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Active allergic disease diminishes life satisfaction in childhood: population-based study

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Abstract

Objective: To assess the impact of allergic diseases on the subjective well-being and life satisfaction of primary school children.

Design: Population-based cohort.

Setting: Finnish sample of children aged10 and 12 from the International Survey of Children's Well-Being.

Participants: Nationally representative sample of 1947 school children.

Main outcome measure: Two different instruments to assess the child´s own perception of well-being; the short version of Student Life Satisfaction Scale (SLSS) and the Brief Multidimensional Student Life Satisfaction Scale (BMSLSS).

Results: Altogether 51,4% of children reported having at least one allergic condition (10,1% asthma, 23,8% eczema, and 40,3% seasonal allergic rhinitis). A distinction in life satisfaction emerged between non-allergic and allergic children, significantly inferior in the latter. In particular, children with eczema were more likely to report a reduction in life satisfaction compared to non-allergic children (SLSS β = -128.220; BMSLSS β = -90.694; $p < 0.01$). Apart from freedom from eczema, good life satisfaction was associated with a physically active life style.

Conclusions: Active allergic disease reduces the child's own perception of well-being. During clinical visits, more attention should be paid to the psychosocial status and children's impairments which may differ substantially from those of parents or medical authorities.

Keywords: allergy; asthma; eczema; life satisfaction, physical activity

Strengths and limitations of this study

- The first nationally representative survey on well-being and quality of life in primary-school children revealed that active allergic disease is a major determinant of children´s well-being in various domains.
- The study did not directly and objectively assess the symptoms in question. The research focus was on children´s own perception of life-satisfaction, not on disease severity.
- The questionnaire was administered only to the children, the responses not being corroborated by parents or medical experts. However, ten-year-old children are already capable of answering reliably to surveys.
- The data of the present study are cross-sectional, and any causal relationship between the predictors and outcome variables thus remains obscure.

INTRODUCTION

Societies worldwide are faced with a progressively increasing risk of immune-mediated health problems such as allergic, autoimmune and inflammatory disease, the velocity of propagation being highest in children. Allergic diseases, the first manifestation of these conditions, comprise the most common chronic disease in childhood, with a prevalence ranging from 7% (eczema) to 14.6% (asthma and rhinitis) in 13-14-year –old children.[1] Thus, allergic diseases hold a key position regarding the burden not only for society and the family, but also for the affected individual.

The severity of allergic disease is assessed by the extent of symptoms in daily life. A vicious circle of symptoms of allergic disease such as allergy flares and emotional stress has been documented, potentially contributing to the burden of disease as experienced.[2] Despite a growing interest in life satisfaction during childhood, little is known as to how chronic diseases such as asthma or eczema affect children's subjective well-being (SWB), this comprising psychosocial contentment. In fact, the burden of allergic disorders may extend well beyond mere physical functioning. The importance of the disease burden may culminate in children, whose recognition of self and self-esteem is still evolving, with a long-term impact on personal well-being and quality of life.

The objective of the present study was to assess the impact of allergic diseases on subjective well-being and life satisfaction in primary-school children. Conventionally, children's well-being has been determined indirectly, using proxies such as household income, mortality, life expectancy, or using parental reports on child well-being[3 4] thus ignoring the child's own point of view.

Recent research has provided tools as indicators of self-reported perceptions of quality of life, satisfaction or other emotional and behavioural elements in children's

lives. [5] In context of allergic diseases, we applied for the first time two summary measures of life satisfaction; the Student Life Satisfaction Scale (SLSS, measure of children's overall life satisfaction) and the Brief Multidimensional Student Life Satisfaction Scale (BMSLSS, measure of children's overall life satisfaction). [5 6 7]

METHODS

Study population and setting

This study is part of an international Children Worlds survey (http://www.isciweb.org).[8] The Ethics Committee of the University of Turku has approved the study in a statement obtained 15.2.2016. Cross-sectional data collected in Finland were used, comprising randomly selected, nationally representative data from 43 primary schools (4th graders 35, 6th graders 39 classes). Informed consent was obtained from the participants before the survey. Finally, in each school at least 40 pupils from both grades (4th and 6th) were recruited. In total, 1947 pupils (67.6% response rate, 48.7% boys, mean age 11 years) completed an online anonymous questionnaire.

Outcome variables

Global life satisfaction

A reduced version of Huebner's[5] SLSS was incremented with one item assessing children's overall life satisfaction, adapted from Diener[6]. The SLSS hypothesizes that children are able to formulate judgments of their overall life satisfaction, over and above judgments concerning specific domains (e.g., family, friends, community)[5]. Instead of dissatisfaction and negative life judgments, the SLSS focuses on positive,

affective conceptualizations of how life is going. This provides complementary information on children's own perception of their optimal development.

Domain-specific life satisfaction

The BMSLSS[7] measures satisfaction in life in more general terms than the SLSS. The evaluation comprises five important life domains: family life, friendships, school experience, body image, and child's living environment.

In both scales the scoring system was modified from the original version ('Not at all agree' to 'Totally agree') to an 11-point scale (0-10). A higher score reflects higher life satisfaction. By calculating the mean of all five items, subscales were summed and transformed into a scale of 0-100.

SLSS and BMSLSS are validated measures of children's experiences of life satisfaction by scales including psychometric properties targeted to age groups from 8 to 18 years. These measures have been successfully used in experience sampling studies; however, to date only few studies have assessed them in the context of chronic conditions.[9 10]

Characterizing the allergic conditions

Three questions, modified from ISAAC Phase One core questionnaires investigating the prevalence of doctor-diagnosed asthma, allergic rhinitis and eczema in children worldwide,[11] were used to recognize allergic disease in this general population. The children were asked if they used inhaled asthma medication (no/yes use of inhalator) prescribed by a doctor. In like manner, the presence of itchy rash sometimes appearing and disappearing (no/yes) was inquired and interpreted to represent atopic eczema. The

manifestation of runny or blocked nose and sneezing in seasons of birch pollen or hay (no/yes allergic cold) was considered to represent seasonal allergic rhinitis in Finland.

Data on background variables

Self-reported sex, age, immigration and parent's employment status were used as socio-demographic background variables. Additionally, we used data on pets (a pet in the family when born or currently in the household). After-school physical activity (sports or exercising) was self-reported.

Statistical analysis

Continuous non-normally distributed outcome variables SLSS and BMSLSS were characterized using means, standard deviations, medians and mean ranks, which were used instead of original values for outcome variables in all analyses. Student's t-test for independent samples was applied in comparisons. In the second phase the significant background variables on either SLSS or BMSLSS and all five asthma variables were taken for linear regression analysis. The interactions were evaluated, but excluded as non-significant from the final regression models. Imputation of the data was not applied to statistical analysis. Statistical analyses were carried out using SAS for Windows version 9.4 (SAS, Cary, NC, USA) and p-values below 0.05 were considered statistically significant.

RESULTS

Overall, the Finnish children here evaluated their wellbeing as excellent; more than 80% of 10- and 12-years-olds are very satisfied with their lives. Altogether 51,4% (n=965) reported having at least one allergic disease; 10,1% (n=188) doctor-diagnosed

asthma, 23,8% (n=452) eczema, and 40,3% (n=769) seasonal allergic rhinitis, while 3% (n=61) of the sample reported having all these allergic conditions.

A significant difference in life satisfaction emerged between non-allergic and allergic children on both scales (Table 1). In particular, eczema was associated with reduced well-being as compared with children not manifesting atopic eczema: for SLSS ($p < .001$) and for BMSLSS ($p < .01$). In contrast, no associations were detected between asthma or allergic rhinitis and life satisfaction. It is of note that all subjects with an asthma diagnosis were on appropriate medication.

The determinants of good life satisfaction were measured by a multivariable model (Table 2). Children not having eczema, aged 10 years (grade 4), having working parents and a physically active life style were found to be more satisfied with their lives than other children. Having had pets in early infancy or having pets currently had no impact on life satisfaction.

Taken together, the strongest predictor of good life satisfaction was a physically active life style ($\beta = 194.05$, $p < .001$), while reduced life satisfaction was explained by eczema ($\beta = -128.22$, $p < .001$).

DISCUSSION

This first nationally representative survey on well-being and quality of life in primary-school children revealed that active allergic disease is a major determinant of children´s well-being in various domains. In particular, eczema was seen to reduce both the global life satisfaction related to children´s moods and feelings (SLSS) and life satisfaction as measured in broader terms of living (BMSLSS). In accord with national [12] and

international[13] reports, half of the children in the present general population reported having at least one allergic condition, indicating that our results may be generalizable.

Not only do allergic diseases comprise the most common chronic disorder of childhood;[14] they also represent the first manifestation of the growing epidemic of non-communicable diseases [15] which tend to share environmental risk factors and pathomechanisms and frequently coexist.[16 17 18] Besides their well-known economic burden, chronic diseases exert a substantial psychosocial impact on children and their families. This notwithstanding, health-related quality of life research has only recently attracted scientific interest.[19 10 20]

The importance of life satisfaction may culminate in childhood. Children, specifically on the very edge of puberty, are vulnerable to exterior influences such as peer acceptance.[21] This phase of life is especially important as regards self-acceptance and relation to self. Specifically, the increase in sensitivity to social rejection during adolescence is associated with mental disorders such as depression.[22] Previous studies mainly on the adult population indicate that active allergic diseases are related to lowered well-being, manifested in fewer relationships, limited daily functioning and decreased self-acceptance, and the emotions.[23 19 24 20] Our results further underline that allergic diseases not only affect separate domains of children´s lives but also entail a holistic effect; the intricacy of the allergic burden is manifested in children's overall life satisfaction. For example, skin conditions distress psychosocial well-being by virtue of the stigma resulting from the visibility of dermatological symptoms.[24] Furthermore, children with persistent or late-onset eczema or with persistent wheeze were demonstrated to have psychosocial problems at school.[20]

In the present study, respiratory allergy seemed to have less influence on children´s life-satisfaction as compared to eczema. An alternative explanation would be

that the lacking effects rather designate these symptoms as treatable. Interestingly, previous studies suggest that symptom-free patients report even better well-being than the population in average,[25] suggesting that it is not the chronic disease *per se* which impacts on the quality of life of the affected, but the manifestations thereof. Treating asthma promotes a physically active life style,[26] and a physically active life style was strongly associated with life satisfaction in the present survey. Thus, the benefit of balanced asthma treatment may extend far beyond physical health to psychosocial consequences and overall improvements in the quality of life.[27]

Several limitations of this study need to be acknowledged. Firstly, the study did not directly and objectively assess the symptoms in question. In point of fact, the research focus was on children´s own perception of life-satisfaction, not on disease severity. Secondly, the questionnaire was administered only to the children, the responses not being corroborated by parents or medical experts. However, ten-year-old children are already capable of answering reliably to surveys.[8] Lastly, the data of the present study are cross-sectional, and any causal relationship between the predictors and outcome variables thus remains obscure.

Taken together, our results suggest that control of symptoms, encouragement of physical exercise and monitoring of psychological well-being reduce the burden of allergic diseases, which affect half of the general paediatric population. Accordingly, children diagnosed with allergic conditions will benefit from thorough monitoring of their overall well-being. The focus in medical practice should thus not be limited to medical treatment of symptoms but should also take account of also on children´s perceived impairments.[24] In fact, these may differ substantially from those of parents or medical authorities.[28]

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: This study was approved by the Ethics Committee of the University of Turku.

Data sharing: No additional data available.

Transparency: The lead author (LH) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Table 1. Socio-economic background variables, pet status, and allergy variables affecting children's life satisfaction analyzed by T-test for independent samples*

	SLSS					BMSLSS				
	n	**Mean(sd)**	**Md**	**Mean rank**	**p**	**n**	**Mean(sd)**	**Md**	**Mean rank**	**p**
Gender					0.7642					0.0685
boy	946	90.3(14.0)	96	824.7		867	88.8(11.4)	92	807.4	
girl	998	89.8(14.8)	96	818.9		938	89.3(12.1)	92	848.5	
Grade					< 0.0001					< 0.0001
4	942	91.0(14.4)	96	864.4		863	90.7(11.4)	94	924.9	
6	1002	89.2(14.4)	94	781.6		942	87.5(11.8)	90	740.7	
Ethnicity					0.6146					0.1949
no	1880	90.1(14.5)	96	822.6		1743	89.1(11.7)	92	831.5	
yes	64	89.8(12.7)	96	795.4		62	86.7(13.6)	90	751.3	
Parental employment status					<0.0295					
no	577	88.8(16.0)	94	794.5		542	88.2(12.9)	92	808.0	0.1292
yes	1342	90.9(13.4)	96	840.2		1241	89.6(10.9)	92	845.3	
Sports and exercise					<0.0020					< 0.0001
no	78	83.1(21.4)	94	678.2		65	79.8(16.4)	82	511.4	
yes	1803	90.4(14.0)	96			1686	89.4(11.4)	92	843.8	
A pet when born					0.1852					0.3060
no	962	90.4(13.3)	96	841.4		894	89.6(11.1)	92	849.6	
yes	766	89.3(15.9)	96	814.2		711	88.7(12.6)	92	824.9	
A pet now					0.3202					< 0.0102
no	703	90.5(13.8)	96	835.7		660	89.9(11.3)	92	867.0	
yes	1227	89.8(14.7)	96	815.7		1132	88.5(12.0)	92	806.7	
Asthma					0.5263					0.8561
no	1678	90(14.2)	96	817.6		1566	89.0(11.6)	92	827.2	
yes	191	899.3(16.9)	96	838.2		174	88.3(13.7)	92	820.2	
Eczema					<0.0001					< 0.0018
no	1446	90.8(13.7)	96	843.3		1350	89.6(11.0)	92	848.5	
yes	452	87.5(16.6)	92	745.8		414	87.2(13.4)	90	764.6	
Perennial rhinitis					0.6494					0.6441
no	1140	89.9(14.6)	96	816.0		1061	89.0(11.6)	92	823.5	
yes	764	90.0(14.3)	96	825.1		709	89.1(11.9)	92	834.2	

*By Kruskall-Wallis non-parametric tests.

Table 2. Children's life satisfaction explained by grade, parental employment status, physical activity, pet status, and allergy variables*

	SLSS			BMSLSS		
	β	**t-value**	**p**	***β***	**t-value**	**p**
Grade	-60.880	-4.41	< 0.001	-106.225	-7.97	< 0.001
Parental employment status	65.682	2.17	< 0.05	70.065	2.40	< 0.05
Sports and exercise	194.053	2.87	< 0.001	307.704	4.47	< 0.001
A pet when born	-22.414	0.75	0.4511	-7.676	-0.27	0.7898
A pet now	-28.816	-0.94	0.3464	-47.133	-1.59	0.1113
Asthma	60.220	1.29	0.1959	1.662	0.04	0.9707
Eczema	-128.220	-3.94	< 0.01	-90.694	-2.88	< 0.01
Perennial rhinitis	29.331	1.01	0.3122	19.440	0.70	0.4868

*By linear regression analysis.

REFERENCES

[1] Mallol J, Crane J, von Mutius E, Odhiambo J, Keil U, Stewart A. The international study of asthma and allergies in childhood (ISAAC) phase three: a global synthesis. *Allergol Immunopathol* (Madr) 2013;41(2):73-85. doi: 10.1016/j.aller.2012.03.001.

[2] Patterson AM, Yildiz VO, Klatt MD, Malarkey WB. *Perceived stress predicts allergy flares.* Annals of Allergy, Asthma & Immunology: Official Publication of the American College of Allergy, Asthma, & Immunology 2014;112(4):317-321. doi.org/10.1016/j.anai.2013.07.013.

[3] Coffey, JK, Warren MT, Gottfried AV. Does infant happiness forecast adult life satisfaction? Examining subjective well-being in the first quarter century of life. *J Happiness Stud* 2015;16(6):1401-1421. Doi 10.1007/s10902-014-9556-x.

[4] Sourander A, Helstelä L, Helenius H. Parent-adolescent agreement on emotional and behavioral problems. *Soc Psychiatry Psychiatr Epidemiol* 1999;34:657-663.

[5] Diener E, Emmons RA, Larsen RJ, Griffin S. The satisfaction with life scale. *J Pers Assess* 1985;49:71-75.

[6] Huebner SE. Further validation of the students' life satisfaction scale: The independence of satisfaction and affect ratings. *J Psychoed Assess* 1991;9:363-368. Doi: 10.1177/073428299100900408.

[7] Seligson JL, Huebner ES, Valois RF. Preliminary validation of the brief multidimensional students' life satisfaction scale (BMSLSS). *Soc Ind Res* 2003;61:121-145. doi: 10.1007/s10488-011-0385-5.

[8] Children's worlds. 2017. http://www.isciweb.org.

[9] Lippman LH, Anderson Moore K, McIntosh H. *Positive indicators of child well-being: a conceptual framework, measures and methodological issue*s. Innocenti Working Paper No. 2009-21; 2009. Florence, UNICEF Innocenti Research Centre.

[10] McDougall J, Wright W, Nichols M, Miller L. Assessing the psychometric properties of both a global and a domain-specific perceived quality of life measure when used with youth who have chronic conditions. *Soc Indic Res* 2013;114:1243-1257. Doi 10.1007/s11205-012-0200-z.

[11] Asher MI, Weiland SK on behalf of the ISAAC steering committee. The international study of asthma and allergies in childhood (ISAAC). *Clin Exp Allergy* 1998;28 Supp 5:52-66.

[12] Jousilahti P, Haahtela T, Laatikainen T, Mäkelä M, Vartiainen E. Asthma and respiratory allergy prevalence is still increasing among Finnish young adults. *Eur Respir J* 2016;47:985-987. Doi:10.1183/13993003.01702-2015.

[13] Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006;368:733-43. Doi: 10.1016/S0140-6736(06)69283-0.

[14] Masoli M, Fabian D, Holt S, Beasley R for the Global Initiative for Asthma (GINA) Program. The global burden of asthma: executive summary of the GINA dissemination committee report. *Allergy* 2004;59:469-478. Doi: 10.1111/j.1398-9995.2004.00526.x.

[15] NCD Risk factor collaboration. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. *Lancet* 2016;387:1377-96. Doi: 10.1016/S0140-6736(16)30054-X.

[16] Campbell DE, Boyle RJ, Thornton CA, Prescott SL. Mechanisms of allergic disease – environmental and genetic determinants for the development of allergy. *Clin Exp Allergy* 2015;45:844-858. Doi: 10.1111/cea.12531.

[17] Hersoug L-G, Linneberg A. The link between the epidemics of obesity and allergic diseases: does obesity induce decreased immune tolerance? *Allergy* 2007;62:1205-13. Doi: 10.1111/j.1398-9995.2007.01506.x.

[18] Rautava S, Luoto R, Salminen S, Isolauri E. Microbial contact during pregnancy, intestinal colonization and human disease. *Nature Reviews Gastroenterology & Hepatology* 2012; 9: 565-76. doi:10.1038/nrgastro.2012.144.

[19] Baiardini I, Braido F, Giardini A, Majani G, Cacciola C, Rogaku A, Scordamaglia A, Canonica GW. Adherence to treatment: assessment of an unmet need in asthma. *J Investig Allergol Clin Immunol* 2006;16(4):218-23. Free full text.

[20] Teyhan A, Galobardes B, Henderson J. Child allergic symptoms and well-being at school: Findings from ALSPAC, a UK cohort study. *J PLoS ONE.* 2015;10(8):e0135271. doi:10.1371/journal. pone.0135271.

[21] Rutter M, Rutter M. *Developing minds. Challenge and continuity across the life span*. England; Clays Ltd, 1993.

[22] Silk JS, Siegle GJ, Lee KH, Nelson EE, Stroud LR, Dahl RE. Increased neural response to peer rejection associated with adolescent depression and pubertal development. *SCAN* 2014;9:1798-1807. Doi: doi.org/10.1093/scan/nst175.

[23] Juniper EF. How important is quality of life in pediatric asthma? *Pediatr Pulmonol Suppl* 1997;15:17-21. Doi: 10.1002/(SICI)1099-0496(199709)15+<17::AID-PPUL5>3.0.CO;2-O.

[24] Tuckman A. The Potential Psychological Impact of Skin Conditions. *Dermatol Ther* (Heidelb)2017;7(Suppl 1):53-57. doi: 10.1007/s13555-016-0169-7.

[25] Osman LR, Caldman C, Robertson R, et al. Symptoms, quality of life, and health service contact among young adults with mild asthma. *Am J Respir Crit Care Med* 2000;61:498-503.

[26] Jago R, Searl A, Henderson AJ, Turner KM. Designing a physical activity intervention for children with asthma: a qualitative study of the views of healthcare professionals, parents and children with asthma. *BMJ Open* 2017;24:7(3):e014020.doi: 10.1136/bmjopen-2016-014020.

[27] Cui W, Zack MM, HS Zahran. Health-related quality of life and asthma among United States adolescents. *J Pediatr* 2015;166(2):358-364. Doi: 10.1016/j.jpeds.2014.10.005.

[28] Akeson N, Worth A, Sheikh A. The psychosocial impact of anaphylaxis on young people and their parents. *Clin Exp Allergy* 2007;37:1213-20. Doi: 10.1111/j.1365-2222.2007.02758.x.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
✓ **Title and abstract**	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract, p. 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found, p. 2
Introduction		
✓ Background/rationale	2	Explain the scientific background and rationale for the investigation being reported, p. 4
✓ Objectives	3	State specific objectives, including any prespecified hypotheses, p. 4
Methods		
✓ Study design	4	Present key elements of study design early in the paper, p. 5
✓ Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection, p. 5
✓ Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants, p. 5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
✓ Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable, p. 5-7
✓ Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group, p. 5-7
✓ Bias	9	Describe any efforts to address potential sources of bias, p. 7

✓	Study size	10	Explain how the study size was arrived at, p. 5
✓	Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why, p. 7
✓	Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding, p. 7
			(*b*) Describe any methods used to examine subgroups and interactions
			(*c*) Explain how missing data were addressed
			(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy, p. 5
			(*e*) Describe any sensitivity analyses

Continued on next page

Results			
✓	Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed, p. 12
			(b) Give reasons for non-participation at each stage
			(c) Consider use of a flow diagram
✓	Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders, p. 7-8, 12
			(b) Indicate number of participants with missing data for each variable of interest
			(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
✓	Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
			Case-control study—Report numbers in each exposure category, or summary measures of exposure
			Cross-sectional study—Report numbers of outcome events or summary measures, p. 5
✓	Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included, p.12
			(*b*) Report category boundaries when continuous variables were categorized
			(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
✓	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion			
✓	Key results	18	Summarise key results with reference to study objectives, p. 8-10
✓	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias, p. 10
✓	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence, p. 9-10
✓	Generalisability	21	Discuss the generalisability (external validity) of the study results, p. 9
Other information			

✓	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based, p. 11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The association of allergic diseases with children's life satisfaction: population-based study in Finland

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Abstract

Objective: To assess the impact of allergic diseases on the subjective well-being and life satisfaction of primary school children.

Design: Population-based cohort.

Setting: Finnish sample of children ages 10 and 12 from the International Survey of Children's Well-Being.

Participants: Nationally representative sample of 1947 school children.

Main outcome measure: Two different instruments to assess the child's own perception of well-being; the short version of the Student Life Satisfaction Scale (SLSS) and the Brief Multidimensional Student Life Satisfaction Scale (BMSLSS).

Results: Altogether, 51.4% of children reported having at least one allergic condition (10.1% asthma, 23.8% eczema, and 40.3% seasonal allergic rhinitis). A statistically significant distinction in life satisfaction emerged between non-allergic and allergic children (inferior in the latter). In particular, children with eczema were more likely to report a reduction in life satisfaction compared to non-allergic children (SLSS $\beta = -128.220$; BMSLSS $\beta = -90.694$; $p < 0.01$). Apart from freedom from eczema, good life satisfaction was associated with a physically active life style.

Conclusions: Active allergic disease reduces the child's own perception of well-being. During clinical visits, more attention should be paid to the child's psychosocial status and impairments, which may differ substantially from those of parents or medical authorities.

Keywords: allergy; asthma; eczema; life satisfaction, physical activity

Strengths and limitations of this study

- The first nationally representative survey on subjective life satisfaction in primary-school children in Finland.
- The first national study that observed allergic diseases with relation to children´s life satisfaction.
- The study did not directly and objectively assess the allergy symptoms in question. The research focus was on children's own perception of life-satisfaction rather than on disease severity.
- The data used in the present study are cross-sectional, and any causal relationship between the predictors and outcome variables thus remains obscure.

INTRODUCTION

Societies worldwide are faced with a progressively increasing risk of immune-mediated health problems such as allergic, autoimmune, and inflammatory diseases, and the velocity of propagation is highest in children.[1 2] Allergic diseases, the first manifestation of these conditions, comprise the most common chronic disease among children, with a prevalence ranging from 7% (eczema) to 14.6% (asthma and rhinitis) in 13- to 14-year-old children.[3] Thus, allergic diseases represent a significant burden not only for society and the family but also for the affected individual.

The severity of allergic disease is assessed by the extent of symptoms in daily life. A vicious circle of symptoms of allergic disease such as allergy flares and emotional stress has been documented, and these symptoms can potentially contribute to the experienced burden of the disease.[4] Despite a growing interest in life satisfaction during childhood, little is known about how chronic diseases such as asthma or eczema affect children's subjective well-being (SWB), that is, psychosocial contentment. In fact, the burden of allergic disorders may extend well beyond mere physical functioning.

Youth with a chronic illness are at increased risk for poor self-concept[5] and show significantly higher rates of emotional and behavioural problems.[6] Self-concept, as a fundamental part of a child's psychological function, is strongly affected by parental and peer approval, physical appearance and perceived competence in domains of importance, such as athletics.[7] For example, for children with asthma, a decreased quality of life has been found to be related to limited activities and participation in sports.[8]

The importance of the disease burden may culminate in children, whose recognition of self and self-esteem are still evolving, and thus disease may have a long-term impact on personal well-being and quality of life.[6 9 10 11] In the medical literature,

quality of life refers to a 'uniquely personal perception, denoting the way that individual patients feel about their health status and/or nonmedical aspects of their lives'.[12] On one hand, health is considered a major component affecting one's quality of life and on the other hand, good quality of life is an important outcome of successful treatment of diseases.[8]

The objective of the study presented here was to assess the impact of allergic diseases on subjective well-being and life satisfaction among primary-school children. Conventionally, children's well-being has been determined indirectly, using proxies such as household income, mortality, or life expectancy or using parental reports on child well-being,[13 14] thus ignoring the child's own point of view. However, children's and parents' perceptions of a child's quality of life often differ; thus, obtaining information directly from the child is advisable.[9 12] Another gap in the research literature regards the lack of attention to ethnically and racially diverse samples.[10 15 16] Research on racially diverse groups of children with allergic diseases would increase our knowledge of the association between allergy and childhood quality of life in populations of children who may already be at increased risk of impaired well-being.[10]

Recent research has provided tools that can be used to evaluate self-reported perceptions of quality of life, satisfaction, or other emotional and behavioural elements of children's lives.[17] In the context of allergic diseases, we applied for the first time two summary measures of life satisfaction: the Student Life Satisfaction Scale (SLSS, measuring children's overall life satisfaction) and the Brief Multidimensional Student Life Satisfaction Scale (BMSLSS, measuring children's overall life satisfaction). [17 18 19]

METHODS

Study population and setting

This study is part of an international Children's Worlds survey (http://www.isciweb.org),[20] which is an international survey on school-aged children's subjective well-being. The purpose of the study is to improve children's well-being by creating awareness among children, their parents, and their communities, as well as among other parties involved in children's lives, such as policy decision makers or teachers. The study was approved by the Ethics Committee of the University of Turku (statement obtained 15 February 2016). Cross-sectional data collected in Finland were used, comprising a random selection of nationally representative data from 43 primary schools (35 classes of 4th graders, 39 classes of 6th graders). Informed consent was obtained from the participants and their parents prior to administering the survey. Finally, in each school at least 40 pupils in each of grades 4 and 6 were recruited. In total, 1947 pupils (67.6% response rate; 48.7% boys; mean age, 11 years) completed an online anonymous questionnaire.

Outcome variables

Global life satisfaction

A reduced version of Huebner's[17] SLSS was expanded by one item assessing children's overall life satisfaction ('the things in my life are excellent'), adapted from Diener.[18] The SLSS hypothesizes that children are able to formulate judgments of their overall life satisfaction over and above judgments concerning specific domains (e.g., family, friends, community).[17] Instead of asking about dissatisfaction and negative life judgments, the SLSS focuses on positive, affective conceptualizations of the child's life. This provides information that is complementary to children's own perceptions of their

optimal development. The internal consistency of the SLSS items was tested via Cronbach's alpha, resulting in $\alpha = 0.94$, indicating internal consistency and reliability.

Domain-specific life satisfaction

The BMSLSS[19] measures satisfaction in life in more general terms than the SLSS. The evaluation covers five important life domains, using one item per domain: family life, friendships, school experience, body image, and child's living environment ($\alpha = 0.78$).

Scoring and validity

In both scales, the scoring system was modified from the original version (1 = 'Strongly disagree' to 6 = 'Strongly agree') to an 11-point scale (0–10). A higher score reflects higher life satisfaction. After calculating the mean of all five items, the subscales were summed and transformed into a scale of 0–100.

SLSS and BMSLSS are validated measures of children's experiences of life satisfaction including psychometric properties, targeted to age groups from 8 to 18 years. These measures have been successfully used in other experience sampling studies; however, to date only a few studies have used them in the context of chronic conditions.[21 22]

Characterization of the allergic conditions

Three questions, modified from the ISAAC Phase One core questionnaires investigating the prevalence of doctor-diagnosed asthma, allergic rhinitis, and eczema in children worldwide,[23] were used to characterize allergic disease among the study population. In Finland, the ISAAC core questions on asthma have been validated against anti-asthmatic medication reimbursement data from the Finnish Social Insurance Institution

and were found to be highly valid.[24] The participants were asked whether they used inhaled asthma medication (no/yes) prescribed by a doctor. In like manner, children were asked about the presence of itchy rash sometimes appearing and disappearing (no/yes), which was interpreted to represent atopic eczema. Although ISAAC questions on eczema have not been specifically validated in the Finnish language, it has been shown that, in general, ISAAC-questionnaire-derived symptom prevalence is sufficiently precise at the population level.[25] Runny or blocked nose and sneezing in seasons of birch pollen or hay (no/yes) was considered to represent seasonal allergic rhinitis in Finland.

Data on background variables

Self-reported sex, age, ethnic background and parent's employment status were used as socio-demographic background variables. Children were asked for the employment status of both parents (mother and father working: yes, no, do not know) and a recoded variable was formed (parents working: no, yes). Ethnic background was determined based on three items: were you / your mother / your father born in Finland (yes, no, I am not sure). Additionally, we used data on pets (a pet in the family when the child was born or currently in the household; yes, no, I do not know). After-school physical activity (sports or exercising) was self-reported.

Statistical analysis

Continuous non-normally distributed SLSS and BMSLSS outcome variables were characterized using means, standard deviations, medians and mean ranks. Ranks, counted over the total data, were used in analyses because of the extremely left skewed distributions of the outcome variables SLSS and BMSLSS. Student's *t*-test for

independent samples was applied in comparisons between variables. In the second phase of analysis, the significant background variables from both SLSS and BMSLSS and all five asthma variables (A pet when born, A pet now, Asthma, Eczema, Perennial rhinitis) were subjected to linear regression analysis. The interactions were evaluated, but all were excluded as non-significant from the final regression models. Imputation of the data was not applied to statistical analysis. However, the analyses were conducted using weighting coefficients calculated for Finnish data.[20] This takes into account non-response, varying probabilities of selection, and variations between characteristics of the sample and the population from which the sample was drawn. Statistical analyses were carried out using SAS for Windows version 9.4 (SAS, Cary, NC, USA) and *p*-values below 0.05 were considered statistically significant.

RESULTS

Overall, the Finnish children in this study evaluated their well-being as excellent; more than 80% of 10- and 12-years-olds were very satisfied with their lives. Altogether, 51.4% (n = 965) reported having at least one allergic disease – 10.1% (n = 188) doctor-diagnosed asthma, 23.8% (n = 452) eczema, and 40.3% (n = 769) seasonal allergic rhinitis.

A significant difference in life satisfaction emerged between non-allergic and allergic children on both scales (Table 1). In particular, eczema was associated with reduced well-being when compared with children not manifesting atopic eczema: the difference on both scales was statistically significant (SLSS, $p < 0.001$; BMSLSS, $p < 0.01$). In contrast, no associations were detected between asthma or allergic rhinitis and life satisfaction. It is of note that all subjects with an asthma diagnosis were on prescribed inhaled asthma medication. An additional correlation analysis showed that

all the domains of BMSLSS were statistically significantly associated with eczema. The most affected domain was body image ($r = -0.10$, $p < 0.001$).

The determinants of good life satisfaction were measured by a multivariable model (Table 2). Children not having eczema, aged 10 years (grade 4), with working parents and a physically active life style were found to be more satisfied with their lives than other children. Having had pets in early infancy or having pets currently had no impact on life satisfaction.

Taken together, the strongest predictor of good life satisfaction was a physically active life style ($\beta = 194.05$, $p < .001$), while reduced life satisfaction was correlated with eczema ($\beta = -128.22$, $p < 0.001$).

DISCUSSION

This study, which is the first nationally representative survey on subjective life satisfaction and allergic diseases in primary-school children, revealed that active allergic disease is a major determinant of children's well-being in various domains. In particular, eczema was seen to reduce both global life satisfaction related to children's moods and feelings (SLSS) and life satisfaction as measured across broader domains of living (BMSLSS). In accord with national[26] and international[27] reports, half of the children in the studied sample reported having at least one allergic condition, indicating that our results may be generalizable.

Not only do allergic diseases comprise the most common chronic disorder of childhood;[28] they also represent the first manifestation of the growing epidemic of non-communicable diseases,[29] which tend to share environmental risk factors and patho-mechanisms and frequently coexist.[2 30 31] Besides their well-known economic burden,

chronic diseases exert a substantial psychosocial impact on children and their families. This notwithstanding, health-related quality of life research has only recently attracted scientific interest.[22 32 33]

The importance of life satisfaction may be highest in childhood. Children, specifically those on the very edge of puberty, are vulnerable to external influences such as peer acceptance.[34] This phase of life is especially important with regards to self-acceptance and relation to self. As also demonstrated in this study, younger children were more content in terms of their life satisfaction than older ones. Hence, our study results tend to substantiate those of previous research[5] according to which age is related to perceptions of well-being, for example in the context of emotional well-being. However, the lack of interaction between the variables of age, allergies, and life satisfaction indicates that the experience of life satisfaction is influenced by the burdens presented by allergies and age individually.

Previous studies mainly on adult populations indicate that active allergic diseases are related to decreased well-being, as manifested in fewer relationships, limited daily functioning and decreased self-acceptance, as well as decreased emotional well-being.[32 33 35 36] Our results further underline that allergic diseases not only affect separate domains of children's lives but also have a holistic effect; the intricacy of the allergic burden is manifested in children's overall life satisfaction. For example, skin conditions distress psychosocial well-being by virtue of the stigma resulting from the visibility of dermatological symptoms.[33] Furthermore, children with persistent or late-onset eczema or with persistent wheeze were demonstrated to have psychosocial problems at school.[33]

Our study results show no association between ethnic background, allergic diseases, and life satisfaction. This suggests that the impact of allergic diseases does not differ between ethnically Finnish children and children with an immigrant background.

Parental employment status was significantly related to life satisfaction, indicating that children of working parents were more satisfied with their lives than those of non-working parents. This association, however, was not associated with allergic diseases.

In the present study, respiratory allergy seemed to have less influence on children's life-satisfaction than eczema. An alternative explanation would be that the absence of effects indicates that the symptoms of these allergies are treatable. Interestingly, previous studies suggest that symptom-free patients report better well-being than the population on average,[37] suggesting that it is not the chronic disease *per se* which impacts the quality of life of those affected but the manifestations thereof (symptoms). Treating asthma promotes a physically active life style,[38] and a physically active life style was strongly associated with life satisfaction in the present survey. Thus, the benefit of balanced asthma treatment may extend far beyond physical health to psychosocial consequences and overall improvements in the quality of life.[39]

Several limitations of this study need to be acknowledged. Firstly, the study did not directly and objectively assess the symptoms in question. Rather, the research focused on children's own perception of disease severity. Similarly, there is a potential for error in children's reports of parental employment status and pet ownership at child's birth. Using objective measures or medical records to verify diagnoses and disease severity and, for instance, parental reports to verify employment status is one way for future studies to improve upon the current study assessing self-reported diseases as correlates of children's life satisfaction. Lastly, the data used in the present study are cross-sectional, and any causal relationship between the predictors and outcome variables thus remains obscure.

Taken together, our results suggest a call to monitor the psychological well-being of children affected by allergic diseases, which are the most common chronic diseases

in childhood. In medical care, consideration should be given to the children's perceived impairments,[37] as these may differ substantially from the perceptions of parents or medical authorities.[40]

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Ethical approval: This study was approved by the Ethics Committee of the University of Turku.

Data sharing: No additional data available.

Transparency: The lead author (LH) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Table 1. Socio-economic background variables, pet status, and allergy variables affecting children's life satisfaction analysed by t-test for independent samples.*

	SLSS					BMSLSS				
	n	**Mean(sd)**	**Md**	**Mean rank**	***p***	***n***	**Mean(sd)**	**Md**	**Mean rank**	***p***
Gender					0.7642					0.0685
boy	946	90.3(14.0)	96	824.7		867	88.8(11.4)	92	807.4	
girl	998	89.8(14.8)	96	818.9		938	89.3(12.1)	92	848.5	
Grade					<0.0001					<0.0001
4	942	91.0(14.4)	96	864.4		863	90.7(11.4)	94	924.9	
6	1002	89.2(14.4)	94	781.6		942	87.5(11.8)	90	740.7	
Born in Finland					0.6146					0.1949
no	1880	90.1(14.5)	96	822.6		1743	89.1(11.7)	92	831.5	
yes	64	89.8(12.7)	96	795.4		62	86.7(13.6)	90	751.3	
Parents working					<0.0295					
no	577	88.8(16.0)	94	794.5		542	88.2(12.9)	92	808.0	0.1292
yes	1342	90.9(13.4)	96	840.2		1241	89.6(10.9)	92	845.3	
Doing sports					<0.0020					<0.0001
no	78	83.1(21.4)	94	678.2		65	79.8(16.4)	82	511.4	
yes	1803	90.4(14.0)	96			1686	89.4(11.4)	92	843.8	
A pet when born					0.1852					0.3060
no	962	90.4(13.3)	96	841.4		894	89.6(11.1)	92	849.6	
yes	766	89.3(15.9)	96	814.2		711	88.7(12.6)	92	824.9	
A pet now					0.3202					=0.0102
no	703	90.5(13.8)	96	835.7		660	89.9(11.3)	92	867.0	
yes	1227	89.8(14.7)	96	815.7		1132	88.5(12.0)	92	806.7	
Asthma					0.5263					0.8561
no	1678	90(14.2)	96	817.6		1566	89.0(11.6)	92	827.2	
yes	191	89.3(16.9)	96	838.2		174	88.3(13.7)	92	820.2	
Eczema					<0.0001					=0.0018
no	1446	90.8(13.7)	96	843.3		1350	89.6(11.0)	92	848.5	
yes	452	87.5(16.6)	92	745.8		414	87.2(13.4)	90	764.6	
Seasonal rhinitis					0.6494					0.6441
no	1140	89.9(14.6)	96	816.0		1061	89.0(11.6)	92	823.5	
yes	764	90.0(14.3)	96	825.1		709	89.1(11.9)	92	834.2	

*By Kruskall-Wallis non-parametric tests.

Table 2. Children's life satisfaction explained by grade, parental employment status, physical activity, pet status, and allergy variables.*

	SLSS			BMSLSS		
	β	**SE**	***p***	**β**	**SE**	***p***
Grade	−60.880	13.799	<0.001	−106.225	13.322	<0.001
Parents working	65.682	30.324	<0.05	70.065	29.141	<0.05
Doing sports	194.053	67.723	<0.001	307.704	68.914	<0.001
A pet when born	−22.414	29.734	0.4511	−7.676	28.794	0.7898
A pet now	−28.816	30.597	0.3464	−47.133	29.577	0.1113
Asthma	60.220	46.539	0.1959	1.662	45.248	0.9707
Eczema	−128.220	32.575	<0.01	−90.694	31.441	<0.01
Seasonal rhinitis	29.331	29.015	0.3122	19.440	27.947	0.4868

*By linear regression analysis.

REFERENCES

[1] Bach JF. The effect of infections on susceptibility to autoimmune and allergic diseases. *N Engl J Med.* 2002;347;12:911-920. Doi: 10.1056/NEJMra020100.

[2] Rautava S, Luoto R, Salminen S, Isolauri E. Microbial contact during pregnancy, intestinal colonization and human disease. *Nat. Rev. Gastroenterol. Hepatol.* 2012;9:565-576. doi: 10.1038/nrgastro.2012.144.

[3] Mallol J, Crane J, von Mutius E, Odhiambo J, Keil U, Stewart A. The international study of asthma and allergies in childhood (ISAAC) phase three: a global synthesis. *Allergol Immunopathol* (Madr) 2013;41(2):73-85. doi: 10.1016/j.aller.2012.03.001.

[4] Patterson AM, Yildiz VO, Klatt MD, Malarkey WB. *Perceived stress predicts allergy flares.* Annals of Allergy, Asthma & Immunology: Official Publication of the American College of Allergy, Asthma, & Immunology 2014;112(4):317-321. doi.org/10.1016/j.anai.2013.07.013.

[5] Ferro M, Boyle M. Self-concept among youth with a chronic illness: A meta-analytic review. *Health Psychol* 2013;32;8: 839-848. Doi: 10.1037/a0031861.

[6] Ferro MA, Van Lieshout RJ, Ohayon J, Scott JG. Emotional and behavioral problems in adolescents and young adults with food allergy. *Allergy* 2016;71:532-540. Doi: 10.1111/all.12829.

[7] Harter S. *The Construction of the Self: A Developmental Perspective.* New York, NY, USA; Guilford, 1999.

[8] Glazebrook C, McPherson AC, Macdonald IA, Swift JA, Ramsay C, Newbould R, Smyth A. Asthma as a barrier to children's physical activity: implications for body mass index and mental health. *Pediatrics* 2006;118;6:2443-2449. Doi: 10.1542/peds.2006-1846.

[9] Merikallio VJ, Mustalahti K, Remes ST, Valovirta EJ, Kaila M. Comparison of quality of life between asthmatic and healthy school children. *Pediatr Allergy Immunol* 2005;16:332-340. Doi: 10.1111/j.1399-3038.2005.00286.x

[10] Everhart RS, Fiese BH. Asthma severity and child quality of life in pediatric asthma: A systematic review. *Patient Educ Couns* 2009;75:162-168. Doi: 10.1016/j.pec.2008.10.001.

[11] Heinl D, Chalmers J, Nankervis H, Apfelbacher CJ. Eczema Trials: Quality of Life Instruments Used and Their Relation to Patient-Reported Outcomes. A Systematic Review. *Acta Derm Venereol* 2016;96:596-601. Doi: 10.2340/00015555-2322.

[12] Gill TM, Feinstein AR. A critical appraisal of the quality of quality-of-life measurements. *JAMA* 1994;272;8:619-626. Doi:10.1001/jama.1994.03520080061045.

[13] Coffey, JK, Warren MT, Gottfried AV. Does infant happiness forecast adult life satisfaction? Examining subjective well-being in the first quarter century of life. *J Happiness Stud* 2015;16(6):1401-1421. doi 10.1007/s10902-014-9556-x.

[14] Sourander A, Helstelä L, Helenius H. Parent-adolescent agreement on emotional and behavioral problems. *Soc Psychiatry Psychiatr Epidemiol* 1999;34:657-663.

[15] McQuaid EL, Farrow ML, Esteban CA, Jandasek BN, Rudders SA. Topical Review: Pediatric Food Allergies among Diverse Children. *J Pediatr Psychol* 2016;41;4:391-396. Doi: 10.1093/jpepsy/jsv051.

[16] Shaw TE, Currie, GP, Koudelka CW, Simpson EL. Eczema prevalence in the United States: Data from the 2003 national survey of children´s health. *J Invest Dermatol* 2011;131;1:67-73. Doi: 10.1038/jid.2010.251.

[17] Diener E, Emmons RA, Larsen RJ, Griffin S. The satisfaction with life scale. *J Pers Assess* 1985;49:71-75.

[18] Huebner SE. Further validation of the students' life satisfaction scale: The independence of satisfaction and affect ratings. *J Psychoed Assess* 1991;9:363-368. Doi: 10.1177/073428299100900408.

[19] Seligson JL, Huebner ES, Valois RF. Preliminary validation of the brief multidimensional students' life satisfaction scale (BMSLSS). *Soc Ind Res* 2003;61:121-145. doi: 10.1007/s10488-011-0385-5.

[20] Children's worlds. 2017. http://www.isciweb.org.

[21] Lippman LH, Anderson Moore K, McIntosh H. *Positive indicators of child well-being: a conceptual framework, measures and methodological issue*s. Innocenti Working Paper No. 2009-21; 2009. Florence, UNICEF Innocenti Research Centre.

[22] McDougall J, Wright W, Nichols M, Miller L. Assessing the psychometric properties of both a global and a domain-specific perceived quality of life measure when used with youth who have chronic conditions. *Soc Indic Res* 2013;114:1243-1257. Doi 10.1007/s11205-012-0200-z.

[23] Asher MI, Weiland SK on behalf of the ISAAC steering committee. The international study of asthma and allergies in childhood (ISAAC). *Clin Exp Allergy* 1998;28 Supp 5:52-66.

[24] Nwaru BI, Lumia M, Kaila M, Luukkainen P, Tapanainen H, Erkkola M. Validation of the Finnish ISAAC questionnaire on asthma against anti-asthmatic medication reimbursement database in 5-year-old children. *Clin Respir J* 2011;5:211-8. Doi: 10.1111/j.1752-699X.2010.00222.x.

[25] Flohr C, Weinmayr G, Weiland SK (deceased), Addo-Yobo E, Annesi-Maesano I. How well do questionnaires perform compared with physical examination in detecting flexural eczema? Findings from the International Study of Asthma and Allergies in

Childhood (ISAAC) Phase Two. *Br J Dermatol* 2009;161:846-53. Doi: 10.1111/j.1365-2133.2009.09261.x.

[26] Jousilahti P, Haahtela T, Laatikainen T, Mäkelä M, Vartiainen E. Asthma and respiratory allergy prevalence is still increasing among Finnish young adults. *Eur Respir J* 2016;47:985-987. Doi:10.1183/13993003.01702-2015.

[27] Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006;368:733-43. Doi: 10.1016/S0140-6736(06)69283-0.

[28] Masoli M, Fabian D, Holt S, Beasley R for the Global Initiative for Asthma (GINA) Program. The global burden of asthma: executive summary of the GINA dissemination committee report. *Allergy* 2004;59:469-478. Doi: 10.1111/j.1398-9995.2004.00526.x.

[29] NCD Risk factor collaboration. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. *Lancet* 2016;387:1377-96. Doi: 10.1016/S0140-6736(16)30054-X.

[30] Campbell DE, Boyle RJ, Thornton CA, Prescott SL. Mechanisms of allergic disease – environmental and genetic determinants for the development of allergy. *Clin Exp Allergy* 2015;45:844-858. Doi: 10.1111/cea.12531.

[31] Hersoug L-G, Linneberg A. The link between the epidemics of obesity and allergic diseases: does obesity induce decreased immune tolerance? *Allergy* 2007;62:1205-13. Doi: 10.1111/j.1398-9995.2007.01506.x.

[32] Baiardini I, Braido F, Giardini A, Majani G, Cacciola C, Rogaku A, Scordamaglia A, Canonica GW. Adherence to treatment: assessment of an unmet need in asthma. *J Investig Allergol Clin Immunol* 2006;16(4):218-23. Free full text.

[33] Teyhan A, Galobardes B, Henderson J. Child allergic symptoms and well-being at school: Findings from ALSPAC, a UK cohort study. *J PLoS ONE.* 2015;10(8):e0135271. doi:10.1371/journal. pone.0135271.

[34] Rutter M, Rutter M. *Developing minds. Challenge and continuity across the life span*. England; Clays Ltd, 1993.

[35] Juniper EF. How important is quality of life in pediatric asthma? *Pediatr Pulmonol Suppl* 1997;15:17-21. Doi: 10.1002/(SICI)1099-0496(199709)15+<17::AID-PPUL5>3.0.CO;2-O.

[36] Tuckman A. The Potential Psychological Impact of Skin Conditions. *Dermatol Ther* (Heidelb)2017;7(Suppl 1):53-57. doi: 10.1007/s13555-016-0169-7.

[37] Osman LR, Caldman C, Robertson R, et al. Symptoms, quality of life, and health service contact among young adults with mild asthma. *Am J Respir Crit Care Med* 2000;61:498-503.

[38] Jago R, Searl A, Henderson AJ, Turner KM. Designing a physical activity intervention for children with asthma: a qualitative study of the views of healthcare professionals, parents and children with asthma. *BMJ Open* 2017;24:7(3):e014020.doi: 10.1136/bmjopen-2016-014020.

[39] Cui W, Zack MM, HS Zahran. Health-related quality of life and asthma among United States adolescents. *J Pediatr* 2015;166(2):358-364. Doi: 10.1016/j.jpeds.2014.10.005.

[40] Akeson N, Worth A, Sheikh A. The psychosocial impact of anaphylaxis on young people and their parents. *Clin Exp Allergy* 2007;37:1213-20. Doi: 10.1111/j.1365-2222.2007.02758.x.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
✓ **Title and abstract**	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract, p. 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found, p. 2
Introduction		
✓ Background/rationale	2	Explain the scientific background and rationale for the investigation being reported, p. 4
✓ Objectives	3	State specific objectives, including any prespecified hypotheses, p. 4
Methods		
✓ Study design	4	Present key elements of study design early in the paper, p. 5
✓ Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection, p. 5
✓ Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants, p. 5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
✓ Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable, p. 5-7
✓ Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group, p. 5-7
✓ Bias	9	Describe any efforts to address potential sources of bias, p. 7

✓	Study size	10	Explain how the study size was arrived at, p. 5
✓	Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why, p. 7
✓	Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding, p. 7
			(*b*) Describe any methods used to examine subgroups and interactions
			(*c*) Explain how missing data were addressed
			(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy, p. 5
			(*e*) Describe any sensitivity analyses

Continued on next page

Results			
✓	Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed, p. 12
			(b) Give reasons for non-participation at each stage
			(c) Consider use of a flow diagram
✓	Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders, p. 7-8, 12
			(b) Indicate number of participants with missing data for each variable of interest
			(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
✓	Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
			Case-control study—Report numbers in each exposure category, or summary measures of exposure
			Cross-sectional study—Report numbers of outcome events or summary measures, p. 5
✓	Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included, p.12
			(*b*) Report category boundaries when continuous variables were categorized
			(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
✓	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion			
✓	Key results	18	Summarise key results with reference to study objectives, p. 8-10
✓	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias, p. 10
✓	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence, p. 9-10
✓	Generalisability	21	Discuss the generalisability (external validity) of the study results, p. 9
Other information			

✓	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based, p. 11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The association of allergic diseases with children's life satisfaction: population-based study in Finland

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The association of allergic diseases with children's life satisfaction: population-based study in Finland

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Abstract

Objective: To assess the impact of allergic diseases on the subjective well-being and life satisfaction of primary school children.

Design: Population-based cohort.

Setting: Finnish sample of children ages 10 and 12 from the International Survey of Children's Well-Being.

Participants: Nationally representative sample of 1947 school children.

Main outcome measure: Two different instruments to assess the child's own perception of well-being; the short version of the Student Life Satisfaction Scale (SLSS) and the Brief Multidimensional Student Life Satisfaction Scale (BMSLSS).

Results: Altogether, 51.4% of children reported having at least one allergic condition (10.1% asthma, 23.8% eczema, and 40.3% seasonal allergic rhinitis). A statistically significant distinction in life satisfaction emerged between non-allergic and allergic children (inferior in the latter). In particular, children with eczema were more likely to report a reduction in life satisfaction compared to non-allergic children (SLSS $\beta = -128.220$; BMSLSS $\beta = -90.694$; $p < 0.01$). Apart from freedom from eczema, good life satisfaction was associated with a physically active life style.

Conclusions: Active allergic disease reduces the child's own perception of well-being. During clinical visits, more attention should be paid to the child's psychosocial status and impairments, which may differ substantially from those of parents or medical authorities.

Keywords: allergy; asthma; eczema; life satisfaction, physical activity

Strengths and limitations of this study

- The first nationally representative survey on subjective life satisfaction in primary-school children in Finland.
- The first national study that observed allergic diseases with relation to children´s life satisfaction.
- The study did not directly and objectively assess the allergy symptoms in question. The research focus was on children's own perception of life-satisfaction rather than on disease severity.
- The data used in the present study are cross-sectional, and any causal relationship between the predictors and outcome variables thus remains obscure.

INTRODUCTION

Societies worldwide are faced with a progressively increasing risk of immune-mediated health problems such as allergic, autoimmune, and inflammatory diseases, and the velocity of propagation is highest in children.[1 2] Allergic diseases, the first manifestation of these conditions, comprise the most common chronic disease among children, with a prevalence ranging from 7% (eczema) to 14.6% (asthma and rhinitis) in 13- to 14-year-old children.[3] Thus, allergic diseases represent a significant burden not only for society and the family but also for the affected individual.

The severity of allergic disease is assessed by the extent of symptoms in daily life. A vicious circle of symptoms of allergic disease such as allergy flares and emotional stress has been documented, and these symptoms can potentially contribute to the experienced burden of the disease.[4] Despite a growing interest in life satisfaction during childhood, little is known about how chronic diseases such as asthma or eczema affect children's subjective well-being (SWB), that is, psychosocial contentment. In fact, the burden of allergic disorders may extend well beyond mere physical functioning.

Youth with a chronic illness are at increased risk for poor self-concept[5] and show significantly higher rates of emotional and behavioural problems.[6] Self-concept, as a fundamental part of a child's psychological function, is strongly affected by parental and peer approval, physical appearance and perceived competence in domains of importance, such as athletics.[7] For example, for children with asthma, a decreased quality of life has been found to be related to limited activities and participation in sports.[8]

The importance of the disease burden may culminate in children, whose recognition of self and self-esteem are still evolving, and thus disease may have a long-term impact on personal well-being and quality of life.[6 9 10 11] In the medical literature,

quality of life refers to a 'uniquely personal perception, denoting the way that individual patients feel about their health status and/or nonmedical aspects of their lives'.[12] On one hand, health is considered a major component affecting one's quality of life and on the other hand, good quality of life is an important outcome of successful treatment of diseases.[8]

The objective of the study presented here was to assess the impact of allergic diseases on subjective well-being and life satisfaction among primary-school children. Conventionally, children's well-being has been determined indirectly, using proxies such as household income, mortality, or life expectancy or using parental reports on child well-being,[13 14] thus ignoring the child's own point of view. However, children's and parents' perceptions of a child's quality of life often differ; thus, obtaining information directly from the child is advisable.[9 12] Another gap in the research literature regards the lack of attention to ethnically and racially diverse samples.[10 15 16] Research on racially diverse groups of children with allergic diseases would increase our knowledge of the association between allergy and childhood quality of life in populations of children who may already be at increased risk of impaired well-being.[10]

Recent research has provided tools that can be used to evaluate self-reported perceptions of quality of life, satisfaction, or other emotional and behavioural elements of children's lives.[17] In the context of allergic diseases, we applied for the first time two summary measures of life satisfaction: the Student Life Satisfaction Scale (SLSS, measuring children's overall life satisfaction) and the Brief Multidimensional Student Life Satisfaction Scale (BMSLSS, measuring children's overall life satisfaction). [17 18 19]

METHODS

Study population and setting

This study is part of an international Children's Worlds survey (http://www.isciweb.org),[20] which is an international survey on school-aged children's subjective well-being. The purpose of the study is to improve children's well-being by creating awareness among children, their parents, and their communities, as well as among other parties involved in children's lives, such as policy decision makers or teachers. The study was approved by the Ethics Committee of the University of Turku (statement obtained 15 February 2016). Cross-sectional data collected in Finland were used, comprising a random selection of nationally representative data from 43 primary schools (35 classes of 4th graders, 39 classes of 6th graders). Informed consent was obtained from the participants and their parents prior to administering the survey. Finally, in each school at least 40 pupils in each of grades 4 and 6 were recruited. In total, 1947 pupils (67.6% response rate; 48.7% boys; mean age, 11 years) completed an online anonymous questionnaire.

Outcome variables

Global life satisfaction

A reduced version of Huebner's[17] SLSS was expanded by one item assessing children's overall life satisfaction ('the things in my life are excellent'), adapted from Diener.[18] The SLSS hypothesizes that children are able to formulate judgments of their overall life satisfaction over and above judgments concerning specific domains (e.g., family, friends, community).[17] Instead of asking about dissatisfaction and negative life judgments, the SLSS focuses on positive, affective conceptualizations of the child's life. This provides information that is complementary to children's own perceptions of their

optimal development. The internal consistency of the SLSS items was tested via Cronbach's alpha, resulting in $\alpha = 0.94$, indicating internal consistency and reliability.

Domain-specific life satisfaction

The BMSLSS[19] measures satisfaction in life in more general terms than the SLSS. The evaluation covers five important life domains, using one item per domain: family life, friendships, school experience, body image, and child's living environment ($\alpha = 0.78$).

Scoring and validity

In both scales, the scoring system was modified from the original version (1 = 'Strongly disagree' to 6 = 'Strongly agree') to an 11-point scale (0–10). A higher score reflects higher life satisfaction. After calculating the mean of all five items, the subscales were summed and transformed into a scale of 0–100.

SLSS and BMSLSS are validated measures of children's experiences of life satisfaction including psychometric properties, targeted to age groups from 8 to 18 years. These measures have been successfully used in other experience sampling studies; however, to date only a few studies have used them in the context of chronic conditions.[21 22]

Characterization of the allergic conditions

Three questions, modified from the ISAAC Phase One core questionnaires investigating the prevalence of doctor-diagnosed asthma, allergic rhinitis, and eczema in children worldwide,[23] were used to characterize allergic disease among the study population. In Finland, the ISAAC core questions on asthma have been validated against anti-asthmatic medication reimbursement data from the Finnish Social Insurance Institution and were found to be highly valid.[24] The participants were asked whether they used inhaled asthma medication (no/yes) prescribed by a doctor. In like manner, children

were asked about the presence of itchy rash sometimes appearing and disappearing (no/yes), which was interpreted to represent atopic eczema. Although ISAAC questions on eczema have not been specifically validated in the Finnish language, it has been shown that, in general, ISAAC-questionnaire-derived symptom prevalence is sufficiently precise at the population level.[25] Runny or blocked nose and sneezing in seasons of birch pollen or hay (no/yes) was considered to represent seasonal allergic rhinitis in Finland.

Data on background variables

Self-reported sex, age, ethnic background and parent's employment status were used as socio-demographic background variables. Children were asked for the employment status of both parents (mother and father working: yes, no, do not know) and a recoded variable was formed (parents working: no, yes). Ethnic background was determined based on three items: were you / your mother / your father born in Finland (yes, no, I am not sure). Additionally, we used data on pets (a pet in the family when the child was born or currently in the household; yes, no, I do not know). After-school physical activity (sports or exercising) was self-reported.

Statistical analysis

Continuous non-normally distributed SLSS and BMSLSS outcome variables were characterized using means, standard deviations, medians and mean ranks. Ranks, counted over the total data, were used in analyses because of the extremely left skewed distributions of the outcome variables SLSS and BMSLSS. Student's *t*-test for independent samples was applied in comparisons between variables. In the second phase of analysis, the significant background variables from both SLSS and BMSLSS

and all five asthma variables (A pet when born, A pet now, Asthma, Eczema, Perennial rhinitis) were subjected to linear regression analysis. The interactions were evaluated, but all were excluded as non-significant from the final regression models. Imputation of the data was not applied to statistical analysis. However, the analyses were conducted using weighting coefficients calculated for Finnish data.[20] This takes into account non-response, varying probabilities of selection, and variations between characteristics of the sample and the population from which the sample was drawn. Statistical analyses were carried out using SAS for Windows version 9.4 (SAS, Cary, NC, USA) and *p*-values below 0.05 were considered statistically significant.

RESULTS

Overall, the Finnish children in this study evaluated their well-being as excellent; more than 80% of 10- and 12-years-olds were very satisfied with their lives. Altogether, 51.4% (n = 965) reported having at least one allergic disease – 10.1% (n = 188) doctor-diagnosed asthma, 23.8% (n = 452) eczema, and 40.3% (n = 769) seasonal allergic rhinitis.

A significant difference in life satisfaction emerged between non-allergic and allergic children on both scales (Table 1). In particular, eczema was associated with reduced well-being when compared with children not manifesting atopic eczema: the difference on both scales was statistically significant (SLSS, $p < 0.001$; BMSLSS, $p < 0.01$). In contrast, no associations were detected between asthma or allergic rhinitis and life satisfaction. It is of note that all subjects with an asthma diagnosis were on prescribed inhaled asthma medication. An additional correlation analysis showed that all the domains of BMSLSS were statistically significantly associated with eczema. The most affected domain was body image ($r = -0.10$, $p < 0.001$).

The determinants of good life satisfaction were measured by a multivariable model (Table 2). Children not having eczema, aged 10 years (grade 4), with working parents and a physically active life style were found to be more satisfied with their lives than other children. Having had pets in early infancy or having pets currently had no impact on life satisfaction.

Taken together, the strongest predictor of good life satisfaction was a physically active life style ($\beta = 194.05$, $p < .001$), while reduced life satisfaction was correlated with eczema ($\beta = -128.22$, $p < 0.001$).

DISCUSSION

This study, which is the first nationally representative survey on subjective life satisfaction and allergic diseases in primary-school children, revealed that active allergic disease is a major determinant of children's well-being in various domains. In particular, eczema was seen to reduce both global life satisfaction related to children's moods and feelings (SLSS) and life satisfaction as measured across broader domains of living (BMSLSS). In accord with national[26] and international[27] reports, half of the children in the studied sample reported having at least one allergic condition, indicating that our results may be generalizable.

Not only do allergic diseases comprise the most common chronic disorder of childhood;[28] they also represent the first manifestation of the growing epidemic of non-communicable diseases,[29] which tend to share environmental risk factors and patho-mechanisms and frequently coexist.[2 30 31] Besides their well-known economic burden, chronic diseases exert a substantial psychosocial impact on children and their families. This notwithstanding, health-related quality of life research has only recently attracted scientific interest.[22 32 33]

The importance of life satisfaction may be highest in childhood. Children, specifically those on the very edge of puberty, are vulnerable to external influences such as peer acceptance.[34] This phase of life is especially important with regards to self-acceptance and relation to self. As also demonstrated in this study, younger children were more content in terms of their life satisfaction than older ones. Hence, our study results tend to substantiate those of previous research[5] according to which age is related to perceptions of well-being, for example in the context of emotional well-being. However, the lack of interaction between the variables of age, allergies, and life satisfaction indicates that the experience of life satisfaction is influenced by the burdens presented by allergies and age individually.

Previous studies mainly on adult populations indicate that active allergic diseases are related to decreased well-being, as manifested in fewer relationships, limited daily functioning and decreased self-acceptance, as well as decreased emotional well-being.[32 33 35 36] Our results further underline that allergic diseases not only affect separate domains of children's lives but also have a holistic effect; the intricacy of the allergic burden is manifested in children's overall life satisfaction. For example, skin conditions distress psychosocial well-being by virtue of the stigma resulting from the visibility of dermatological symptoms.[33] Furthermore, children with persistent or late-onset eczema or with persistent wheeze were demonstrated to have psychosocial problems at school.[33]

Our study results show no association between ethnic background, allergic diseases, and life satisfaction. This suggests that the impact of allergic diseases does not differ between ethnically Finnish children and children with an immigrant background. Parental employment status was significantly related to life satisfaction, indicating that children of working parents were more satisfied with their lives than those of non-working parents. This association, however, was not associated with allergic diseases.

In the present study, respiratory allergy seemed to have less influence on children's life-satisfaction than eczema. An alternative explanation would be that the absence of effects indicates that the symptoms of these allergies are treatable. Interestingly, previous studies suggest that symptom-free patients report better well-being than the population on average,[37] suggesting that it is not the chronic disease *per se* which impacts the quality of life of those affected but the manifestations thereof (symptoms). Treating asthma promotes a physically active life style,[38] and a physically active life style was strongly associated with life satisfaction in the present survey. Thus, the benefit of balanced asthma treatment may extend far beyond physical health to psychosocial consequences and overall improvements in the quality of life.[39]

This study was the first to investigate the subjectively measured quality of life focusing on children with or without allergic diseases in a large, nationally representative, sample of 10–12-year-old Finnish children. However, some limitations of this study need to be acknowledged. Firstly, the study did not directly and objectively assess the symptoms in question. Rather, the research focused on children's own perception of disease severity. Similarly, there is a potential for error in children's reports of parental employment status and pet ownership at child's birth. Using objective measures or medical records to verify diagnoses and disease severity and, for instance, parental reports to verify employment status is one way for future studies to improve upon the current study assessing self-reported diseases as correlates of children's life satisfaction. Lastly, the data used in the present study are cross-sectional, and any causal relationship between the predictors and outcome variables thus remains obscure.

Taken together, our results suggest a call to monitor the psychological well-being of children affected by allergic diseases, which are the most common chronic diseases

in childhood. In medical care, consideration should be given to the children's perceived impairments,[37] as these may differ substantially from the perceptions of parents or medical authorities.[40]

Contributors: L. Haanpää drafted the final version of this manuscript, and all authors (L. Haanpää, P. af Ursin, M. Nermes, A. Kaljonen, E. Isolauri) drafted different sections and paragraphs of this work, critically revised this work for important intellectual content, approved the final version to be published, and agreed on the accuracy and integrity of this work. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare the following: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: This study was approved by the Ethics Committee of the University of Turku.

Data sharing: No additional data available.

Transparency: The lead author (LH) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Table 1. Socio-economic background variables, pet status, and allergy variables affecting children's life satisfaction analysed by t-test for independent samples.*

	SLSS					BMSLSS				
	n	**Mean(sd)**	**Md**	**Mean rank**	***p***	***n***	**Mean(sd)**	**Md**	**Mean rank**	***p***
Gender					0.7642					0.0685
boy	946	90.3(14.0)	96	824.7		867	88.8(11.4)	92	807.4	
girl	998	89.8(14.8)	96	818.9		938	89.3(12.1)	92	848.5	
Grade					<0.0001					<0.0001
4	942	91.0(14.4)	96	864.4		863	90.7(11.4)	94	924.9	
6	1002	89.2(14.4)	94	781.6		942	87.5(11.8)	90	740.7	
Born in Finland					0.6146					0.1949
no	1880	90.1(14.5)	96	822.6		1743	89.1(11.7)	92	831.5	
yes	64	89.8(12.7)	96	795.4		62	86.7(13.6)	90	751.3	
Parents working					<0.0295					
no	577	88.8(16.0)	94	794.5		542	88.2(12.9)	92	808.0	0.1292
yes	1342	90.9(13.4)	96	840.2		1241	89.6(10.9)	92	845.3	
Doing sports					<0.0020					<0.0001
no	78	83.1(21.4)	94	678.2		65	79.8(16.4)	82	511.4	
yes	1803	90.4(14.0)	96			1686	89.4(11.4)	92	843.8	
A pet when born					0.1852					0.3060
no	962	90.4(13.3)	96	841.4		894	89.6(11.1)	92	849.6	
yes	766	89.3(15.9)	96	814.2		711	88.7(12.6)	92	824.9	
A pet now					0.3202					=0.0102
no	703	90.5(13.8)	96	835.7		660	89.9(11.3)	92	867.0	
yes	1227	89.8(14.7)	96	815.7		1132	88.5(12.0)	92	806.7	
Asthma					0.5263					0.8561
no	1678	90(14.2)	96	817.6		1566	89.0(11.6)	92	827.2	
yes	191	89.3(16.9)	96	838.2		174	88.3(13.7)	92	820.2	
Eczema					<0.0001					=0.0018
no	1446	90.8(13.7)	96	843.3		1350	89.6(11.0)	92	848.5	
yes	452	87.5(16.6)	92	745.8		414	87.2(13.4)	90	764.6	
Seasonal rhinitis					0.6494					0.6441
no	1140	89.9(14.6)	96	816.0		1061	89.0(11.6)	92	823.5	
yes	764	90.0(14.3)	96	825.1		709	89.1(11.9)	92	834.2	

*By Kruskall-Wallis non-parametric tests.

Table 2. Children's life satisfaction explained by grade, parental employment status, physical activity, pet status, and allergy variables.*

	SLSS			BMSLSS		
	β	**SE**	***p***	**β**	**SE**	***p***
Grade	−60.880	13.799	<0.001	−106.225	13.322	<0.001
Parents working	65.682	30.324	<0.05	70.065	29.141	<0.05
Doing sports	194.053	67.723	<0.001	307.704	68.914	<0.001
A pet when born	−22.414	29.734	0.4511	−7.676	28.794	0.7898
A pet now	−28.816	30.597	0.3464	−47.133	29.577	0.1113
Asthma	60.220	46.539	0.1959	1.662	45.248	0.9707
Eczema	−128.220	32.575	<0.01	−90.694	31.441	<0.01
Seasonal rhinitis	29.331	29.015	0.3122	19.440	27.947	0.4868

*By linear regression analysis.

REFERENCES

[1] Bach JF. The effect of infections on susceptibility to autoimmune and allergic diseases. *N Engl J Med.* 2002;347;12:911-920. Doi: 10.1056/NEJMra020100.

[2] Rautava S, Luoto R, Salminen S, Isolauri E. Microbial contact during pregnancy, intestinal colonization and human disease. *Nat. Rev. Gastroenterol. Hepatol.* 2012;9:565-576. doi: 10.1038/nrgastro.2012.144.

[3] Mallol J, Crane J, von Mutius E, Odhiambo J, Keil U, Stewart A. The international study of asthma and allergies in childhood (ISAAC) phase three: a global synthesis. *Allergol Immunopathol* (Madr) 2013;41(2):73-85. doi: 10.1016/j.aller.2012.03.001.

[4] Patterson AM, Yildiz VO, Klatt MD, Malarkey WB. *Perceived stress predicts allergy flares.* Annals of Allergy, Asthma & Immunology: Official Publication of the American College of Allergy, Asthma, & Immunology 2014;112(4):317-321. doi.org/10.1016/j.anai.2013.07.013.

[5] Ferro M, Boyle M. Self-concept among youth with a chronic illness: A meta-analytic review. *Health Psychol* 2013;32;8: 839-848. Doi: 10.1037/a0031861.

[6] Ferro MA, Van Lieshout RJ, Ohayon J, Scott JG. Emotional and behavioral problems in adolescents and young adults with food allergy. *Allergy* 2016;71:532-540. Doi: 10.1111/all.12829.

[7] Harter S. *The Construction of the Self: A Developmental Perspective.* New York, NY, USA; Guilford, 1999.

[8] Glazebrook C, McPherson AC, Macdonald IA, Swift JA, Ramsay C, Newbould R, Smyth A. Asthma as a barrier to children's physical activity: implications for body mass index and mental health. *Pediatrics* 2006;118;6:2443-2449. Doi: 10.1542/peds.2006-1846.

[9] Merikallio VJ, Mustalahti K, Remes ST, Valovirta EJ, Kaila M. Comparison of quality of life between asthmatic and healthy school children. *Pediatr Allergy Immunol* 2005;16:332-340. Doi: 10.1111/j.1399-3038.2005.00286.x

[10] Everhart RS, Fiese BH. Asthma severity and child quality of life in pediatric asthma: A systematic review. *Patient Educ Couns* 2009;75:162-168. Doi: 10.1016/j.pec.2008.10.001.

[11] Heinl D, Chalmers J, Nankervis H, Apfelbacher CJ. Eczema Trials: Quality of Life Instruments Used and Their Relation to Patient-Reported Outcomes. A Systematic Review. *Acta Derm Venereol* 2016;96:596-601. Doi: 10.2340/00015555-2322.

[12] Gill TM, Feinstein AR. A critical appraisal of the quality of quality-of-life measurements. *JAMA* 1994;272;8:619-626. Doi:10.1001/jama.1994.03520080061045.

[13] Coffey, JK, Warren MT, Gottfried AV. Does infant happiness forecast adult life satisfaction? Examining subjective well-being in the first quarter century of life. *J Happiness Stud* 2015;16(6):1401-1421. doi 10.1007/s10902-014-9556-x.

[14] Sourander A, Helstelä L, Helenius H. Parent-adolescent agreement on emotional and behavioral problems. *Soc Psychiatry Psychiatr Epidemiol* 1999;34:657-663.

[15] McQuaid EL, Farrow ML, Esteban CA, Jandasek BN, Rudders SA. Topical Review: Pediatric Food Allergies among Diverse Children. *J Pediatr Psychol* 2016;41;4:391-396. Doi: 10.1093/jpepsy/jsv051.

[16] Shaw TE, Currie, GP, Koudelka CW, Simpson EL. Eczema prevalence in the United States: Data from the 2003 national survey of children´s health. *J Invest Dermatol* 2011;131;1:67-73. Doi: 10.1038/jid.2010.251.

[17] Diener E, Emmons RA, Larsen RJ, Griffin S. The satisfaction with life scale. *J Pers Assess* 1985;49:71-75.

[18] Huebner SE. Further validation of the students' life satisfaction scale: The independence of satisfaction and affect ratings. *J Psychoed Assess* 1991;9:363-368. Doi: 10.1177/073428299100900408.

[19] Seligson JL, Huebner ES, Valois RF. Preliminary validation of the brief multidimensional students' life satisfaction scale (BMSLSS). *Soc Ind Res* 2003;61:121-145. doi: 10.1007/s10488-011-0385-5.

[20] Children's worlds. 2017. http://www.isciweb.org.

[21] Lippman LH, Anderson Moore K, McIntosh H. *Positive indicators of child well-being: a conceptual framework, measures and methodological issue*s. Innocenti Working Paper No. 2009-21; 2009. Florence, UNICEF Innocenti Research Centre.

[22] McDougall J, Wright W, Nichols M, Miller L. Assessing the psychometric properties of both a global and a domain-specific perceived quality of life measure when used with youth who have chronic conditions. *Soc Indic Res* 2013;114:1243-1257. Doi 10.1007/s11205-012-0200-z.

[23] Asher MI, Weiland SK on behalf of the ISAAC steering committee. The international study of asthma and allergies in childhood (ISAAC). *Clin Exp Allergy* 1998;28 Supp 5:52-66.

[24] Nwaru BI, Lumia M, Kaila M, Luukkainen P, Tapanainen H, Erkkola M. Validation of the Finnish ISAAC questionnaire on asthma against anti-asthmatic medication reimbursement database in 5-year-old children. *Clin Respir J* 2011;5:211-8. Doi: 10.1111/j.1752-699X.2010.00222.x.

[25] Flohr C, Weinmayr G, Weiland SK (deceased), Addo-Yobo E, Annesi-Maesano I. How well do questionnaires perform compared with physical examination in detecting flexural eczema? Findings from the International Study of Asthma and Allergies in

Childhood (ISAAC) Phase Two. *Br J Dermatol* 2009;161:846-53. Doi: 10.1111/j.1365-2133.2009.09261.x.

[26] Jousilahti P, Haahtela T, Laatikainen T, Mäkelä M, Vartiainen E. Asthma and respiratory allergy prevalence is still increasing among Finnish young adults. *Eur Respir J* 2016;47:985-987. Doi:10.1183/13993003.01702-2015.

[27] Asher MI, Montefort S, Björkstén B, Lai CK, Strachan DP, Weiland SK, et al. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006;368:733-43. Doi: 10.1016/S0140-6736(06)69283-0.

[28] Masoli M, Fabian D, Holt S, Beasley R for the Global Initiative for Asthma (GINA) Program. The global burden of asthma: executive summary of the GINA dissemination committee report. *Allergy* 2004;59:469-478. Doi: 10.1111/j.1398-9995.2004.00526.x.

[29] NCD Risk factor collaboration. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. *Lancet* 2016;387:1377-96. Doi: 10.1016/S0140-6736(16)30054-X.

[30] Campbell DE, Boyle RJ, Thornton CA, Prescott SL. Mechanisms of allergic disease – environmental and genetic determinants for the development of allergy. *Clin Exp Allergy* 2015;45:844-858. Doi: 10.1111/cea.12531.

[31] Hersoug L-G, Linneberg A. The link between the epidemics of obesity and allergic diseases: does obesity induce decreased immune tolerance? *Allergy* 2007;62:1205-13. Doi: 10.1111/j.1398-9995.2007.01506.x.

[32] Baiardini I, Braido F, Giardini A, Majani G, Cacciola C, Rogaku A, Scordamaglia A, Canonica GW. Adherence to treatment: assessment of an unmet need in asthma. *J Investig Allergol Clin Immunol* 2006;16(4):218-23. Free full text.

[33] Teyhan A, Galobardes B, Henderson J. Child allergic symptoms and well-being at school: Findings from ALSPAC, a UK cohort study. *J PLoS ONE.* 2015;10(8):e0135271. doi:10.1371/journal. pone.0135271.

[34] Rutter M, Rutter M. *Developing minds. Challenge and continuity across the life span*. England; Clays Ltd, 1993.

[35] Juniper EF. How important is quality of life in pediatric asthma? *Pediatr Pulmonol Suppl* 1997;15:17-21. Doi: 10.1002/(SICI)1099-0496(199709)15+<17::AID-PPUL5>3.0.CO;2-O.

[36] Tuckman A. The Potential Psychological Impact of Skin Conditions. *Dermatol Ther* (Heidelb)2017;7(Suppl 1):53-57. doi: 10.1007/s13555-016-0169-7.

[37] Osman LR, Caldman C, Robertson R, et al. Symptoms, quality of life, and health service contact among young adults with mild asthma. *Am J Respir Crit Care Med* 2000;61:498-503.

[38] Jago R, Searl A, Henderson AJ, Turner KM. Designing a physical activity intervention for children with asthma: a qualitative study of the views of healthcare professionals, parents and children with asthma. *BMJ Open* 2017;24:7(3):e014020.doi: 10.1136/bmjopen-2016-014020.

[39] Cui W, Zack MM, HS Zahran. Health-related quality of life and asthma among United States adolescents. *J Pediatr* 2015;166(2):358-364. Doi: 10.1016/j.jpeds.2014.10.005.

[40] Akeson N, Worth A, Sheikh A. The psychosocial impact of anaphylaxis on young people and their parents. *Clin Exp Allergy* 2007;37:1213-20. Doi: 10.1111/j.1365-2222.2007.02758.x.

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation
✓ **Title and abstract**	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract, p. 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found, p. 2
Introduction		
✓ Background/rationale	2	Explain the scientific background and rationale for the investigation being reported, p. 4
✓ Objectives	3	State specific objectives, including any prespecified hypotheses, p. 4
Methods		
✓ Study design	4	Present key elements of study design early in the paper, p. 5
✓ Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection, p. 5
✓ Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants, p. 5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case
✓ Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable, p. 5-7
✓ Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group, p. 5-7
✓ Bias	9	Describe any efforts to address potential sources of bias, p. 7

✓	Study size	10	Explain how the study size was arrived at, p. 5
✓	Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why, p. 7
✓	Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding, p. 7
			(*b*) Describe any methods used to examine subgroups and interactions
			(*c*) Explain how missing data were addressed
			(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy, p. 5
			(*e*) Describe any sensitivity analyses

Continued on next page

Results			
✓	Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed, p. 12
			(b) Give reasons for non-participation at each stage
			(c) Consider use of a flow diagram
✓	Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders, p. 7-8, 12
			(b) Indicate number of participants with missing data for each variable of interest
			(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)
✓	Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time
			Case-control study—Report numbers in each exposure category, or summary measures of exposure
			Cross-sectional study—Report numbers of outcome events or summary measures, p. 5
✓	Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included, p.12
			(*b*) Report category boundaries when continuous variables were categorized
			(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
✓	Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion			
✓	Key results	18	Summarise key results with reference to study objectives, p. 8-10
✓	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias, p. 10
✓	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence, p. 9-10
✓	Generalisability	21	Discuss the generalisability (external validity) of the study results, p. 9
Other information			

✓	Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based, p. 11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.