8) n=22	p>0.05
Median Exhaled Nitric Oxide (IQR), parts per billion				16 (11, 32) n=21	26 (13, 74) n=47	<0.001

E-Table 4. Results of univariate analyses comparing domains of quality of life (QoL) with variables which were plausibly associated with or confounders for QoL.

		Median QoL activity score for category or Rho value	p value	Median QoL symptoms score for category or Rho value	p value	Median QoL emotions score for category or Rho value	p value
Environment al exposure	Number of smokers	None 3.4 (n=385)	0.288	None 6.1 (n=385)	<0.001	None 6.5 (n=385)	<0.001
		One 3.5 (n=104)		One 5.6 (n=104)		One 6.1 (n=104)	
		>One 3.0 (n=46)		>One 5.2 (n=46)		>One 5.7 (n=46)	
	Visible damp	Yes 3.0 (n=60)	0.097	Yes 5.6 (n=61)	0.114	Yes 6.1(n=61)	0.165
		No 3.4 (n=489)		No 5.9(n=489)		No 6.4 (n=489)	
	Exposure to dog	Yes 3.4 (n=255)	0.535	Yes 5.9 (n=256)	0.110	Yes 6.3 (n=256)	0.097
		No 3.4 (n=294)		No 6.0(n=294)		No 6.5 (n=256)	
	Exposure to cat	Yes 3.4 (n=186)	0.482	Yes 5.9 (n=186)	0.664	Yes 6.4 (n=186)	0.618
		No 3.4 (n=363)		No 5.9 (n=364)		No 6.4 (n=364)	
	Co morbidity	Weight category	Healthy 3.2 (n=188)	0.205	Healthy 5.8 (n=187)	0.012	Healthy 6.1 (n=187)
Overweight 3.6 (n=36)			Overweight 5.2 (n=36)		Overweight 5.8 (n=36)		
Obese 3.0 (n=53)			Obese 5.0 (n=53)		Obese 5.3 (n=53)		
Current rhinitis		Yes 3.4 (n=209)	0.521	Yes 5.7 (n=210)	<0.001	Yes 6.1 (n=210)	<0.001
		No 3.4 (n=340)		No 6.0 (n=340)		No 6.5 (n=340)	
Current eczema		Yes 3.4 (n=214)	0.888	Yes 5.8 (n=215)	0.080	Yes 6.3 (n=215)	0.379
		No 3.4 (n=335)		No 6.0 (n=335)		No 6.5 (n=335)	
Confounders		Socioeconomi c status	Rho 0.119 (n=532)	0.006	Rho 0.140 (n=524)	0.001	Rho 0.124(n=524)
	BTS treatment step	1 3.8 (n=47)	0.036	1 6.2 (n=47)	<0.001	1 6.6 (n=47)	<0.001
		2 3.4 (n=218)		2 6.3(n=219)		2 6.8 (n=219)	
		3 3.4(n=238)		3 5.7 (n=238)		3 6.0 (n=238)	
		4 and 5 2.8		4 and 5 3.4		4 and 5 4.5	

		(n=43)		(n=43)		(n=43)	
	Sex	Male 3.6 (n=311)	0.218	Male 6.0 (n=311)	0.143	Male 6.4 (n=311)	0.246
		Female 3.6 (n=229)		Female 5.8 (n=229)		Female 6.3 (n=229)	
	Age	Rho 0.081 (n=551)	0.059	Rho -0.079 (n=552)	0.062	Rho -0.007 (n=552)	0.877

E-Table 5. Factors associated with quality of life (QoL) score within the three domains of overall QoL in multivariate models.

		% reduction in activity domain of QoL [95% CI]	% reduction in symptoms domain of QoL [95% CI]	% reduction in emotions domain of QoL [95% CI]
Number of resident smokers	1 (ref to none)		5 [-3;13]	7 [-1;15]
	2 (ref to none)		12 [1;23]	13 [-2;25]
Current rhinitis	(ref to none)		10 [4;16]	9 [3;15]
BTS treatment step	2 (ref to 1)	3 [-10;17]	7 [-3;19]	6 [-5; 18]
	3 (ref to 1)	6 [-7;21]	5 [-6;16]	7 [-4; 19]
	4 and 5 (ref to 1)	29 [9;52]	44 [25;65]	38 [20;58]
Socioeconomic status	Per quartile change relative to most affluent quartile	3 [1;6]	4 [1;6]	2 [0.2;5]
		n=522	n=506	n=506