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Perceived triggers of asthma impair quality of life in children with asthma

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Abstract

Background: Data on the impact of the number and nature of perceived asthma triggers on health-related quality of life (HRQL) in children are scarce.

Objective: To investigate the impact of perceived asthma triggers on both asthma-specific and generic HRQL in children.

Methods: A cross-sectional study was conducted among children (7-18 years) with asthma in secondary and tertiary care. Children were screened with electronic questionnaires regarding respiratory and allergic symptoms. Asthma-specific HRQL was assessed using the Pediatric Asthma Quality of Life Questionnaire (PAQLQ) (score range 1-7) and generic HRQL using the RAND questionnaire (score range 7-32). The Kruskal-Wallis test and one-way ANOVA were used to test the difference of, respectively, the PAQLQ and RAND scores across the number of perceived asthma triggers (0, 1-2, 3-4, or ≥ 5). Univariable and multivariable linear regression analyses were performed to evaluate the association between individual triggers and HRQL.

Results: A total of 527 children with a mean (SD) age of 12.1 (2.9) years were included. Children with a higher number of perceived triggers had significantly lower PAQLQ and RAND scores (ie poorer HRQL). The difference in PAQLQ scores was clinically relevant between children with 0 versus 3-4 or ≥ 5 triggers and 1-2 versus ≥ 5 triggers (mean difference 0.66, 1.02 and 0.63, respectively). Especially, non-allergic triggers (physical exercise, the weather, (cigarette) smoke and emotions) were significantly associated with reduced PAQLQ scores. Emotions and food/drinks were associated with reduced RAND scores.

Conclusion and Clinical Relevance: A higher number of perceived triggers of asthma were associated with reduced HRQL in children with asthma. Especially, non-allergic triggers were associated with reduced HRQL.

Abbreviations: ANOVA, Analysis of variance; CI, Confidence interval; HRQL, Health-related quality of life; ISAAC, International study of asthma and allergies in childhood; MCID, Minimal clinically important difference; PAQLQ, Pediatric Asthma Quality of Life Questionnaire; RAND, RAND general health-rating index; SE, Standard error.

KEYWORDS
asthma, paediatrics, quality of life

1 | INTRODUCTION

Asthma presents as one of the most common chronic inflammatory diseases in children in the developed world, affecting up to 9% of children.[1] Asthma causes significant morbidity and has a negative impact on health-related quality of life (HRQL).[2] HRQL can be measured with asthma-specific and generic questionnaires. Asthma-specific HRQL reflects the perceived impact of asthma on a patient's life, while generic HRQL allows direct comparison between different diseases. Asthma-specific HRQL is especially reduced in girls, in children with uncontrolled asthma and in those with frequent or severe asthma exacerbations.[3,4] Children with asthma report poorer generic HRQL than children in the general population and children with allergic rhinitis, food allergy, atopic dermatitis and diabetes mellitus, but better generic HRQL than children with juvenile chronic arthritis.[5,6]

Asthma symptoms and exacerbations can be elicited by a range of allergic triggers (ie pollen, house dust or pets) and non-allergic triggers (ie physical exercise, respiratory tract infections, emotions or exposure to tobacco smoke).[7] Only scarce data on the impact of perceived asthma triggers on HRQL in children are available. A higher number of perceived triggers of asthma can exert a toll on asthma-specific HRQL in children with severe or difficult-to-treat asthma.[8,9] Data in children with mild or moderate asthma are lacking. Furthermore, it has been shown that allergic disease-specific HRQL in children was associated with grass pollen exposure and airway inflammation[10] and generic HRQL in children was reduced during pollen season.[11] In adults, previous research has suggested that mainly non-allergic asthma triggers are associated with reduced asthma-specific HRQL.[12]

The aim of this study was to investigate the single and composite impact of perceived allergic and non-allergic triggers of asthma on asthma-specific and generic HRQL in children referred to secondary or tertiary care.

2 | METHODS

2.1 | Domain and data collection

A cross-sectional study was performed among children referred with respiratory or allergic complaints to 8 secondary care centres and 1 tertiary care centre in the Netherlands between June 2011 and August 2018. Eligible children were aged 7-18 years with parent-reported physician-diagnosed asthma. All children were invited for the electronic portal (EP) before an outpatient visit. The details of the EP have been previously published.[13] In short, the EP is a web-based system with electronic questionnaires for children and their parents developed to collect information on asthma, allergic rhinitis, food allergy, atopic dermatitis and recurrent respiratory tract infections. This study was approved by the Medical Ethical Review Board of the University Medical Center in Utrecht, the Netherlands, number 10/348, and all parents and/or children gave informed consent before enrolment.

2.2 | Measurements

2.2.1 | Asthma-specific and generic HRQL

Asthma-specific HRQL in children was assessed using the child-reported Pediatric Asthma Quality of Life Questionnaire (PAQLQ).[14] The PAQLQ is a validated instrument with 23 items in three domains: symptoms, activity limitation and emotional function. All PAQLQ items are scored on a 7-point Likert response scale (ie 1 = extremely bothered; 7 = not bothered) with a 1-week recall period. The final overall PAQLQ score is the mean score of all 23 items, and domain-scores are the means of the items in the individual domains. The mean difference (MD) in PAQLQ scores between patients can be interpreted using the minimal clinically important differences (MCIDs). The MCID is the smallest change score that is considered clinically relevant.[15] The MCID for the PAQLQ is 0.5 as estimated previously.[16]

Generic HRQL in children was assessed using the parent-reported RAND questionnaire.[17] The RAND is a validated general health-rating index for children with 7 questions that ask parents to assess the overall health status of their child with a 1-month recall period. The final RAND score is the summed score ranging from 7 to 32 with higher scores indicating better general health. The MCID of the RAND questionnaire is 5.3.[18]

2.2.2 | Perceived triggers of asthma

Children (≥12 years) or parents (children 7-12 years) were asked if, in the last 12 months, symptoms of wheezing in the chest were worsened after exposure to one or more of the following triggers: dust, pollen, pets, physical exercise, the weather, cold or the flu, (cigarette) smoke, emotions, food or drinks, detergent, or wool clothing. Dust, pollen and pets were categorized as allergic triggers; all other triggers were categorized as non-allergic triggers.

2.2.3 | Clinical data

Information on patients' demographic and environmental characteristics was obtained using the electronic questionnaires in the EP. Asthma control during the last month was assessed using the Asthma Control Test (ACT). The previously defined cut-off was used to classify children as having well-controlled asthma (ACT score ≥ 20) or uncontrolled asthma (<20).[19,20] Furthermore, the

ISAAC core questionnaires for wheezing, allergic rhinitis and atopic dermatitis were used.[21] Comorbidities—that is allergic rhinitis, food allergy, atopic dermatitis and recurrent respiratory tract infections—were defined based on a combination of questions in the EP (see Table S1 in the Supporting Information).

2.3 | Statistical analyses

Children with complete HRQL data, information on perceived asthma triggers and clinical data used as confounders in the multivariable analysis were included in the analysis. Differences between children with complete and incomplete data were statistically evaluated by the chi-square test for categorical variables, the unpaired t-test for normally distributed continuous variables and the Mann-Whitney U tests for non-normally distributed continuous variables with Bonferroni correction for multiple testing. Descriptive statistics were presented as number and percentages, means with standard deviations (SD) for normally distributed data and medians with interquartile ranges (IQR) for non-normally distributed data. The Kruskal-Wallis test was used to compare the non-normally distributed PAQLQ score and one-way analysis of variance (ANOVA) was used to compare the normally distributed RAND score across the total number of perceived asthma triggers (0, 1-2, 3-4 or ≥ 5), the number of allergic triggers (0, 1, 2 or 3) and the number of non-allergic triggers (0, 1-2, 3-4 or ≥ 5). Furthermore, the difference between the mean HRQL scores (mean difference, MD) of children in the different categories of triggers (e.g. 0 vs. 1-2 triggers) was calculated along with the 95% confidence interval (95% CI) to interpret the change score using the minimal clinically important difference (MCID). In addition, the standardized mean difference (SMD) was calculated using Cohen's statistics to estimate the effect size.[22] Based on Cohen's criteria, a SMD of 0.2 is considered small, 0.5 is moderate, and >0.8 is large.[22]

The association between the individual perceived asthma triggers and HRQL was estimated using univariable and multivariable linear regression analyses. The multivariable linear regression analyses were performed with all triggers and adjusted for age, sex, living environment, asthma control (well-controlled vs. uncontrolled according to the Asthma Control Test) and the presence of allergic rhinitis, food allergy, atopic dermatitis or recurrent respiratory tract infections. The unadjusted and adjusted unstandardized regression coefficients for the difference in the outcome between patients with and without the trigger were estimated along with the 95% CI and *P*-value. A *P*-value of <0.05 was considered statistically significant. All analyses were performed in SPSS Statistics for Windows (version 25.0. Armonk, NY: IMB Corp).

3 | RESULTS

3.1 | Patients' characteristics

A total of 1869 children aged 7-18 years were included in the electronic portal in one of the participating secondary (*n* = 8) or tertiary care (*n* = 1) centres: 1743 (93%) completed the screening questionnaires, and the parents of 764 children (44%) reported their child to have physician-diagnosed asthma. A total of 527 children (69%) had

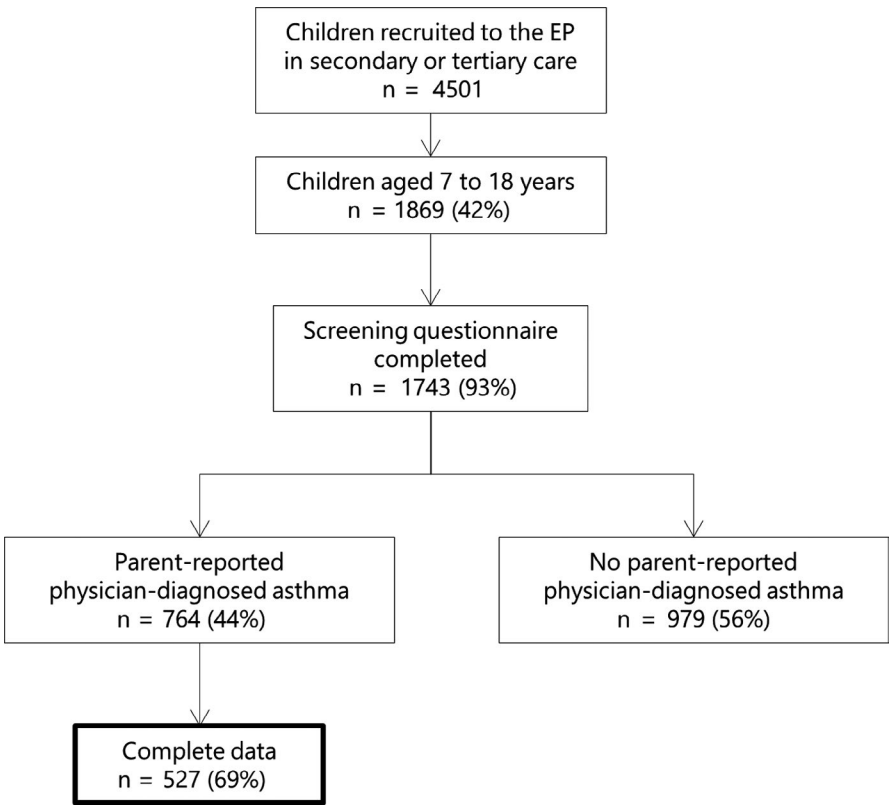

FIGURE 1 Study population flow chart. EP, electronic portal; n, number

TABLE 1 Clinical characteristics of children with asthma

		n
Age in years, mean (SD)	12.1 (2.9)	527
Male sex	304 (58)	527
Both parents Dutch	458 (88)	523
Maternal education level		
Elementary school or lower secondary education	68 (13)	524
Intermediate or higher secondary education	212 (41)	524
Higher education or university	244 (47)	524
Any asthma trigger	417 (79)	527
Both allergic and non-allergic asthma triggers	278 (53)	527
Only non-allergic asthma triggers	129 (24)	527
Only allergic asthma triggers	10 (2)	527
No asthma triggers	110 (21)	527
Family history of		
Asthma	239 (45)	526
Allergic rhinitis	353 (67)	525
Atopic dermatitis	268 (51)	525
Food allergy	53 (14)	379
Current living environment		
Rural	318 (60)	527
Urban	209 (40)	527
Pet ownership	234 (44)	527
Asthma characteristics		
Uncontrolled asthma (ACT < 20)	200 (38)	527
Nocturnal wheezing/coughing in the past year	271 (51)	527
Daily inhaled corticosteroids	264 (66)	403
Inhaled short-acting β2-agonists in the past week	271 (51)	527
Comorbidities		
Allergic rhinitis	296 (56)	527
Food allergy	153 (29)	527
Atopic dermatitis	215 (41)	527
Recurrent respiratory tract infections in the past year	250 (47)	527
Referred to		
Secondary care	367 (70)	527
Tertiary care	160 (30)	527
Referral reason		
Asthma	209 (50)	415
Food allergy	124 (30)	415
Allergic rhinitis	32 (8)	415
Atopic dermatitis	32 (8)	415
Recurrent respiratory tract infections	10 (2)	415
Other	19 (5)	415

Note: Data are n (%) unless otherwise stated.
Abbreviations: ACT, Asthma Control Test; n, number; SD, standard deviation.

complete data and were included in the analysis (Figure 1). Children included in the analysis were older compared to the children with incomplete data, but did not differ in the frequency of having any perceived trigger of asthma, the level of asthma control, asthma-specific health-related quality of life (HRQL) and generic HRQL (see Table S2 in the Supporting Information).

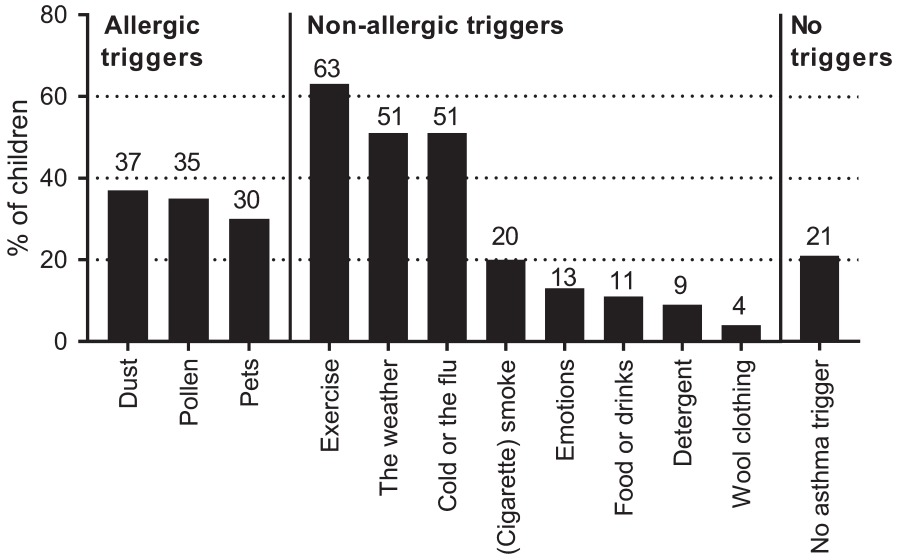

FIGURE 2 Proportion of asthma triggers in children with asthma, *n* = 527

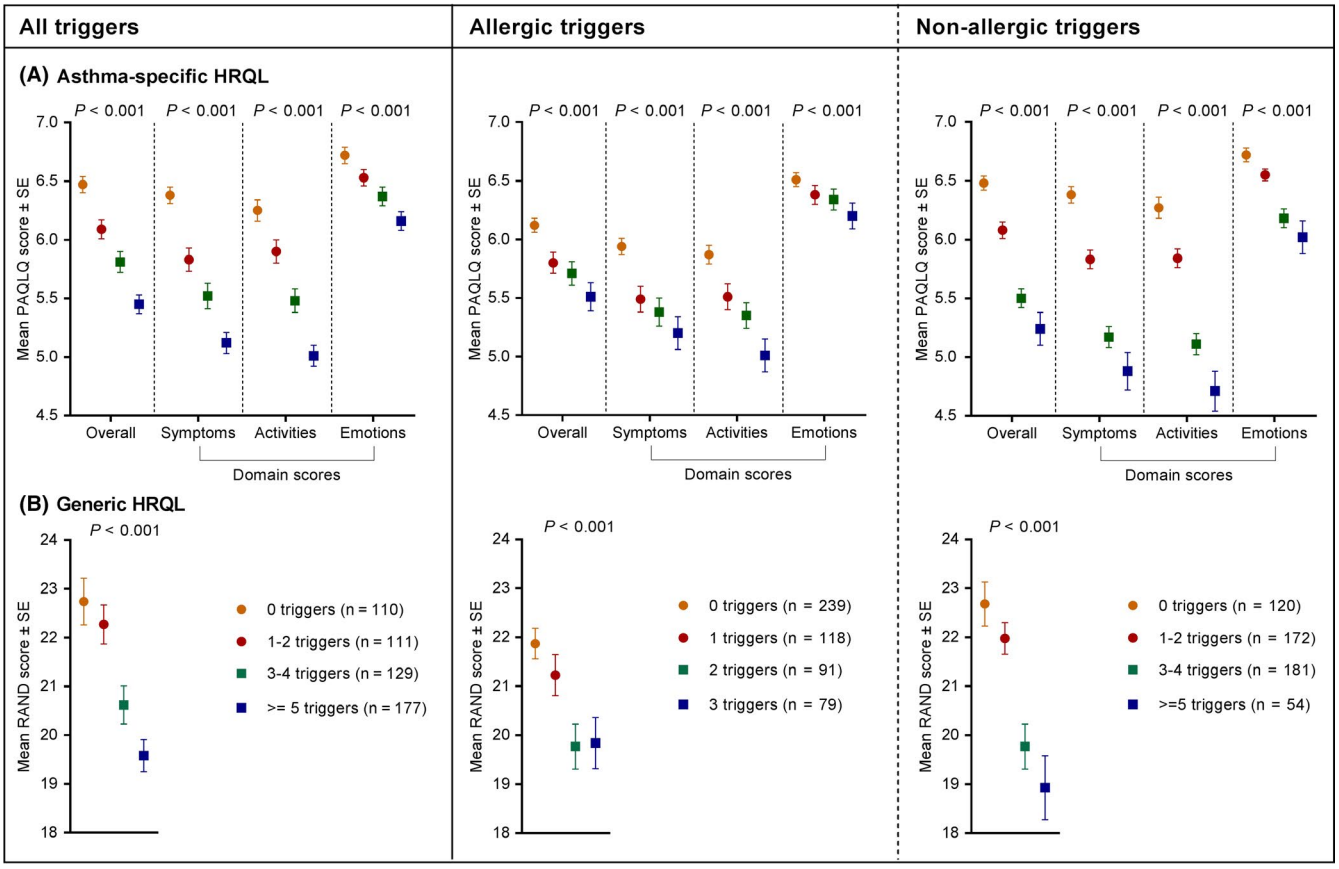

FIGURE 3 Association between the number of asthma triggers and asthma-specific (A) and generic (B) quality of life. All triggers included allergic triggers (dust, pollen and pets) and non-allergic triggers (physical exercise, the weather, cold or the flu, (cigarette) smoke, emotions, food or drinks, detergent, wool clothing). n, number; PAQLQ, Pediatric Asthma Quality of Life; RAND, RAND general health-rating index; SE, standard error

Patients' characteristics are presented in Table 1. Children had a mean (SD) age of 12.1 (2.9) years, 58% were male, 88% were Dutch, and 79% reported worsening of symptoms of wheezing in the chest after exposure to one or more asthma trigger in the past year. Half of the children reported both perceived allergic and non-allergic asthma triggers (53%). Figure 2 shows the proportion of individual triggers. The three most common perceived triggers of asthma were all non-allergic: physical exercise (*n* = 331; 63%), the weather (*n* = 269; 51%) and a cold or the flu (*n* = 268; 51%).

TABLE 2 The number of asthma triggers and asthma-specific (PAQLQ) and generic (RAND) quality of life scores

	n	PAQLQ score				RAND score
		Overall	Domain symptoms	Domain activities	Domain emotions	
All triggers[a]						
0 triggers	110	6.47 ± 0.07	6.38 ± 0.07	6.25 ± 0.09	6.72 ± 0.07	22.74 ± 0.48
1-2 triggers	111	6.09 ± 0.08	5.83 ± 0.10	5.90 ± 0.10	6.53 ± 0.07	22.27 ± 0.40
3-4 triggers	129	5.81 ± 0.08	5.52 ± 0.11	5.48 ± 0.10	6.37 ± 0.08	20.62 ± 0.39
≥5 triggers	177	5.45 ± 0.08	5.12 ± 0.09	5.01 ± 0.09	6.16 ± 0.08	19.58 ± 0.33
P-value[b]		<0.001	<0.001	<0.001	<0.001	<0.001
Allergic triggers						
0 triggers	239	6.12 ± 0.06	5.94 ± 0.07	5.87 ± 0.08	6.51 ± 0.06	21.87 ± 0.31
1 triggers	118	5.80 ± 0.09	5.49 ± 0.11	5.51 ± 0.11	6.38 ± 0.08	21.23 ± 0.42
2 triggers	91	5.71 ± 0.10	5.38 ± 0.12	5.35 ± 0.11	6.34 ± 0.09	19.77 ± 0.46
3 triggers	79	5.51 ± 0.12	5.20 ± 0.14	5.01 ± 0.14	6.20 ± 0.11	19.84 ± 0.52
P-value[b]		<0.001	<0.001	<0.001	<0.001	<0.001
Non-allergic triggers						
0 triggers	120	6.48 ± 0.06	6.38 ± 0.07	6.27 ± 0.09	6.72 ± 0.06	22.68 ± 0.45
1-2 triggers	172	6.08 ± 0.07	5.83 ± 0.08	5.84 ± 0.08	6.55 ± 0.05	21.98 ± 0.32
3-4 triggers	181	5.50 ± 0.08	5.17 ± 0.09	5.11 ± 0.09	6.18 ± 0.08	19.77 ± 0.46
≥5 triggers	54	5.24 ± 0.14	4.88 ± 0.16	4.71 ± 0.17	6.12 ± 0.14	18.93 ± 0.65
P-value[b]		<0.001	<0.001	<0.001	<0.001	<0.001

Note: Data are mean ± SE, unless otherwise stated.
Abbreviations: n, number; PAQLQ, Pediatric Asthma Quality of Life Questionnaire; RAND, RAND general health-rating index; SE, standard error.
[a]All triggers included allergic triggers (dust, pollen and pets) and non-allergic asthma triggers (physical exercise, the weather, cold or the flu, (cigarette) smoke, emotions, food or drinks, detergent, wool clothing).
[b]Statistical comparisons between trigger categories using Kruskal-Wallis test for the PAQLQ scores and one-way ANOVA for the RAND score with *P* values of <0.004 taken to be significant according to Bonferroni correction for multiple testing.

3.2 | The association between the number of asthma triggers and HRQL

3.2.1 | Asthma-specific HRQL

A higher number of perceived triggers of asthma were associated with reduced asthma-specific HRQL (Figure 3a). Children with a higher number of triggers had significantly lower PAQLQ scores (Table 2). The same association was observed for the domain-specific PAQLQ scores and after stratification by allergic and non-allergic triggers.

The difference of the overall PAQLQ score was considered clinically relevant between children with 0 and 3-4 triggers and 0 and ≥ 5 triggers (mean difference [MD] 0.66 and 1.02, respectively) with respectively moderate and large effect size (standardized mean difference [SMD] 0.74 and 1.10). Furthermore, the difference was clinically relevant between children with 1-2 and ≥ 5 triggers (MD 0.63) with moderate effect size (SMD 0.65) (see Table S3 in the Supporting Information). In addition, clinically relevant differences of the domain-specific PAQLQ scores were observed (see Table S3 in the Supporting Information).

Children with only non-allergic asthma triggers had a significantly lower median (IQR) PAQLQ score (ie worse HRQL) (6.1 (5.2-6.7); *n* = 129) compared to children with only allergic asthma triggers (6.7 (6.1-6.9); *n* = 10) (*P* = 0.029).

3.2.2 | Generic health-related HRQL

A higher number of perceived triggers of asthma were associated with reduced generic HRQL as assessed with the RAND questionnaire (Figure 3b). Children with a higher number of triggers had significantly lower RAND scores (Table 2). The same association was observed if the analysis was stratified by allergic and non-allergic triggers. The difference in RAND scores was not considered clinically relevant as the minimal clinically important difference was not exceeded. The effect size was moderate between children with 0 and ≥ 5 triggers (SMD 0.68) and between children with 1-2 and ≥ 5 triggers (SMD 0.62) (see Table S3 in the Supporting Information).

The RAND score was comparable between children with only non-allergic asthma triggers (mean (SD) 21.1 (4.4)) and children with only allergic asthma triggers (22.1 (3); *n* = 10) (*P* = 0.494).

3.3 | Single and composite effects of asthma triggers

3.3.1 | Asthma-specific HRQL

In univariable linear regression analysis, all allergic asthma triggers were associated with a lower overall PAQLQ score (ie poorer asthma-specific

TABLE 3 Linear regression analysis for asthma-specific (a) and generic (b) quality of life

	Univariable analysis			Multivariable analysis		
	β	95% CI	*P*-value	aβ[a]	95% CI	*P*-value
a. Overall PAQLQ score						
Allergic triggers						
Dust	−0.51	−0.68 to −0.34	<0.001	−0.09	−0.25 to 0.08	0.293
Pollen	−0.27	−0.45 to −0.08	0.004	0.15	−0.03 to 0.33	0.095
Pets	−0.35	−0.53 to −0.16	<0.001	−0.03	−0.19 to 0.14	0.760
Non-allergic triggers						
Physical exercise	−0.70	−0.87 to −0.53	<0.001	**−0.16**	−0.32 to 0.00	0.047
The weather	−0.66	−0.83 to −0.50	<0.001	**−0.17**	−0.33 to −0.01	0.038
Cold or the flu	−0.55	−0.71 to −0.38	<0.001	0.00	−0.16 to 0.15	0.954
(Cigarette) smoke	−0.75	−0.96 to −0.55	<0.001	**−0.27**	−0.47 to −0.08	0.006
Emotions	−0.75	−1.00 to −0.50	<0.001	**−0.28**	−0.49 to −0.08	0.007
Food or drinks	−0.29	−0.57 to −0.02	0.037	−0.14	−0.36 to 0.08	0.201
Detergent	−0.68	−0.97 to −0.38	<0.001	0.05	−0.20 to 0.31	0.670
Wool clothing	−0.31	−0.73 to 0.11	0.153	0.22	−0.10 to 0.55	0.181
b. RAND score						
Allergic triggers						
Dust	−2.07	−2.89 to −1.26	<0.001	−0.65	−1.55 to 0.26	0.162
Pollen	−1.24	−2.08 to −0.40	0.004	0.27	−0.71 to 1.25	0.594
Pets	−0.92	−1.79 to −0.05	0.039	0.20	−0.74 to 1.14	0.676
Non-allergic triggers						
Physical exercise	−1.46	−2.28 to −0.63	0.001	0.46	−0.41 to 1.34	0.299
The weather	−1.88	−2.67 to −1.09	<0.001	−0.17	−1.06 to 0.73	0.717
Cold or the flu	−2.21	−2.99 to −1.42	<0.001	−0.55	−1.41 to 0.31	0.212
(Cigarette) smoke	−1.79	−2.78 to −0.79	<0.001	0.00	−1.08 to 1.08	0.998
Emotions	−2.75	−3.94 to −1.56	<0.001	**−1.49**	−2.64 to −0.35	0.011
Food or drinks	−2.24	−3.51 to −0.96	0.001	**−1.86**	−3.09 to −0.63	0.003
Detergent	−2.10	−3.49 to −0.72	0.003	−0.06	−1.47 to 1.35	0.930
Wool clothing	−1.02	−2.99 to 0.96	0.312	0.85	−0.98 to 2.67	0.362

Note: Bold values indicate a significant association between the asthma trigger and HRQL in multivariable analysis.
A negative β-value indicates a negative impact on HRQL scores (ie poorer HRQL).
Abbreviations: (a)β, (adjusted) unstandardized regression coefficient; CI, confidence interval; PAQLQ, Pediatric Asthma Quality of Life Questionnaire; RAND, RAND general health-rating index.
[a]Adjusted for age, gender, living environment, asthma control, allergic rhinitis, food allergy, atopic dermatitis and recurrent respiratory tract infections.

HRQL) (Table 3a). In addition, all non-allergic asthma triggers except wool clothing were associated with a lower overall PAQLQ score. In the adjusted multivariable analysis, physical exercise, the weather, (cigarette) smoke and emotions were independently associated with a lower overall PAQLQ score. None of the perceived allergic triggers was independently associated with the overall PAQLQ score.

The multivariable analysis was repeated with the domain-specific PAQLQ scores as the outcome (see Table S4 in the Supporting

Information). Physical exercise and (cigarette) smoke were independently associated with a lower symptom domain score. Pets, physical exercise, the weather and (cigarette) smoke were independently associated with a lower activity limitations domain score. The asthma trigger emotions were independently associated with a lower emotional function domain score.

3.4 | Generic HRQL

In univariable linear regression analysis, all allergic asthma triggers were associated with a lower RAND score (ie poorer generic HRQL) (Table 3b). Again, all non-allergic asthma triggers except wool clothing were associated with a lower RAND score. In the adjusted multivariable analysis, only emotions and food or drinks were independently associated with a lower RAND score. None of the perceived allergic triggers was independently associated with the RAND score.

4 | DISCUSSION

Our cross-sectional study demonstrated that among a broad population of children with asthma, a higher number of perceived allergic and non-allergic asthma triggers were strongly associated with reduced asthma-specific and generic health-related quality of life (HRQL). The majority of children (79%) reported one or more perceived trigger(s) of asthma. Non-allergic asthma triggers were independently associated with reduced HRQL: physical exercise, the weather, (cigarette) smoke and emotions with asthma-specific HRQL, and emotions and food/drinks with generic HRQL.

Our study is the first to indicate that not only asthma-specific HRQL was reduced in children with a higher number of asthma triggers but also generic HRQL was reduced. Previous research showed an association between a higher number of perceived triggers of asthma and reduced asthma-specific HRQL in children and adolescents with severe or difficult-to-treat asthma,[8,9] and in children participating in an asthma education programme with symptom perception interventions.[23] We were able to confirm these findings in children and adolescents with asthma of varying severity in secondary or tertiary care. The impact of asthma triggers on HRQL may be explained by the fact that asthma triggers are associated with greater severity and frequency of asthma exacerbations, emergency treatments, healthcare visits and hospitalization.[12,24] In addition, a higher number of asthma triggers may result in an increased perceived burden of asthma. Furthermore, children with a higher number of asthma triggers may try to avoid asthma triggers, which may have an additional negative impact on asthma-specific and generic HRQL.

Our study suggests that especially non-allergic triggers were independently associated with HRQL. It can be hypothesized that triggers that are difficult to control, that is the weather, (cigarette) smoke and emotions, exert a greater influence on HRQL than triggers that are more easily controlled or treated. Allergic triggers, that is pets, dust or pollen, might exert less influence on HRQL because adequate treatment is available to reduce the symptoms caused by these triggers. However, we might not have detected an association between allergic triggers and HRQL as data on allergen sensitization were not available. Interestingly, the asthma trigger emotions were consistently associated with both asthma-specific and generic HRQL in our study population. Strong emotions such as fear, excitement, stress, anger or laughter may cause asthma symptoms due to an abnormal breathing pattern. Furthermore, the asthma trigger emotions might indicate the presence of psychiatric comorbidities, for example depression and anxiety. Psychiatric comorbidities are known to be more prevalent among patients with asthma and are associated with worse asthma control, increased asthma exacerbations and emergency visits.[7]

Our results highlight the importance of trigger identification in children with asthma. Physicians should pay attention to the identification of asthma triggers and, in turn, instruct children and parents regarding avoidance strategies or treatment of the identified triggers. For instance, the impact of the trigger physical exercise on HRQL might be reduced when children are advised to use a short-acting β2-agonist before exercising[7] and the impact of the trigger emotions might be reduced when children seek psychological support to reduce emotional stress. Although allergic triggers were not independently associated with HRQL in our analysis, we showed that a higher cumulative number of allergic and non-allergic asthma triggers were associated with reduced asthma-specific and generic HRQL. Therefore, specific instructions directed at children with allergic triggers might be beneficial as well. For instance, the impact of the trigger dust on HRQL might be reduced when instructions are given on house cleaning and the impact of the trigger pollen might be reduced when adequate (pharmacological) treatment is initiated.

The major limitation of the present study is that the asthma diagnosis and asthma triggers were self-reported by parents. Furthermore, data on allergen sensitization were not available. However, patient-reported data do provide meaningful insight into the perception of allergic and non-allergic asthma triggers and HRQL among parents and children. Additionally, asthma-specific and generic HRQL cannot be directly compared as asthma-specific HRQL was assessed in children and generic HRQL in parents. Previous research reported a lack of agreement between children's self-reported and parent proxy-reported HRQL and suggested to include both perspectives in HRQL research as both are complementary to each other.[25,26] In addition, we were not able to assess asthma severity as we did not collect data on the frequency of asthma exacerbations, emergency department visits and hospitalizations. Finally, the cross-sectional design of this study limits the assessment of possible long-term effects. Strengths of this study are the large sample size, reliable data collection in routine secondary and tertiary care using validated questionnaires in children and parents and the assessment of both asthma-specific and generic HRQL.

In summary, we demonstrated that a higher number of perceived allergic and non-allergic triggers of asthma were strongly associated with reduced asthma-specific and generic health-related

quality of life (HRQL) in children with asthma. Especially, non-allergic asthma triggers were independently associated with reduced HRQL. Accurate identification and, in turn, avoidance and/or treatment of triggers in children with asthma may improve health-related quality of life.

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CONFLICTS OF INTEREST

None.

AUTHORS' CONTRIBUTIONS

HK substantially contributed to design, concept, acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be published and agreed to be accountable for all aspects of the work. TL, FE and CE substantially contributed to design, interpretation of data, drafting the article, final approval of the version to be published and agreed to be accountable for all aspects of the work. YM, CU and AK substantially contributed to interpretation of data, revising critically for important intellectual content, final approval of the version to be published and agreed to be accountable for all aspects of the work.

DATA AVAILABILITY

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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