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Physical activity and asthma development in childhood: Prospective birth cohort study

Marianne Eijkemans MD[1,2] | Monique Mommers PhD[1] | Teun Remmers PhD[1,3] | Jos M. Th. Draaisma MD, PhD[4,5] | Martin H. Prins MD, PhD[1] | Carel Thijs MD, PhD[1]

[1]Care and Public Health Research Institute (CAPHRI), Maastricht University, Maastricht, The Netherlands

[2]Department of Pediatrics, Catharina Hospital, Eindhoven, The Netherlands

[3]School of Sport Studies, Fontys University of Applied Sciences, Eindhoven, The Netherlands

[4]Department of Pediatrics, Radboudumc Amalia Children's Hospital, Nijmegen, The Netherlands

[5]Department of Pediatrics, Viecuri Medical Centre, Venlo, The Netherlands

Correspondence
Marianne Eijkemans, Department of Epidemiology, Maastricht University, PO Box 616, 6200 MD, Maastricht, The Netherlands.
Email: Marianne.eijkemans@maastrichtuniversity.nl

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Abstract

Background: Sedentary behavior and decreased physical activity are possible risk factors for developing asthma. This longitudinal study investigates the association between physical activity and subsequent asthma. We hypothesize that children with decreased physical activity at early school age, have higher risk of developing asthma.

Methods: One thousand eight hundred thirty-eight children from the KOALA Birth Cohort Study were analyzed. Children who were born prematurely or with congenital defects/diseases with possible influence on either physical activity or respiratory symptoms were excluded. Physical activity, sedentary behavior, and screen time were measured at age 4 to 5 years by questionnaire and accelerometry in a subgroup (n = 301). Primary outcome was asthma, assessed by repeated ISAAC questionnaires between age 6 and 10. Secondary outcome was lung function measured by spirometry in a subgroup (n = 485, accelerometry subgroup n = 62) (forced expiratory volume in 1 second [FEV1], forced vital capacity [FVC] and FEV1/FVC ratio) at age 6 to 7 years.

Results: Reported physical activity was not associated with reported asthma nor lung function. Accelerometry data showed that daily being 1 hour less physically active was associated with a lower FEV1/FVC (z score β, −0.65; 95% confidence interval, −1.06 to −0.24).

Conclusions: Physical activity at early school age was not associated with reported asthma development later in life. However, lung function results showed that sedentary activity time was associated with lower FEV1/FVC later in childhood. As this is the first longitudinal study with objectively measured physical activity and lung function, and because the subgroup sample size was small, this result needs replication.

KEYWORDS

accelerometry, asthma, exercise, spirometry

1 | INTRODUCTION

Asthma is one of the most common chronic diseases in childhood and is associated with increased Westernization.[1] Sedentary behavior and decreased physical activity (PA) are also associated with

Abbreviations: BMI, body mass index; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; GLI, Global Lung Function Initiative; ISAAC, International Study of Asthma and Allergies in Childhood; MVPA, moderate to vigorous physical activity; OR, odds ratio; PA, physical activity.

prosperity.[2] PA has been identified as a possible protective factor in several chronic illnesses, such as diabetes, high blood pressure, heart disease, and asthma.[3,4] The role of PA in asthma is subject to debate. Several studies have suggested that asthmatic children are less physically active than their healthy peers,[5,6] however other studies showed no difference.[7] Exercising induces a beneficial effect on allergic inflammation,[8] on quality of life, and cardiopulmonary fitness in asthmatics, but it has no effect on lung function.[9] The role of PA in asthma prevention is still unclear. To establish a causal role of PA in asthma development there is a need for longitudinal studies. In adults, these longitudinal studies are not conclusive: some showed no association,[10,11] others designated low PA as potential risk factor for developing asthma,[12,13] and one study found a reverse association.[14] In children, only a few longitudinal studies were conducted on this subject: Byberg et al[15] showed that low PA at age 3 to 6 years was associated with asthma later in childhood. Parents of 617 children were asked if their child was “not so active,” “active,” or “very active.” Sherriff et al[16] showed that children who watched more TV at age 3 years had a higher risk of developing asthma at age 11.5 years.

In this study, we aim to evaluate PA preceding asthma development in childhood. We measured PA at age 4 to 5 years, lung function at age 6 years, and asthma at several ages between 6 and 10 years. We hypothesize that low PA in childhood increases the risk of asthma development later in life. To our knowledge, this is the first longitudinal study in childhood on PA and asthma using questionnaires as well as objective measurements for both the exposure and the outcome (accelerometry and spirometry).

2 | MATERIALS AND METHODS

This prospective study was embedded in the KOALA (Child, Parent, and Health: Lifestyle and Genetic Constitution [in Dutch]) Birth Cohort Study,[17] which focuses on potential risk factors for atopy and asthma development in childhood. In total, 2834 pregnant women were recruited and completed a questionnaire at 34 weeks of gestation. The birth cohort consists of two recruitment groups, based on lifestyle (alternative and conventional). Children born to these mothers were followed at several ages (ie, 3 and 7 months, 1 year, 2 years, 4 to 5 years, 6 to 7 years, 6 to 8 years, 7 to 9 years, and 8 to 10 years).

Inclusion criteria for the present study were: all children for whom their parents completed a questionnaire on PA at age 4 to 5 years and at least one questionnaire at any age between 6 and 10 years on asthma symptoms. We excluded children born with congenital defects or diseases with possible influence on either PA or respiratory symptoms, such as for example cystic fibrosis, Down’s syndrome, or rheumatic disease (for the complete list, see appendix). Other exclusion criteria were prematurity with a gestational age of less than 37 weeks, birth weight of less than 2000 g, and use of growth hormone.

All parents gave written informed consent. Ethical approval was obtained from the medical ethics committee of Maastricht University and Academic Hospital of Maastricht, The Netherlands.

2.1 | Physical activity

2.1.1 | Questionnaires

At age 4 to 5 years PA was assessed using questionnaires. Parents were asked about their child’s frequency (days per week) and duration of activities (minutes per day) during the last 4 weeks: walking or cycling to school, school gymnastics, sports club, and playing outside. The total time that a child was physically active was added and converted in total PA in hours per day. Screen time was calculated by adding the frequency and duration of TV watching and playing computer games into one variable (screen time in hours per day).

2.1.2 | Accelerometry

A subgroup of 4- to 5-year-olds was invited to participate in accelerometry, based on the location of their home addresses (all children who lived within a range of 20 km from the communal building from where the accelerometers were distributed).[18] These children were instructed to wear an accelerometer (ActiGraph 7164; ActiGraph, Fort Walton Beach, FL) on the right hip during daytime for at least 5 days. Children were instructed to only remove the accelerometer when water was involved, as in swimming or showering. PA counts were registered in epochs of 15 seconds, for young children are known for their short and intermittent movement bursts.[19] This was transformed in counts per minute to express total activity. Four intensity-levels were distinguished: sedentary, light, moderate, and vigorous PA, based on cut-off values established by Evenson et al.[20,21] Time in these PA levels was expressed in hours per day, to make it comparable with PA from questionnaire data. Only accelerometer data with at least 400 minutes (ie, 6.7 hours) of wear time per day (during at least 3 weekdays and 1 weekend day) were included in analyses.[22] All analyses with accelerometry were adjusted for wear time.

2.2 | Asthma

2.2.1 | Questionnaires

Asthma was identified through parental questionnaires at several ages between 6 and 10 years. Asthma was defined according to the International Study of Asthma and Allergies in Childhood Questionnaire (ISAAC)[23]: doctor’s diagnosed asthma combined with clinical symptoms in the last 12 months (ie, wheezing or shortness of breath) and/or if they used asthma medication in the last 12 months. Asthma medication was defined as regular use of short-acting bronchodilators or the use of inhaled corticosteroids. Regular use was defined as everyday use for a period of at least 2 months or use associated with PA of the child. Asthma at the age 6 to 10 years was considered present if at least one questionnaire in this age period met the asthma definition.

2.2.2 | Lung function

In a subgroup children's lung function was assessed at age 6 to 7 years. Children were selected for this subgroup if their mothers participated in an earlier study in a subgroup for which they had to donate a blood sample at 34 weeks of pregnancy. Lung function was assessed using the handheld Medikro Spirostar USB spirometer (Medikro, Kuopio, Finland) according to the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines.[24,25] This was assessed by trained research assistants during home visits. Lung function was performed after 10 minutes rest in an upright seated position. Each child performed forced expiration until three acceptable curves were achieved. Acceptable curves met the reproducibility criteria defined by the ATS/ERS. Forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), and Tiffeneau-Pinelli index (FEV1/FVC) were transferred into *z* scores using the GLI-2012 (Global Lung Function Initiative) reference values for spirometry, corrected for the child's sex, age, and height.[26] We presented FEV1/FVC as primary lung function outcome, because in children it gives a better indication of asthma severity than FEV1, which can be normal even in severe persistent childhood asthma.[27]

2.3 | Statistical analysis

Data were analyzed using SPSS 22.0 for Windows (SPSS Inc, Chicago, IL). The total number of missing values ranged from none (eg, sex, birth weight, environmental tobacco smoke exposure) up to 6.1% for body mass index (BMI). In 10.8% of the children one or more variables were missing. Missing data were imputed using multiple imputation in SPSS, using the regression method with five iterations. The missing data pattern was evaluated as random. The imputed variables were parent-reported PA variables and all confounding variables. Logistic regression analysis was used for evaluating the association between PA, screen time, and asthma. Linear regression analysis was used for evaluating the associations between PA, screen time, and lung function. We adjusted for the following potential confounders: sex, atopic family history (father's and/or mother's history of asthma, eczema, or allergy), maternal education level, maternal age, maternal BMI, smoking during pregnancy, birth weight, breastfeeding (exclusively in the first 3 months), environmental tobacco smoke in first 4 years of life, and recruitment group.[17] The accelerometry data were adjusted for wear time. Children's BMI measures were transferred into *z* scores adjusted for age and sex, using reference values from the Fourth Dutch Growth Study.[28] Protopathic bias is a major potential issue in longitudinal studies on this subject: it consists of the hypothesis that PA can be restricted by respiratory symptoms preceding asthma diagnosis. Sensitivity analyses were performed by comparing models without and with parent-reported wheeze in the 12 months before exposure to evaluate protopathic bias. Possible effect modification was assessed by testing for interaction by wheeze and BMI. In order not to miss nonmonotonous confounding or effect modification by BMI we also used BMI as a categorical variable (lower/normal/overweight based on lower and upper quartiles).

3 | RESULTS

In total, 1957 children met the inclusion criteria at the age of 4 to 5 years. Of these, 1838 children (94%) completed at least one questionnaire at any age between 6 and 10 years on asthma symptoms. Table 1 shows the characteristics of participants and their PA levels at age 4 to 5 years for the total group and for the subgroups of children that participated in accelerometry (n = 301), lung function (n = 485), and both measurements (n = 62). There were no obvious differences between the total cohort and the subgroups. On average, children participated in PA 1.9 hours per day, and they were engaged in screen time 1.0 hour per day (questionnaire based). Boys were reported to be more physically active than girls (mean 2.0 hours per day vs 1.8 hours per day). Accelerometry data confirmed that there was a difference in PA between boys and girls (666 vs 615 counts per minute). Table 2 shows the characteristics of accelerometry data. A weak correlation was found between parent-reported PA and counts per minute in accelerometry ($r = 0.20$, $P < .01$), and also between parent-reported sedentary activity and time spent in sedentary activity level in accelerometry ($r = 0.05$, $P < .05$).

3.1 | Asthma

A total of 186 children (10.1%) met the ISAAC definition of asthma between the age of 6 and 10. The majority of these children (n = 101, 56%) had already wheezed at the age of 4 to 5 years.

We found no association between PA and asthma (Table 3). Sensitivity analyses for wheeze showed no difference between the children that had already wheezed at age 4 to 5 years and the children that had not wheezed at that age in relation to PA and asthma. BMI *z* scores or categories (under/normal/overweight) did not affect the relation between PA and asthma either.

3.1.1 | Lung function

There was no association between parent-reported PA and FEV1 or FVC (results in supplement) or FEV1/FVC (Table 3).

A small subgroup (n = 62) participated in accelerometry as well as lung function. Accelerometry data in this group showed a significant association between sedentary time and lung function on follow-up: children who had spent more time being physically inactive (ie, in PA level sedentary) at age 4 to 5 years had a lower FEV1/FVC at age 6 to 7 years (Table 3). In a sensitivity analysis we evaluated whether protopathic bias could explain this association, by repeating the analyses with and without wheeze at age 4 to 5 years as covariable in the model. This did not influence the association between sedentary time and FEV1/FVC. BMI did not influence the association either. There was no association between sedentary time and FEV1 or FVC separately (results in supplement). Total activity (counts per minute) and time spent in moderate to vigorous physical activity (MVPA) were not associated with lung function.

TABLE 1 Characteristics of participants of the KOALA Birth Cohort Study, The Netherlands

Characteristic	All participants (n = 1838)	Participants who had accelerometry (n = 301)	Participants who had lung function (n = 485)	Participants who had accelerometry and lung function (n = 62)
Sex n (%)				
Boy	939 (51)	146 (49)	230 (47)	31 (50)
Girl	899 (49)	155 (52)	255 (53)	31 (50)
Atopic family history[a] n (%)				
Yes	1100 (60)	190 (63)	316 (65)	43 (69)
No	738 (40)	111 (37)	169 (35)	19 (31)
Maternal education level n (%)				
Low	156 (8)	25 (8)	35 (7)	5 (8)
Moderate	675 (37)	100 (33)	183 (38)	15 (24)
High	1007 (55)	176 (58)	267 (55)	42 (68)
Smoking during pregnancy n (%)				
Yes	87 (5)	13 (4)	18 (4)	1 (2)
No	1751 (95)	288 (96)	467 (96)	61 (98)
Birth weight n (%)				
2000-3000 g	177 (10)	23 (8)	51 (11)	3 (5)
3000-4000 g	1353 (74)	226 (75)	361 (74)	47 (76)
>4000 g	308 (17)	52 (17)	73 (15)	12 (19)
Breastfeeding[b] n (%)				
Yes	991 (54)	122 (41)	221 (46)	24 (39)
No	847 (46)	179 (59)	264 (54)	38 (61)
Environmental tobacco smoke n (%)				
Yes	310 (17)	58 (19)	70 (14)	13 (21)
No	1528 (83)	243 (81)	415 (86)	49 (79)
Physical activity (parent-reported). Mean (SD)				
Physical activity, h/d[c]	1.9 (0.9)	1.7 (0.8)	1.9 (0.9)	1.6 (0.8)
Screen time, h/d[d]	1.0 (0.7)	1.1 (0.6)	0.9 (0.6)	1.0 (0.6)
Wheeze at time of exposure n (%)				
Yes	181 (10)	31 (10)	55 (11)	6 (10)
No	1648 (90)	269 (90)	426 (89)	56 (90)
Asthma at age 6-10 y n (%)				
Yes	186 (10)	26 (9)	66 (14)	7 (11)
No	1652 (90)	275 (91)	419 (86)	55 (89)

[a]Father and/or mother history of asthma, eczema, or allergy.
[b]Exclusively breastfeeding in the first 3 months.
[c]Hours per day engaging in physical activity: walking or cycling to school, school gymnastics, sports club, and playing outside.
[d]Hours per day watching television or playing computer games.

4 | DISCUSSION

This study did not confirm an association between lower PA levels and asthma development in childhood. Sedentary time as measured by accelerometry, however, was associated with lower FEV1/FVC.

PA and asthma is a subject of an ongoing debate and numerous studies looked into this subject. However, no convincing evidence was shown yet. In 2012, we performed a systematic review and meta-analysis on PA and asthma.[5] We identified 34 cross-sectional studies, of which a large portion showed a significant association between PA and asthma. Unfortunately, due to large clinical and statistical heterogeneity, it was not possible to perform a pooled analysis. Five longitudinal studies were identified and these showed that adults with high PA levels had lower asthma incidence in follow-up. No high quality longitudinal studies in children were identified at that time.

Since then, two systematic reviews on PA and childhood asthma were published, both in 2016. Lochte et al[6] identified eight cross-sectional studies, which were considered too heterogenous for pooling. Three longitudinal studies were identified and pooled, which showed a positive association of low PA and new-onset asthma.

Cassim et al[7] focused on accelerometry studies and found no difference in PA and childhood asthma in 10 cross-sectional, 1 case-control, and 1 cohort study. No longitudinal studies with PA as exposure were identified in this meta-analysis. A very recent publication by Pike et al[29] showed no association between MVPA in accelerometry and asthma status in their cross-sectional analysis. No longitudinal analysis was reported in this publication.

The most important strength of this study is that it is a longitudinal study with PA as exposure preceding the outcome measurement of asthma and lung function. A longitudinal study

TABLE 2 Descriptive information on physical activity derived from accelerometry at age 4-5 years (n = 301)

	Percentage of wear time[d]	Mean (SD)	Range	Median	25th percentile	75th percentile
Wear time, h/d		11.0 (0.8)	5.4	11.0	10.4	11.5
Total activity, cpm[a]		640 (153)	916	617	521	728
Time in activity level in h/d[b]						
Sedentary PA	47%	5.2 (0.7)	4.5	5.2	4.7	5.6
Light PA	45%	5.0 (0.7)	3.6	5.0	4.5	5.4
Moderate PA	6%	0.6 (0.2)	0.9	0.6	0.5	0.7
Vigorous PA	2%	0.2 (0.1)	0.8	0.2	0.1	0.3
MVPA[c]	8%	0.8 (0.3)	1.6	0.8	0.6	1.0

[a]Total activity measured by accelerometry in average daily counts per minute (cpm).
[b]Time in physical activity (PA) levels, converted to hours per day for reasons of comparability.
[c]Moderate to vigorous physical activity (MVPA) (sum of time in moderate physical activity and time in vigorous physical activity).
[d]Time in physical activity levels, calculated in percentage of total wear time.

design is necessary to ensure that cause (PA) precedes effect (asthma development). Another strength of this study is the use of objective measures for assessing PA and asthma in a subgroup.

This study has several limitations. An important issue in the debate is reverse causation and protopathic bias: is asthma caused by low PA or is the child less physically active because of its asthmatic symptoms? Asthma is often preceded by wheeze symptoms in early childhood. However, asthma can be difficult to diagnose before the age of 6 years because spirometry is often not possible before this age. Children that wheeze at a young age and eventually develop asthma are sometimes difficult to distinguish from the children with viral-induced wheeze: children that wheeze due to respiratory infections in combination with small airways but who outgrow it and do not develop asthma.[30] In this study, 72% of the children with asthma diagnosis at the age of 6 to 10 years had already wheezed at the age of 4 to 5 years. In contrast, 44% of the children who had wheezed at age 4 to 5 years did not meet the ISAAC definition of asthma at the age of 6 to 10 years. To evaluate protopathic bias, we performed sensitivity analysis by adding and removing the variable wheeze at the age of exposure in all analyses. This did not show any relevant influence on the results. A recent study on this subject performed bidirectional longitudinal analyses and found no association between high PA levels and asthma in childhood.[31] For lung function, this is less clear. Unfortunately, we have no objective data on long function at time of exposure, because children were too young to perform spirometry at that time (ie, 4-5 years). It is possible that children with lower lung function capacities are (subsequently) becoming less physically active. Therefore, some level of reverse causation is not ruled out.

TABLE 3 Asthma and FEV1/FVC in relation to physical activity earlier in childhood

	Asthma		FEV1/FVC	
	OR (95% CI)	Adjusted OR (95% CI)[#]	B (95% CI)	Adjusted B (95% CI)[e]
Questionnaires	n = 1838		n = 485	
Physical activity[a]	1.13 (0.95 to 1.34)	1.07 (0.90 to 1.27)	−0.08 (−0.16 to 0.00)	−0.08 (−0.16 to 0.01)
Screen time[b]	1.10 (0.99 to 1.23)	0.98 (0.77 to 1.23)	−0.07 (−0.20 to 0.05)	−0.09 (−0.22 to 0.05)
Accelerometry	n = 301		n = 62	
Total activity, cpm[c]	1.00 (0.99 to 1.00)	1.00 (0.99 to 1.00)	0.00 (−0.00 to 0.00)	0.00 (−0.00 to 0.00)
Time in sedentary PA[d]	0.72 (0.39 to 1.32)	0.75 (0.37 to 1.52)	−0.32 (−0.64 to 0.00)	−0.65 (−1.06 to −0.24)
Time in MVPA[e]	0.87 (0.22 to 3.51)	1.11 (0.25 to 4.98)	−0.03 (−0.90 to 0.83)	0.10 (−0.91 to 1.11)

Note: OR and 95% CI for asthma in relation to PA earlier in childhood. β (B) and 95% CI for FEV1/FVC (in z scores) in relation to physical activity. Abbreviations: BMI, body mass index; CI, confidence interval; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; MVPA, moderate to vigorous physical activity; OR, odds ratio; PA, physical activity.
[#]Adjusted for sex, birth weight, smoking during pregnancy, environmental tobacco smoke, atopic family history, maternal education level, maternal age, maternal BMI, breastfeeding, recruitment group, wear time (in accelerometry data). (Sensibility analyses for wheeze and BMI did not show significant differences, results not shown).
[a]Hours per day engaging in physical activity: walking or cycling to school, school gymnastics, sports club, and playing outside.
[b]Hours per day watching television or playing computer games.
[c]Total activity measured by accelerometry on average daily counts per minute (cpm).
[d]Time in activity level sedentary physical activity, converted to hours per day for reasons of comparability.
[e]Time in activity levels MVPA (sum of time in moderate physical activity and time in vigorous physical activity), converted to hours per day for reasons of comparability.

Another limitation of this study is that although the accelerometer used (ActiGraph 7164) has established validity and reliability for assessing PA,[32] it is less suited for measuring sedentary activity. The accelerometer underestimates activities such as bicycling, because of its uniaxial measurement. Moreover, it is not possible to measure the posture of the child (sitting, lying, standing up). More recent literature advises to use triaxial accelerometers worn on the thigh for assessing sedentary behavior.[33]

To our knowledge, the finding of an association between sedentary activity and FEV1/FVC later in childhood has not been reported before. In cross-sectional studies, no association between PA and lung function was found in nonasthmatic children,[34] nor in exercise studies in asthmatic children.[9] Most studies focused on PA levels and asthma found no significant association.[7,31] It could be possible that contrasting results are caused by different methods to measure PA. This study suggests that sedentary activity possibly is a more important factor in developing asthma than high PA levels, which is consistent with earlier studies on sedentary activity.[16,35] It should be noted that our results were based only on a small sample (n = 62) from the whole cohort with both accelerometry and lung function measurements available, warranting replication in larger groups.

For future research, it is important to focus on PA and especially sedentary behavior and subsequent asthma and lung function development in (larger) longitudinal studies, taking into account protopathic bias, to prove causality.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

ORCID

Marianne Eijkemans http://orcid.org/0000-0003-4550-8628
Monique Mommers http://orcid.org/0000-0002-6341-3596
Teun Remmers http://orcid.org/0000-0002-5921-7509
Jos M. Th. Draaisma http://orcid.org/0000-0003-4829-6173
Carel Thijs http://orcid.org/0000-0001-6646-5458

REFERENCES

1. Lai CK, Beasley R, Crane J, et al. Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma And Allergies in Childhood (ISAAC). *Thorax*. 2009;64(6):476-483.
2. Hallal PC, Andersen LB, Bull FC, et al. Global physical activity levels: surveillance progress, pitfalls, and prospects. *Lancet*. 2012;380(9838):247-257.
3. Humphreys BR, McLeod L, Ruseski JE. Physical activity and health outcomes: evidence from Canada. *Health Econ*. 2014;23(1):33-54.
4. Marques A, Santos T, Martins J, Matos MG, Valeiro MG. The association between physical activity and chronic diseases in European adults. *Euro J Sport Sci*. 2018;18(1):140-149.
5. Eijkemans M, Mommers M, Draaisma JM, Thijs C, Prins MH. Physical activity and asthma: a systematic review and meta-analysis. *PLOS One*. 2012;7(12):e50775.
6. Lochte L, Nielsen KG, Petersen PE, Platts-Mills TA. Childhood asthma and physical activity: a systematic review with meta-analysis and graphic appraisal tool for epidemiology assessment. *BMC Pediatr*. 2016;16:50.
7. Cassim R, Koplin JJ, Dharmage SC, et al. The difference in amount of physical activity performed by children with and without asthma: a systematic review and meta-analysis. *J Asthma*. 2016;53(9):882-892.
8. Del Giacco SR, Firinu D, Bjermer L, Carlsen KH. Exercise and asthma: an overview. *Eur Clin Respir J*. 2015;2:27984.
9. Carson KV, Chandratilleke MG, Picot J, Brinn MP, Esterman AJ, Smith BJ. Physical training for asthma. *Cochrane Database Syst Rev*. 2013;(9):CD001116.
10. Beckett WS, Jacobs DR Jr., Yu X, Iribarren C, Williams OD. Asthma is associated with weight gain in females but not males, independent of physical activity. *Am J Respir Crit Care Med*. 2001;164(11):2045-2050.
11. Benet M, Varraso R, Kauffmann F, et al. The effects of regular physical activity on adult-onset asthma incidence in women. *Respir Med*. 2011;105(7):1104-1107.
12. Huovinen E, Kaprio J, Koskenvuo M. Factors associated to lifestyle and risk of adult onset asthma. *Respir Med*. 2003;97(3):273-280.
13. Lucke J, Waters B, Hockey R, et al. Trends in women's risk factors and chronic conditions: findings from the Australian Longitudinal Study on Women's Health. *Womens Health*. 2007;3(4):423-432.
14. Thomsen SF, Ulrik CS, Kyvik KO, et al. Risk factors for asthma in young adults: a co-twin control study. *Allergy*. 2006;61(2):229-233.
15. Byberg KK, Eide GE, Forman MR, Júlíusson PB, Øymar K. Body mass index and physical activity in early childhood are associated with atopic sensitization, atopic dermatitis and asthma in later childhood. *Clin Transl Allergy*. 2016;6(1):33.
16. Sherriff A, Maitra A, Ness AR, et al. Association of duration of television viewing in early childhood with the subsequent development of asthma. *Thorax*. 2009;64(4):321-325.
17. Kummeling I, Thijs C, Penders J, et al. Etiology of atopy in infancy: the KOALA Birth Cohort Study. *Pediatr Allergy Immunol*. 2005;16(8):679-684.
18. Eijkemans M, Mommers M, de Vries SI, et al. Asthmatic symptoms, physical activity, and overweight in young children: a cohort study. *Pediatrics*. 2008;121(3):e666-e672.
19. Ward DS, Evenson KR, Vaughn A, Rodgers AB, Troiano RP. Accelerometer use in physical activity: best practices and research recommendations. *Med Sci Sports Exerc*. 2005;37(11 suppl):S582-S588.
20. Evenson KR, Catellier DJ, Gill K, Ondrak KS, McMurray RG. Calibration of two objective measures of physical activity for children. *J Sports Sci*. 2008;26(14):1557-1565.
21. Trost SG, Loprinzi PD, Moore R, Pfeiffer KA. Comparison of accelerometer cut points for predicting activity intensity in youth. *Med Sci Sports Exerc*. 2011;43(7):1360-1368.
22. Trost SG, Pate RR, Freedson PS, Sallis JF, Taylor WC. Using objective physical activity measures with youth: how many days of monitoring are needed? *Med Sci Sports Exerc*. 2000;32(2):426-431.

23. Beasley R. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC. *Lancet*. 1998; 351(9111):1225-1232.
24. Miller MR, Crapo R, Hankinson J, et al. General considerations for lung function testing. *Eur Respir J*. 2005;26(1):153-161.
25. Miller MR, Hankinson J, Brusasco V, et al. Standardisation of spirometry. *Eur Respir J*. 2005;26(2):319-338.
26. Quanjer PH, Stanojevic S, Cole TJ, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. *Eur Respir J*. 2012;40(6):1324-1343.
27. Bacharier LB, Strunk RC, Mauger D, White D, Lemanske RF Jr., Sorkness CA. Classifying asthma severity in children: mismatch between symptoms, medication use, and lung function. *Am J Respir Crit Care Med*. 2004;170(4):426-432.
28. Fredriks AM, van Buuren S, Wit J, Verloove-Vanhorick SP. Body index measurements in 1996-7 compared with 1980. *Arch Dis Child*. 2000;82(2):107-112.
29. Pike KC, Griffiths LJ, Dezateux C, Pearce A. Physical activity among children with asthma: cross-sectional analysis in the UK millennium cohort. *Pediatr Pulmonol*. 2019;54:962-969.
30. Martinez FD, Wright AL, Taussig LM, Holberg CJ, Halonen M, Morgan WJ. Asthma and wheezing in the first six years of life. *N Engl J Med*. 1995;332(3):133-138.
31. Cassim R, Milanzi E, Koplin JJ, Dharmage SC, Russell MA. Physical activity and asthma: cause or consequence? A bidirectional longitudinal analysis. *J Epidemiol Community Health*. 2018;72: 770-775.
32. Cliff DP, Reilly JJ, Okely AD. Methodological considerations in using accelerometers to assess habitual physical activity in children aged 0-5 years. *J Sci Med Sport*. 2009;12(5):557-567.
33. Byrom B, Stratton G, Mc Carthy M, Muehlhausen W. Objective measurement of sedentary behaviour using accelerometers. *Int J Obes*. 2016;40(11):1809-1812.
34. Smith MP, von Berg A, Berdel D, et al. Physical activity is not associated with spirometric indices in lung-healthy German youth. *Eur Respir J*. 2016;48(2):428-440.
35. Vogelberg C, Hirsch T, Radon K, et al. Leisure time activity and new onset of wheezing during adolescence. *Eur Respir J*. 2007;30(4):672-676.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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