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Physical activity, sedentary behaviour, and childhood asthma: a European collaborative analysis

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ABSTRACT

Objectives To investigate the associations of physical activity (PA) and sedentary behaviour in early childhood with asthma and reduced lung function in later childhood within a large collaborative study.

Design Pooling of longitudinal data from collaborating birth cohorts using meta-analysis of separate cohort-specific estimates and analysis of individual participant data of all cohorts combined.

Setting Children aged 0–18 years from 26 European birth cohorts.

Participants 136 071 individual children from 26 cohorts, with information on PA and/or sedentary behaviour in early childhood and asthma assessment in later childhood.

Main outcome measure Questionnaire-based current asthma and lung function measured by spirometry (forced expiratory volume in 1 s (FEV_1), FEV_1/forced vital capacity) at age 6–18 years.

Results Questionnaire-based and accelerometry-based PA and sedentary behaviour at age 3–5 years was not associated with asthma at age 6–18 years (PA in hours/day adjusted OR 1.01, 95% CI 0.98 to 1.04; sedentary behaviour in hours/day adjusted OR 1.03, 95% CI 0.99 to 1.07). PA was not associated with lung function at any age. Analyses of sedentary behaviour and lung function showed inconsistent results.

Conclusions Reduced PA and increased sedentary behaviour before 6 years of age were not associated with the presence of asthma later in childhood.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Sedentary behaviour and decreased physical activity have been identified as possible risk factors for developing asthma.

WHAT THIS STUDY ADDS

⇒ This study shows no indication that physical activity and sedentary behaviour in early childhood are associated with asthma or reduced lung function in later childhood.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study contributes to the growing knowledge of lifestyle and asthma. Physical activity seems not to play a role in asthma prevention.

INTRODUCTION

Asthma is the most common non-communicable chronic disease in childhood.[1]

Among lifestyle risk factors, obesity[2] and physical inactivity[3] have received particular attention. Results from cross-sectional studies suggest that adults and children with asthma might be less physically active compared with their peers.[4–8] Since higher levels of physical activity (PA) have been found to be associated with better lung function and asthma control,[3] the hypothesis emerged that PA could possibly protect against asthma development by influencing inflammatory processes important in the development of asthma. Fernandes *et al*[9] showed that PA modulates pulmonary allergic inflammation by increasing anti-inflammatory cytokines and decreasing proinflammatory cells and mediators.

Several researchers have investigated possible longitudinal associations between PA and asthma onset and found contrasting results. In adult populations, some longitudinal studies found that low levels of PA at baseline were associated with higher asthma odds later in life.[10–12] However, most studies did not find evidence for an association between PA and new-onset asthma in adults.[13–16] In children, studies also show conflicting results. Cassim *et al* published a systematic review focusing on cohort studies in children with PA measurements preceding asthma and lung function outcomes.[17] The results were highly inconsistent and showed insufficient evidence to suggest that PA influences the risk of new-onset asthma or improves lung function in children. In a recent study performed by our group, we did not find an association between PA at age 4–5 years and subsequent asthma at age 6–10 years in the KOALA Birth Cohort Study.[18] However, in a small subgroup of children with both accelerometry and lung function data available, we observed an association between sedentary behaviour and subsequently lower lung function. In the literature, sedentary behaviour and physical inactivity have been regarded as two different entities.[19] Sedentary behaviour is described as activities with an energy expenditure of 1.5 or less metabolic equivalent of a task in sitting, lying or reclining position, during wake time, which is not necessarily the same as physical inactivity (ie, not meeting the PA guidelines). Sherriff *et al* and Protudjer *et al* both found a positive association between screen time and new-onset asthma in childhood.[20 21] Chen *et al* demonstrated a pathway from central obesity to childhood asthma, via physical fitness and sedentary behaviour.[22]

The relation between childhood PA and lung function has been described in a few studies before higher PA levels in childhood have been associated with higher lung function in adolescent boys[23] and girls.[24] These findings could be relevant for respiratory health across the life course since lung function has been positively associated with aerobic fitness, and higher fitness levels during childhood are associated with larger adult lung volumes.[24]

Limitations of earlier studies are the relatively small study sizes in childhood studies compared with adult studies and little information on sedentary behaviour and lung function. In this large collaborative study, we gathered information on PA, sedentary behaviour, asthma and lung function from birth to age 18 years from 26 cohorts in Europe. We aimed to investigate PA and sedentary behaviour in relation to asthma and lung function at different ages in childhood. Our hypothesis was that higher PA before the age of six protects against asthma development later in childhood and that sedentary behaviour increases asthma risk. We also hypothesised that a higher level of PA is positively associated with lung function in later childhood.

METHODS

Design

Meta-analysis of cohort-specific association estimates from separate analyses of longitudinal data within the collaborating birth cohorts and individual participant data.

Study population

European cohorts identified from existing collaborations on childhood asthma or asthma-related outcomes (www.birthcohorts.net; www.birthcohortsenrieco.net; www.chicosproject.eu) were invited to participate if they had data on PA that preceded information on asthma. Criteria for exclusion of individual children were congenital birth defects and diseases (other than asthma) that could influence either PA or respiratory function (such as cystic fibrosis, intellectual disability, or rheumatic disorders).

37 potentially eligible cohorts were identified, 26 agreed to participate. Of the 11 studies not participating, 2 had no data on PA, 1 had no data on asthma and 5 studies only had cross-sectional data on PA and asthma. Three other cohorts did not reply or were not interested in participating. In total, we included 136 071 individual children from 26 birth cohorts across Europe.

Participating cohorts signed a data transfer agreement, and pseudonymised datasets were transferred to Maastricht University for analysis. Cohort-specific informed consent was signed by the parents or legal guardians in the original cohorts.

Patient and public involvement

No patients were involved in the design or implementation of this study.

Age groups

Cohorts were asked to provide their available exposure (PA, sedentary behaviour) and outcome data (asthma, lung function) for separate age groups: 0–2 years, 3–5 years, 6–8 years, 9–14 years and 15–18 years. If cohorts had multiple measurements for one age group, the age with the largest number of variables relevant to this study was selected.

PA and sedentary behaviour

Information on PA and sedentary behaviour was obtained by cohort-specific questionnaires in all cohorts and activity monitors (accelerometry, four cohorts). Parents were asked how much time on average their child spent on different physical activities, such as cycling, walking, playing outside, exercising and physical education lessons. In case both the child and its parents filled out a questionnaire, we selected the parent-reported data. The total amount of time being physically active was converted into hours per day. All cohorts had questionnaire-based information on PA for at least one age group totalling to 134 929 individual participants (available data per age group in table 1, detailed information for the individual cohorts in online supplemental appendix table A). 24 cohorts had information on sedentary behaviour for at least one age group in 117 473 participants. Sedentary behaviour was calculated as the amount of time (expressed as hours per day) the child on average spent on sedentary activities (eg, watching television, playing computer games, travelling by car and reading). To harmonise the data, the total amount of time spent on PA or sedentary behaviour was also categorised into (cohort-specific) tertiles.

PA as measured by accelerometry was available in four cohorts in 1905 children in total. Cohort-specific protocols with information on the type of activity monitor used, and intensity level cut-off values is presented in online supplemental appendix table A. Accelerometry data that were requested from the cohorts were mean activity counts per minute (cpm) per day, time spent in different intensity levels (sedentary, moderate to vigorous PA (MVPA)) and mean wear time per day. In general, children wore the activity monitor all day, also during school time.

Asthma and lung function

Asthma was measured using parent-completed ISAAC (International Study of Asthma and Allergies in Childhood) questionnaires in all cohorts (136 067 children).[25] We requested different asthma definitions: parent-reported physician-diagnosed asthma, ISAAC-based current asthma[18] and MeDALL (Mechanisms of the Development of Allergy) based current asthma.[26] ISAAC-based current asthma was defined as presence of (1) physician-diagnosed asthma and (2) dyspnoea or wheeze in last 12 months, or (3) regular use of asthma medication in the last 12 months. MeDALL-based definition of current asthma was constructed requiring the presence of two out of three criteria (1) physician-diagnosed asthma, (2) wheeze in the last 12 months, (3) use of asthma medication in the last 12 months). Not all cohorts provided physician-diagnosed asthma, in that case it was replaced by asthma ever in order to complete the current asthma definitions. A detailed overview of information on asthma questions of each individual cohort is presented in online supplemental appendix table B. 25 cohorts provided asthma data at the age of 6–18 years (n=125 250 children), from which 24 cohorts provided physician-diagnosed asthma (n=95 122), 22 cohorts (n=117 143) had ISAAC-based current asthma definition and 21 cohorts had MeDALL-based current asthma definition (n=90 576). It has to be noted that these numbers do not add up because most cohorts provided more than one definition. The primary outcome was current asthma; a child was defined as a current asthma case if it had either physician-diagnosed asthma or met the ISAAC or MeDALL-based definition. Separate analyses were performed with ISAAC and MeDALL-based definition as outcome.

Lung function was measured by spirometry in seventeen cohorts, totalling to 19 314 individual participants. The spirometry was performed according to American Thoracic Society/European Respiratory Society guidelines.[27 28] Measures of interest were forced expiratory volume in 1 s (FEV_1) and FEV_1/forced vital capacity (FVC) ratio. All lung function results were converted into sex-adjusted, age-adjusted and height-adjusted z-scores based on the Global Lung Initiative-2012 reference values.[29]

Statistical analysis

Data were analysed by using SPSS V.23.0 for Windows (SPSS). The main analysis consisted of PA and sedentary behaviour in hours/day at ages 0–2 years and 3–5 years with current asthma at age 6–18 years as outcome. Secondary analyses were performed with PA and sedentary behaviour, categorised in tertiles and by using accelerometry data, combined with current asthma at age 6–18 years as outcome. Age-specific analyses for PA and sedentary behaviour in each age group (ie, 0–2 years, 3–5 years, 6–8 years, 9–14 years) and asthma and lung function in the consecutive age group were performed in order to gain more insight into age dependent associations. In cohorts that had information available on wheeze and/or asthma at age 3–5 years, we were able to perform additional analyses excluding children with wheeze or asthma present at the time of exposure measurement, in order to reduce the risk of reverse causation or protopathic bias.

First, we performed cohort-specific regression analyses: logistic regression analysis was used for evaluating the associations of PA, sedentary behaviour and accelerometry with current asthma. Linear regression analysis was used for the associations of PA, sedentary behaviour and accelerometry with lung function z-scores. Cohort-specific association estimates were pooled using random effects meta-analysis in Review Manager (RevMan, V.5.3, Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Heterogeneity among studies was assessed using the χ^2 test and Higgins I^2 test.[30] We excluded each separate cohort one by one to examine the influence of any particular cohort on the results. Second, we performed pooled analyses using individual participant data, using generalised linear and logistic mixed models with a random intercept for cohort. When

Table 1 Data availability per cohort

	0–2 years			3–5 years					6–8 years					9–14 years					15–18 years				
Name cohort	PA	Sed	Acc	PA	Sed	Acc	Asthma	LF	PA	Sed	Acc	Asthma	LF	PA	Sed	Acc	Asthma	LF	PA	Sed	Acc	Asthma	LF
ABCD	0	0	0	2769	2836	0	0	0	0	0	0	2872	0	0	0	0	0	0	0	0	0	0	0
ABIS	0	0	0	7202	7127	0	6960	0	3925	3947	0	3845	0	0	0	0	0	0	0	0	0	0	0
BAMSE	0	0	0	0	0	0	3104	0	0	0	0	3039	1685	2712	2668	0	3040	0	2750	2860	0	3043	1962
CHOP	0	0	0	0	0	0	0	0	515	502	432	558	0	523	497	434	573	0	0	0	0	0	0
$COPSAC_{2000}$	0	0	0	0	143	236	272	0	0	31	40	272	259	0	0	0	272	0	0	0	0	272	0
DNBC	66 409	0	0	0	0	0	0	0	53 092	53 172	0	54 602	0	45 928	46 082	0	80 350	0	0	0	0	0	0
EDEN	753	734	0	608	629	0	100	876	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
G21	0	0	0	6975	5964	0	7125	0	5831	5831	0	5788	1605	0	0	0	0	0	0	0	0	0	0
Gen R	0	0	0	3919	4027	0	0	0	3787	4390	0	4401	0	0	0	0	4484	4583	0	0	0	0	0
GINIplus	0	0	0	0	0	0	0	0	3837	3848	0	3855	744	2695	3267	0	3300	626	2447	3047	0	3167	1822
HUMIS	0	694	0	686	685	0	681	0	292	369	0	371	0	0	0	0	0	0	0	0	0	0	0
INMA Asturias	0	0	0	340	340	0	0	0	0	0	0	340	0	0	0	0	0	0	0	0	0	0	0
INMA Gipuzkoa	0	0	0	351	351	0	0	284	0	0	0	351	331	0	0	0	0	0	0	0	0	0	0
INMA Menorca	0	0	0	0	0	0	471	0	470	471	0	463	0	425	425	0	425	395	288	286	0	287	269
INMA Sabadell	0	0	0	534	534	0	0	415	0	0	0	534	433	0	0	0	0	0	0	0	0	0	0
INMA Valencia	0	0	0	450	460	0	0	0	0	0	0	460	446	0	0	0	0	0	0	0	0	0	0
KOALA	2089	2181	0	1787	1835	301	2009	0	1889	1944	367	1971	519	0	0	0	1810	0	0	0	0	0	0
Lifeways	0	0	0	552	544	0	379	0	0	0	0	0	0	0	0	0	226	0	0	0	0	0	0
LISA	0	0	0	2409	2409	0	2346	0	2181	2185	0	2188	50	1429	1705	0	1756	111	1383	1661	0	1729	934
LRC	15	0	0	3671	3596	0	4937	0	4450	4381	0	4402	0	3244	3224	0	3635	499	0	0	0	659	0
LucKi	0	0	0	773	807	0	813	0	0	0	0	333	0	0	0	0	0	0	0	0	0	0	0
PIAMA	0	0	0	3439	3436	0	3506	0	3227	3229	0	3307	1055	2626	2629	0	2642	1292	2082	1995	0	1874	721
SEATON	0	0	0	0	0	0	199	0	0	0	0	0	0	212	0	0	206	147	0	0	0	156	126
STEPS Study	145	101	0	696	508	0	690	0	636	151	0	598	0	0	0	0	0	0	0	0	0	0	0
SWS	0	0	0	2542	2547	537	2547	0	0	0	0	1962	921	0	0	0	0	0	0	0	0	0	0
WHISTLER	0	0	0	599	0	0	580	579	46	0	0	15	20	0	0	0	0	0	0	0	0	0	0
Total cohorts	5	5	0	19	19	3	17	4	14	14	3	23	12	9	8	1	13	7	5	5	0	8	6
Total participants	69 411	3725	0	40 302	38 778	1074	37 495	2154	84 178	84 451	839	96 527	8068	59 794	60 497	434	102 719	7653	8950	9849	0	11 187	5834

Overview of data availability of participating cohorts. Numbers of observations for the different variables and age groups.
PA, physical activity; Sed, sedentary behaviour; Acc, accelerometry data; LF, lung function.

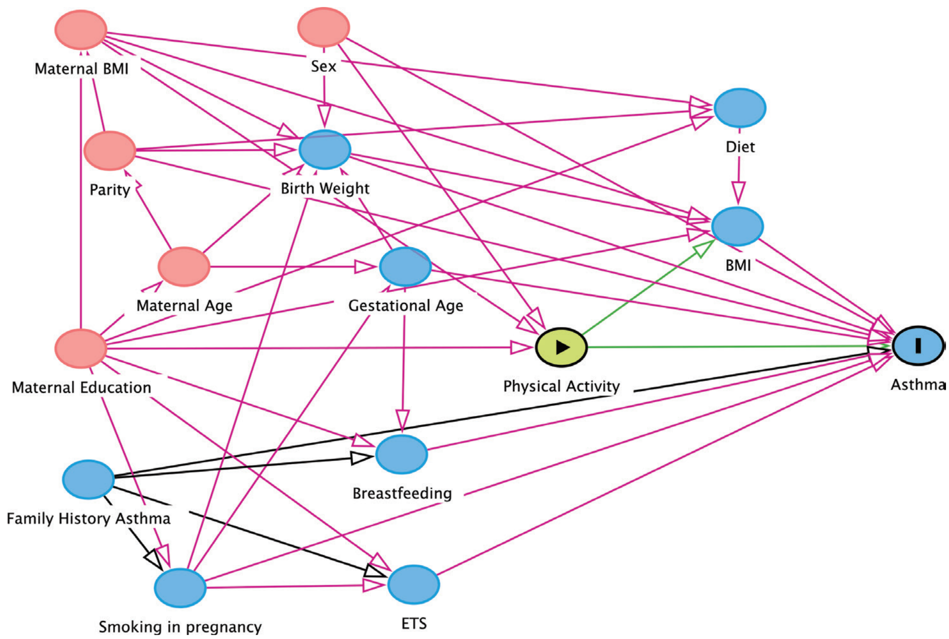

Figure 1 Directed Acyclic Graph (DAG) of possible covariables on the association between physical activity and asthma. Minimal dataset was identified as sex, maternal education, and maternal BMI. BMI, body mass index. ETS, environmental tobacco smoke.

there were too few cohorts to make a valid estimation of the variance, we used fixed effects models with cohort as a covariable. Usually, this occurred when only two or three cohorts had data availability for a specific age group.

We considered the following potential confounders a priori: sex, gestational age at birth, birth weight, maternal smoking during pregnancy, environmental tobacco smoke, highest maternal education level, maternal age, maternal body mass index (BMI), breast feeding, parity, family history of asthma and family history of atopy. These variables were collected in cohort-specific parent-based questionnaires. Some cohorts measured height and weight of the child in order to calculate BMI, others used parent reported height and weight. A child's BMI in each age group was converted into WHO z-scores adjusted for age and sex.[31] We used a directed acyclic graph (DAG) approach in order to select the expected most important set of covariables for adjustment in multivariable models (figure 1). The graph was constructed using DAGitty V.2.3.[32] We included the minimal sufficient adjustment set for estimating the total effect of PA on asthma as covariables in the multivariable analyses: maternal BMI, maternal education and sex. We assumed this confounder set to be the same for the other analyses (ie, sedentary behaviour and lung function). All analyses using accelerometry data were additionally adjusted for wear time. The child's BMI was considered to have a potential interaction with PA and was, therefore, not adjusted for in the main analyses. Additional analyses were performed by testing for interaction between PA and BMI (z-scores as continuous variable) with and without adjustment for the other covariables. We reported such interactions if the interaction term was statistically significant (Wald test $p<0.05$).

RESULTS

Participant characteristics

The data available on exposure and outcome for each cohort are shown in table 1. At age 3–5 years, most cohorts had data available on PA and/or sedentary behaviour (ie, 19 cohorts). All cohorts except one (ie, EDEN) had data available for the age of 6 years and older. Characteristics of the study population are shown in online supplemental appendix table C.

PA and sedentary behaviour

Children were reported to be physically active for an average of 2.1 hours per day (all age groups combined), with children being the most active at age 6–8 years (mean 2.7 hours per day) and least active at age 9–14 years (mean 0.9 hours per day). Children engaged in sedentary behaviour for 2.7 hours per day on average over all age groups. At age 9–14 years sedentary behaviour peaked (mean 4.3 hours per day), whereas children aged 0–2 years were reported to spend the least amount of time engaging in sedentary behaviour (ie, screen time) (0.4 hours per day).

Accelerometry data showed an average mean count per minute per day of 400 cpm, varying from 323 at age 3–5 years to 606 at age 6–8 years. Large differences were observed between the different cohorts, depending on which type of accelerometer was used. Children spent on average 1.6 hours per day in MVPA, with children aged

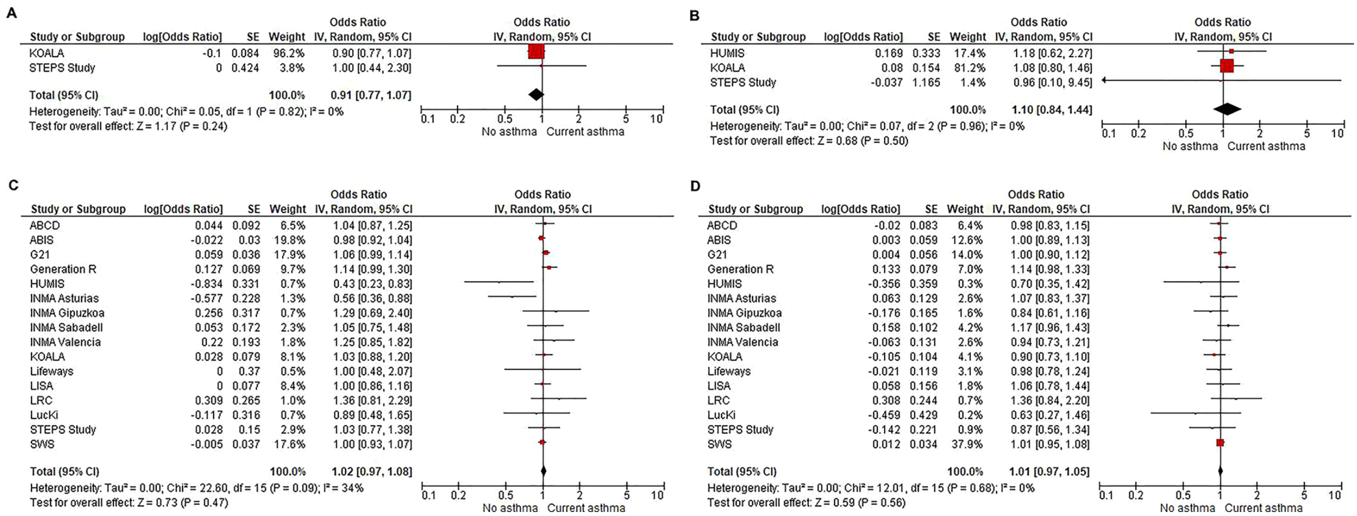

Figure 2 Overview of meta-analyses of per-cohort longitudinal analyses on questionnaire derived physical activity and sedentary behaviour at ages 0–2 and 3–5 years and current asthma at age 6–18 years. (A) Exposure: physical activity in hours/day at ages 0–2 years—outcome: current asthma at age 6–18 years. (B) Exposure: sedentary behaviour in hours/day at ages 0–2 years—outcome: current asthma at age 6–18 years. (C) Exposure: physical activity in hours/day at age 3–5 years—outcome: current asthma at age 6–18 years. (D) Exposure: sedentary behaviour in hours/day at age 3–5 years—outcome: current asthma at age 6–18 years. Current asthma is defined as physician-diagnosed asthma, ISAAC-based current asthma definition or MeDALL-based current asthma definition. Per-cohort multivariable logistic regression using a random effects model with minimum data set as confounders (sex, maternal education level and maternal BMI for all cohorts except LRC which did not have information on maternal BMI, therefore, was corrected for sex and maternal education level). BMI, body mass index; ISAAC, International Study of Asthma and Allergies in Childhood.

9–14 years being the least active (1.4 hours in MVPA daily) compared with 3–5 year olds being the most active (1.8 hours in MVPA daily). The range of measured sedentary activity was very broad among the different cohorts (5.2–14.0 hours at age 3–5 years) due to differences in wear time: some cohorts included sleeping hours as wear time, while others limited the measuring time to waking hours.

Asthma

In total, 11.3% (n=14 112) of the children had current asthma at any age between 6 ando 18 years, ranging from 6.2% in G21 to 29.2% in LRC. When using parent-reported physician-diagnosed asthma only, 11.9% (n=11 349; range 3.8%–27.3%) of the children were defined as having asthma, compared with 7.4% (n=8633; range 1.7%–21.8%) according to the ISAAC-based current asthma definition and 7.9% (n=7155; range 2.5%–21.6%) according to the MeDALL-based current asthma definition.

We found no association between PA at ages 0–2 years or 3–5 years and the presence of asthma at age 6–18 years. Meta-analysis of cohort-specific association estimates showed no association between PA in hours/day at age 3–5 years and asthma at age 6–18 years (adjusted OR 1.02, 95% CI 0.97 to 1.08) (figure 2). The pooled analysis of the individual participant data showed comparable results: adjusted OR 1.01, 95% CI 0.98 to 1.04 (table 2). When excluding wheeze and asthma at baseline (in a subgroup), no association was found either (adjusted OR 1.00, 95% CI 0.95 to 1.04) (online supplemental appendix table D). Also, analysing each asthma definition (ISAAC-based and MeDALL-based current asthma definition) separately did not reveal an association between PA and asthma (online supplemental appendix tables E,F), neither for PA measured by questionnaires nor for accelerometry. When PA was categorised in tertiles, only the youngest age group (0–2 years) showed a possible association between PA and lower asthma incidence: PA in the highest two tertiles at ages 0–2 years was associated with a lower asthma incidence at age 6–18 years compared with PA in the lowest tertile (adjusted OR highest tertile 0.80, 95% CI 0.68 to 0.95) (online supplemental appendix tables G,H). The result was driven by data of one cohort (DNBC) using the question: 'Do you think he/she is more or less active than kids the same age?'. When this cohort was excluded, no association between PA in tertiles and subsequent asthma was found. The other two cohorts that had questionnaire-based information on PA at ages 0–2 years measured PA by the amount of time the child spent playing outside. No accelerometry data were available at this age.

Sedentary behaviour was not associated with the presence of asthma at subsequent follow-ups age 6–18 years, regardless of the PA method and asthma definition that was used. Accelerometry data for sedentary behaviour were also analysed for each cohort separately, due to large differences in wear time. In none of the separate analyses, nor the meta-analysis, an association between time spent in sedentary level and subsequent asthma was seen (online supplemental appendix figure A).

Table 2 Longitudinal analyses on physical activity (PA), sedentary behaviour and current asthma between age 6 and 18 years

	n (n asthma cases)	n cohorts		aOR (95% CI)*
Questionnaire based				
PA (hours/day) age 0–2 years	2024 (282)	2	a	0.91 (0.77 to 1.07)
Age 3–5 years	21 927 (2204)	16	b	1.01 (0.98 to 1.04)
Sedentary behaviour (hours/day) age 0–2 years	2380 (329)	3	c	1.05 (0.80 to 1.37)
Age 3–5 years	21 643 (2180)	15	d	1.03 (0.99 to 1.07)
Accelerometry				
Total activity (counts/min) age 3–5 years	775 (131)	2	e	1.00 (1.00 to 1.00)
Sedentary activity age 3–5 years	775 (131)	2	e	1.00 (0.86 to 1.16)
MVPA				
Age 3–5 years	775 (131)	2	e	0.99 (0.66 to 1.50)

Generalised logistic mixed models on questionnaire-based PA in hours per day, sedentary behaviour in hours per day and accelerometry data at ages 0–2 years and 3–5 years; and current asthma at age 6–18 years.
Multivariable analyses corrected for sex, maternal education level, maternal BMI.
Included cohorts: (a) KOALA, STEPS Study, (b) ABCD, ABIS, G21, Generation R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, Lifeways, LISA, LucKi, STEPS Study, SWS, Whistler, (c) HUMIS, KOALA, STEPS Study, (d) ABCD, ABIS, G21, Generation R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, Lifeways, LISA, LucKi, STEPS Study, SWS. : KOALA, SWS.
*aORs indicate the increase in odds of current asthma between age 6 and 18 years for each hour per day of parent reported PA or sedentary behaviour in the age periods between age 0 and 2 or 3 and 5 years; and time in sedentary activity or MVPA recorded by accelerometry between age 3 and 5 years. Current asthma is defined as physician-diagnosed asthma, ISAAC-based current asthma definition or MeDALL-based current asthma definition.
aOR, adjusted OR; BMI, body mass index; ISAAC, International Study of Asthma and Allergies in Childhood; MeDALL, Mechanisms of the Development of Allergy; MVPA, moderate to vigorous PA .

Age-specific analyses of PA and sedentary behaviour and asthma in the consecutive age group showed no associations at any age in the multivariable analyses (online supplemental appendix tables I–L), except again for PA in tertiles at ages 0–2 years and asthma at age 6–8.

The interaction term child's BMI×PA was tested in both univariable and multivariable models but was not statistically significant at any age (online supplemental appendix tables M,N).

Lung function

No associations between questionnaire-based PA and lung function in the age-specific analyses were observed at any age (online supplemental appendix tables O,P). Children who spent more time in MVPA at age 3–5 years (as measured by accelerometry) had a higher FEV_1 at age 6–8 years (B 0.27 SD, 95% CI 0.07 to 0.46). This means that every 1 hour per day more engaging in MVPA level at age 3–5 years results in a 0.27 SD (reported as z-score) higher FEV_1 at age 6–8 years. This association disappeared when we excluded the children with wheeze or asthma at baseline (online supplemental appendix tables Q,P).

For questionnaire-based sedentary behaviour, children who engaged more time in sedentary behaviour at age 6–8 years had a slightly higher FEV_1 at age 9–14 years (B 0.03 SD, 95% CI 0.00 to 0.06 for every additional hour of sedentary behaviour per day). Children aged 9–14 years old who spent more time in sedentary behaviour had slightly higher FEV_1/FVC at age 15–18 years (B 0.04 SD, 95% CI 0.00 to 0.07). Children who displayed more time in sedentary behaviour (as measured by accelerometry) at age 3–5 years had a lower FEV_1 at age 6–8 years (B −0.13 SD, 95% CI −0.20 to −0.06). This association persisted after excluding children with wheeze or asthma at baseline. At all other ages no association between PA or sedentary behaviour and lung function was observed.

DISCUSSION

Overall, in this large collaborative study, we found no evidence that PA or sedentary behaviour during early childhood was associated with the presence of asthma in later childhood. Both PA measured by questionnaire and by accelerometry showed no association. This is in line with more recent studies that have shown that PA is not associated with subsequent asthma in childhood.[17 18] Cassim *et al* performed a bidirectional longitudinal analysis on PA and childhood asthma and found no association in any direction.[33] Recently, Russell *et al* described the association between PA and asthma incidence over 10 years in a multicentre study and found no benefit from vigorous PA in reducing the risk of asthma development in adults.[34] Garcia-Aymerich *et al* performed hypothetical interventions on BMI and PA in 76 470 asthma-free women and found no effect of PA intervention on new-onset asthma.[35]

Unfortunately, we were not able to collect reliable information on PA in the youngest age group (under 2 years) to draw conclusions for this age. Habitual PA in infants and toddlers differs from PA at older ages, and no validated questionnaires on PA at this young age exist. Earlier studies on this subject have stressed the importance of using accelerometry for measuring PA in infants and toddlers.[36 37] However, a recent systematic review and meta-analysis on accelerometry in infants and toddlers showed that accelerometry measurements in infants still are inconclusive due to a lack of existing validated cut-points at this age. In toddlers (ie, in general 1–3 years) validated cut-points are available for some accelerometer devices (eg, Actigraph) but consistency and reliability remains problematic.[38]

We found no clear associations between PA and lung function at any age (0–18 years). The analyses of sedentary behaviour and lung function measured a few years later showed a few associations: questionnaire-based sedentary behaviour at age 6–8 years was associated with a marginally higher FEV_1 at age 9–14 years, whereas accelerometry measured sedentary behaviour at age 3–5 years was associated with a slightly lower FEV_1 at age 6–8. FEV_1/FVC was lower at age 15–18 years when children had spent more time in sedentary behaviour at age 9–14 years. All other analyses on sedentary behaviour and lung function showed no associations.

In the literature, we only found one study that focused on the longitudinal association between sedentary behaviour and lung function in childhood: da Silva *et al*[39] found that adolescents who spent less time in sedentary behaviour at ages 11–18 years had higher FVC at age 18 years. Earlier studies on PA and lung function are inconsistent: cross-sectionally, no association between PA and lung function in adolescents was found.[40] In contrast to studies in adults, where a weak positive association between higher PA level and FEV_1 was found.[41] Longitudinally, in adolescents and young adults, aerobic fitness was positively associated with FEV_1 and FVC but not with FEV_1/FVC.[42] It is possible that our findings are the result of chance finding because of multiple testing. The clinical relevance of these small differences is not known either.

Obesity was a priori considered to have a possible interaction with PA in relation to asthma. However, models including BMI×PA as interaction term did not show any modifying effect of BMI on the association between PA and asthma. Bédard *et al* investigated the role of PA in the obesity-asthma link in adult women and found an independent association between obesity and asthma but no independent causal effect of PA on asthma.[16]

The most important strength of this study is that it is a large collaboration of 26 European birth cohorts, which all delivered individual-level information on PA, sedentary behaviour and asthma from 0 to 18 years. By including children from different geographical areas residual confounding was indirectly taken into account. By virtue of the longitudinal design, with information on several age groups, we were able to reduce the risk of reverse causality. We evaluated protopathic bias by excluding children with asthma and wheeze in the 12 months preceding the exposure date. In this asthma-and-wheeze free population, there was no association between PA levels or sedentary behaviour and new-onset asthma at ages 6–8 years. Unfortunately, we were not able to perform repeated measures analysis as most cohorts had only one or two measurements of PA, all at different ages.

An important limitation of this study is the heterogeneity in data collection between the different cohorts. Especially the data on PA and sedentary behaviour differed across the cohorts. For example, some cohorts had more detailed questionnaires on PA than others, some included questions on school activities while others only included activities outside of school hours. To harmonise the data, we performed additional analyses after conversion into tertiles. These showed comparable results. Accelerometry data also showed large differences across the cohorts due to different methodologies, especially for the time spent in sedentary activity level. However, the separate cohort-specific analyses displayed comparable results and meta-analysis showed little statistical heterogeneity. Asthma outcome data were less heterogeneous: all cohorts used ISAAC core questionnaires and/or MeDALL-based asthma definition and separate analyses on these different asthma outcomes showed comparable results. Recruitment bias could also be an issue: most birth cohorts consist of relatively highly educated parents, which is a selection of the real population. Low socioeconomic status is a known risk factor for severe asthma and is possibly under-represented in this study.[43 44]

This study focuses on the association between PA and asthma development later in childhood. It is important to notice that this study did not focus on asthma severity, which can still be related to PA and sedentary behaviour, for example, due to symptoms of breathlessness.

In conclusion, we found no indication of a relation between PA and sedentary behaviour in early childhood and asthma in later childhood. There is very sparse information about the PA levels in the youngest age group (under 2 years) and subsequent asthma so no conclusion can be drawn for this age. The results of the effects of PA and sedentary behaviour on lung function were inconsistent.

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Overview of the included cohorts:

1. ABCD[45]
2. ABIS[46]
3. BAMSE[47]
4. CHOP[48]
5. COPSAC$_{2000}$[49]
6. DNBC[50]
7. EDEN[51]
8. G21[52]
9. Generation R[53]

10. GINI plus[54]
11. HUMIS[55]
12. INMA Asturias[56]
13. INMA Gipuzkoa[56]
14. INMA Menorca[56]
15. INMA Sabadell[56]
16. INMA Valencia[56]
17. KOALA[57]
18. Lifeways[58]
19. LISA[59]
20. LRC[60]
21. LucKi[61]
22. PIAMA[62]
23. SEATON[63 64]
24. STEPS Study[65]
25. SWS[66]
26. WHISTLER[67]

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Ethics approval All parents gave written informed consent. Ethical approval was obtained from the local authorised institutional review boards of the individual cohorts: ABCD: The Central Committee on Research Involving Human Subjects in the Netherlands, the medical ethics review committees of the participating hospitals and the Registration of the Municipality of Amsterdam approved the protocol of the ABCD study and written informed consent of all the participants was obtained. ABIS: The ABIS project was approved by the Research Ethics Committees of the Faculty of Health Science at the University of Linköping, Linköping, Sweden and the Medical Faculty at the University of Lund, Lund, Sweden (Dnr 99227, Dnr 99321). BAMSE: The BAMSE study and subsequent follow-ups were approved by the Regional Ethical Review Board, Karolinska Institutet, Stockholm, Sweden, and all parents provided informed consent for data collection and analysis. CHOP:Belgium: Comitè d'Ethique Medicale de Centre Hospitalier Chretien Liege; No. OM87Germany: Bayerische Landesärztekammer Ethik-Kommission, No. 02070Italy: Azienda Ospedaliera San Paolo Comitato Etico, No 14/2002Poland: Instytut Pomnik-Centrum Zdrowia Dziecka Komitet Etyczny, No 243/KE/2001Spain: Comité ético de investigación clínica del Hospital Universitario de Tarragona Joan XXIII, Comité ético de investigación clínica del Hospital Universitario Sant Joan de ReusCOPSAC2000: The study was conducted in accordance with the guiding principles of the Declaration of Helsinki and was approved by the Local Ethics Committee (COPSAC2000: KF 01-289/96, COPSAC2000 18 University College Hospital, Galway, Ireland; St. Vincent's University Hospital, Dublin, Ireland; Irish College of General Practitioners; National University of Ireland, Galway, Ireland; University College Dublin, Ireland. LISA: For the LISA study, the ethical approval was given by the Bavarian Board of Physicians (12067), the Board of Physicians of Saxony (EK-BR02/13-1) and the Board of Physicians of North Rhine-Westphalia (2012446). LRC: The Leicestershire Health Authority Research Ethics Committee approved this study. LUCKI: The study was approved by the medical ethics committee of Maastricht University and Academic Hospital of Maastricht, Netherlands (MEC 09-4-058). PIAMA: Start project—Rotterdam, MEC (Medisch Ethische Commisie Erasmus Universiteit Rotterdam/Academische Ziekenhuizen Rotterdam) 132.636/1994/39, 13 June 1994 and 137.326/1994/130, 16 February 1995—Groningen, MEC (Medisch Ethische Commisie Academisch ziekenhuis Groningen) 94/08/92, 26 August 1994—Utrecht/Bilthoven, MEC-TNO (Medisch Ethische Commisie—Toegepast Natuurwetenschappelijk Onderzoek) 95/50, 28 February 1996 Age 4 years Utrecht, CCMO (Centrale Commissie Mensgebonden Onderzoek) P000777C, 25 September 2000 Age 8 years Utrecht, CCMO (Centrale Commissie Mensgebonden Onderzoek) P04.0071C, 5 August 2004 (Utrecht, METC-protocol number 04—101/K, 27 July 2004; Rotterdam, P04.0071C/MEC 2004-152, 1 July 2004; Groningen, P04.0071C/ M 4.019912, 28 June 2004) Age 12 years Utrecht, METC (Medisch Ethische ToetsingsCommissie) protocol number 07-337/K, 20 May 2008 Age 16 years Utrecht, METC (Medisch Ethische ToetsingsCommissie) protocol number 12-019/K, 25 May 2012; Amendement 1, 12 July 2012; Amendement 2, 20 September 2012; Groningen, METC (Medisch Ethische ToetsingsCommissie) protocol number 12-019/K; Amendement, 16 August 2012 Age 18 years Utrecht (Medisch Ethische Toetsingscommissie), onderzoeksvoorstel 15/170, PIAMA studie Preventie en Incidentie van Astma en Mijt Allergie, opvragen van huisarts JGZ en PRN gegevens SEATON: North of Scotland Research Ethics Committee (13/NS/0108). STEPS Study: The STEPS Study was approved by the Ethics Committee of the Hospital District of Southwest Finland (27 February 2007). SWS: The SWS received ethics approval for all waves of the cohort study from Southampton and South-West Hampshire Local Research Ethics Committee. WHISTLER: The WHISTLER birth cohort study was approved by the paediatric Medical Ethical Committee of the University Medical Center Utrecht. Parents gave informed consent for participating in the study. Participants gave informed consent to participate in the study before taking part.

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Data availability statement Due to data protection reasons, the datasets generated during the current study cannot be made publicly available. The cohort-specific datasets are available to interested researchers on reasonable request, provided the release is consistent with the obtained consent of the study participants of the cohort. This will not be possible for all cohorts involved. Ethical approval might be necessary to be obtained for the release and a data transfer agreement must be accepted.

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