Asthma

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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.

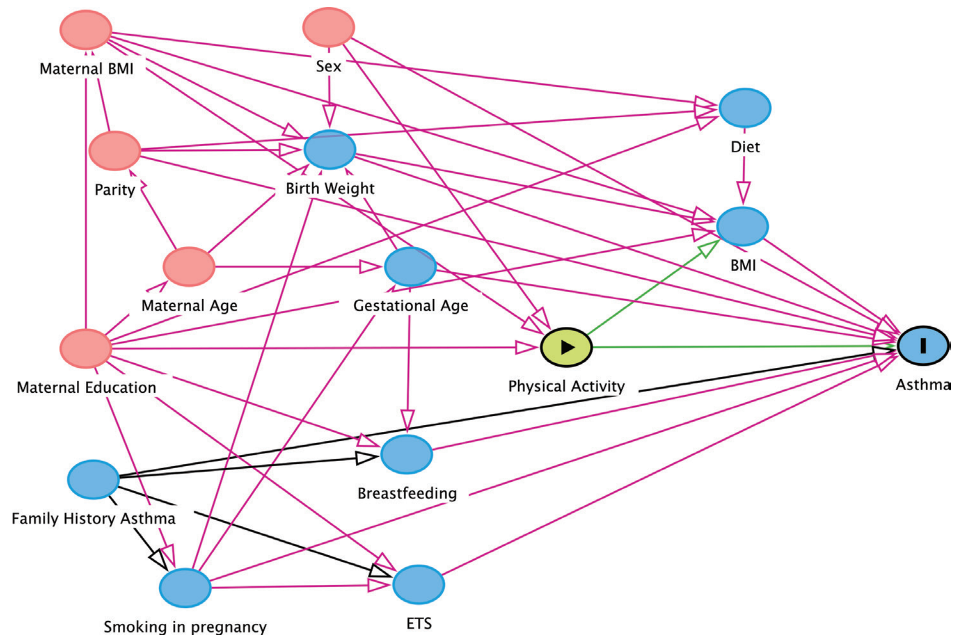

Figure 1 Directed Acyclic Graph (DAG) of possible covariables on the association between physical activity and asthma. Minimal dataset was identified as sex, maternal education, and maternal BMI. BMI, body mass index. ETS, environmental tobacco smoke.

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

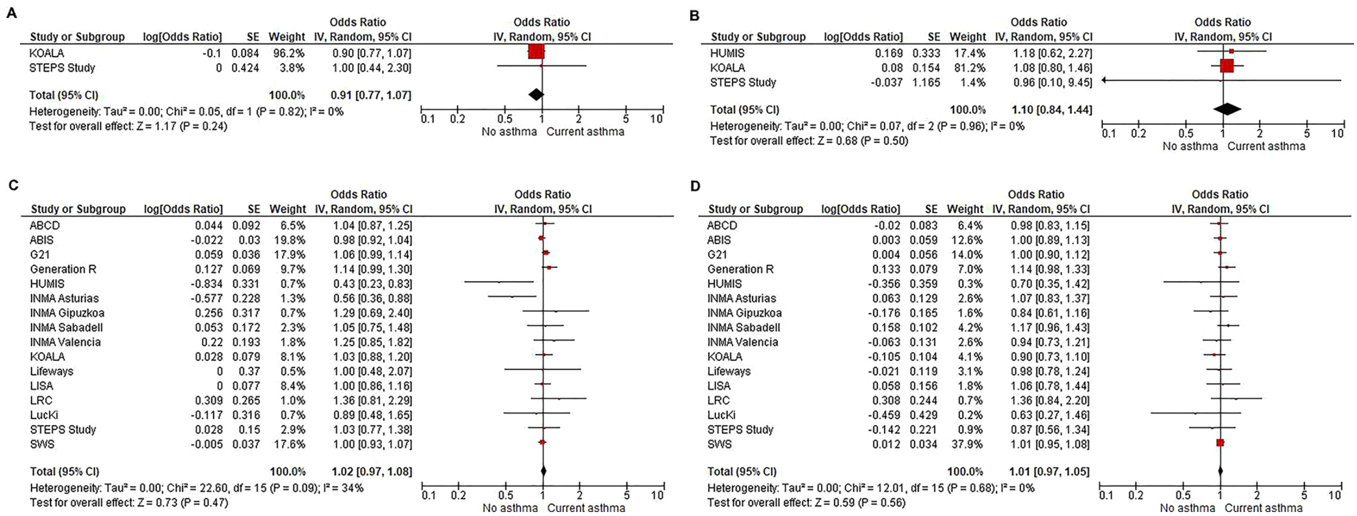

Figure 2 Overview of meta-analyses of per-cohort longitudinal analyses on questionnaire derived physical activity and sedentary behaviour at ages 0–2 and 3–5 years and current asthma at age 6–18 years. (A) Exposure: physical activity in hours/day at ages 0–2 years—outcome: current asthma at age 6–18 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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Appendix

Table A. Overview of cohort-specific questionnaires and accelerometry on physical activity and sedentary behaviour

Cohort	Physical Activity / sedentary behaviour
ABCD	**Questionnaire on physical activity. Questions on 5-6 and 7-8 years old:** *- 'How many hours a day does your child play outside in the summer?' (same question for the winter)* *- 'How many times a week does your child walk to or from school?' (same question for cycling)* *- 'How many hours a week does your child play sport at sport club(s)?'* **Questionnaire on sedentary behaviour. Questions on 5-6 and 7-8 years old:** *- 'How many hours a day does your child watch television, a DVD or a video at home or at a friend's house?'* *- How many hours a day does your child sit at home or at a friend's house playing on the computer, Playstation or X-box?*
ABIS	hours per day in exercise playing outside jumping running hours per day TV,watching computer internet
BAMSE	***Parental questionnaire at age 8 years:*** Does your child participate in any type of organized physical activity or sport (excl school phys.)? ***Parental web-questionnaire at age 12 years:*** Does your child engage in sports or physical activity in his/her leisure time? How long does your child exercise on each occasion, on the average? ***Participant web-questionnaire at age 16 years:*** Over the past 12 months, how many hours during an ordinary week have you engaged in very strenuous activities? Over the past 12 months, how many hours during an ordinary week have you engaged in fairly strenuous activities? Over the past 12 months, how many hours during an ordinary week have you engaged in activities that are not strenuous? At school, how many class hours of physical education do you participate in per week? How many hours per day do you watch TV, use a computer, play computer- or video games or read?
CHOP	**Questionnaire at age 3-6 years** Hours/day **Questionnaire at age 8, 11 years** PAQ-score **Accelerometry at age 6, 11 years** Sensewear Pro Armband, epoch length 60 seconds, total energy expenditure, sleeping time, time in different activity levels. Count cut-offs based on METs: 0-3 sedentary 3-6 moderate 6-9 vigorous Above 9 very vigorous
$COPSAC_{2000}$	**Accelerometry at age 5 years** Omnidirectional Actical accelerometer (Philips Respironics, Murrysville, PA)
DNBC	***Computer-assisted telephone interview with the mother (child age 1.5 years):*** D149: Do you think he/she is MORE or LESS active than kids the same age? ***Web-based or paper-mailed questionnaire to mother/parent (child age 7 years):*** Z014: "How many hours is your daughter physically active in kindergarten, school or at the leisure centre/school leisure centre, e.g. running, hopping, climbing, cycling, training sport or other activities, which require a lot of movement (Tick one box only)?" Z015: "How many hours is your daughter physically active with e.g. running, hopping, climbing, cycling, training sport or other activities, which require a lot of movement? Please assess how physically active she is on a normal weekday after kindergarten, school or the leisure centre/ school leisure centre compared to a normal day during the weekend. (Tick one box in each column)" Additional relevant questions: Z070: Is she/he "Restless, overactive, cannot stay still for long",

	Z076: where you (the mother) "restless, "hyperactive", had problems keeping quiet long" in childhood? ***Web-based questionnaire to child when aged 11 years:*** E057: How many sports lessons per week (lessons of 45 minutes) does your school timetable include? E058: Do you get out of breath or break sweat during the sports lessons? E059: How do you usually use your body during the breaks? Think about the last month when choosing your answer. E060 How do you usually use your body during your leisure time? Think about the last month when choosing your answer. E061: Do you do sports in your leisure time? E062_1-12: What kind of sports do you do? Tick all the activities you participate in. E062_1A - 12A: How many times per week do you play …… [asked for each kind of sport mentioned in E062_1-12] E063-E066 may be considered questions on activity or inactivity. They are described in under physical inactivity. Additional relevant questions to adult: Is she/he "Restless, overactive, cannot stay still for long" ***Web-based or paper-mailed questionnaire to mother/parents (child age 7 years):*** Z016: How many hours is your daughter physically inactive on a normal weekday/day during the weekend, i.e. rests, sleeps during the day, reads, watches TV, plays computer games, is tutored, etc. after school or school leisure centre/leisure centre? (Tick one box in each column). ***Web-based questionnaire to child when aged 11 years:*** E049/E050: How much of your leisure time do you spend in front of the computer? Count all the time you sit in front of a computer. (Weekday computer). E051/E052: How much of your leisure time do you spend playing computer games? (Both on a computer or on a Playstation, Xbox, PSP, Nintendo, Wii). (Weekday gaming). E053/E054: How much of your leisure time do you spend watching tv? (include DVD/video or watching films on your computer). (Weekdays TV/DVD/Video). E055/E056: How much of your leisure time do you spend reading, playing boardgames, drawing, resting, etc.? (including homework). (Weekdays read, play, rest). E063: How do you usually get to school? E064: How long does it usually take you to get to school? E065: How do you usually get back from school? E066: How long does it usually take you to get back from school?
EDEN	Questionnaire at age 0-2 and 3-5 years on physical activities and sedentary behaviour in hours per week.
G21	**Questionnaire on physical activity** (How many hours per day does your child play outside during week days? And, how many hours per day does your child play outside during the weekend?) **Questionnaire on physical inactivity** (How many hours per day does your child watch television, plays videogames, during week days? And (How many hours per day does your child watch television, plays videogames, during the weekend?)
Gen R	Playing outside (no of times (**4, 6, 9y** and duration (**3, 4, 6, 9y**)) Walking or cycling from/to school (no of times and duration (**6, 9y**)) Participation in sports (duration (**9y**)) Physical education lesson (no of times and duration (**6y**)) Swimming lesson (no of times and duration (**6y**)) Watching TV/video/DVD (no of times (**4, 6, 9y**) and duration (**2, 3, 4, 6, 9y**)) Computer use (no of times (**6, 9y**) and duration (**3, 6, 9y**)) **NB:** at 2, 3, 6 and 9y separate for weekday and weekend
GINIplus	**Questionnaire on physical activity at age 6**: "How many hours per day does your child spend outside during summer/during winter?"; **Questionnaire on physical activity at age 10 and 15:** How many hours per week during summer/during winter does the child spend in light activity (no sweating, normal respiration, e.g. walking) moderate activity (some sweating, moderately increased respiration, e.g. cycling, swimming, skating) vigorous activity (strong sweating, fast respiration, e.g. ball games, training) **Questionnaire on sedentary behaviour at age 6, 10 and 15:** "How many hours per day does your child spend in front of a screen (TV, PC)?" (for 10 and 15 years, it was differentiated between summer and winter)
HUMIS	**3 year questionnaire:**

	"How often is your child outside at present? Seldom; Frequently, but less than 1 hour a day on average; 1-3 hours a day on average; more than 3 hours a day" "How many hours on average does your child sit in front of a TV/video every day? 4 hours or more; 3 hours; 1-2 hours; less than 1 hour; seldom/never" 7 year questionnaire: "Outside of school, on a regular week day: How many hours per day does the child usually spend watching TV, videos, playing electronic video games, DVDs or using a computer? Summer… Winter… Less than 1 hr per day; 1-2 hrs/day 3-5 hrs/day >5 hrs or more/day" **7 year questionnaire:** "Outside of school: Approximately how many times per week is the child physically active/ takes part in sports such that he/she become short of breath or sweaty? X times per week" "Outside of school: Approximately how many hours per week does the child spend on physical activity/sports (soccer, handball, skiing or gymnastics/dance or similar)? <1 hr/wk; 1-2 hr/wk; 3-4 hr/wk; 5-7 hr/wk; 8-10 hr/wk; 11 hr/wk" "Outside of school on a regular week day: Approximately how many hours per day is the child usually outdoors? Summer / Winter X hrs/day" "How often does the child get to school by? Walking/riding a bike… Car… Public transportation: never; sometimes; usually; always" "How far is the child's home from school? Less than 1 km; 1-2 km; 3-4 km; >4 km"
INMA	**Global physical activity** (questionnaire on physical activity): *"Overall, considering all physical activity of your child: Do you think your child is?"* **Physical activity at school** (questionnaire on physical activity): *"How long usually do physical activities in the school? Include pool and playing in the yard. Specify activities"* **Energy expenditure in physical activity at school** (Calculations based on activities specified in the previous question) ** **Walk to school** (questionnaire on physical activity): *"How usually your child goes or comes back to school?* *1 walking min/day: going____ return____"* **Energy expenditure walk to school** (Calculations based on **) **Extracurricular physical activity**(questionnaire on physical activity): (see annex 1) *"During a typical week, how long your child usually does extracurricular physical activity each day, (for example. dance lessons / swimming) or just play, running, biking, skating, swimming, etc. (exclude play Wii games and the trip to school). Specify activities."* **Energy expenditure in extracurricular physical activity** (Calculations based on activities specified in the previous question) ** **Physical inactivity** (Sum of inactivity questions): *"How many hours a day usually sleeps your child? Including naps"* *"How many hours your child spend watching tv or videos a day?"* *"Outside school hours, how much time your child spends in sedentary games or activities (eg puzzles, reading, dolls / games, homework, etc.) a day? (Exclude television, videos and Wii-sports)"* **Energy expenditure in physical inactivity** (Calculations based on activities specified in the previous question)**
KOALA	**Questionnaire at age 1-2 years:** How often does your child play outside? How often does your child watch TV? How often does your child play on the computer? **Questionnaire at age 4-5 years and 6-7 years:** How often does your child walk or cycle to school? How often does your child sport on school? How often does your child sport outside of school? How often does your child play outside? How often does your child watch TV? How often does your child play on the computer? How often does your child sit in the car? **Accelerometry data at age 4-5 years and 6-7 years:** Actigraph 7164 during day time for at least 5 days. Epoch length 15 seconds. Counts per minute. Four intensity levels: sedentary, light, moderate and vigorous PA based on cut-off values established by Evenson et al.
Lifeways	Hours activity/inactivity

LISA	**Questionnaire on physical activity at age 4 and 6:** “How many hours per day does your child spend outside during summer/during winter?”; **Questionnaire on physical activity at age 10 and 15:** How many hours per week during summer/during winter does the child spend in • light activity (no sweating, normal respiration, e.g. walking) • moderate activity (some sweating, moderately increased respiration, e.g. cycling, swimming, skating) • vigorous activity (strong sweating, fast respiration, e.g. ball games, training) **Questionnaire on sedentary behaviour at age 4, 6, 10 and 15**: “How many hours per day does your child spend in front of a screen (TV, PC)?” (for 10 and 15 years, it was differentiated between summer and winter)
LRC	**Age 4-8 (2001)** At the weekend, how many hours per day does your child usually: Play outdoors? Watch TV or play video games? Which of the following descriptions fits your child best? (categories: Not very active, moderately active, or very active) **Age 6-10 (2003)** At the weekend, how many hours per day does your child usually: Play outdoors? Watch TV or play video games? On average, how many hours a week does your child spend on sports, games or vigorous physical activity? How does your child usually go to school? (categories: by walking, by car, by bus, by bicycle) Which of the following descriptions fits your child best? (categories: Not very active, moderately active, or very active) **Age 9-13 (2006)** On average, how many hours a week does your child spend on sports, games or vigorous physical activity? Which of the following descriptions fits your child best? (categories: Not very active, moderately active, or very active) **Age 13-17 (2010)** In the past month, did you participate in any physical activities or exercises such as running, football, fitness, gym, or other active sports? IF YES: What activity? How often In a typical week, do you do vigorous physical activities for at least 10 minutes at a time? IF YES: On how many days do you do vigorous physical activities in a typical week days per week? How much time in total do you usually spend on one of those days doing vigorous physical activities? In a typical week, do you do moderate physical activities for at least 10 minutes at a time? IF YES: On how many days do you do moderate physical activities in a typical week days per week? How much time in total do you usually spend on one of those days doing moderate physical activities? How many hours per day do you spend, on average, doing following activities, outside working or school time? Watching TV, computer games, video games Quiet activities: reading, studying, listening to music
LucKi	How often does your child walk or cycle to school? How often does your child sport on school? How often does your child sport outside of school? How often does your child play outside? How often does your child watch TV? How often does your child play on the computer? How often does your child sit in the car?
PIAMA	**Age 5, 7, 8:** - cycling/ walking to school (time per day) - frequency physical education (gym) at school - sport club membership (incl swimming lessons, ballet etc) - time spent (per day) in physically active play (e.g. ball games, playing tag, skipping rope) - playing outside (times p. week) - watching TV/ video’s / computer (hrs p.d.)

	Age 11: - cycling/ walking to school (time per day) - Sport frequency (incl sport outside sport club) (times p.wk) - sport club member yes/no - use of asthma medication when sporting (never, sometimes, most of the time) - number of days p. wk on which physically active during at least 1 hr - TV/ video/ dvd (days p. wk and time p. day) - computer/ Gameboy (days p. wk and time p. day) **Age 14:** Questions age 11 + On how many days p. wk intensive phys act (with sweating and heavy breathing) during at least 0.5 hr - TV/ dvd (days p. wk and time p. day) - computer (incl laptop, Ipad, spel-computer, etc) (days p. wk and time p. day) **Age 17:** Questions on age 14 + Cycling (days p. wk and time p. day) Time spent sedentary per day during transport; during work or school/ study; with TV, computer, tablet, smartphone;during other leisure time activities
SEATON	**Fels PAQ** 1. In the last year, what sports did your child play at school (e.g. dancing, walking, jogging, running, badminton, tennis, basket ball, football, rugby, field hockey, aerobics)? 2. In the last year, what sports or physically active games did your child play outside of school (e.g. dancing, dog walking, running, football, rugby, field hockey, skateboarding, bicycle riding, bowling)? 3. When my child plays sports or games (s)he sweats 4. During leisure time my child plays sports 5. During leisure time my child watches television or reads 6. How often does your child walk and/or bicycle to and from school? 7. What jobs around the house does your child do that are physically active and how often do they do them (e.g. carrying laundry baskets, carrying food bags, watering flowers, weeding garden, feeding pets, walking large pet, picking up rubbish, picking up sticks, mowing the lawn)?
Steps Study	**At 1, 2 and 4 yrs:** “How many hours per day does your child play outside?” Additional questions about attitudes towards physical activity. At 5 yrs: “Does your child attend an instructed sports (or related) activity? How many times per week, how long time per session” **Yearly 1 to 5 years:** “How many hours per day does your child watch television, DVD, play videogames, use computer?”
SWS	Hours actively on the move per day (derived from detailed questions about time spent sleeping, sitting etc) Questionnaire: On a typical day, how many hours does he/she generally spend watching television? Hours sitting per day (derived from detailed questions about time spent sleeping, sitting etc) **Accelerometry at age 3-5 years:** Epoch length 60 seconds. Counts per minute (cpm), intensity levels light (>20 cpm), moderate (>400 cpm), vigorous (>600 cpm) during day time.
WHISTLER	Transportation to school (walking, cycling), outside of school walking, cycling, playing outside, playing inside, sports.

Table B. Overview of cohort-specific questionnaires on asthma, wheeze, and medication use

Cohort	**Asthma definition / wheeze / medication use**
ABCD	**ISAAC based questionnaire at age 7-8 years:** *'Has your child ever had asthma? If yes, was this diagnosed by a doctor?'* *'Has your child ever had wheezing or whistling in the chest at any time in the past?' and 'Has your child had wheezing or whistling in the chest in the past 12 months?'* <u>No</u> specific question about asthma medication. Only a general question about medicine use on 5 years old. *'Has your child been prescribed medicine by a doctor in the last 6 months?'*
ABIS	Parental questionnaire/ISAAC, and physician-diagnosed, health register data
BAMSE	At least 3 episodes of wheeze in the last 12 months and/or at least 1 episode of wheeze in the last 12 months combined with prescription of inhaled steroids for symptoms of asthma. Has a doctor diagnosed your child as having asthma? At least 1 episode of wheeze in the last 12 months Has your child been prescribed any medicines for treatment of asthma or breathing difficulties the last 12 months?
CHOP	Did a physician ever diagnose asthma in your child No question on wheeze Medication use in general (not specifically for asthma)
$COPSAC_{2000}$	Physician diagnosed asthma
DNBC	***Web-based or paper-mailed questionnaire to mother/parent (child age 7 years):*** Z048. Has your child ever had asthma? Z051. Has a doctor ever said that your daughter/son had asthma? ***Web-based questionnaire to adult when child aged 11 years:*** F085 Has [child name] ever had asthma? (no questions on doctor-diagnosis) F086 How old was [child name] when [child name] had [his/hers] first asthma attack? F087 Has [child name] had an asthma attack in the past year? F088 How old was [child name] when [child name] had his/ her latest asthma attack? F097 Has [child name] a peakflow-meter at home? ***Web-based or paper-mailed questionnaire to mother/parent (child age 7 years):*** Z043. Has your child ever had wheezing or whistling in the chest at any time in the past? Z044. Has your child had wheezing or whistling in the chest in the last 12 months? Z045. How many attacks of wheezing has your child had in the last 12 months? ***Web-based questionnaire to adult when child aged 11 years:*** F082 How many periods of wheezing has [child name]s had during the past year? F089 Has [child name]s breathing sounded wheezy during or after exercise in the past year? (and more questions on nightly cough etc) ***Web-based or paper-mailed questionnaire to mother/parent (child age 7 years):*** Z052. Has your daughter/son taken asthma medicine during the past 12 months? If yes: Which type of medicine? ***Web-based questionnaire to adult when child aged 11 years:*** F091 Has [child name] been given medicine for [his/hers] wheezy breathing or asthma (e.g. inhalators, spray or pills) in the past year? F092_1-4 What type of medicine has [child name] received? F093, F094, F095: What was the name of the type? How often has [child names] received these products?
EDEN	Physician-diagnosed asthma, ISAAC questionnaire
G21	**ISAAC based questionnaire (4 and 7 years of age):** "has you child ever had asthma diagnosed by a doctor?" "if so, in the last 12 months, has your child had an asthma attack?" ISAAC questions on physician diagnosed allergy, eczema, rhinitis. ISAAC based questionnaire: *"Has your child ever had wheezing in the chest?* *"Has your child ever had wheezing in the chest in the past 12 months?" number of wheezing attacks in the last 12 months.* *"In the last 12 months, how often did he/she wake up due to wheezing?"* *"In the last 12 months, did he/she become short of breath during a conversation due to wheezing?"*

	Questionnaire: "Did your child use any prescription medication in the past 12 months for asthma?" (name of the medication/quantity per day/how many times per day/duration (days)) (4 years)
Gen R	ISAAC based questionnaire: "has you child ever had asthma diagnosed by a doctor?" "has you child ever suffered from a whistling noise in the chest?" (**1y**); "has your child had problems with a wheezing chest during the last year?" (**2,3, 4, 9y**); "Did your child ever suffer from chest wheezing?" "If yes, during the past 12 months, did you child ever suffer from chest wheezing?" (**6y**) Questionnaire: "Did your child use any prescription medication in the past 12 months for complaints of the lungs, allergy or skin?"
GINIplus	**Questionnaire (at each follow-up):** it was asked from birth to age 15 for each year of life since the previous follow-up whether the child was diagnosed with asthma by a physician ("doctor diagnosis at the age of x years: asthma") **Questionnaire (at 6, 10, 15 years):** "Has your child ever had asthma?" **Questionnaire (at each follow-up):** "Has your child had wheezing or whistling in the chest in the past 12 months?" (asked for age 1,2,3 and 4) "Has your child had wheezing or whistling in the chest during the past 12 months?" (asked at ages 6, 10 and 15) **Questionnaire:** at age 6: "Has your child been treated for asthma in the 5th or 6th year of life?" at ages 10 and 15: "Has your child been treated for asthma in the past 12 months?"
HUMIS	Has your child ever suffered, or is currently suffering from any of the following long-term illnesses or health problems? Asthma… no/yes; If yes, was the illness/problem confirmed by a doctor. Additionally, linkage to **Norwegian Patient Registry** "Has the child ever had, or does the child have, any of the following symptoms or health problems? **Tightness/wheezing/whistling in the chest**… Tightness/wheezing in the chest during or after physical exercise no/yes; At what age? 3 years or older; Number of times last 12 months: XX" "During the last year, has the child used medication, spray, inhaler or other medications for treatment of asthma? No/yes; If yes, Name of medication used on a regular basis: XXX; Name of medications used during attacks: XXX; When did your child last use medications for asthma? Yesterday; Last 7 days; Last month; Last year"
INMA	Parental questionnaire *"In the last 12 months, Has your child had ever suffered asthma?"* *"Has your child ever been diagnosed by a doctor as having asthma?"* Parental questionnaire *"Has your child ever had wheezing in the chest in the past 12 months?"* *"Has your child ever had wheezing in the chest in the past 24 months?"* Parental questionnaire *"Has your child taken any medicines for asthma in the last 24 months? (include any inhalers, nebulisers, tablets, oral corticosteroids or liquid medicines)"* *"Has your child taken any medicines for asthma/breathing difficulties in last 12 months?"*
KOALA	ISAAC questionnaire on asthma, wheezing, physician diagnosed asthma, asthma medication use
Lifeways	Questionnaire/physician diagnosed.
LISA	**Questionnaire (at each follow-up):** it was asked for ages 1, 1.5, and 2 years whether the child was diagnosed with asthma by a physician during the past 6 months it was asked from age 3 to age 15 for each year of life since the previous follow-up whether the child was diagnosed with asthma by a physician ("doctor diagnosis at the age of x years: asthma") **Questionnaire (at 6, 10, 15 years):** "Has your child ever had asthma?" **Questionnaire (at each follow-up):** "Has your child had wheezing or whistling in the chest during the past 6 months?" (asked for age 0.5, 1, 1.5 and 2)

	"Has your child had wheezing or whistling in the chest during the past 12 months?" (asked at age 4, 6, 10 and 15) **Questionnaire:** at age 6: "Has your child been treated for asthma in the 5th or 6th year of life?" at ages 10 and 15: "Has your child been treated for asthma in the past 12 months?"
LRC	**Age 1-5 years (1998) and 4-8 years (2001):** Has any doctor or hospital told you that he/she has asthma or bronchitis? Does your child attend a clinic or see a doctor for wheezing? (or asthma or bronchitis?) Has your child had wheezing or whistling in the chest in the last 12 months? Has your child ever taken any medicine for wheezing? (or asthma or bronchitis) **6-10 years (2003):** Has any doctor or hospital told you that he/she has asthma or bronchitis? Has your child had wheezing or whistling in the chest in the last 12 months? Did your child take any of the following during the last 12 months? (Salbutamol, Ventolin, Bricanyl, Pulmicort, Flixotide, Becotide, Beclovent, Serevent, Seretide, Symbicort) **Age 13-17 years (2010):** Have you ever been diagnosed with asthma by a doctor or a nurse? Have you had wheezing or whistling in the chest in the last 12 months? In the last 12 months, did you take any of the following medicines or inhalers? (Salbutamol, Ventolin, Bricanyl, Pulmicort, Flixotide, Becotide, Beclovent, Serevent, Seretide, Symbicort)
LucKi	ISAAC questions on physician diagnosed asthma (bronchitis, allergy, eczema) and prescribed asthma medication. Full ISAAC module questions on wheeze (number of attacks etc.) Pharmacy registry data
PIAMA	**At ages 1,2,3,4,5,6,7,8,11,14,17: ISAAC questions** **At ages 3,4,5,6,7,8,11,14,17 'MeDALL asthma definition'** (= presence of 2 out of the 3 following items: doctor diagnosed asthma ever; wheeze in the last 12 months; use of asthma medication in the last 12 months) **At ages 3,4,5,6,7,8,11,14,17:** questionnaire based different types of asthma medication, incl ICS and bronchodilators
SEATON	Physician diagnosed asthma
Steps Study	ISAAC based questionnaires on asthma and wheezing "Did a physician ever diagnose asthma in your child?" "Did your child ever experience wheezing?" "Did your child experience wheezing during the last 12 months?" Questions on frequency and severity of wheezing symptoms during the last 12 months Open question on medications: "Does your child have any long-term medication? Please name the medication"
SWS	Questionnaire asking about physician-diagnosed asthma ISAAC questionnaire ISAAC Questionnaire: Has he/she received inhalers or other medication for asthma prescribed by a doctor in the past 12 months?
WHISTLER	Did your child ever suffer from asthma? Did your child ever suffer from wheezing? Did your child suffer from wheezing in the last 12 months? Pharmacy registry data and GP registry data

Table C. Covariables of participating cohorts

Cohort (country)	n	Sex		Gestational Age		Birth weight		Parity		Parental history of asthma		Parental history of atopy		Maternal smoke in pregnancy		Environmental Tobacco Smoke	
		boy %(n)	missing %(n)	mean (SD)	missing %(n)	mean (SD)	missing %(n)	firstborn %(n)	missing %(n)	yes %(n)	missing %(n)	yes %(n)	missing %(n)	yes %(n)	missing %(n)	yes %(n)	missing %(n)
ABCD (Netherlands)	2,887	51.3 (1,481)	0.0 (0)	39.5 (1.7)	0.2 (5)	3499 (533)	0.5 (14)	57.8 (1,670)	0.0 (0)	14.4 (371)	10.9 (314)	51.4 (1322)	10.9 (315)	7.2 (208)	0.0 (0)	6.7 (192)	0.0 (1)
ABIS (Sweden)	8,327	52.3 (4,355)	0.0 (0)	39.7 (1.7)	3.4 (286)	3584 (548)	1.8 (153)	42.0 (3423)	2.1 (173)	9.3 (776)	0.0 (0)	28.8 (2,400)	0.0 (0)	7.9 (644)	1.9 (159)	4.8 (331)	17.9 (1,488)
BAMSE (Sweden)	3,181	49.7 (1,581)	0.0 (0)	39.8 (2.0)	0.0 (0)	3530 (560)	1.0 (31)	52.6 (1,672)	0.0 (0)	19.6 (620)	0.7 (23)	- -	- -	13.6 (431)	0.1 (2)	18.0 (564)	1.2 (39)
CHOP (Multiple)*	632	47.8 (302)	0.0 (0)	39.8 (1.2)	0.2 (1)	3298 (345)	0.0 (0)	57.9 (365)	0.3 (2)	- -	- -	40.9 (256)	0.9 (6)	18.9 (119)	0.2 (1)	- -	- -
COPSAC$_{2000}$ (Denmark)	272	48.9 (133)	0.0 (0)	39.9 (1.6)	0.0 (0)	3541 (545)	0.0 (0)	61.0 (166)	0.0 (0)	100.0 (272)	0.0 (0)	100.0 (272)	0.0 (0)	22.4 (61)	0.0 (0)	26.2 (71)	0.4 (1)
DNBC (Denmark)	80,633	50.9 (41,042)	0.0 (0)	39.6 (1.7)	0.1 (108)	3595 (553)	0.5 (386)	45.5 (34,033)	7.3 (5,915)	8.4 (6,471)	5.0 (4,004)	21.3 (16,307)	5.2 (4,219)	25.6 (20,471)	0.7 (584)	14.8 (11,239)	5.8 (4,713)
Eden (France)	876	53.4 (468)	0.0 (0)	39.3 (1.7)	0.0 (0)	3290 (494)	0.0 (0)	29.6 (206)	20.5 (180)	18.4 (161)	0.0 (0)	17.9 (157)	0.0 (0)	21.7 (173)	8.8 (77)	35.5 (274)	11.9 (104)
G21 (Portugal)	7,310	50.9 (3,723)	0.0 (0)	38.5 (1.9)	0.1 (8)	3155 (528)	0.0 (0)	57.8 (4,149)	1.9 (138)	5.4 (380)	4.3 (315)	- -	- -	21.7 (1,562)	1.6 (115)	17.2 (1170)	6.8 (498)
Gen R (Netherlands)	5,149	49.8 (2,566)	0.0 (0)	39.8 (1.9)	0.6 (31)	3433 (573)	0.1 (7)	58.8 (2,933)	3.1 (160)	15.7 (554)	31.3 (1,613)	59.9 (2,350)	23.8 (1,226)	21.9 (1,011)	10.5 (539)	13.0 (556)	16.7 (859)
GINIplus (Germany)	4,010	50.9 (2,043)	0.0 (0)	39.7 (1.4)	16.9 (676)	3469 (467)	4.2 (170)	- -	- -	14.2 (562)	1.0 (40)	53.7 (2,131)	1.1 (43)	14.0 (553)	1.4 (56)	30.8 (1,201)	2.8 (113)
HUMIS (Norway)	763	50.5 (324)	15.9 (121)	39.8 (2.1)	15.9 (121)	3574 (641)	15.9 (121)	45.8 (283)	19.0 (145)	14.3 (85)	21.9 (167)	45.2 (268)	22.3 (170)	7.2 (45)	17.8 (136)	5.6 (42)	1.7 (13)
INMA Asturias (Spain)	340	54.1 (184)	0.0 (0)	39.4 (1.6)	0.0 (0)	3254 (474)	0.0 (0)	62.4 (212)	0.0 (0)	14.4 (49)	0.0 (0)	21.8 (74)	0.0 (0)	27.1 (88)	4.4 (15)	56.6 (192)	0.3 (1)
INMA Gipuzkoa (Spain)	351	49.9 (175)	0.0 (0)	39.8 (1.5)	0.0 (0)	3294 (438)	0.9 (3)	56.7 (199)	0.0 (0)	13.7 (48)	0.0 (0)	29.3 (103)	0.0 (0)	21.4 (73)	2.8 (10)	47.1 (165)	0.3 (1)
INMA Menorca (Spain)	471	51.2 (241)	0.0 (0)	39.3 (1.8)	0.2 (1)	3209 (471)	3.0 (14)	41.8 (197)	0.0 (0)	12.4 (58)	0.6 (3)	51.7 (215)	11.7 (55)	35.3 (165)	0.6 (3)	48.3 (210)	7.6 (36)
INMA Sabadell (Spain)	534	52.4 (280)	0.0 (0)	39.8 (1.4)	0.0 (0)	3276 (423)	0.0 (0)	55.9 (295)	1.1 (6)	15.0 (70)	12.4 (66)	35.7 (168)	11.8 (63)	26.3 (138)	1.9 (10)	52.1 275)	1.1 (6)
INMA Valencia (Spain)	460	50.9 (234)	0.0 (0)	39.6 (1.7)	0.0 (0)	3233 (493)	0.0 (0)	56.7 (261)	0.0 (0)	13.3 (61)	0.0 (0)	31.1 (143)	0.0 (0)	37.6 (173)	0.0 (0)	64.9 (298)	0.2 (1)

Cohort (country)	n	Sex		Gestational Age		Birth weight		Parity		Parental history of asthma		Parental history of atopy		Maternal smoke in pregnancy		Environmental Tobacco Smoke	
		boy %(n)	missing %(n)	mean (SD)	missing %(n)	mean (SD)	missing %(n)	firstborn %(n)	missing %(n)	yes %(n)	missing %(n)	yes %(n)	missing %(n)	yes %(n)	missing %(n)	yes %(n)	missing %(n)
KOALA (Netherlands)	2,222	50.7 (1,126)	0.0 (0)	39.5 (1.5)	0.4 (9)	3516 (506)	0.0 (1)	44.5 (980)	0.9 (21)	17.7 (386)	1.9 (43)	59.6 (1,307)	1.4 (30)	5.4 (119)	0.0 (0)	10.2 (227)	0.0 (1)
Lifeways (Ireland)	555	47.9 (266)	0.0 (0)	39.9 (1.9)	9.2 (51)	3526 (566)	0.9 (5)	41.9 (229)	1.6 (9)	16.9 (69)	26.3 (146)	- -	- -	17.6 (95)	2.5 (14)	36.3 (200)	0.7 (4)
LISA (Germany)	2,493	51.5 (1,284)	0.0 (0)	39.8 (1.2)	1.5 (37)	3476 (444)	0.0 (0)	53.0 (1,314)	0.6 (14)	11.5 (273)	4.7 (116)	56.2 (1,306)	6.8 (170)	15.3 (367)	3.6 (89)	27.2 (677)	0.1 (3)
LRC (United Kingdom)	5,948	52.0 (3,093)	0.0 (0)	39.2 (1.9)	2.7 (160)	3305 (578)	2.5 (151)	41.7 (2,415)	2.7 (163)	30.5 (1,495)	17.6 (1,049)	55.8 (2,801)	15.6 (926)	14.2 (726)	14.3 (852)	32.8 (1,841)	5.7 (339)
LucKi (Netherlands)	828	49.5 (410)	0.0 (0)	39.2 (1.8)	0.2 (2)	3404 (525)	0.2 (2)	50.8 (410)	2.5 (21)	21.7 (171)	5.0 (41)	65.9 (519)	5.0 (41)	10.6 (88)	0.0 (0)	7.6 (63)	0.0 (0)
PIAMA (Netherlands)	3,591	51.7 (1,855)	0.0 (1)	39.9 (1.6)	0.3 (11)	3520 (541)	0.5 (18)	49.9 (1,788)	0.1 (5)	13.1 (466)	0.9 (32)	50.0 (1,796)	0.0 (0)	16.8 (597)	0.8 (29)	24.2 (867)	0.1 (4)
SEATON (United Kingdom)	212	49.5 (105)	0.0 (0)	39.6 (1.6)	5.2 (11)	3521 (540)	5.7 (12)	38.3 (77)	5.2 (11)	25.9 (55)	0.0 (0)	67.5 (137)	4.2 (9)	17.5 (37)	0.0 (0)	19.0 (40)	0.9 (2)
STEPS Study (Finland)	832	52.0 (433)	0.0 (0)	39.8 (1.6)	1.3 (11)	3514 (511)	1.3 (11)	58.1 (483)	0.0 (0)	19.8 (131)	20.4 (170)	34.3 (230)	19.5 (162)	2.1 (13)	26.2 (218)	19.0 (151)	4.6 (38)
SWS (United Kingdom)	2,549	52.1 (1,329)	0.0 (0)	39.8 (1.8)	0.0 (0)	3443 (544)	1.0 (26)	53.2 (1,354)	0.1 (3)	36.9 (839)	10.8 (276)	67.1 (1,433)	16.2 (414)	14.4 (349)	4.6 (117)	35.8 (905)	0.9 (23)
WHISTLER (Netherlands)	645	47.9 (304)	1.7 (11)	39.5 (1.4)	2.9 (19)	3537 (496)	2.9 (19)	- -	- -	13.8 (81)	8.7 (56)	65.6 (356)	15.8 (102)	16.8 (105)	3.1 (20)	6.4 (41)	0.2 (1)

Continues on next page

Table C. (continued)

Cohort (country)	Maternal age		Maternal education				Maternal BMI		Breastfeeding		Breastfeeding duration in months	
	mean (SD)	missing %(n)	low %(n)	mid %(n)	high %(n)	missing %(n)	mean (SD)	missing %(n)	yes %(n)	missing %(n)	mean (SD)	missing %(n)
ABCD	32.3	0.0	9.1	18.6	72.3	0.3	22.8	5.1	85.2	0.0	4.9	0.0
(Netherlands)	(4.2)	(0)	(262)	(535)	(2,080)	(10)	(3.7)	(148)	(2,459)	(1)	(3.7)	(1)
ABIS	29.9	0.1	6.2	58.3	35.5	2.0	23.7	21.1	96.2	20.8	7.2	21.1
(Sweden)	(4.5)	(7)	(510)	(4,756)	(2,896)	(165)	(3.8)	(1,755)	(6,342)	(1,734)	(2.3)	(1,734)
BAMSE	30.8	0.0	32.1	24.7	43.1	0.4	-	-	97.2	0.0	8.7	2.8
(Sweden)	(4.5)	(1)	(1,018)	(783)	(1,366)	(14)	-	-	(3,092)	(0)	(3.4)	(89)
CHOP	31.2	0.2	17.9	50.6	31.5	0.0	23.4	3.3	33.4	0.0	-	-
(Multiple)*	(4.7)	(1)	(113)	(320)	(199)	(0)	(4.2)	(21)	(211)	(0)	-	-
COPSAC$_{2000}$	30.2	0.0	38.8	46.9	14.2	4.4	-	-	99.3	0.0	9.0	0.0
(Denmark)	(4.2)	(0)	(101)	(122)	(37)	(12)	-	-	(270)	(0)	(5.5)	(0)
DNBC	30.0	0.0	8.8	37.4	53.8	5.2	23.5	6.4	98.4	20.4	5.2	20.4
(Denmark)	(4.3)	(0)	(6,748)	(28,606)	(41,111)	(4,168)	(4.2)	(5,147)	(63,170)	(16,457)	(1.5)	(16,457)
Eden	30.3	0.0	22.7	17.3	60.0	1.0	23.4	0.8	72.0	0.1	-	-
(France)	(4.8)	(0)	(197)	(150)	(520)	(9)	(4.5)	(7)	(630)	(1)	-	-
G21	29.3	0.0	46.4	27.3	26.3	0.6	23.9	7.8	93.1	2.4	10.3	27.9
(Portugal)	(5.4)	(0)	(3,370)	(1,987)	(1,910)	(43)	(4.3)	(570)	(6,640)	(178)	(10.1)	(2,039)
Gen R	31.5	0.0	4.9	39.1	56.1	5.1	24.5	10.7	92.5	14.7	5.1	36.0
(Netherlands)	(4.6)	(0)	(238)	(1,908)	(2,740)	(263)	(4.1)	(550)	(4,062)	(756)	(3.8)	(1,854)
GINIplus	31.2	0.0	15.1	39.9	45.0	6.0	22.7	37.4	87.1	4.3	4.3	4.5
(Germany)	(4.1)	(1)	(570)	(1,502)	(1,696)	(242)	(3.4)	(1,501)	(3,344)	(171)	(2.3)	(179)
HUMIS	30.1	15.9	4.8	9.2	85.9	16.1	23.9	16.3	98.7	19.0	11.8	24.5
(Norway)	(4.5)	(121)	(31)	(59)	(550)	(123)	(4.1)	(124)	(610)	(145)	(5.3)	(187)
INMA Asturias	33.3	0.0	14.1	44.1	41.8	0.0	23.7	0.0	76.1	4.1	5.1	4.1
(Spain)	(4.2)	(0)	(48)	(150)	(142)	(0)	(4.1)	(0)	(248)	(14)	(6.9)	(14)
INMA Gipuzkoa	32.7	0.0	10.9	35.4	53.7	0.3	22.9	0.0	90.8	4.0	6.8	4.0
(Spain)	(3.2)	(0)	(38)	(124)	(188)	(1)	(3.5)	(0)	(306)	(14)	(4.7)	(14)
INMA Menorca	30.0	3.0	58.5	28.1	13.4	3.4	22.8	3.6	82.4	0.0	1.1	0.0
(Spain)	(4.6)	(14)	(266)	(128)	(61)	(16)	(3.7)	(17)	(388)	(0)	(1.0)	(0)
INMA Sabadell	31.8	0.2	22.9	44.1	32.9	2.8	23.8	2.4	93.6	0.2	6.3	0.2
(Spain)	(4.3)	(1)	(119)	(229)	(171)	(15)	(4.5)	(13)	(499)	(1)	(4.5)	(1)
INMA Valencia	31.8	0.7	27.2	42.4	30.4	0.0	23.6	0.0	83.9	0.0	5.5	0.0
(Spain)	(4.2)	(3)	(125)	(195)	(140)	(0)	(4.2)	(0)	(386)	(0)	(4.5)	(0)

Cohort (country)	Maternal age		Maternal education				Maternal BMI		Breastfeeding		Breastfeeding duration in months	
	mean (SD)	missing %(n)	low %(n)	mid %(n)	high %(n)	missing %(n)	mean (SD)	missing %(n)	yes %(n)	missing %(n)	mean (SD)	missing %(n)
KOALA (Netherlands)	32.2 (3.8)	0.1 (2)	8.8 (196)	36.5 (811)	54.1 (1,189)	1.2 (26)	23.7 (3.9)	0.5 (10)	85.5 (1,899)	0 (0)	5.3 (4.3)	0.0 (0)
Lifeways (Ireland)	31.6 (5.3)	0.0 (0)	0.2 (1)	44.6 (244)	55.2 (302)	1.4 (8)	23.8 (3.9)	15.1 (84)	54.4 (298)	1.3 (7)	3.1 (3.7)	47.9 (266)
LISA (Germany)	31.4 (4.4)	0.1 (2)	7.6 (187)	38.0 (936)	54.4 (1,340)	1.2 (30)	22.6 (3.8)	2.2 (54)	94.4 (2,329)	1.1 (27)	4.8 (1.9)	1.1 (28)
LRC (United Kingdom)	28.9 (5.2)	(0.1) (4)	43.0 (1,130)	34.1 (898)	22.9 (602)	55.8 (3,318)	- -	- -	62.0 (3,224)	12.6 (751)	2.8 (3.0)	12.6 (751)
LucKi (Netherlands)	30.8 (4.2)	52.9 (438)	8.7 (41)	80.9 (382)	10.4 (49)	43.0 (356)	24.1 (4.4)	67.5 (559)	62.3 (514)	0.4 (3)	- -	- -
PIAMA (Netherlands)	30.5 (3.8)	0.5 (17)	22.3 (795)	42.1 (1,500)	35.6 (1,271)	0.7 (25)	22.8 (3.4)	9.3 (334)	82.6 (2,932)	1.1 (40)	3.5 (3.5)	1.1 (40)
SEATON (United Kingdom)	30.8 (4.3)	0.0 (0)	41.7 75	11.7 21	46.7 84	15.1 32	- -	- -	76.2 (157)	2.8 (6)	3.5 (3.8)	3.8 (8)
STEPS Study (Finland)	31.3 (4.4)	0.0 (0)	16.9 (138)	42.3 (345)	40.7 (332)	2.0 (17)	24.2 (4.7)	1.8 (15)	98.5 (657)	19.8 (165)	9.3 (4.8)	19.8 (165)
SWS (United Kingdom)	30.9 (3.8)	0.0 (0)	38.8 (986)	32.1 (816)	29.1 (740)	0.3 (7)	25.2 (4.7)	0.9 (24)	83.4 (2,042)	4.0 (102)	4.3 (5.1)	4.0 (102)
WHISTLER (Netherlands)	32.8 (3.5)	9.8 (63)	32.2 (180)	0.0 (0)	67.8 (379)	13.3 (86)	24.8 (4.1)	11.3 (73)	80.5 (503)	3.1 (20)	3.0 (2.9)	4.5 (29)

The numbers shown are based on the inclusion criteria for this study (participants with information on physical activity and asthma for at least one age group). Cohort-specific details on study population and covariables can be found in the reference of the specific cohort.
* CHOP study included participants in multiple countries: Belgium, Germany, Italy, Poland, and Spain.

Table D. Longitudinal analyses on physical activity, sedentary behaviour and current asthma between age 6 and 18 years – exclusion of wheeze and asthma at baseline

	n (n asthma cases)	n cohorts		aOR (95% CI) #
Questionnaire based				
Physical activity (hours/day)				
age 3-5 years	12972 (836)	10	a	1.00 (0.95 to 1.04)
Sedentary behaviour (hours/day)				
age 3-5 years	12595 (828)	9	b	1.04 (0.98 to 1.10)
Accelerometry				
Total activity (counts/min)				
age 3-5 years	732 (99)	2	c	1.00 (1.00 to 1.00)
Sedentary activity				
age 3-5 years	732 (99)	2	c	1.04 (0.89 to 1.21)
MVPA				
age 3-5 years	732 (99)	2	c	1.00 (0.64 to 1.57)

Generalized logistic mixed models on questionnaire based physical activity (PA) in hours per day, sedentary behaviour in hours per day, and accelerometry data at age 3-5 years; and current asthma at age 6-18 years. Subgroup analysis with exclusion of partcipants with wheeze or asthma at baseline.
adjusted odds ratios (aOR) indicate the increase in odds of current asthma between age 6 and 18 years for each hour per day of parent reported physical activity or sedentary behaviour at the age of 3-5 years; and time in sedentary activity or moderate to vigorous physical activity (MVPA) recorded by accelerometry between age 3-5 years. Current asthma is defined as physician diagnosed asthma, ISAAC based current asthma definition or MeDALL based current asthma definition.
95% CI: 95% confidence intervals.
Multivariable analyses adjusted for sex, maternal education level, maternal BMI.

Included cohorts:
a: ABIS, G21, HUMIS, KOALA, Lifeways, LISA, LucKi, STEPS Study, SWS, Whistler
b: ABIS, G21, HUMIS, KOALA, Lifeways, LISA, LucKi, STEPS Study, SWS
c: KOALA, SWS

Table E. Longitudinal analyses on physical activity, sedentary behaviour and ISAAC based definition of current asthma between age 6 and 18 years

	n (n asthma cases)	n cohorts		aOR (95% CI) #
Questionnaire based				
Physical activity (hours/day)				
age 0-2 years	2024 (182)	2	a	0.92 (0.75 to 1.11)
age 3-5 years	15968 (1256)	14	b	1.02 (0.98 to 1.06)
Sedentary behaviour (hours/day)				
age 0-2 years	2379 (205)	3	c	1.00 (0.72 to 1.38)
age 3-5 years	16014 (1259)	13	d	1.03 (0.98 to 1.08)
Accelerometry				
Total activity (counts/min)				
age 3-5 years	775 (116)	2	e	1.00 (1.00 to 1.00)
Sedentary activity				
age 3-5 years	775 (116)	2	e	1.03 (0.89 to 1.19)
MVPA				
age 3-5 years	775 (116)	2	e	0.94 (0.62 to 1.43)

Generalized logistic mixed models on questionnaire based physical activity (PA) in hours per day, sedentary behaviour in hours per day, and accelerometry data at ages 0-2 years and 3-5 years; and ISAAC based definition of current asthma at age 6-18 years. ISAAC based current asthma is defined as (1) asthma ever and (2) dyspnea or wheeze in the last 12 months, or (3) regular use of asthma medication in the last 12 months.
adjusted odds ratios (aOR) indicate the increase in odds of (ISAAC based) current asthma between age 6 and 18 years for each hour per day of parent reported physical activity or sedentary behaviour in the age periods between age 0-2 or 3-5 years; and time in sedentary activity or moderate to vigorous physical activity (MVPA) recorded by accelerometry between age 3-5 years.
95% CI: 95% confidence intervals.
Multivariable analyses adjusted for sex, maternal education level, maternal BMI.

Included cohorts:
a: KOALA, STEPS Study
b: ABCD, ABIS, Generation R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, LucKi, STEPS Study, SWS, Whistler
c: HUMIS, KOALA, STEPS Study
d: ABCD, ABIS, Generation R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, LucKi, STEPS Study, SWS
e: KOALA, SWS

Table F. Longitudinal analyses on physical activity, sedentary behaviour and MeDALL based definition of current asthma between age 6 and 18 years

	n (n asthma cases)	n cohorts		aOR (95% CI) #
Questionnaire based				
Physical activity (hours/day)				
age 0-2 years	1879 (171)	1	a	0.96 (0.79 to 1.18)
age 3-5 years	15069 (1194)	12	b	1.01 (0.97 to 1.05)
Sedentary behaviour (hours/day)				
age 0-2 years	2264 (200)	2	c	1.00 (0.71 to 1.39)
age 3-5 years	15225 (1200)	12	b	1.01 (0.95 to 1.06)
Accelerometry				
Total activity (counts/min)				
age 3-5 years	766 (71)	2	d	1.00 (1.00 to 1.00)
Sedentary activity				
age 3-5 years	766 (71)	2	d	0.96 (0.79 to 1.17)
MVPA				
age 3-5 years	766 (71)	2	d	1.14 (0.67 to 1.94)

Generalized logistic mixed models on questionnaire based physical activity (PA) in hours per day, sedentary behaviour in hours per day, and accelerometry data at ages 0-2 years and 3-5 years; and MeDALL based definition of current asthma at age 6-18 years. MeDALL based current asthma is defined as presence of 2 out of 3 criteria (1) asthma ever, (2) wheeze in the last 12 months, (3) use of asthma medication in the last 12 months.
adjusted odds ratios (aOR) indicate the increase in odds of (MeDALL based) current asthma between age 6 and 18 years for each hour per day of parent reported physical activity or sedentary behaviour in the age periods between age 0-2 or 3-5 years; and time in sedentary activity or moderate to vigorous physical activity (MVPA) recorded by accelerometry between age 3-5 years.
95% CI: 95% confidence intervals.
Multivariable analyses adjusted for sex, maternal education level, maternal BMI.

Included cohorts:
a: KOALA
b: ABCD, ABIS, Generation R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, LucKi, SWS
c: HUMIS, KOALA
d: KOALA, SWS

Table G. Longitudinal analyses on physical activity and sedentary behaviour in tertiles and current asthma at age 6-18 years (multivariable)

Physical activity in tertiles	n (n cases asthma)	n cohort		Low tertile aOR (95% CI)	Mid tertile aOR (95% CI)	High tertile aOR (95% CI)
age 0-2 years	64658 (6086)	3	a	ref	0.69 (0.59 to 0.82)	0.80 (0.68 to 0.95)
age 3-5 years	24912 (2681)	17	b	ref	1.03 (0.93 to 1.14)	1.10 (0.99 to 1.22)
Sedentary behaviour in tertiles						
age 0-2 years	2380 (329)	3	c	ref	0.99 (0.77 to 1.27)	1.28 (0.88 to 1.87)
age 3-5 years	22449 (2515)	15	d	ref	0.94 (0.85 to 1.05)	0.99 (0.89 to 1.11)

Generalized logistic mixed models on physical activity in tertiles and sedentary behaviour in tertiles at ages 0-2 years and 3-5 years; and 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.
aOR adjusted Odds Ratio; 95% CI 95% confidence interval.
Multivariable analyses adjusted for sex, maternal education level, maternal BMI.

Included cohorts:
a: DNBC, KOALA, STEPS Study
b: ABCD, ABIS, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, Lifeways, LISA, LucKi, PIAMA, STEPS Study, SWS, WHISTLER
c: HUMIS, KOALA, STEPS Study
d: ABCD, ABIS, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, Lifeways, LucKi, PIAMA, STEPS Study, SWS

Table H. Longitudinal analyses on physical activity and sedentary behaviour in tertiles and current asthma at age 6-18 years (univariable)

Physical activity in tertiles	n (n cases asthma)	n cohort		Low tertile OR (95% CI)	Mid tertile OR (95% CI)	High tertile OR (95% CI)
age 0-2 years	68482 (6451)	4	a	ref	0.71 (0.56 to 0.89)	0.82 (0.65 to 1.04)
age 3-5 years	30109 (3739)	18	b	ref	1.06 (0.97 to 1.16)	1.17 (1.07 to 1.28)
Sedentary behaviour in tertiles						
age 0-2 years	2467 (338)	4	c	ref	1.07 (0.83 to 1.37)	1.36 (0.95 to 1.95)
age 3-5 years	27661 (3629)	17	d	ref	1.03 (0.95 to 1.12)	1.11 (1.00 to 1.22)

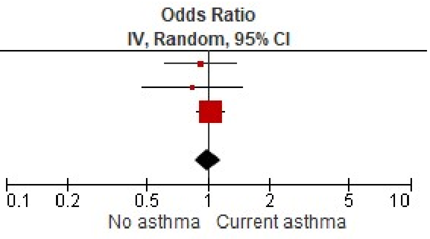
Generalized logistic mixed models on physical activity in tertiles and sedentary behaviour in tertiles at ages 0-2 years and 3-5 years; and current asthma at age 6-18 years. Current asthma is defined as physician diagnosed asthma, ISAAC based current asthma definition or MeDALL based current asthma definition.
OR Odds Ratio; 95% CI 95% confidence interval
Univariable analyses.

Included cohorts:
a: DNBC, KOALA, LRC, STEPS Study
b: ABCD, ABIS, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, Lifeways, LISA, LRC, LucKi, PIAMA, STEPS Study, SWS, WHISTLER
c: HUMIS, KOALA, LRC, STEPS Study
d: ABCD, ABIS, $COPSAC_{2000}$, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, Lifeways, LRC, LucKi, PIAMA, STEPS Study, SWS

Figure A. Meta-analysis of longitudinal data on sedentary behaviour measured with accelerometry and current asthma at age 6-18 years

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
COPSAC2000	-0.086	0.211	11.8%	0.92 [0.61, 1.39]
KOALA	-0.18	0.29	6.2%	0.84 [0.47, 1.47]
SWS	0.024	0.08	82.0%	1.02 [0.88, 1.20]
Total (95% CI)			**100.0%**	**1.00 [0.87, 1.15]**

Heterogeneity: Tau² = 0.00; Chi² = 0.64, df = 2 (P = 0.73); I² = 0%
Test for overall effect: Z = 0.02 (P = 0.98)



Meta-analysis of longitudinal data on sedentary behviour measured with accelerometry and current asthma at age 6-18 years. Meta-analysis of cohort-specific logistic regression analyses. Current asthma is defined as physician diagnosed asthma, ISAAC based current asthma definition or MeDALL based current asthma definition.
95% CI 95% confidence interval
Multivariable analyses adjusted for sex, maternal education level, maternal BMI (maternal BMI available for KOALA and SWS, not available for $COPSAC_{2000}$).

Table I. Longitudinal age-specific analyses on physical activity in hours/day and sedentary behaviour in hours/day and current asthma (multivariable)

Age at exposure	Age at outcome		Current asthma		
Physical activity in hours/day		**n (n cases asthma)**	**n cohort**		**aOR (95% CI)**
age 0-2 years	age 3-5 years	2735 (295)	3	a	1.01 (0.85 to 1.20)
age 0-2 years	age 6-8 years	1918 (218)	2	b	0.89 (0.74 to 1.07)
age 3-5 years	age 6-8 years	21155 (1875)	15	c	1.01 (0.97 to 1.04)
age 6-8 years	age 9-14 years	58324 (2731)	6	d	1.00 (0.97 to 1.03)
age 9-14 years	age 15-18 years	3311 (201)	3	e	0.90 (0.77 to 1.05)
Sedentary behaviour in hours/day					
age 0-2 years	age 3-5 years	3287 (316)	4	f	1.19 (0.89 to 1.58)
age 0-2 years	age 6-8 years	2269 (263)	3	g	0.93 (0.69 to 1.25)
age 3-5 years	age 6-8 years	20856 (1852)	14	h	1.02 (0.98 to 1.06)
age 6-8 years	age 9-14 years	59337 (2827)	7	i	1.02 (0.98 to 1.05)
age 9-14 years	age 15-18 years	5482 (436)	4	j	1.01 (0.92 to 1.11)

Generalized logistic mixed models on physical activity in hours/day and sedentary in hours/day and subsequent current asthma for each age group. Current asthma is defined as physician diagnosed asthma, ISAAC based current asthma definition or MeDALL based current asthma definition.
aOR adjusted Odds Ratio; 95% CI 95% confidence interval.
Multivariable analyses adjusted for sex, maternal education level, maternal BMI.

Included cohorts:
a: EDEN, KOALA, STEPS Study
b: KOALA, STEPS Study
c: ABCD, ABIS, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, LucKi, STEPS Study, SWS, Whistler
d: DNBC, Gen R, GINIplus, INMA Menorca, KOALA, LISA
e: GINIplus, INMA Menorca, LISA
f: EDEN, HUMIS, KOALA, STEPS Study
g: HUMIS, KOALA, STEPS Study
h: ABCD, ABIS, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, LucKi, STEPS Study, SWS
i: CHOP, DNBC, GenR, GINIplus, INMA Menorca, KOALA, LISA
j: GINIplus, INMA Menorca, LISA, PIAMA

Table J. Longitudinal age-specific analyses on physical activity in hours/day and sedentary behaviour in hours/day and current asthma (univariable)

Age at exposure	Age at outcome		Current asthma		
Physical activity in hours/day		**n (n cases asthma)**	**n cohort**		**OR (95% CI)**
age 0-2 years	age 3-5 years	2792 (299)	4	a	1.05 (0.88 to 1.25)
age 0-2 years	age 6-8 years	1965 (223)	3	b	0.92 (0.75 to 1.13)
age 3-5 years	age 6-8 years	25463 (2585)	16	c	1.02 (0.99 to 1.05)
age 6-8 years	age 9-14 years	65888 (3741)	7	d	1.00 (0.98 to 1.03)
age 9-14 years	age 15-18 years	6934 (828)	5	e	1.02 (0.92 to 1.13)
Sedentary behaviour in hours/day					
age 0-2 years	age 3-5 years	3440 (325)	5	f	1.30 (0.99 to 1.71)
age 0-2 years	age 6-8 years	2354 (268)	4	g	1.08 (0.83 to 1.42)
age 3-5 years	age 6-8 years	25116 (2554)	15	h	1.05 (1.01 to 1.09)
age 6-8 years	age 9-14 years	66965 (3825)	8	i	1.03 (0.99 to 1.07)
age 9-14 years	age 15-18 years	9311 (1078)	6	j	1.01 (0.97 to 1.05)

Generalized logistic mixed models on physical activity in hours/day and sedentary in hours/day and subsequent current asthma for each age group. Current asthma is defined as physician diagnosed asthma, ISAAC based current asthma definition or MeDALL based current asthma definition.
OR Odds Ratio; 95% CI 95% confidence interval
Univariable analyses.

Included cohorts:
a: EDEN, KOALA, LRC, STEPS Study
b: KOALA, LRC, STEPS Study
c: ABCD, ABIS, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, LRC, LucKi, STEPS Study, SWS, WHISTLER
d: DNBC, Gen R, GINIplus, INMA Menorca, KOALA, LISA, LRC
e: BAMSE, GINIplus, INMA Menorca, LISA, LRC
f: EDEN, HUMIS, KOALA, LRC, STEPS Study
g: HUMIS, KOALA, LRC, STEPS Study
h: ABCD, ABIS, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, LRC, LucKi, STEPS Study, SWS
i: CHOP, DNBC, Gen R, GINIplus, INMA Menorca, KOALA, LISA, LRC
j: BAMSE, GINIplus, INMA Menorca, LISA, LRC, PIAMA

Table K. Longitudinal age-specific analyses on physical activity in tertiles and current asthma (multivariable)

Age at exposure	Age at outcome	Current asthma					
Physical activity in tertiles		**n (n cases asthma)**	**n cohort**		**Low tertile aOR (95% CI)**	**Mid tertile aOR (95% CI)**	**High tertile aOR (95% CI)**
age 0-2 years	age 3-5 years	2735 (295)	3	a	ref	1.05 (0.78 to 1.40)	1.17 (0.84 to 1.64)
age 0-2 years	age 6-8 years	42788 (4948)	3	b	ref	0.64 (0.54 to 0.77)	0.75 (0.62 to 0.91)
age 3-5 years	age 6-8 years	24061 (2212)	16	c	ref	1.01 (0.90 to 1.13)	1.07 (0.95 to 1.20)
age 6-8 years	age 9-14 years	61102 (3057)	8	d	ref	0.93 (0.86 to 1.02)	1.03 (0.94 to 1.13)
age 9-14 years	age 15-18 years	4929 (406)	4	e	ref	0.87 (0.69 to 1.11)	0.83 (0.64 to 1.09)
Sedentary behaviour in tertiles							
age 0-2 years	age 3-5 years	3287 (316)	4	f	ref	1.18 (0.91 to 1.53)	1.42 (0.98 to 2.06)
age 0-2 years	age 6-8 years	2269 (263)	3	g	ref	1.00 (0.76 to 1.32)	1.09 (0.71 to 1.67)
age 3-5 years	age 6-8 years	21675 (2121)	14	h	ref	0.91 (0.82 to 1.02)	0.97 (0.86 to 1.10)
age 6-8 years	age 9-14 years	61667 (3112)	8	i	ref	0.98 (0.90 to 1.08)	1.06 (0.97 to 1.16)
age 9-14 years	age 15-18 years	5482 (436)	4	j	ref	0.94 (0.74 to 1.20)	0.97 (0.76 to 1.24)

Generalized logistic mixed models on physical activity in tertiles and sedentary in tertiles and subsequent current asthma for each age group. Current asthma is defined as physician diagnosed asthma, ISAAC based current asthma definition or MeDALL based current asthma definition.
aOR adjusted Odds Ratio; 95% CI 95% confidence interval.
Multivariable analyses adjusted for sex, maternal education level, maternal BMI.

Included cohorts:
a: EDEN, KOALA, STEPS Study
b: DNBC, KOALA, STEPS Study
c: ABCD, ABIS, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, LucKi, PIAMA, STEPS Study, SWS, WHISTLER
d: CHOP, DNBC, Gen R, GINIplus, INMA Menorca, KOALA, LISA, PIAMA
e: GINIplus, INMA Menorca, LISA, PIAMA
f: EDEN, HUMIS, KOALA, STEPS Study
g: HUMIS, KOALA, STEPS Study
h: ABCD, ABIS, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LucKi, PIAMA, STEPS Study, SWS
i: CHOP, DNBC, Gen R, GINIplus, INMA Menorca, KOALA, LISA, PIAMA
j: GINIplus, INMA Menorca, LISA, PIAMA

Table L Longitudinal age-specific analyses on physical activity in tertiles and current asthma (univariable)

Age at exposure	Age at outcome		Current asthma				
Physical activity in tertiles		**n (n cases asthma)**	**n cohort**		**Low tertile OR (95% CI)**	**Mid tertile OR (95% CI)**	**High tertile OR (95% CI)**
age 0-2 years	age 3-5 years	2792 (299)	4	a	ref	1.05 (0.81 to 1.37)	1.20 (0.97 to 1.76)
age 0-2 years	age 6-8 years	45159 (5254)	4	b	ref	0.65 (0.51 to 0.82)	0.76 (0.60 to 0.97)
age 3-5 years	age 6-8 years	28630 (2958)	17	c	ref	1.01 (0.91 to 1.12)	1.13 (1.02 to 1.25)
age 6-8 years	age 9-14 years	68858 (4093)	9	d	ref	0.94 (0.87 to 1.02)	1.05 (0.97 to 1.14)
age 9-14 years	age 15-18 years	8818 (1078)	7	e	ref	1.00 (0.85 to 1.17)	1.09 (0.93 to 1.28)
Sedentary behaviour in tertiles							
age 0-2 years	age 3-5 years	3440 (325)	5	f	ref	1.25 (0.98 to 1.61)	1.62 (1.13 to 2.31)
age 0-2 years	age 6-8 years	2354 (268)	4	g	ref	1.07 (0.80 to 1.43)	1.26 (0.81 to 1.97)
age 3-5 years	age 6-8 years	26276 (2862)	16	h	ref	1.00 (0.91 to 1.09)	1.10 (0.99 to 1.22)
age 6-8 years	age 9-14 years	69504 (4138)	10	i	ref	0.97 (0.89 to 1.06)	1.10 (1.01 to 1.20)
age 9-14 years	age 15-18 years	9311 (1078)	6	j	ref	1.12 (0.96 to 1.32)	1.00 (0.86 to 1.18)

Generalized logistic mixed models on physical activity in tertiles and sedentary in tertiles and subsequent current asthma for each age group. Current asthma is defined as physician diagnosed asthma, ISAAC based current asthma definition or MeDALL based current asthma definition.
OR Odds Ratio; 95% CI 95% confidence interval.
Univariable analyses.

Included cohorts:
a: EDEN, KOALA, LRC, STEPS Study
b: DNBC, KOALA, LRC, STEPS Study
c: ABCD, ABIS, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, LRC, LucKi, PIAMA, STEPS Study, SWS, WHISTLER
d: CHOP, DNBC, Gen R, GINIplus, INMA Menorca, KOALA, LISA, LRC, PIAMA
e: BAMSE, GINIplus, INMA Menorca, LISA, LRC, PIAMA, SEATON
f: EDEN, HUMIS, KOALA, LRC, STEPS Study
g: HUMIS, KOALA, LRC, STEPS Study
h: ABCD, ABIS, $COPSAC_{2000}$, G21, Gen R, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LRC, LucKi, PIAMA, STEPS Study, SWS
i: CHOP, $COPSAC_{2000}$, DNBC, Gen R, GINIplus, INMA Menorca, KOALA, LISA, LRC, PIAMA
j: BAMSE, GINIplus, INMA Menorca, LISA, LRC, PIAMA

Table M. Longitudinal analyses on physical activity in hours/day and sedentary behaviour in hours/day and current asthma between age 6 and 18 years – interaction with BMI at baseline and physical activity and sedentary behaviour (multivariable)

	n (n asthma cases)	n cohorts		aOR (95% CI) #
Age 0-2 years				
Physical activity (hours/day)	1852 (257)	2	a	0.89 (0.76 to 1.05)
BMI at baseline				1.14 (0.91 to 1.43)
BMI*PA				1.01 (0.87 to 1.19)
Sedentary behaviour (hours/day	2185 (301)	3	b	1.05 (0.79 to 1.38)
BMI at baseline				1.06 (0.89 to 1.27)
BMI*Sed				1.21 (0.94 to 1.54)
Age 3-5 years				
Physical activity (hours/day)	14715 (1468)	14	c	1.03 (0.99 to 1.09)
BMI at baseline				1.10 (0.99 to 1.22)
BMI*PA				1.01 (0.97 to 1.05)
Sedentary behaviour (hours/day	14755 (1474)	13	d	1.05 (1.00 to 1.10)
BMI at baseline				1.16 (1.07 to 1.27)
BMI*Sed				0.99 (0.96 to 1.02)

Generalized logistic mixed models on questionnaire based physical activity (PA) in hours per day and sedentary behaviour in hours per day at ages 0-2 years and 3-5 years; and current asthma at age 6-18 years.
Adjusted odds ratios (aOR) indicate the increase in odds of current asthma between age 6 and 18 years for physical activity and sedentary behaviour, but also for BMI at baseline, and the interaction terms BMI*PA and BMI*Sed, which reflect the interaction of BMI at baseline (i.e. at age 0-2 years or 3-5 years) and physical activity (PA) or sedentary behaviour (Sed).
Current asthma is defined as physician diagnosed asthma, ISAAC based current asthma definition or MeDALL based current asthma definition.
95% CI: 95% confidence intervals
Multivariable analyses adjusted for sex, maternal education level, maternal BMI.

Included cohorts:
a: KOALA, STEPS Study
b: HUMIS, KOALA, STEPS Study
c: ABCD, G21, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, Lifeways, LISA, LucKi, STEPS Study, SWS, Whistler
d: ABCD, G21, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, Lifeways, LISA, LucKi, STEPS Study, SWS

Table N. Longitudinal analyses on physical activity in hours/day and sedentary behaviour in hours/day and current asthma between age 6 and 18 years – interaction with BMI at baseline and physical activity and sedentary behaviour (univariable)

Age at exposure	n (n asthma cases)	n cohorts		OR (95% CI) #
Age 0-2 years				
Physical activity (hours/day)	1882 (261)	2	a	0.89 (0.76 to 1.05)
BMI at baseline				1.14 (0.91 to 1.43)
BMI*PA				1.01 (0.87 to 1.19)
Sedentary behaviour (hours/day)	2216 (305)	3	b	1.05 (0.79 to 1.38)
BMI at baseline				1.06 (0.89 to 1.27)
BMI*Sed				1.21 (0.94 to 1.54)
Age 3-5 years				
Physical activity (hours/day)	15566 (1546)	14	c	1.03 (0.99 to 1.09)
BMI at baseline				1.10 (0.99 to 1.22)
BMI*PA				1.01 (0.97 to 1.05)
Sedentary behaviour (hours/day)	15621 (1553)	13	d	1.05 (1.00 to 1.10)
BMI at baseline				1.16 (1.07 to 1.27)
BMI*Sed				0.99 (0.96 to 1.02)

Generalized logistic mixed models on questionnaire based physical activity (PA) in hours per day and sedentary behaviour in hours per day at ages 0-2 years and 3-5 years; and current asthma at age 6-18 years.
Odds ratios (OR) indicate the increase in odds of current asthma between age 6 and 18 years for physical activity and sedentary behaviour, but also for BMI at baseline, and the interaction terms BMI*PA and BMI*Sed, which reflect the interaction of BMI at baseline (i.e. at age 0-2 years or 3-5 years) and physical activity (PA) or sedentary behaviour (Sed). Current asthma is defined as physician diagnosed asthma, ISAAC based current asthma definition or MeDALL based current asthma definition.
95% CI: 95% confidence intervals
Univariable analyses.

Included cohorts:
a: KOALA, STEPS Study
b: HUMIS, KOALA, STEPS Study
c: ABCD, G21, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, Lifeways, LISA, LucKi, STEPS Study, SWS, Whistler
d: ABCD, G21, HUMIS, INMA Asturias, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, Lifeways, LISA, LucKi, STEPS Study, SWS

Table O. Longitudinal age-specific analyses on physical activity in hours/day and sedentary behaviour in hours/day and lung function

Age at exposure	Age at outcome	FEV$_1$				FEV$_1$/FVC			
Physical activity in hours/day		**n**	**n cohort**		**B (95% CI) #**	**n**	**n cohort**		**B (95% CI) #**
age 0-2 years	age 3-5 years	733	1	a	0.19 (-0.40 to 0.78)	738	1	a	-0.38 (-0.82 to 0.08)
age 0-2 years	age 6-8 years	487	1	b	0.09 (-0.02 to 0.20)	488	1	b	-0.01 (-0.12 to 0.09)
age 3-5 years	age 6-8 years	4008	8	c	-0.01 (-0.03 to 0.02)	3967	7	h	-0.01 (-0.04 to 0.01)
age 6-8 years	age 9-14 years	3716	4	d	-0.02 (-0.05 to 0.01)	3672	4	d	-0.03 (-0.06 to 0.00)
age 9-14 years	age 15-18 years	2052	3	e	-0.02 (-0.06 to 0.02)	2052	3	e	-0.03 (-0.07 to 0.01)
Sedentary behaviour in hours/day									
age 0-2 years	age 3-5 years	715	1	b	-0.20 (-1.16 to 0.76)	720	1	b	-0.03 (-0.76 to 0.69)
age 0-2 years	age 6-8 years	507	1	b	0.04 (-0.16 to 0.23)	508	1	b	-0.06 (-0.24 to 0.12)
age 3-5 years	age 6-8 years	3959	7	f	-0.02 (-0.04 to 0.01)	3919	6	i	-0.02 (-0.04 to 0.01)
age 6-8 years	age 9-14 years	4156	4	d	0.03 (0.00 to 0.06)	4113	4	d	0.01 (-0.02 to 0.04)
age 9-14 years	age 15-18 years	3013	4	g	0.01 (-0.03 to 0.05)	3014	4	g	0.04 (0.00 to 0.07)

Generalized linear mixed models on physical activity in hours/day, sedentary behaviour in hours/day, and lung function.
FEV$_1$ forced expiratory volume in 1 second (in z-score); FVC: forced vital capacity; B Beta; 95% CI 95% confidence interval.
Beta (B) indicates the increase of FEV$_1$ z-score in SDS at age at outcome for each hour per day of parent reported physical activity or sedentary behaviour at age at exposure.
95% CI: 95% confidence intervals.
Multivariable analyses adjusted for sex, maternal education level, maternal BMI

Included cohorts:
a: EDEN
b: KOALA
c: G21, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, SWS, WHISTLER
d: Gen R, GINIplus, INMA Menorca, LISA
e: GINIplus, INMA Menorca, LISA
f: G21, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, SWS
g: GINIplus, INMA Menorca, LISA, PIAMA
h: G21, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, SWS, WHISTLER
i: G21, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, SWS

Table P. Longitudinal age-specific analyses on physical activity in hours/day and sedentary behaviour in hours/day and lung function – exclusion of wheeze and asthma at baseline

Age at exposure	Age at outcome	FEV_1				FEV_1/FVC			
Physical activity in hours/day		**n**	**n cohort**		**B (95% CI) #**	**n**	**n cohort**		**B (95% CI) #**
age 0-2 years	age 3-5 years	618	1	a	0.07 (-0.57 to 0.71)	623	1	a	-0.43 (-0.93 to 0.07)
age 0-2 years	age 6-8 years	412	1	b	0.09 (-0.03 to 0.21)	413	1	b	-0.05 (-0.15 to 0.06)
age 3-5 years	age 6-8 years	3177	8	c	0.00 (-0.02 to 0.03)	3144	7	h	-0.01 (-0.04 to 0.01)
age 6-8 years	age 9-14 years	3014	4	d	-0.02 (-0.04 to 0.01)	2971	4	d	-0.01 (-0.04 to 0.02)
age 9-14 years	age 15-18 years	1809	3	e	-0.03 (-0.07 to 0.01)	1809	3	e	-0.03 (-0.07 to 0.01)
Sedentary behaviour in hours/day									
age 0-2 years	age 3-5 years	602	1	b	-0.10 (-1.12 to 0.93)	607	1	b	0.02 (-0.78 to 0.83)
age 0-2 years	age 6-8 years	426	1	b	0.07 (-0.13 to 0.27)	427	1	b	-0.07 (-0.25 to 0.12)
age 3-5 years	age 6-8 years	3127	7	f	-0.02 (-0.05 to 0.01)	3095	6	i	-0.02 (-0.05 to 0.01)
age 6-8 years	age 9-14 years	3373	4	d	0.03 (0.00 to 0.06)	3331	4	d	0.01 (-0.02 to 0.04)
age 9-14 years	age 15-18 years	2626	4	g	0.01 (-0.03 to 0.04)	2627	4	g	0.03 (-0.00 to 0.07)

Generalized linear mixed models on physical activity in hours/day, sedentary behaviour in hours/day, and lung function.
Subgroup analysis with exclusion of partcipants with wheeze or asthma at baseline.
FEV_1 forced expiratory volume in 1 second (in z-score); FVC: forced vital capacity; B Beta; 95% CI 95% confidence interval.
Beta (B) indicates the increase of FEV_1 z-score in SDS at age at outcome for each hour per day of parent reported physical activity or sedentary behaviour at age at exposure.
95% CI: 95% confidence intervals.
Multivariable analyses adjusted for sex, maternal education level, maternal BMI

Included cohorts:
a: EDEN
b: KOALA
c: G21, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, SWS, WHISTLER
d: Gen R, GINIplus, INMA Menorca, LISA
e: GINIplus, INMA Menorca, LISA
f: G21, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, LISA, SWS
g: GINIplus, INMA Menorca, LISA, PIAMA
h: G21, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, SWS, WHISTLER
i: G21, INMA Gipuzkoa, INMA Sabadell, INMA Valencia, KOALA, SWS

Table Q. Longitudinal age-specific analyses on physical activity measured with accelerometry and lung function

Age at exposure	Age at outcome	FEV$_1$				FEV$_1$/FVC			
Accelerometry in counts/min		**n**	**n cohort**		**B (95% CI) #**	**n**	**n cohort**		**B (95% CI) #**
age 3-5 years	age 6-8 years	361	2	a	0.00 (-0.00 to 0.00)	359	2	a	0.00 (-0.00 to 0.00)
Sedentary level (hours/day)									
age 3-5 years	age 6-8 years	361	2	a	-0.13 (-0.20 to -0.06)	359	2	a	0.01 (-0.05 to 0.08)
MVPA (hours/day)									
age 3-5 years	age 6-8 years	361	2	a	0.27 (0.07 to 0.46)	359	2	a	-0.06 (-0.25 to 0.14)

Generalized linear mixed models on accelerometry data in counts per minute (counts/min), time in ssedentary activity or moderate to vigorous physical activity (MVPA) recorded by accelerometry between age 3-5 years, and lung function. Age specific analyses: no data available at other age groups (0-2, 6-8, 9-14, 15-18 years).
FEV$_1$ forced expiratory volume in 1 second (in z-score); FVC: forced vital capacity; B Beta; 95% CI 95% confidence interval.
Beta (B) indicates the increase of FEV$_1$ z-score in SDS at age at outcome for each hour per day of measured time in sedentary activity or moderate to vigorous physical activity (MVPA) recorded by accelerometry at age at exposure.
Multivariable analyses adjusted for sex, maternal education level, maternal BMI.

Included cohorts:
a: KOALA, SWS

Table R. Longitudinal age-specific analyses on physical activity measured with accelerometry and lung function – exclusion of wheeze and asthma at baseline

Age at exposure	Age at outcome	FEV$_1$				FEV$_1$/FVC			
Accelerometry in counts/min		**n**	**n cohort**		**B (95% CI) #**	**n**	**n cohort**		**B (95% CI) #**
age 3-5 years	age 6-8 years	296	2	a	0.00 (-0.00 to 0.00)	259	2	a	-0.00 (-0.00 to 0.00)
Sedentary level (hours/day)									
age 3-5 years	age 6-8 years	296	2	a	-0.09 (-0.17 to -0.02)	295	2	a	0.04 (-0.03 to 0.11)
MVPA (hours/day)									
age 3-5 years	age 6-8 years	296	2	a	0.18 (-0.02 to 0.39)	295	2	a	-0.09 (-0.30 to 0.11)

Generalized linear mixed models on accelerometry data in counts per minute (counts/min), time in ssedentary activity or moderate to vigorous physical activity (MVPA) recorded by accelerometry between age 3-5 years, and lung function. Age specific analyses: no data available at other age groups (0-2, 6-8, 9-14, 15-18 years). Subgroup analysis with exclusion of partcipants with wheeze or asthma at baseline.
FEV$_1$ forced expiratory volume in 1 second (in z-score); FVC: forced vital capacity; B Beta; 95% CI 95% confidence interval.
Beta (B) indicates the increase of FEV$_1$ z-score in SDS at age at outcome for each hour per day of measured time in sedentary activity or moderate to vigorous physical activity (MVPA) recorded by accelerometry at age at exposure.
Multivariable analyses adjusted for sex, maternal education level, maternal BMI.

Included cohorts:
a: KOALA, SWS

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	4
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	6
Objectives	3	State specific objectives, including any prespecified hypotheses	7
Methods			
Study design	4	Present key elements of study design early in the paper	7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-9
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
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	8, appendix A
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	8, table 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	10
		(*b*) Describe any methods used to examine subgroups and interactions	10
		(*c*) Explain how missing data were addressed	n/a
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a
		(*e*) Describe any sensitivity analyses	10
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	Table 1
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Appendix C
		(b) Indicate number of participants with missing data for each variable of interest	Table 1, Appendix C
		(c) Summarise follow-up time (eg, average and total amount)	n/a
Outcome data	15*	Report numbers of outcome events or summary measures over time	11

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	12-13, Table 2, Figure 2, Appendix D
		(*b*) Report category boundaries when continuous variables were categorized	n/a
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Appendix E-R
Discussion			
Key results	18	Summarise key results with reference to study objectives	13-14
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	15
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	15
Generalisability	21	Discuss the generalisability (external validity) of the study results	15
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	16-19

*Give information separately for exposed and unexposed groups.

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 http://www.strobe-statement.org.