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Early View

Original research article

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Maternal diet in pregnancy and child's respiratory outcomes: an individual participant data meta-analysis of 18,000 children

Sara M. Mensink-Bout, MD[1,2], Evelien R. van Meel, MD[1,2], Johan C. de Jongste, MD PhD[2], Isabella Annesi-Maesano, MD PhD[3], Adrien M. Aubert, MSc[4], Jonathan Y. Bernard, PhD[4,5], Ling-Wei Chen, PhD[6], Cyrus Cooper, FMedSci[7,8], Sarah R Crozier, PhD[7], Wojciech Hanke, PhD[9], Nicholas C. Harvey, PhD[7,8], James R Hébert, MSPH, ScD[10,11], Barbara Heude, PhD[4], Joanna Jerzynska, PhD[12], Cecily C. Kelleher, MD[6], John Mehegan, PhD[6], Fionnuala M. McAuliffe, MD[13], Catherine M. Phillips, PhD[6], Kinga Polanska, PhD[9], Caroline L. Relton, BSc, PGCE, PhD[14], Nitin Shivappa, MBBS, MPH, PhD[10,11], Matthew Suderman, PhD[14], Vincent W.V. Jaddoe, MD PhD[1,15], Liesbeth Duijts, MD PhD[1,2,16]

[1]The Generation R Study Group, Erasmus MC, University Medical Center, Rotterdam, the Netherlands; [2]Department of Pediatrics, Division of Respiratory Medicine and Allergology, Erasmus MC, University Medical Center, Rotterdam, the Netherlands; [3]Institute of Epidemiology and Public Health, EPAR, Sorbonne Université, Inserm, Paris, France; [4]Centre for Research in Epidemiology and StatisticS (CRESS), Université de Paris, Inserm, INRAE, Paris, France; [5]Singapore Institute for Clinical Sciences (SICS), Agency for Science, Technology and Research (A*STAR), Singapore, Singapore [6]HRB Centre for Health and Diet Research, School of Public Health, Physiotherapy, and Sports Science, University College Dublin, Dublin, Republic of Ireland; [7]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton General Hospital, Southampton, United Kingdom; [8]NIHR Southampton Nutrition Biomedical Research Centre, University of Southampton and University Hospital Southampton NHS Foundation Trust, Southampton, United Kingdom [9]Department of Environmental Epidemiology, Nofer Institute of Occupational Medicine, Lodz, Poland; [10]Cancer Prevention and Control Program and Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC, USA; [11] Department of Nutrition Connecting Health Innovations LLC, Columbia, SC USA; [12]Department of Pediatrics and Allergy, Medical University of Lodz, Copernicus Memorial Hospital in Lodz, Poland; [13]UCD Perinatal Research Centre, School of Medicine, University College Dublin, National Maternity Hospital, Dublin, Ireland; [14]MRC Integrative Epidemiology Unit, Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, United Kingdom; [15]Department of Pediatrics, Erasmus MC, University Medical Center, Rotterdam, The Netherlands; [16]Department of Pediatrics, Division of Neonatology, Erasmus MC, University Medical Center, Rotterdam, The Netherlands;

Corresponding author Dr. Liesbeth Duijts, MD, PhD, Erasmus MC - Sophia, University Medical Center Rotterdam, Sp-3435; PO Box 2060, 3000 CB Rotterdam, The Netherlands. Tel: *31 10 7036263, Fax: *31 10 7036811, E-mail: l.duijts@erasmusmc.nl

Contribution of authors to the study

SMB, EM, VJ and LD contributed to the conception and design, acquisition of data, analyses and interpretation of the data, drafted the article, revised it critically for important intellectual content, and gave final approval of the version to be published. JJ, IAM, AA, JB, LWC, CC, SC, WH, NH, JH, BH, JJ, CK, JM, FM, CP, KP, CR, NS and MS contributed to the conception and design, acquisition of local data, revised the drafted manuscript critically for important intellectual content, and gave final approval of the version to be published.

Ethical approvals

Specific cohort approvals are for ALSPAC by the ALSPAC Ethics and Law Committee (IRB00003312) and Local Research Ethics Committees, informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time; for EDEN by the Ethics Committee (CCPPRB) and CNIL (Commission Nationale Informatique et Liberté), the French data privacy institution; for Generation R by the Medical Ethical Committee of the Erasmus Medical Center, Rotterdam; for Lifeways by the University College Dublin Research Ethics Committee and St. Vincent's University Hospital Research Ethics Committee; for REPRO_PL by the Ethical Committee of the Nofer Institute of Occupational Medicine, Łódź, Poland

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Conflict of interest

The study sponsors had no role in the study design, data analysis, interpretation of data, or writing of this report.

Disclosure

Dr. James R. Hébert owns controlling interest in Connecting Health Innovations LLC (CHI), a company that has licensed the right to his invention of the dietary inflammatory index (DII®) from the University of South Carolina in order to develop computer and smart phone applications for patient counselling and dietary intervention in clinical settings. Dr. Nitin Shivappa is an employee of CHI. The subject matter of this paper will not have any direct bearing on that work, nor has that activity exerted any influence on this project.

Take home message

A suboptimal maternal diet in pregnancy, as defined by a higher inflammatory potential or low quality of the diet, does not play an important role in the development of respiratory diseases in childhood.

ABSTRACT

Rationale Severe fetal malnutrition has been related to an increased risk of respiratory diseases later in life, but evidence for the association of a suboptimal diet during pregnancy with respiratory outcomes in childhood is conflicting. We aimed to examine whether a pro-inflammatory or low-quality maternal diet during pregnancy was associated with child's respiratory health.

Methods We performed an individual participant meta-analysis among 18,326 mother-child pairs from seven European birth cohorts. Maternal pro-inflammatory and low-quality diet were estimated by energy-adjusted Dietary Inflammatory Index (E-DII^{TM}) and Dietary Approaches to Stop Hypertension (DASH) scores. Preschool wheezing and school-age asthma were measured by questionnaires and lung function by spirometry.

Results After adjustment for lifestyle and sociodemographic factors, we observed that a higher maternal E-DII score (a more pro-inflammatory diet) during pregnancy was associated only with a lower FVC in children (Z-score difference (95% confidence interval (CI)): -0.05 (-0.08, -0.02), per IQR increase). No linear associations of the maternal E-DII or DASH score with child's wheezing or asthma were observed. When exploratively examining the extremes, a very low DASH score (<10th percentile) (a very low dietary quality) was associated with an increased risk of preschool wheezing and a low FEV_1/FVC (z-score <-1.64) (OR (95% CI) 1.20 (1.06,

1.36), 1.40 (1.06, 1.85), compared to ≥10th percentile), with corresponding population attributable risk fractions of 1.7% and 3.3%.

Conclusion Main results from this individual participant data meta-analysis do not support the hypothesis that maternal pro-inflammatory or low-quality diet in pregnancy are related to respiratory diseases in childhood.

Key words diet; pregnancy; asthma; pulmonary function test; meta-analysis

INTRODUCTION

Asthma is a common disorder in childhood, and associated with respiratory health problems in adulthood [1, 2]. It is therefore important to identify early-life modifiable risk factors. Fetal exposure to a suboptimal diet during pregnancy might affect the maturation of the lungs and immune system, leading to a lower lung function and a higher risk of wheezing and asthma in childhood [3]. Severe malnutrition in pregnancy has previously been associated with an increased risk of respiratory diseases later in life [4]. Studies examining maternal diet during pregnancy and childhood respiratory health mainly focused on the intake of specific nutrients or food groups [5]. However, examining the overall diet might take the interactions within the diet into account and be better translatable to dietary guidelines [6]. The E-DII™ (energy-adjusted Dietary Inflammatory Index) [7] and DASH (Dietary Approaches to Stop Hypertension) [8] provide dietary scores for the inflammatory potential and overall quality of the diet, respectively. Cohort studies showed that a higher maternal E-DII score in pregnancy was associated with a higher risk of an early wheeze trajectory and a lower mid-expiratory flow or a higher risk of asthma in childhood [9, 10]. The relation of the DASH score with respiratory outcomes has been studied only in adults, where a DASH-promoting behavioural intervention seemed to improve asthma control [11]. To date, a pooled analysis across cohorts which examines the relation of the inflammatory potential and overall quality of maternal diet during pregnancy with child's respiratory health is lacking.

We performed an individual participant data meta-analysis among 18,326 children, participating in seven European birth cohort studies. We assessed the associations of maternal diet during pregnancy, as summarized by the E-DII and DASH score, with preschool wheezing, school-age asthma and lung function, and

estimated the impact of these associations on the general population by calculating the population attributable fraction (PAF).

METHODS

This meta-analysis was performed among seven European prospective birth cohorts participating in the ALPHABET consortium, which aims to examine the early-life nutritional programming of non-communicable diseases (supplemental methods) [12, 13]. We included 18,326 mother-child pairs for the current analyses (supplemental methods).

Maternal diet Information obtained from food frequency questionnaires (FFQs) before or during pregnancy was used to generate the maternal E-DII and DASH scores (Table E1, Table E2), as previously described (supplemental methods) [7, 13]. To control for the effect of the total energy intake the E-DII, calculated per 1,000 kilocalories (kcal) of food consumed, was used. The E-DII in ALPHABET was generated from 20-28 dietary parameters, out of 44 possible parameters. A higher E-DII score characterizes a more pro-inflammatory diet [7]. For the seven cohorts in the ALPHABET project, a DASH score was generated. This score was composed of eight food components, based mainly on the Fung method with a scoring system based on quintile rankings in each cohort [8, 13]. A lower DASH score characterizes a lower dietary quality. For the main analyses, we used data collected at one time-point, preferably in early-pregnancy (first or second trimester) (Generation R, Lifeways, REPRO_PL, ROLO, SWS) since this period is of specific importance for lung disease development later in life [14], or, if not available, in late-pregnancy (third trimester) (ALSPAC, EDEN).

Respiratory health Data on preschool wheezing and school-age asthma was mainly obtained from questions adapted from the International Study on Asthma and Allergy in Childhood questionnaire [15]. We defined preschool wheezing as ‘‘ever reported wheezing during the first 4 years of life’’ and school-age asthma as ‘‘asthma diagnosis reported between 5 and 10 years’’ [16]. Cohort-specific information is shown in supplemental methods and Table E1. All cohorts obtained lung function measures by spirometry according to the ATS/ERS guidelines [17]. Lung function measures included forced expiratory volume in 1 second (FEV_1), forced vital capacity (FVC), FEV_1/FVC and forced expiratory flow at 25–75% of FVC ($FEF_{25–75}$), and were converted into sex-, age-, height-, and ethnicity adjusted Z-scores based on the Global Lung Initiative reference values [18].

Covariates Information on lifestyle and sociodemographic related confounders, intermediates and effect modifiers was mainly obtained by questionnaires or clinical examinations at the research center (supplemental methods, Table E1).

Statistical analyses Dietary scores were analysed as continuous variables to study the linear associations, and additionally as dichotomous variables to explore the effect of the extremes. We first conducted one-stage meta-analyses by using multilevel linear regression models or multilevel logistic regression models to study the associations of the maternal E-DII and DASH scores with child’s respiratory outcomes. In these models, individual participant data from all cohorts were combined and modeled simultaneously, taking into account clustering of participants within cohorts [19]. We included a random intercept at cohort level, which allows intercepts to vary across cohorts. More information on the used models is provided in

the supplemental methods. As explorative analyses to examine the effect of an extreme adverse diet in pregnancy, we additionally studied the dichotomous relationships and examined the associations of a very high E-DII score (>90th percentile) or low DASH score (<10th percentile) with wheezing and asthma, and with lung function below the lower limit of normal (LLN) (<5th percentile, equals z-score of -1.64). The highest and lowest 10th percentile cut off for the dietary scores is a common epidemiological approach, in the absence of clinical cut-offs. If consistent associations were observed, we subsequently calculated the population attributable risk fraction (PAF) based on the adjusted odds ratio (OR) and the prevalence of a high E-DII or low DASH score, which indicates the proportion of wheezing, asthma or lung function measures below the LLN attributable to a high E-DII or low DASH score [20]. We considered the linear confounder models as the main models and applied several additional analyses to these models as described in the supplemental methods.

P-values are two-tailed, statistical significance was defined at p-values <0.05. We did not adjust for multiple testing since respiratory outcomes are strongly interrelated [21]. Statistical analyses were performed using SPSS version 24.0 (IBM Corp., Armonk, NY, USA) and RevMan version 5.3 (Nordic Cochrane Centre, Copenhagen, Denmark) and R version 3.6.1 (‘mediation’ package).

RESULTS

Subject characteristics Table 1 shows the main characteristics, maternal dietary scores and child's respiratory outcomes of the cohorts, and Table E3 and Table E4 the corresponding information on maternal and child related baseline characteristics. The median age of the included children at lung function measurement was 8.6 years (95% range 5.4-10.2). Of all participants, 51.9 % (n=8,018) had preschool wheezing and 15.6% (n=2,193) had school-age asthma. The correlation between the E-DII and DASH score was moderate (range Pearson r -0.49 to -0.60, $p<0.001$).

Maternal E-DII and DASH score and child's respiratory outcomes Table 2 shows that after adjustment for confounders, only an association of a higher maternal E-DII score during pregnancy with a lower FVC in the children was observed (Z-score difference (95% CI): -0.05 (-0.08, -0.02)). A lower DASH score was not associated with preschool wheezing, school-age asthma, or lung function measures. We observed no consistent associations for both the maternal E-DII and DASH score with FEF_{25-75} (results not shown).

When exploratively examining the extremes, we observed after adjustment for confounders no associations of a very high maternal E-DII score (>90th percentile) with child's respiratory outcomes compared to a normal maternal E-DII score (≤90th percentile) (Figure 1). A very low DASH score (<10th percentile) was associated with a higher risk of preschool wheezing and an FEV_1/FVC below the LLN, and borderline associated with a higher risk of asthma (OR (95% CI) 1.20 (1.06, 1.36), 1.40 (1.06, 1.85), 1.17 (1.00, 1.39), respectively, as compared to a DASH score ≥10th percentile)). The estimated proportions of wheezing, a FEV_1/FVC below the LLN and asthma attributable to a low DASH score were 1.7%, 3.3% and 1.4%, respectively.

Additional analyses Additional adjustment for early growth factors, lower respiratory tract infections, child's BMI, or child's E-DII score did not materially change the effects (results not shown). Further mediation analyses showed that early growth factors and child's E-DII score only explained 6.2% (95% CI: 2.3, 21.0) and 17.8% (2.6, 48.0) of the association of the E-DII score with FVC. We observed a consistent interaction between the maternal DASH score and child's sex (range p-values interaction terms <0.001 – 0.549), but not between maternal dietary scores and child's atopic predisposition. After stratification by sex, no consistent differences between boys and girls in the association of the maternal E-DII or DASH score with child's respiratory outcomes were observed (Table E5). The two-stage random effect meta-analyses indicated at most moderate heterogeneity (range I^2 0% - 52%) and similar effects as the one-stage meta-analyses (Figure E2, Figure E3). When we examined the dietary scores per time period of assessment in pregnancy, directions of the associations with respiratory outcomes were similar for all time periods (Table E6). Examining the associations of maternal dietary scores with lung function measures in age groups of children showed that among children ≥8 years, a higher maternal E-DII score was associated with a lower FEV_1 and FVC, and a lower maternal DASH score with a lower FEV_1 (Table E7). We repeated the main models restricted to complete cases, to mothers with a European birthplace/ethnic background, and excluding one cohort at a time, and mainly observed similar sizes and directions of the effect estimates (Table E7, Table E8a, Table E8b). Excluding only the intervention arm of the ROLO study did not materially change our results (results not shown).

DISCUSSION

In this individual-participant data meta-analysis among 18,326 children from seven European birth cohorts, we observed that only a more pro-inflammatory diet during pregnancy was associated with a lower FVC in childhood. When studying the extremes, a very low maternal dietary quality was associated with a higher risk of preschool wheezing and a FEV_1/FVC below the LLN in the children, and borderline higher risk of school-age asthma.

Comparison with previous studies To our best knowledge, our study is the first individual participant meta-analysis of prospective birth cohorts that examined the associations of the maternal E-DII score with child's respiratory outcomes. Previous studies showed that a higher E-DII score during pregnancy or in childhood was associated with a higher risk of early wheezing, wheezing trajectories, or asthma, and a lower FEF_{25-75}, but not with other lung function measures or in high risk children only [9, 10, 22]. Differences between results of these studies and our meta-analysis might be due to other definitions of respiratory outcomes. Asthma is difficult to diagnose in children younger than 5 years, and the wheezing pathogenesis including the role of specific viruses in the development of a lower lung function and asthma might differ between age periods [23, 24]. Therefore, we used both preschool wheezing and school-age asthma as outcomes. The association of the E-DII with a lower FVC did not attenuate after additional adjustment for lower respiratory tract infections. However, further studies on the effect of the maternal E-DII score on harmonized longitudinal asthma-symptom phenotypes in the children are needed.

Our study showed no linear associations of the maternal DASH score with child's respiratory outcomes, but a very-low-quality-diet, defined by a very-low DASH score capturing the intake of multiple food groups, was associated with a higher risk of wheezing and airway obstruction. A Mediterranean diet in pregnancy partly overlaps with the high DASH score diet (DASH diet) and has been associated with a lower risk of wheezing, whereas other dietary patterns, defined based on principal component analysis, were not associated with respiratory outcomes [25, 26]. The advantage of the DASH diet, as compared to these approaches, is that it might better reflect the dietary habits in a non-Mediterranean population and is easy to translate into public health guidelines [6].

Interpretation of the results The E-DII score takes many food parameters into account, of which main pro-inflammatory components are trans-fat, saturated fat and cholesterol, and main anti-inflammatory components are nutrients derived from fruits and vegetables and n-3 fatty acids [7]. Underlying mechanisms might be that a high-fat maternal diet leads to fetal lung inflammation and remodelling, which could make the lungs more susceptible to developing asthma later in childhood [27]. Obesity is another factor that is associated with inflammation [28], and this might be the reason why the associations with wheezing and asthma attenuated after adjustment for lifestyle factors including maternal BMI. Also, an indirect effect through early growth factors may play a role in the association of the maternal E-DII score with child's FVC as shown by the moderate percentage of change of the effect estimates [29]. However, the effect of the association of the maternal E-DII score with child's FVC was small and might therefore reflect a subclinical change or chance finding.

A DASH diet is mainly characterized by a high intake of fruits and vegetables which are rich in anti-oxidants, and a low intake of added sugars and sodium [13]. Antioxidants might make the lungs less vulnerable to oxidative stress, and thereby may reduce the risk of asthma and airway obstruction [30]. The DASH diet has also been shown to lower the blood pressure [31]. A higher blood pressure in pregnancy, which might reflect a poorer vascular health, has been associated with a higher risk of wheezing and asthma and a lower FEV_1/FVC in children [32, 33]. We only observed in our explorative analyses that a very low DASH score was associated with a higher risk of preschool wheezing, airway obstruction and borderline with asthma. However, we were not able to take the DASH score of child's current diet into consideration. Also, the effect of maternal diet on child's respiratory outcomes may differ between different periods of pregnancy. Since lung development already starts in the fourth week of pregnancy, adverse exposures in early pregnancy are considered to be specifically important for lung disease development later in life [14]. Further research is needed to understand the effect of maternal diet at different gestational ages during pregnancy and in different periods of early life after birth on lung development across the life course.

Although previous studies showed that high maternal intake of single nutrients including vitamin D and n-3 fatty acids may be beneficial for child's respiratory health [34, 35], we observed no consistent association of the maternal E-DII or DASH score with respiratory outcomes. This suggests that specific supplements may be of more importance than a balanced diet for asthma development.

The moderate correlation between the E-DII and DASH scores suggest that these scores partly represent different factors of the diet. The scores differ in concept as the E-DII is mainly nutrient based and focusses on the inflammatory effects of the

diet whereas the DASH defines the overall quality of the diet based on food components. Our hypothesis for the effect of maternal diet on child's respiratory outcomes was based on a population with an extreme adverse diet [4]. The distribution of maternal diet during pregnancy in Western countries might be within optimal ranges, and any potential adverse effect might lay in the extremes. Therefore, we studied the extremes by using a common epidemiological cut-off approach, the highest and lowest 10th percentiles, since clinical cut-offs are lacking. Categorization is prone to bias and our analyses are explorative and should be considered as hypothesis-generating. Results suggesting that the associations of an adverse diet with clinically relevant respiratory outcomes only exist in those exposed to an extreme adverse diet should therefore be carefully interpreted. In addition, if we assume that these relationships are causal, the average proportions of wheezing, asthma and an FEV_1/FVC below the LLN attributable to a low DASH are tenuous. Whether targeting maternal diet, in addition to other lifestyle and sociodemographic factors, improves child's respiratory outcomes, could be the subject for future intervention trials but in a population of mothers with an extreme adverse diet only.

Strengths and limitations A major strength of this meta-analysis is the use of individual participant data. This resulted in a large sample size and enabled us to harmonize the data, and to reduce the risk of publication bias. However, some limitations do apply. First, dietary scores as well as wheezing and asthma were defined based on questionnaires which could have led to reporting errors. FFQs may also not adequately assess the intake of specific nutrients, such as sodium, a component of the DASH score or the specific food parameters for the E-DII score. Also, missing data in the FFQs might have biased the estimation of the dietary

scores. Clearly, we cannot know the effect of foods eaten that are not on the FFQ. Nevertheless, most cohorts used validated questionnaires [13, 15]. Second, although the dietary scores were calculated in all cohorts according to the same methods, there were differences in the included food parameters, length and content of the FFQs, assessed time periods in pregnancy and assessment years. However, two-stage meta-analyses gave similar results and showed limited heterogeneity between the cohort estimates. Although none of the cohorts had information on all 44 possible parameters for the E-DII score, a previous validation study showed that an DII score based on 28 parameters had a good predictive ability, and an additional study showed that a score based on 17 parameters was related to inflammatory markers [36, 37]. Thus, our E-DII score gives a valid, if imprecise, estimation of the inflammatory potential of the diet. We were not able to take potential changes in a mothers diet due to seasonal variation or food aversions into consideration. Also, we did not have information for all cohorts on the exact gestational age at which diet was assessed. However, FFQs are considered an adequate method to measure the usual dietary intake over an extensive period of time, and dietary patterns are suggested not to change much during pregnancy [38, 39]. Thus, our dietary measurements across cohorts were appropriate and support our findings. Third, although the participating cohorts were carefully selected based on a priori power calculations, data availability, and spread throughout Europe, most participants come from two cohorts and have a European birthplace/ethnic background. Therefore, results may not be generalizable to mothers in other geographical regions. Fourth, we did not measure changes in the associations of maternal diet with child's respiratory outcomes over time. Fifth, to date, no validated method to calculate child's DASH score is available. Although results remained similar after adjustment for child's BMI,

potential mediating effect of child's DASH score cannot be fully ruled out. Last, we adjusted for major potential confounders but, as in all observational studies, residual confounding due to unmeasured or insufficiently harmonised factors, such as other socio-demographic factors, environmental pollution, the use of supplements or medication in pregnancy or the duration of breastfeeding, remains an issue. Future randomized controlled intervention trials might minimise the risk of confounding factors influencing the results, but should be carefully considered given the absence of a consistent association in our current study.

CONCLUSION

A more pro-inflammatory diet of mothers during pregnancy was only related to a lower FVC in childhood. Both the inflammatory potential and quality of the diet were not consistently related to wheezing or asthma in childhood. Main results from this individual participant data meta-analysis do not support the hypothesis that maternal pro-inflammatory or low-quality diet in pregnancy are related to respiratory diseases in childhood.

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Table 1. Characteristics of participating cohorts

	ALSPAC (United Kingdom)	**EDEN (France)**	**Generation R (The Netherlands)**	**Lifeways (Ireland)**	**REPRO_PL (Poland)**	**ROLO (Ireland)**	**SWS (United Kingdom)**
Total participants	10,130	843	4,263	224	523	301	2,042
Inclusion years	1990-1992	2003-2006	2002-2006	2001-2003	2007-2011	2007-2011	1998-2002
Pregnancy							
FFQ (GA in weeks)***	32	24-28 Birth	<24	12-16	20-24	≤28	PP 11 34
FFQ assessed period	LP	PP LP	EP	EP	EP	EP	PP EP LP
E-DII score*	0.51 (1.82)	0.76 (1.65)	-0.43 (1.10)	-0.12 (1.43)	-1.10 (1.54)	0.12 (1.74)	0.27 (1.49)
DASH score*	24.1 (4.0)	24.3 (4.1)	24.4 (4.4)	25.2 (4.5)	24.1 (4.4)	24.2 (4.1)	24.1 (4.3)
Preschool wheezing							
N	9,313	840	2,876	NA	370	NA	2,037
Age (years)***	0-3.5	0-4	1-4	NA	1,2	NA	0-3
Yes %, (N)	54.4 (5,070)	36.8 (309)	49.7 (1,429)	NA	18.4 (68)	NA	56.1 (1,142)
School-age asthma							
N	7,506	842	3,510	224	275	301	1,421

Age (years)***	8	5,8	9	9	7-8	5	5
Yes %, (N)	20.3 (1,525)	12.1 (102)	8.9 (312)	5.4 (12)	6.2 (17)	7.6 (23)	14.2 (202)
Lung function							
N	5,766	838	3,651	NA	264	NA	730
Age (years)**	8.6 (8.3 - 9.5)	5.6 (5.4 - 6.0)	9.8 (9.4 - 10.7)	NA	7.2 (7.0 - 8.8)	NA	6.5 (6.2 - 6.9)
FEV_1 (z-score)*	-0.03 (1.01)	-0.70 (1.45)	0.17 (0.98)	NA	-0.32 (1.74)	NA	0.09 (0.98)
FVC (z-score)*	-0.04 (1.02)	-1.00 (1.48)	0.21 (0.93)	NA	-0.44 (1.85)	NA	0.15 (1.06)
FEV_1/FVC (z-score)*	0.05 (1.07)	0.87 (1.06)	-0.11 (0.95)	NA	0.30 (1.25)	NA	-0.08 (1.06)
FEF_{25-75} (z-score)*	-0.15 (1.02)	-0.39 (1.09)	0.43 (1.08)	NA	-0.14 (1.01)	NA	-0.25 (0.92)

Values are valid percentages (absolute numbers), *means (SD), **medians (95% range), or ***time period of questionnaire assessment. Number of participants (N). Food frequency questionnaire (FFQ). Pre pregnancy (PP), early pregnancy (EP): first or second trimester, late pregnancy (LP): third trimester. Gestational age (GA). Forced Expiratory Flow in 1 second (FEV_1), Forced Vital Capacity (FVC). Not available (NA).

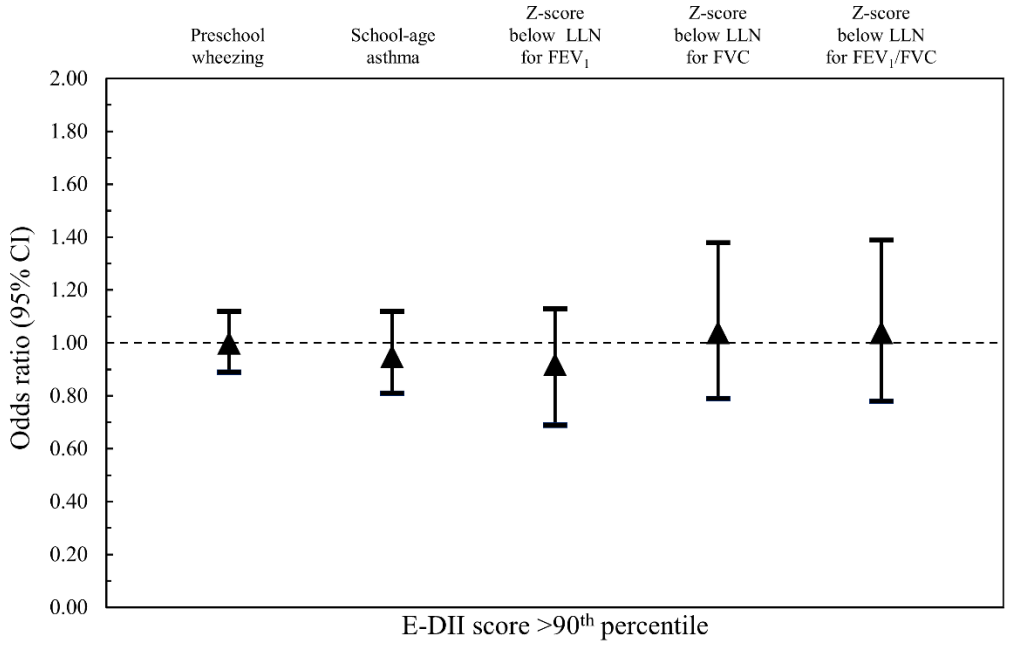
Table 2. Linear associations of maternal E-DII and DASH score with preschool wheezing and school-age asthma and lung function

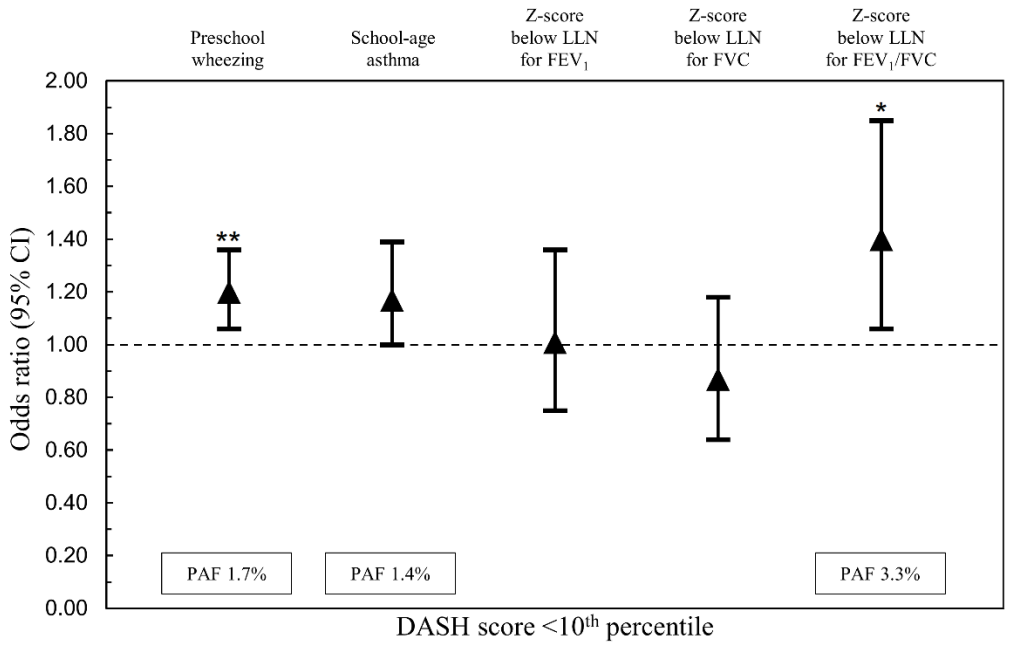
	Preschool wheezing OR (95% CI) n = 15,436	**School-age asthma OR (95% CI) n = 14,079**	**FEV_1 Z-score change (95% CI) n = 11,249**	**FVC Z-score change (95% CI) n = 11,249**	**FEV_1/FVC Z-score change (95% CI) n = 11,249**
E-DII score, per IQR increase					
Basic model	**1.14 (1.09, 1.20)****	**1.07 (1.00, 1.15)***	-0.03 (-0.05, 0.00)	**-0.04 (-0.07, -0.01)***	0.02 (-0.01, 0.05)
P-value	*<0.001*	*0.047*	*0.082*	*0.010*	*0.11*
Confounder model	1.02 (0.97, 1.07)	1.00 (0.93, 1.07)	-0.03 (-0.06, 0.00)	**-0.05 (-0.08, -0.02)****	0.03 (-0.00, 0.06)
P-value	*0.484*	*0.883*	*0.057*	*0.003*	*0.051*
DASH score, per IQR decrease					
Basic model	**1.15 (1.10, 1.21)****	**1.16 (1.08, 1.24)****	-0.01 (-0.04, 0.02)	-0.01 (-0.04 0.02)	-0.02 (-0.05, 0.01)
P-value	*<0.001*	*<0.001*	*0.421*	*0.865*	*0.122*
Confounder model	1.04 (0.98, 1.09)	1.06 (0.99, 1.14)	-0.02 (-0.05, 0.01)	-0.01 (-0.04, 0.02)	-0.02 (-0.05, 0.01)
P-value	*0.180*	*0.123*	*0.250*	*0.506*	*0.170*

Values are derived from multilevel logistic or linear regression models and reflect Odds ratios or changes in Z-scores with their corresponding 95% confidence interval (95% CI) per inter quartile range (IQR) increase in the E-DII score or per IQR decrease in the DASH score. Forced

Expiratory Flow in 1 second (FEV_1), and Forced Vital Capacity (FVC). Basic models are adjusted for child's sex, and basic models with DASH as exposure are additionally adjusted for maternal energy intake. The main models are additionally adjusted for maternal BMI, education, birthplace/ethnic background, smoking during pregnancy and parity, and child's breastfeeding. *P-value <0.05. **P-value <0.01.

Figure 1. Associations of a high E-DII and low DASH score in pregnancy with preschool wheezing, and school-age asthma and lung function





Values are derived from multilevel logistic regression models and reflect changes in Odds ratios with 95% confidence interval (95% CI) as compared to the reference group (≤90th percentile for the E-DII score and ≥10th percentile for the DASH score). The population attributable risk fractions (PAFs) indicate the proportion of preschool wheezing, school-age asthma or FEV_1/FVC below the lower limit of normal (LLN) attributable to a low DASH score.

LLN is defined as z-score for lung function outcome <1.64. Forced Expiratory Volume in 1 second (FEV1) and Forced Vital Capacity (FVC). The models are adjusted for maternal BMI, education, birthplace/ethnic background, smoking during pregnancy and parity, and child's sex and breastfeeding, and the models with DASH as exposure are additionally adjusted for maternal energy intake. *P-value <0.05. **P-value<0.01.

Maternal diet in pregnancy and child's respiratory outcomes: an individual participant data meta-analysis of 18,000 children

SUPPORTING INFORMATION

Figure E3 Associations of maternal DASH score with child's respiratory outcomes assessed by a two-stage IPD meta-analysis

SUPPLEMENTAL METHODS

This meta-analysis was performed among seven European prospective birth cohorts participating in the ALPHABET consortium, which aims to examine the early-life nutritional programming of non-communicable diseases [E1, E2]. The birth cohorts were the Avon Longitudinal Study of Parents and Children (ALSPAC) from the United Kingdom [E3, E4], the study on the pre- and early postnatal determinants of child health and development (EDEN) from France [E5], the Generation R Study (Generation R) from The Netherlands [E6], the Lifeways Cross-Generation Cohort Study (Lifeways) from Ireland [E7], the Polish Mother and Child Cohort (REPRO_PL) [E8] from Poland and the Southampton Women's Survey (SWS) from the United Kingdom [E9], which were observational birth cohorts, and the Randomised cOntrol trial of LOw glycaemic index diet versus no dietary intervention to prevent recurrence of fetal macrosomia study (ROLO) from Ireland [E10], which was originally a randomized controlled trial. Participants from both the intervention and non-intervention arm of this study were included for the main analyses. All participating cohorts obtained ethical approval from their local institutional review boards.

We included 23,466 singleton children with information on maternal dietary scores. To avoid extreme misreporting, participants with a likely implausible maternal energy intake (<500 or >3,500 kcal per day) (n=353), were excluded based on the availability of data in the ALPHABET consortium and according to a commonly used cut-off [E2, E11]. Furthermore, children with missing information on respiratory outcomes (n=4,787) were excluded, resulting in 18,326 mother-child pairs for the current analyses.

Maternal diet Information on maternal dietary intake was obtained from food frequency questionnaires (FFQs) (Table E1). All FFQs were adapted to the country-specific diet and validated, except for the ALSPAC cohort that uses a FFQ which covers all the main foods consumed in Britain but has not formally been validated [E12-E18]. To control for the effect of the total energy intake the E-DII, calculated per 1,000 kilocalories (kcal) of food consumed, was used instead of the standard DII (Dietary Inflammatory Index) score. Briefly, for the E-DII score, the food parameters for each cohort were linked to a regionally representative world database. This database was constructed based on eleven datasets from populations from different regions of the world and provides a global mean and standard deviation for each food parameter per 1000 kcal included in the E-DII score [E19]. A z-score was created by subtracting the "energy-adjusted standard global mean" from the amount reported and by dividing this value by the standard deviation. To calculate a food parameter-specific E-DII score, the obtained z-score for each food parameter was converted to a proportion and centered on zero by doubling and subtracting 1, then multiplied by its respective parameter-specific inflammatory effect score based on literature. These scores were summed up to create the overall E-DII score for each participant. When a parameter was not available, this parameter was imputed as missing. Based on the availability of the dietary parameters in each cohort, the E-DII was generated from 20-28 dietary parameters, out of 44 possible parameters (Table E2). Energy was not included in the score since the E-DII was adjusted for it. A higher E-DII score characterizes a more pro-inflammatory diet [E19, E20]. For the seven cohorts in the ALPHABET project, a DASH score was generated in a harmonized way and adapted to the length and content of the FFQs used in the different cohorts (Table E2) [E2]. This score was composed of eight food

components, based mainly on the Fung method with a scoring system based on quintile rankings in each cohort [E2, E21]. An item not filled in was imputed with zero. For intakes of total grains, vegetables, fruits, non-full-fat dairy products, and nuts/seeds/legumes, women received a score from 1 (lowest quintile) to 5 (highest quintile). At the opposite, for intakes of red and processed meats, sugar-sweetened beverages/sweets/added sugars, and sodium, women were scored on a reverse scale. The food component scores were summed to calculate an overall DASH score for each participant. A lower DASH score characterizes a lower dietary quality.

Respiratory health The ALSPAC study collected lung function data at multiple time points, and we used the measurement closest to the mean age at lung function measurement of the children of other cohorts for this meta-analysis. Five cohorts (ALSPAC, EDEN, Generation R, REPRO_PL and SWS) had information on preschool wheezing and school-age lung function. All cohorts had information on school-age asthma.

Covariates Information on lifestyle and sociodemographic related confounders, intermediates and effect modifiers was mainly obtained by questionnaires or clinical examinations at the research center (Table E1), and included maternal energy intake (kcal), pre-pregnancy or early-pregnancy body mass index (BMI) according to World Health Organization cut-offs (underweight, normal weight, overweight, obesity), educational level (low, medium, high), birthplace/ethnic background (European, non-European), smoking during pregnancy (no, yes), parity (nulliparous, multiparous), history of asthma (no, yes), and child's sex (boy, girl), gestational age at birth (weeks), birthweight (grams), whether the child was ever breastfed (no, yes),

attended daycare (no, yes), was exposed to pets (no, yes), or to dampness in the house (no, yes), had lower respiratory tract infections at the age of 2 years (no, yes), and about child's inhalant allergic sensitization obtained by skin prick tests (no, yes) and BMI in childhood. All cohorts, except for the EDEN cohort, had information available on child's dietary intake. This information was collected by using parental-reported questionnaires developed to capture foods eaten by children, and child's E-DII score was calculated according to a validated method (Table E2) [E22].

Statistical analyses Model 1 (basic model) was adjusted for maternal energy intake (only with DASH as the exposure) and child's sex. Model 2 (confounder model) was additionally adjusted for lifestyle-related confounders including maternal BMI, smoking during pregnancy, whether the child was ever breastfed, and socio-demographic factors including maternal educational level, birthplace/ethnic background and parity. Confounders were selected based on previous knowledge and visualised in a directed acyclic graph (DAG) by using DAGitty version 2.3 (Figure E1). We included variables in our models that were identified by the DAG. Consequently, child's daycare attendance, pet keeping and dampness in the house were not included in our models. To prevent exclusion of non-complete cases, we categorized all covariates and defined the missing values as an additional category.

We considered the linear confounder models as the main models and applied several additional analyses to these models. First, for the consistent associations, we additionally adjusted for potential intermediates gestational age at birth and birthweight, lower respiratory tract infections, child's BMI and, only for the models with maternal E-DII as exposure, for child's E-DII score. The percentage of the total effect that was explained by intermediates with the corresponding 95% confidence

interval (CI) was calculated by using causal mediation analysis implemented in R [E23]. Second, to examine effect modification due to atopic predisposition factors (maternal history of asthma or child's inhalant allergic sensitisation) or child's sex, we added the product term of the potential effect modifier and E-DII or DASH score to the model, one at a time. Third, we performed two-stage random effect meta-analyses to study the associations of maternal diet with respiratory outcomes in each cohort and to test for heterogeneity between cohorts [E24]. Fourth, we performed several restrictive analyses. Because of the potential effect of the timing in pregnancy of an adverse maternal diet on child's respiratory outcomes and of the age of the children when adequate lung function measures on a population-based level could be performed, we repeated the analyses in groups of different time periods in pregnancy (early, mid, late) and ages of the children (<8 and ≥8 years). We repeated our analyses restricted to complete cases to explore differences between complete and non-complete cases. Also, we repeated our models restricted to mothers with a European birthplace/ethnic background, since the FFQs were mainly developed for a European population. Last, to determine the influence of any particular population, we left one cohort out at a time.

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Table E1. Data collection on maternal diet and child's respiratory outcomes per cohort.

	Maternal E-DII and DASH			Child's respiratory outcomes			Covariates
Cohort name (country)	**Method**	**Total of food items in FFQ**	**Assessed period**	**Preschool wheezing**	**Spirometry**	**School-age asthma**	
ALSPAC (United Kingdom)	Non-quantitative FFQ	43	Preceding 3 months	Annual questionnaires to mother from 6 months to 42 months	Vitalograph 2120 hand-held spirometer (Spirotrac IV, Vitalograph, UK), according to ATS/ERS protocol	Questionnaire, parental report of doctor diagnosis at age 8 years	Questionnaires at 18 and 32 weeks gestation and annually from 6 months of age. At age 7 years, BMI was measured and skin prick tests were used to measure inhalant allergic sensitization.
EDEN (France)	Semi-quantitative FFQ	137	Preceding year	ISAAC based questionnaire at 4, 8, 12 months, 2 years, 3 years, 4years	Spirobank G (Medical International Research, Rome, Italy), according to ATS/ERS protocol	Parent reported questionnaire at 5 and 8 years on ever doctor-diagnosed asthma	Questionnaires and clinical exams during pregnancy and at 1, 3 and 5 years of age

Generation R (The Netherlands)	Semi-quantitative FFQ	293	Preceding 3 months	ISAAC based questionnaire, age 1, 2, 3 and 4 years: Has your child ever suffered from a whistling noise in the chest?	MS-Pneumo, (Vyaire, Würzburg, Germany), according to ATS/ERS protocol	ISAAC based questionnaire, physician diagnosed asthma ever, age 9 years	Questionnaires 1st - 3rd trimester of pregnancy, and at age 1-4, 6 and 9 years. At age 9 years, BMI was measured and skin prick tests were used to measure inhalant allergic sensitization.
Lifeways (Ireland)	Semi-quantitative FFQ	158	First 12-16 weeks of pregnancy	NA	NA	Asthma diagnosed between age 5 and age 9 years was reported by the general practitioner	Baseline questionnaire at ante-natal stage, mother and baby hospital records, questionnaires age 5 and 10 years, and measurements age 10 years.
REPRO_PL (Poland)	Non-quantitative FFQ	66	Preceding 3 months	ISAAC based questionnaire, age 1 and at 2 years: Has you	Jaeger MasterScreen Body/Diffusion (Viasys,	ISAAC based questionnaire at age 7-8 years, parental report	Questionnaires 1st, 2nd and 3rd trimester of pregnancy, age 1

				child ever suffered from a whistling noise in the chest?	Hoechberg, Germany). According to ATS/ERS protocol.	of ever doctor-diagnosed asthma	year, age 2 years and age 7-8 years. At age 7 years, BMI was measured and skin prick tests were used to measure inhalant allergic sensitization.
ROLO (Ireland)	Semi-quantitative FFQ	158	Preceding 3 months	NA	NA	Maternal reported doctor-diagnosed asthma at age 5 years	Baseline questionnaire at ante-natal stage, mother and baby hospital records, questionnaires and measurements at age 5 years

SWS (United Kingdom)	Non-quantitative FFQ	104	Preceding 3 months	ISAAC-based questionnaire at 6, 12 and 36 months of life: Has your child had any episodes of chestiness associated with wheezing or whistling in his/her chest? (includes wheezy bronchitis, asthma)	Koko spirometer and incentive software (KoKo version 4; PDS Instrumentation ; Louisville, CO, USA) . According to ATS/ERS protocol but without noseclips.	ISAAC based questionnaire, physician diagnosed asthma ever, age 5 years. ICPC codes reported by the GP	Questionnaires at 11 and 34 weeks gestation and at 6, 12 and 36 months of life. At age 6-7 years, BMI was measured and skin prick tests were used to measure inhalant allergic sensitization.

Food frequency questionnaire (FFQ); International Study on Asthma and Allergy in Childhood (ISAAC); American Thoracic Society/ European Respiratory Society (ATS/ERS); not available (NA)

Table E2. Cohort specific information on the food items included in the dietary scores

	ALSPAC (United Kingdom)	EDEN (France)	Generation R (The Netherlands)	Lifeways (Ireland)	REPRO_PL (Poland)	ROLO (Ireland)	SWS (United Kingdom)
Maternal E-DII score							
Total parameters	28	25	20	28	28	28	24
Food parameters	Beta Carotene, Folic Acid, Vitamin A, Alcohol, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Niacin, Protein, Polyunsaturated fatty acids, Riboflavin, Saturated fat, Selenium, Thiamin, Vitamin B12, Vitamin B6, Vitamin C, Vitamin D, Vitamin E, Zinc, Tea, Caffeine, Omega 3, Trans Fat	Beta Carotene, Folic Acid, Vitamin A, Alcohol, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Niacin, Protein, Polyunsaturated fatty acids, Riboflavin, Saturated fat, Thiamin, Vitamin B12, Vitamin B6, Vitamin C, Vitamin D, Vitamin E, Tea, Omega 3, Omega 6	Alcohol, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Protein, Polyunsaturated fatty acids, Riboflavin, Saturated fat, Vitamin B6, Vitamin C, Zinc, Garlic, Onion, Tea, Caffeine, Omega 6	Beta Carotene, Folic Acid, Vitamin A, Alcohol, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Niacin, Protein, Polyunsaturated fatty acids, Riboflavin, Saturated fat, Selenium, Thiamin, Vitamin B12, Vitamin B6, Vitamin C, Vitamin D, Vitamin E, Zinc, Garlic, Onion, Tea, Caffeine	Beta Carotene, Folic Acid, Vitamin A, Alcohol, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Niacin, Protein, Polyunsaturated fatty acids, Riboflavin, Saturated fat, Selenium, Thiamin, Vitamin B12, Vitamin B6, Vitamin C, Vitamin D, Vitamin E, Zinc, Tea, Caffeine, Omega 3, Omega 6	Beta Carotene, Folic Acid, Vitamin A, Alcohol, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Niacin, Protein, Polyunsaturated fatty acids, Riboflavin, Saturated fat, Selenium, Thiamin, Vitamin B12, Vitamin B6, Vitamin C, Vitamin D, Vitamin E, Zinc, Garlic, Onion, Tea, Caffeine	Beta Carotene, Folic Acid, Vitamin A, Alcohol, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Niacin, Protein, Polyunsaturated fatty acids, Riboflavin, Saturated fat, Vitamin B12, Vitamin B6, Vitamin C, Vitamin D, Vitamin E, Zinc, Onion, Tea
Child's E-DII score							

Assessment method	FFQ	NA	FFQ	FFQ	24-hour dietary recall	FFQ	FFQ
Assessment age	8.5 years	NA	8 years	5 years	7 years	5 years	3 years
Total parameters	23	NA	15	23	23	23	19
Food parameters	Beta Carotene, Folic Acid, Vitamin A, Alcohol, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Niacin, Protein, Polyunsaturated fatty acids, Riboflavin, Saturated fat, Selenium, Thiamin, Vitamin B12, Vitamin B6, Vitamin C, Vitamin E, Zinc		Cholesterol, Fat, Fiber, Iron, Magnesium, Niacin, Protein, Riboflavin, Saturated fat, Selenium, Vitamin B12, Vitamin B6, Vitamin C, Vitamin D, Zinc	Beta Carotene, Folic Acid, Vitamin A, Alcohol, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Niacin, Protein, Polyunsaturated fatty acids, Riboflavin, Saturated fat, Selenium, Thiamin, Vitamin B12, Vitamin B6, Vitamin C, Vitamin E, Zinc	Beta Carotene, Folic Acid, Vitamin A, Alcohol, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Niacin, Protein, Polyunsaturated fatty acids, Riboflavin, Saturated fat, Selenium, Thiamin, Vitamin B12, Vitamin B6, Vitamin C, Vitamin E, Zinc	Beta Carotene, Folic Acid, Vitamin A, Alcohol, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Niacin, Protein, Polyunsaturated fatty acids, Riboflavin, Saturated fat, Selenium, Thiamin, Vitamin B12, Vitamin B6, Vitamin C, Vitamin E, Zinc	Folic Acid, Vitamin A, Carbohydrate, Cholesterol, Fat, Fiber, Iron, Magnesium, Monounsaturated fatty acids, Niacin, Protein, Riboflavin, Saturated fat, Thiamin, Vitamin B12, Vitamin B6, Vitamin C, Vitamin E, Zinc
Maternal DASH score							
Total grains	7 Rice; Pasta; Oat cereals; Wholegrain or bran cereals; Other cereals; Crispbreads; Bread or rolls or chappatis	7 Bread; Whole bread or special bread; Rusk or equal; Cereals; Pasta; Rice; Semolina or Wheat	20 White pasta; Whole grain pasta; Cereal products; White rice; Brown rice; Seitan; White bread; Wholegrain bread; Multigrain bread; Muesli bread; White baguette; Wholegrain baguette; Dutch cake; Rye bread; Muesli; Cornflakes;	14 White bread; Brown bread; Wholemeal bread; Crisp bread; Brown soda; All bran; Branflakes; Cornflakes; Muesli; Sugar coated cereals; White rice; Brown rice; White green pasta; Wholemeal pasta	5 White bread; Whole bread; Groats; Rice or pasta; Cereal	14 White bread; Brown bread; Wholemeal bread; Crisp bread; Brown soda; All bran; Branflakes; Cornflakes; Muesli; Sugar coated cereals; White rice; Brown rice; White green pasta; Wholemeal pasta	8 White bread; Brown or wholemeal bread; Wholemeal or rye crackers; 'Bran' breakfast cereals; Other breakfast cereals; Added bran to foods; Brown or white rice; Pasta or dumplings

			Oatmeal; Whole cereal; Bran; Wheat germ				
Vegetables (excluding potatoes and condiments)	5	16	33	24	12	24	16
	Cabbage or brussels sprouts or kale or other green leafy vegetables; Other green vegetables (cauliflower, runner beans, leeks, etc.); Carrots; Other root vegetables (turnip, swede, parsnip, etc.); Salad (lettuce, tomato, cucumber, etc.)	<u>Raw vegetables:</u> Salad or endive or cress or spinach; Grated carrot; Other raw vegetables (celery, tomato, beet, cabbage, cucumber, radish, etc.); Avocado; Raw soybeans <u>Cooked vegetables:</u> Green beans; Endive or spinach or watercress; Leeks or cabbage (green cabbage, cauliflower, brussels sprouts, etc.); Broccoli; Cooked carrots; Courgette or eggplant (ratatouille, etc.); green peas; Other cooked vegetables (turnip, chards, etc.); Vegetable soup; Sweetcorn; Pumpkins or sweet potato	<u>Raw vegetables:</u> Kool; Endive salad; Winter carrot; Root or carrot; Endive or spinach; Lettuce; Cucumber; Celery. <u>Cooked vegetables:</u> Cauliflower; Broccoli; Brussels sprouts or cabbage; Beetroot; Chard; Green beans or snow peas; Garden peas or broad beans; Sweetcorn; Endive chicory; Leek; Endive or spinach; Mixed stir-fry vegetables; Carrots or stew; Kale; Sauerkraut. <u>Vegetables for family/household:</u> Onion; Tomato; Zucchini; Mushrooms; Bean sprouts; Paprika; Eggplant.	Carrots; Spinach; Broccoli; Brussel sprouts; Cabbage; Peas; Green beans; Marrow; Cauliflower; Parsnips; Leeks; Onions; Mushrooms; Sweet peppers; Bean sprouts; Green salad; Cucumber or celery; Watercress; Tomatoes; Beetroot; Coleslaw; Avocado; Vegetable soup; Sweetcorn	Carrot or root parsley; Beetroot; Lettuce; Tomato; Cucumber; Pepper; Radish; Onions or garlic; Cauliflower or broccoli or cabbage; Mushrooms; Other vegetables; Vegetable juice.	Carrots; Spinach; Broccoli; Brussel sprouts; Cabbage; Peas; Green beans; Marrow; Cauliflower; Parsnips; Leeks; Onions; Mushrooms; Sweet peppers; Bean sprouts; Green salad; Cucumber or celery; Watercress; Tomatoes; Beetroot; Coleslaw; Avocado; Vegetable soup; Sweetcorn.	Tinned vegetables; Peas or green beans; Carrots; Parsnips or swede or turnip; Sweetcorn or mixed vegetables; Tomatoes; Spinach; Broccoli or brussels sprouts or spring greens; Cabbage or cauliflower; Peppers or watercress; Onion; Green salad; Side salads in dressing; Courgettes or marrow or leeks; Mushrooms; Vegetable dishes

Fruits	3 Fresh fruit (apple, pear, banana, orange, bunch of grapes, etc.); Tinned juice; Pure juice not in tin	12 Apricot or melon or mango; Peach or plum or cherry; Banana; Kiwi; Citrus (orange, mandarin, grapefruit, etc.); Apple or pear; Grape; Other fresh fruits (pineapple); Dried apricot or peach; Other dried fruits; Fruit juice (orange, grapefruit, pineapple, apple, grape)	20 Mandarin; Orange or grapefruit; Lemon or lime; Banana; Kiwi; Apple; Pear; Mango; Peaches or nectarines; Apricots; Plums; Strawberries or raspberries; Grapes or cherries; Pineapple or melon; Canned fruit; Orange juice or grapefruit juice from the pack; Other fruit juices from the pack; Fruit juices prepared yourself; Dried fruits; Dried plums <u>Other parts:</u> Avocado; Side dish vegetables; Tomato juice or vegetable juice.	13 Apples; Pears; Oranges; Grapefruit; Bananas; Grapes; Melon; Peaches; Strawberries; Tinned fruit; Pure juice; Dried fruit; Fruit squash	10 Apples; Pears; Plums; Strawberries or raspberries; Cherries; Mandarins or oranges or grapefruit or kiwi; Peaches or apricots; Bananas; Other fruits; Fruit juice	13 Apples; Pears; Oranges; Grapefruit; Bananas; Grapes; Melon; Peaches; Strawberries; Tinned fruit; Pure juice; Dried fruit; Fruit squash	12 Tinned fruit; Cooked fruit; Dried fruit; Apples or pears; Oranges or orange juice; Grapefruit or grapefruit juice; Blackcurrants or ribena or hi-juice blackcurrant drinks; Other fruit juices (not squashes); Bananas; Peaches or plums or cherries or grapes; Strawberries or raspberries; Pineapple or melon or kiwi fruit or other tropical fruit
Non-full-fat dairy products	3 Semi-skimmed milk; Skimmed milk; Dried milk	6 Semi-skimmed milk; skimmed milk; Sour cream or yoghurt 0% fat; Sour cream or yoghurt 20%, 30%, 40% fat;	18 Semi-skimmed milk. Skimmed milk; Buttermilk; Drink yoghurt (natural/ without detail/ with sweeteners/ light);	7 Low-fat yoghurt; Low-fat cheddar; Low-fat milk; Skimmed milk; High low milk; Buttermilk; Dried milk	2 Milk; Yoghurt or kefir or buttermilk	7 Low-fat yoghurt; Low-fat cheddar; Low-fat milk; Skimmed milk; High low milk; Buttermilk; Dried milk	5 Yoghurt or fruit fools; Semi-skimmed pasteurised milk; Skimmed pasteurised milk; Semi-skimmed UHT; Skimmed UHT

		Yoghurt; Low-fat fresh cream	Yoghurt (semi-skimmed natural/ semi-skimmed with fruits/ skimmed natural/ skimmed with fruits/ skimmed with fruits and sweeteners); Cottage cheese (semi-skimmed natural/ semi-skimmed with fruits/ skimmed natural/ skimmed with fruits/ skimmed with fruits and sweeteners/ light); Low-fat cheese				
Nuts, seeds, legumes	7 Baked beans; Peas or sweetcorn or broad beans; Pulses or dried peas or beans or lentils or chick peas; Nuts or nut roast; Bean curd; Tahini; Soya 'meat' or TVP or vegaburgers	4 Nuts, hazelnut, almonds; Legumes (lentils, white bean, chickpea, beans, etc.); Cooked soy; Peanut	14 Legumes; Lentil soup; Lentils; Cooked soy; Tofu or tahoe; Tempeh; Nuts; Peanut butter or nut paste; Tahin (sesame paste); Sunflower seed; Pine nut; Linseed; Peanuts or nuts cocktail; Other nuts	5 Baked beans; Dried lentils; Tofu; Peanuts; Peanut butter	2 Legumes (soybeans, beans, peas, etc.); Seeds or nuts	5 Baked beans; Dried lentils; Tofu; Peanuts; Peanut butter	2 Beans or pulses; Nuts
Red and Processed meat	4	12	20	17	4	17	10

	Sausages or burgers; Pies or pasties (pork pie, steak/meat pie, etc.); Meat (beef, lamb, pork, ham, bacon, etc.); Liver or liver pate or kidney or heart	Beef (except chopped steak); Chopped steak; Pork; Veal; Lamb or ship; Liver (heifer, poultry, etc.); Beef tongue or black pudding, etc.; Dry sausage; Cervelas or mortadella; Pate or rillettes; Ham or bacon; Sausage	<u>Meat:</u> Beef or calf's liver; Veal; Steak or roast beef or tartar; Beef rump or ground beef; Smoked sausage; Half-to-half minced; Pork liver; Cop or pork; Bacon; Sausage or hamburger or minced pork; Pork; Mutton: Horse meat; Lamb; Shoarma meat; Frikandel or croquette. <u>Salty snacks:</u> Frikandel or croquette; Crunchy sausage; Satay or bitterballen or meatball; Slice of sausage meat	Beef roast; Beef steak; Beef mince; Beef stew; Beef burgers; Pork roast; Pork chops; Pork slices; Lamb roast; Lamb chops; Lamb stew; Bacon; Ham; Corned beef; Sausages; Liver; Pate.	Meat (beef, pork, veal); Liver; Other offal; Cooked meats	Beef roast; Beef steak; Beef mince; Beef stew; Beef burgers; Pork roast; Pork chops; Pork slices; Lamb roast; Lamb chops; Lamb stew; Bacon; Ham; Corned beef; Sausages; Liver; Pate	Bacon or gammon; Pork; Lamb; Beef; Minced meat dishes; Liver or kidney; Pate or liver sausage; Faggots or black pudding; Sausages; Ham or luncheon meat
Sugar-sweetened beverages, sweets, and added sugars	5 Sweets; Soft drink; Cola; Spoons of sugar in tea; Spoons of sugar in coffee	8 Honey or jam or marmalade; Sugar (in coffee, yoghurt, etc.); Candies; Drink syrup; Cola "non-light"; Lemonade or soft drinks "non-	11 Honey or sugar or jam; Apple syrup; Ice cream or milkshake; Soft drink (not light); Lemonade syrup; Liquorice; Candy;	5 Sweets; Sugar; Soft drinks; Ice cream; Jam or marmalade	1 Candy or cake or biscuits.	5 Sweets; Sugar; Soft drinks; Ice cream; Jam or marmalade	5 Coke or Pepsi; Soft drinks not including diet drinks (low calorie or low sugar); Other sweets; Ice cream or chocolate

		light"; Ice cream; Ice sorbet.	Rosehip syrup; Added sugar in dairy products; Added sugar in coffee; Added sugar in tea.				desserts; Teaspoons of sugar added
Sodium	Available in grams/day	Available in grams/day	Available in grams/day	Available in grams/day	Available in grams/day	Available in grams/day	Available in grams/day

Food frequency questionnaire (FFQ), Not available (NA).

Table E3. Maternal related baseline characteristics of cohorts

	ALSPAC (United Kingdom)	**EDEN (France)**	**Generation R (The Netherlands)**	**Lifeways (Ireland)**	**REPRO_PL (Poland)**	**ROLO (Ireland)**	**SWS (United Kingdom)**
Maternal BMI							
Underweight	0.2 (15)	7.0 (59)	3.3 (141)	2.5 (5)	8.5 (44)	0.7 (2)	1.3 (27)
Normal weight	38.5 (3,500)	65.4 (547)	69.4 (2,955)	69.5 (141)	73.0 (376)	48.0 (144)	56.4 (1,144)
Overweight	44.6 (4,047)	18.0 (151)	19.2 (816)	21.7 (44)	14.0 (72)	34.3 (103)	28.1 (570)
Obesity	16.8 (1,522)	9.6 (80)	8.1 (343)	6.4 (13)	4.5 (23)	17.0 (51)	14.2 (287)
Missing	*10.3 (1,046)*	*0.7 (6)*	*0.2 (8)*	*9.4 (21)*	*1.5 (8)*	*0.3 (1)*	*0.7 (14)*
Educational level							
Low	17.4 (1,759)	3.7 (31)	5.3 (218)	0.4 (1)	2.7 (14)	0.0 (0)	39.0 (794)
Middle	68.6 (6,920)	18.3 (154)	40.1 (1,664)	35.0 (78)	27.9 (146)	18.1 (54)	37.5 (763)
High	13.9 (1,403)	78.0 (657)	54.6 (2,267)	64.6 (144)	69.4 (363)	81.9 (245)	23.5 (479)
Missing	*0.5 (48)*	*0.1 (1)*	*2.7 (114)*	*0.4 (1)*	*0.0 (0)*	*0.7 (2)*	*0.3 (6)*

Birthplace/ethnic background, European	98.0 (9,932)	98.1 (783)*	72.2 (3,060)	100 (224)	100 (523)	99 (298)	96.8 (1,977)
Missing	*0.0 (0)*	*5.3 (45)*	*0.6 (24)*	*0.0 (0)*	*0.0 (0)*	*1.0 (3)*	*0.0 (0)*
Smoking, yes	24.9 (2,358)	21.1 (177)	23.3 (911)	41.6 (92)	9.9 (52)	6.4 (19)	13.8 (278)
Missing	*6.4 (649)*	*0.4 (3)*	*8.1 (347)*	*1.3 (3)*	*0.2 (1)*	*1.0 (3)*	*1.3 (26)*
Parity, nulliparous	55.9 (4,441)	42.8 (360)	59.4 (2,524)	39.8 (88)	64.2 (315)	0.0 (0)**	52.4 (1,068)
Missing	*21.5 (2,181)*	*0.2 (2)*	*0.3 (14)*	*1.3 (3)*	*6.1 (32)*	*0.0 (0)*	*0.1 (2)*
Asthma, yes	11.5 (1,134)	10.6 (89)	6.8 (261)	10.8 (24)	3.8 (10)	NA	21.8 (444)
Missing	*2.5 (256)*	*0.0 (0)*	*9.9 (424)*	*1.3 (3)*	*49.9 (261)*		*0.0 (1)*

Values are valid percentages (absolute numbers). Not available (NA). *For EDEN, maternal ethnicity was proxied by birthplace because a specific question on ethnicity is not allowed in France. **It was a recruitment criterion in ROLO that mothers were not nulliparous.

Table E4. Child related baseline characteristics of cohorts

	ALSPAC (United Kingdom)	**EDEN (France)**	**Generation R (The Netherlands)**	**Lifeways (Ireland)**	**REPRO_PL (Poland)**	**ROLO (Ireland)**	**SWS (United Kingdom)**
Early life							
Sex, female	48.3 (4,892)	47.2 (398)	50.5 (2,154)	46.9 (105)	50.7 (265)	50.2 (151)	48.0 (981)
Missing	*0.0 (0)*	*0.0 (0)*	*0.0 (0)*	*0.0 (0)*	*0.0 (0)*	*0.0 (0)*	*0.0 (0)*
Gestational age**	40.0	40.0	40.1	39.9	39.0	40.0	40.1
(weeks)	(36.0 - 42.0)	(35.0 - 41.0)	(36.0 - 42.4)	(34.2 - 42.0)	(36.0 - 41.0)	(37.0 - 42.0)	(34.9 - 42.1)
Missing	*0.0 (0)*	*0.0 (0)*	*0.0 (0)*	*8.0 (18)*	*0.2 (1)*	*0.0 (0)*	*0.0 (0)*
Birthweight (grams)*	3,444 (520)	3,287 (504)	3,454 (544)	3,548 (593)	3393 (472)	4,042 (435)	3,451 (559)
Missing	*1.2 (122)*	*0.0 (0)*	*0.1 (5)*	*0.0 (0)*	*4.0 (21)*	*0.0 (0)*	*0.8 (16)*
Ever breastfed	79.1 (7,545)	74.6 (628)	92.5 (3,303)	65.4 (140)	91.7 (343)	67.1 (202)	83.2 (1,641)
Missing	*5.8 (587)*	*0.1 (1)*	*16.3 (694)*	*4.5 (10)*	*28.5 (149)*	*0.0 (0)*	*3.4 (70)*
LRTI age 2 years	NA	39.7 (296)	11.2 (349)	22.5 (16)	30.5 (67)	NA	20.8 (402)
Missing		*11.6 (98)*	*27.2 (1,160)*	*68.3 (153)*	*57.9 (303)*		*5.3 (109)*
Childhood							

Allergy, yes	33.7 (788)	NA	32.0 (887)	NA	53.8 (86)	NA	19.9 (317)
Missing	*76.9 (7,795)*		*34.9 (1,487)*		*69.4 (363)*		*22.1 (452)*
E-DII score*	0.35 (1.00)	NA	-0.36 (0.77)	0.50 (1.10)	-0.10 (1.35)	-0.46 (1.36)	-0.04 (1.07)
Missing	*30.3 (3,070)*		*25.2 (1,073)*	*10.3 (23)*	*55.3 (289)*	*0.3 (1)*	*10.3 (211)*
School-age BMI*	16.2 (2.0)	15.4 (1.3)	17.5 (2.7)	17.9 (3.1)	16.4 (2.5)	16.2 (1.3)	16.1 (1.8)
Missing	*31.9 (3,229)*	*0.1 (1)*	*7.9 (338)*	*0.0 (0)*	*47.6 (249)*	*5.0 (15)*	*31.3 (639)*

Values are valid percentages (absolute numbers), *means (SD) or **medians (95% range), and percentages (absolute numbers) for the amount of missing data. Lower respiratory tract infections (LRTI), not available (NA).

Table E5. Associations of maternal E-DII and DASH score with preschool wheezing and school-age asthma and lung function, stratified by child's sex

	Preschool wheezing OR (95% CI)	**School-age asthma OR (95% CI)**	**FEV_1 Z-score change (95% CI)**	**FVC Z-score change (95% CI)**	**FEV_1/FVC Z-score change (95% CI)**
E-DII score, per IQR increase					
Boys	n = 7,987	n = 7,141	n = 5,631	n = 5,631	n = 5,631
	1.03 (0.96, 1.11)	1.03 (0.94, 1.14)	-0.04 (-0.08, 0.00)	**-0.06 (-0.10, -0.02)****	0.03 (-0.01, 0.07)
Girls	n = 7,449	n = 6,938	n = 5,618	n = 5,618	n = 5,618
	1.00 (0.93, 1.08)	0.95 (0.85, 1.06)	-0.02 (-0.06, 0.02)	-0.03 (-0.07, 0.01)	0.03 (-0.01, 0.07)
DASH score, per IQR decrease					
Boys	n = 7,987	n = 7,141	n = 5,631	n = 5,631	n = 5,631
	1.03 (0.96, 1.11)	1.08 (0.99, 1.19)	0.01 (-0.04, 0.05)	0.00 (-0.04, 0.05)	-0.01 (-0.06, 0.03)
Girls	n = 7,449	n = 6,938	n = 5,618	n = 5,618	n = 5,618
	1.04 (0.97, 1.12)	1.03 (0.92, 1.15)	-0.04 (-0.08, 0.00)	-0.02 (-0.06, 0.02)	-0.03 (-0.07, 0.01)

Values are derived from multilevel logistic or linear regression models and reflect Odds ratios or changes in Z-scores with their corresponding 95% confidence interval (95% CI) per inter quartile range (IQR) increase in the E-DII score or per IQR decrease in the DASH score. Forced

Expiratory Flow in 1 second (FEV_1), and Forced Vital Capacity (FVC). The models are adjusted for maternal BMI, education, birthplace/ethnic background, smoking during pregnancy and parity, and child's breastfeeding, and the models with DASH as exposure are additionally adjusted for maternal energy intake. *P-value <0.05. **P-value<0.01.

Table E6. Associations of maternal E-DII and DASH score with preschool wheezing and school-age asthma and lung function, per time period in pregnancy of maternal diet assessment

	Preschool wheezing OR (95% CI)	**School-age asthma OR (95% CI)**	**FEV_1 Z-score change (95% CI)**	**FVC Z-score change (95% CI)**	**FEV_1/FVC Z-score change (95% CI)**
E-DII score, per IQR increase					
Pre-pregnancy‡	n = 2,854	n = 2,240	n = 1,546	n = 1,546	n = 1,546
	1.01 (0.90, 1.14)	0.85 (0.71, 1.02)	-0.00 (-0.10, 0.09)	-0.01(-0.10, 0.09)	-0.02 (-0.10, 0.06)
Early pregnancy§	n = 5,283	n = 5,731	n = 4,645	n = 4,645	n = 4,645
	0.97 (0.89, 1.05)	1.04 (0.91, 1.18)	-0.02 (-0.06, 0.03)	-0.03 (-0.08, 0.01)	0.02 (-0.02, 0.06)
Late pregnancy‖	n = 11,983	n = 9,616	n = 7,292	n = 7,292	n = 7,292
	1.04 (0.98, 1.10)	0.95 (0.88, 1.03)	-0.03 (-0.07, 0.01)	**-0.05 (-0.09, -0.01)***	0.04 (-0.00, 0.08)
DASH score, per IQR decrease					
Pre-pregnancy‡	n = 2,854	n = 2,240	n = 1,546	n = 1,546	n = 1,546
	1.06 (0.95, 1.18)	0.96 (0.82, 1.13)	-0.01 (-0.10, 0.07)	0.01 (-0.08, 0.10)	-0.07 (-0.14, 0.00)
Early pregnancy§	n = 5,283	n = 5,731	n = 4,645	n = 4,645	n = 4,645

	1.04 (0.95, 1.13)	1.08 (0.94, 1.24)	-0.03 (-0.08, 0.01)	-0.03 (-0.08, 0.02)	-0.02 (-0.07, 0.03)
Late pregnancy[‖]	n = 11,983	n = 9,616	n = 7,292	n = 7,292	n = 7,292
	1.03 (0.98, 1.09)	1.03 (0.95, 1.11)	-0.02 (-0.05, 0.02)	-0.00 (-0.04, 0.03)	-0.03 (-0.07, 0.01)

Values are derived from multilevel logistic or linear regression models and reflect Odds ratios or changes in Z-scores with their corresponding 95% confidence interval (95% CI) per inter quartile range (IQR) increase in the E-DII score or per IQR decrease in the DASH score. Forced Expiratory Flow in 1 second (FEV_1), and Forced Vital Capacity (FVC). The models are adjusted for maternal BMI, education, birthplace/ethnic background, smoking during pregnancy and parity, and child's sex and breastfeeding, and the models with DASH as exposure are additionally adjusted for maternal energy intake. *P-value <0.05. **P-value<0.01.

[‡] Pre-pregnancy includes data from EDEN and SWS

[§] Early pregnancy (first and second trimester) includes data from Generation R, Lifeways, REPRO_PL, ROLO and SWS

[‖] Late pregnancy (third trimester) includes data from ALSPAC, EDEN and SWS

Table E7. Associations of maternal E-DII and DASH score with preschool wheezing and school-age asthma and lung function in complete cases, mothers with a European birthplace/ethnic background, and children aged < 8 years and ≥ 8 years, respectively

	Complete cases	European mothers	Age <8 years	Age ≥ 8 years
		Preschool wheezing		
N	11,676	14,566	NA	NA
E-DII score	0.98 (0.93, 1.04)	1.02 (0.97, 1.08)	NA	NA
DASH score	1.04 (0.98, 1.10)	1.03 (0.98, 1.09)	NA	NA
		School-age asthma		
N	10,408	12,978	NA	NA
E-DII score	0.97 (0.89, 1.05)	0.96 (0.89, 1.04)	NA	NA
DASH score	1.05 (0.96, 1.14)	1.06 (0.98, 1.14)	NA	NA
		FEV_1		
N	8,126	9,992	1,803	9,446
E-DII score	-0.03 (-0.06, 0.01)	-0.03 (-0.06, 0.00)	0.02 (-0.07, 0.12)	**-0.04 (-0.07, -0.01)***
DASH score	-0.03 (-0.06, 0.01)	-0.02 (-0.06, 0.01)	0.07 (-0.02, 0.15)	**-0.04 (-0.07, -0.01)***
		FVC		
N	8,126	9,992	1,803	9,446

E-DII score	**-0.04 (-0.08, -0.01)***	**-0.05 (-0.08, -0.02)**	-0.02 (-0.11, 0.08)	**-0.05 (-0.08, -0.02)****
DASH score	-0.01 (-0.04, 0.03)	-0.02 (-0.05, 0.01)	0.08 (-0.01, 0.17)	-0.03 (-0.06, 0.00)
		FEV_1/FVC		
N	8,126	9,992	1,803	9,446
E-DII score	0.02 (-0.01, 0.06)	**0.04 (0.01, 0.07)***	0.07 (-0.01, 0.14)	0.02 (-0.01, 0.05)
DASH score	**-0.04 (-0.07, -0.00)***	-0.02 (-0.05, 0.01)	-0.06 (-0.13, 0.01)	-0.01 (-0.05, 0.02)

Values are derived from multilevel logistic or linear regression models and reflect Odds ratios or changes in Z-scores with their corresponding 95% confidence interval (95% CI) per inter quartile range (IQR) increase in the E-DII score or per IQR decrease in the DASH score. Forced Expiratory Flow in 1 second (FEV_1), and Forced Vital Capacity (FVC). The models are adjusted for maternal BMI, education, birthplace/ethnic background (except for the models restricted to mothers with a European birthplace/ethnic background), smoking during pregnancy and parity, and child's sex and breastfeeding, and the models with DASH as exposure are additionally adjusted for maternal energy intake. *P-value <0.05. **P-value<0.01.

Table E8a. Associations of maternal E-DII score with preschool wheezing and school-age asthma and lung function, after excluding one cohort at a time

E-DII score, per IQR increase	Preschool wheezing OR (95% CI)	School-age asthma OR (95% CI)	FEV_1 Z-score change (95% CI)	FVC Z-score change (95% CI)	FEV_1/FVC Z-score change (95% CI)
All cohorts	n = 15,436	n = 14,079	n = 11,249	n = 11,249	n = 11,249
	1.02 (0.97, 1.07)	1.00 (0.93, 1.07)	-0.03 (-0.06, 0.00)	**-0.05 (-0.08, -0.02)****	0.03 (-0.00, 0.06)
Excluded cohort					
ALSPAC	n = 6,123	n = 6,573	n = 5,483	n = 5,483	n = 5,483
	0.97 (0.90, 1.05)	1.04 (0.93, 1.18)	-0.01 (-0.05, 0.04)	-0.02 (-0.06, 0.02)	0.02 (-0.01, 0.06)
EDEN	n = 14,596	n = 13,237	n = 10,411	n = 10,411	n = 10,411
	1.02 (0.97, 1.07)	0.99 (0.92, 1.07)	**-0.04 (-0.07, -0.01)***	**-0.05 (-0.08, -0.02)****	0.03 (-0.00, 0.06)
Generation R	n = 12,560	n = 10,569	n = 7,598	n = 7,598	n = 7,598
	1.03 (0.98, 1.09)	0.96 (0.89, 1.04)	-0.04 (-0.08, 0.00)	**-0.06 (-0.10, -0.02)****	**0.04 (0.00, 0.08)***
Lifeways	n = 15,436	n = 13,855	n = 11,249	n = 11,249	n = 11,249
	NA	1.00 (0.93, 1.08)	NA	NA	NA

REPRO_PL	n = 15,066	n = 13,804	n = 10,985	n = 10,985	n = 10,985
	1.01 (0.96, 1.07)	0.99 (0.93, 1.07)	**-0.03 (-0.06, -0.00)***	**-0.05 (-0.08, -0.02)****	**0.03 (0.00, 0.06)***
ROLO	n = 15,436	n = 13,778	n = 11,249	n = 11,249	n = 11,249
	NA	0.99 (0.92, 1.06)	NA	NA	NA
SWS	n = 13,399	n = 12,658	n = 10,519	n = 10,519	n = 10,519
	1.03 (0.97, 1.09)	1.01 (0.94, 1.09)	-0.03 (-0.06, 0.00)	**-0.04 (-0.07, -0.01)***	0.03 (-0.00, 0.06)

Values are derived from multilevel logistic or linear regression models and reflect Odds ratios or changes in Z-scores with their corresponding 95% confidence interval (95% CI) per inter quartile range (IQR) increase in the E-DII score. Forced Expiratory Flow in 1 second (FEV_1), and Forced Vital Capacity (FVC). 'NA' measure is not available in the omitted cohort. The models are adjusted for maternal BMI, education, birthplace/ethnic background, smoking during pregnancy and parity, and child's sex and breastfeeding. *P-value <0.05. **P-value<0.01.

Table E8b. Associations of maternal DASH score with preschool wheezing and school-age asthma and lung function, after excluding one cohort at a time

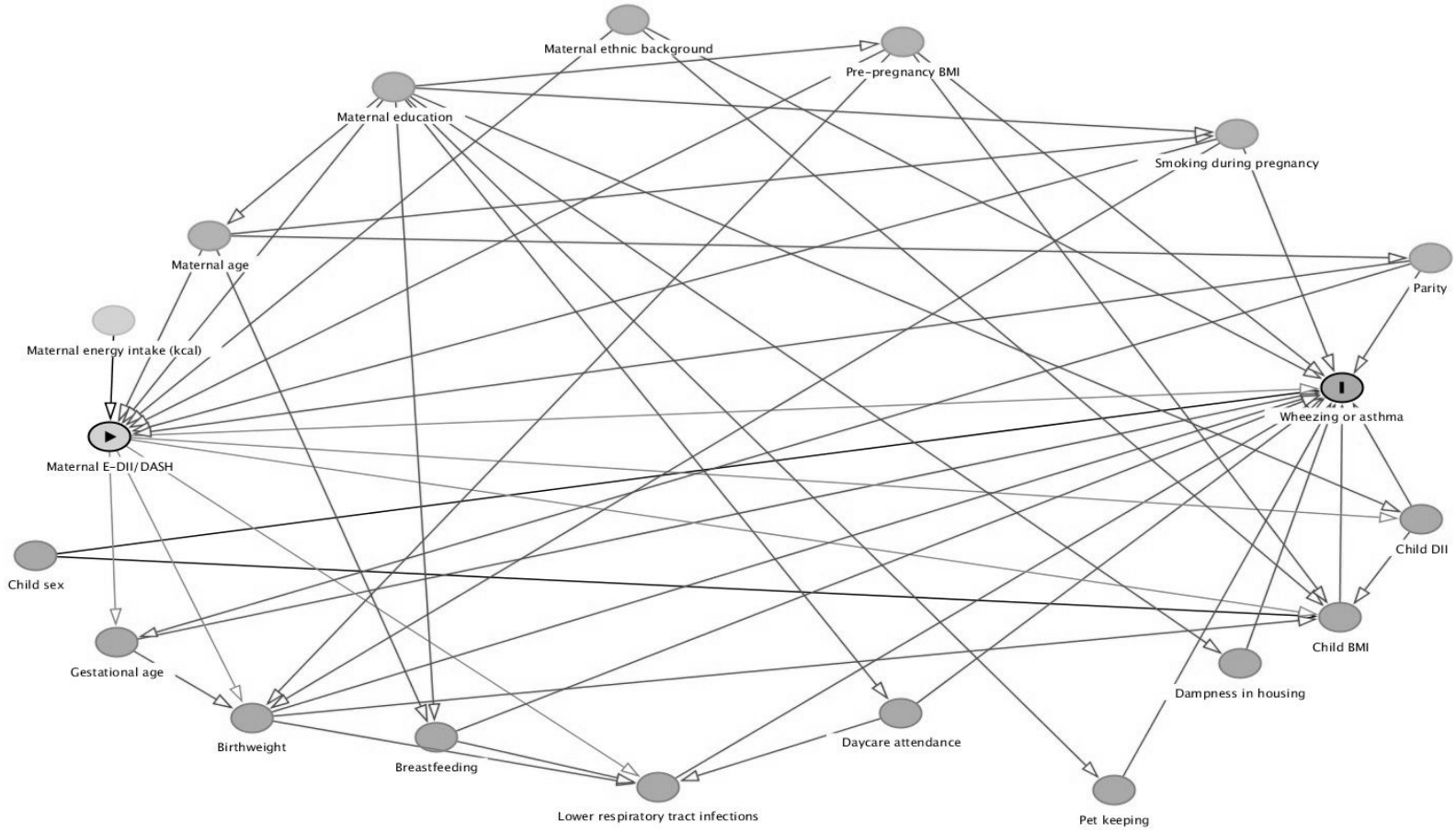
DASH score, per IQR decrease	**Preschool wheezing OR (95% CI)**	**School-age asthma OR (95% CI)**	**FEV_1 Z-score change (95% CI)**	**FVC Z-score change (95% CI)**	**FEV_1/FVC Z-score change (95% CI)**
All cohorts	n = 15,436	n = 14,079	n = 11,249	n = 11,249	n = 11,249
	1.04 (0.98, 1.09)	1.06 (0.99, 1.14)	-0.02 (-0.05, 0.01)	-0.01 (-0.04, 0.02)	-0.02 (-0.05, 0.01)
Omitted cohort					
ALSPAC	n = 6,123	n = 6,573	n = 5,483	n = 5,483	n = 5,483
	1.07 (0.99, 1.16)	1.11 (0.99, 1.26)	-0.00 (-0.05, 0.05)	0.00 (-0.04, 0.05)	-0.02 (-0.06, 0.02)
EDEN	n = 14,596	n = 13,237	n = 10,411	n = 10,411	n = 10,411
	1.02 (0.97, 1.08)	1.05 (0.97, 1.13)	**-0.04 (-0.07, -0.00)***	-0.03 (-0.06, 0.01)	-0.02 (-0.05, 0.01)
Generation R	n = 12,560	n = 10,569	n = 7,598	n = 7,598	n = 7,598
	1.03 (0.97, 1.09)	1.04 (0.96, 1.12)	-0.01 (-0.05, 0.02)	0.00 (-0.04, 0.04)	-0.03 (-0.07, 0.00)
Lifeways	n = 15,436	n = 13,855	n = 11,249	n = 11,249	n = 11,249
	NA	1.06 (0.99, 1.14)	NA	NA	NA
REPRO_PL	n = 15,066	n = 13,804	n = 10,985	n = 10,985	n = 10,985

	1.04 (0.98, 1.09)	1.06 (0.99, 1.14)	-0.02 (-0.05, 0.01)	-0.17 (-0.05, 0.01)	-0.02 (-0.05, 0.01)
ROLO	n = 15,436	n = 13,778	n = 11,249	n = 11,249	n = 11,249
	NA	1.06 (0.98, 1.14)	NA	NA	NA
SWS	n = 13,399	n = 12,658	n = 10,519	n = 10,519	n = 10,519
	1.04 (0.99, 1.10)	1.07 (1.00, 1.16)	-0.01 (-0.04, 0.02)	-0.01 (-0.04, 0.03)	-0.02 (-0.05, 0.02)

Values are derived from multilevel logistic or linear regression models and reflect Odds ratios or changes in Z-scores with their corresponding 95% confidence interval (95% CI) per inter quartile range (IQR) decrease in the DASH score. Forced Expiratory Flow in 1 second (FEV_1), and Forced Vital Capacity (FVC). 'NA' measure is not available in the omitted cohort. The models are adjusted for maternal energy intake, BMI, education, birthplace/ethnic background, smoking during pregnancy and parity, and child's sex and breastfeeding. *P-value <0.05. **P-value<0.01.

Figure E1. Directed acyclyc graph for confounder selection

A. Wheezing and asthma



B. Lung function

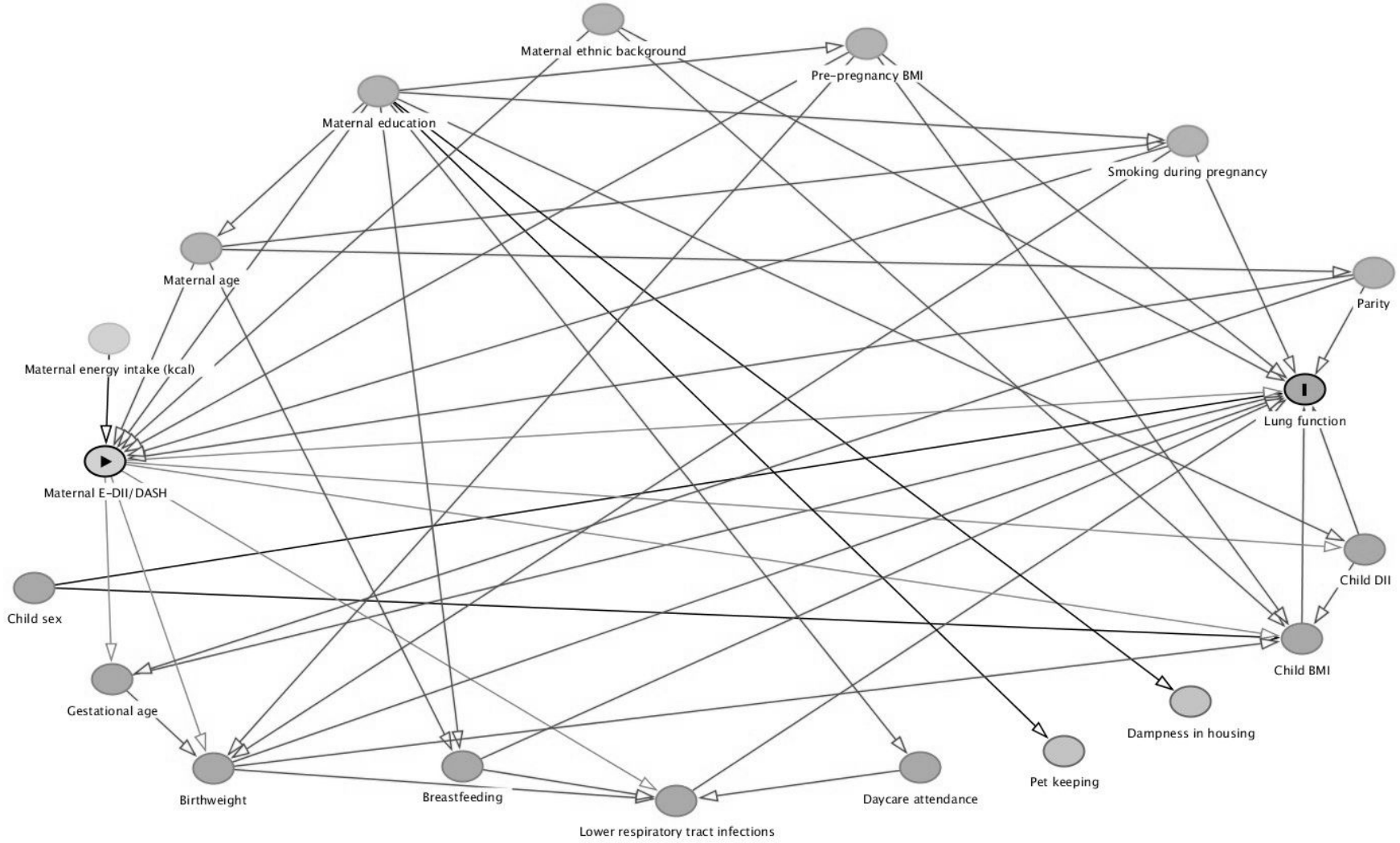
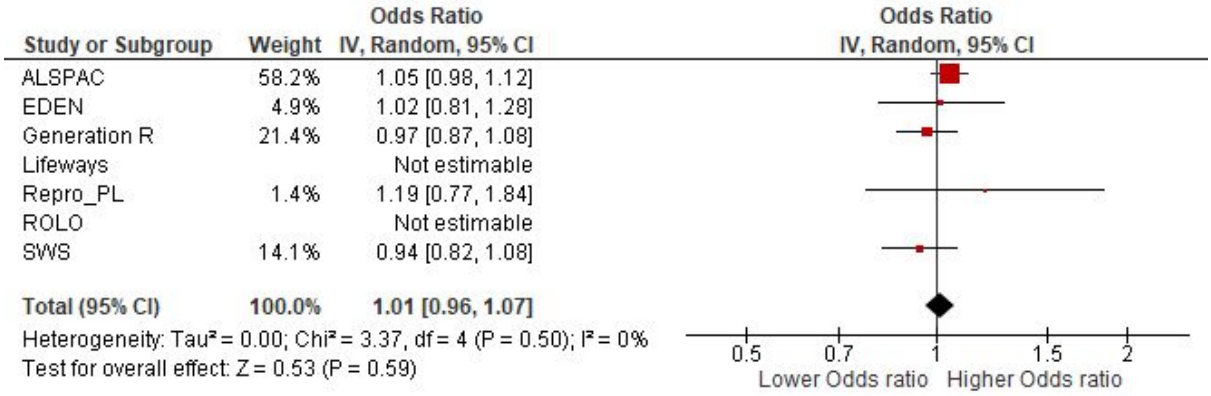
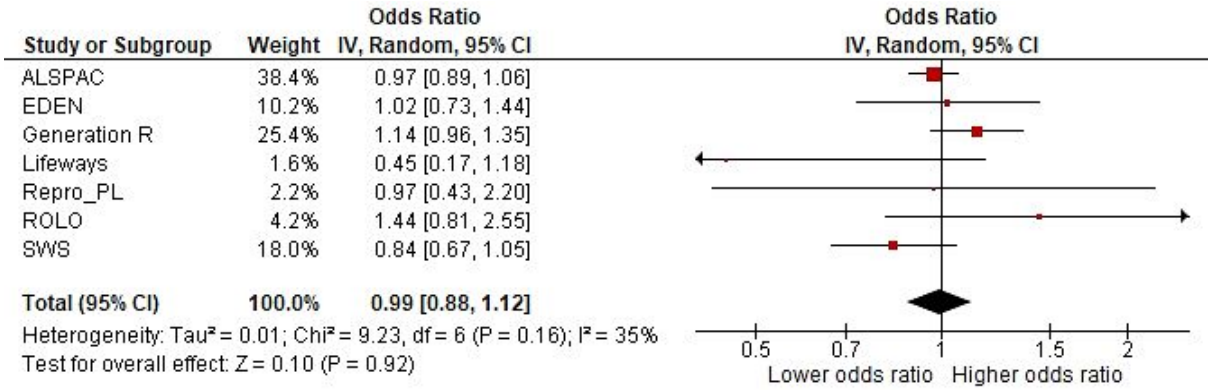


Figure E2. Associations of maternal E-DII score with preschool wheezing and school-age asthma and lung function, assessed by a two-stage individual participant data meta-analysis

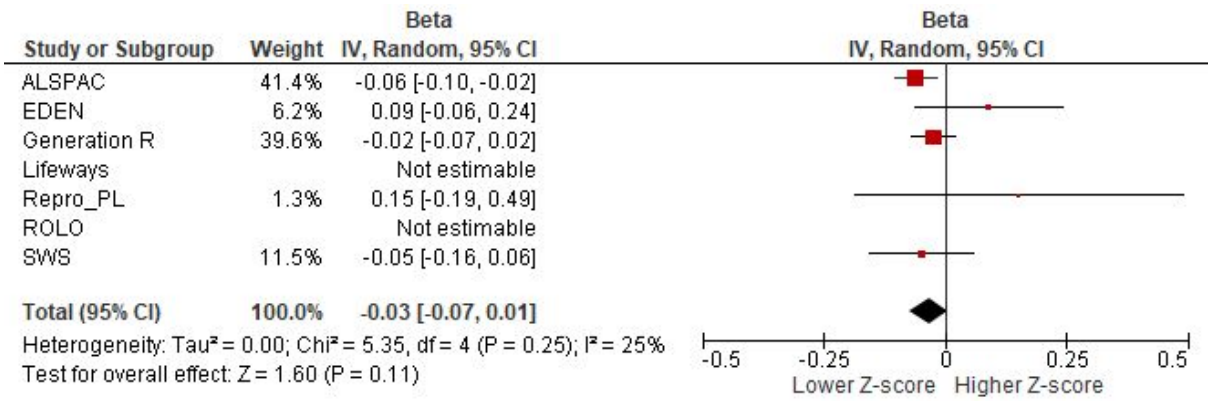
A. Preschool wheezing



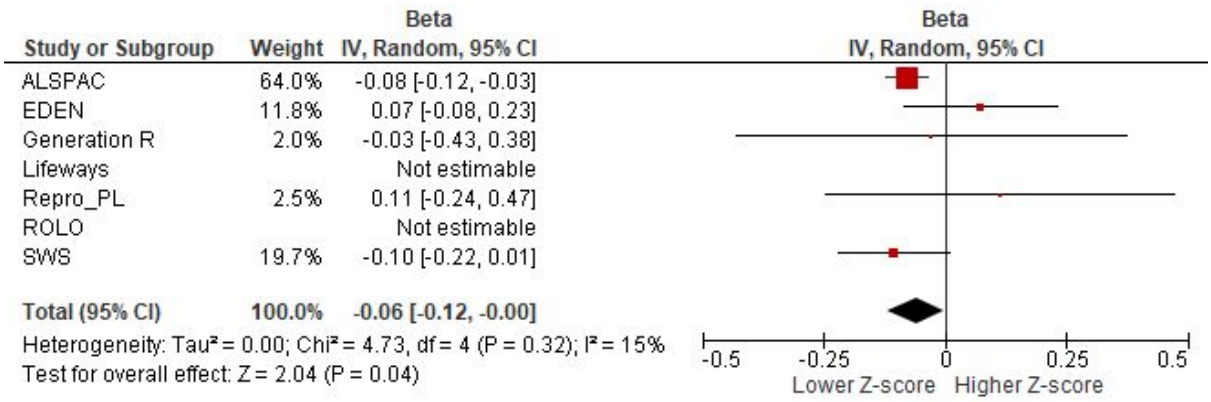
B. School-age asthma



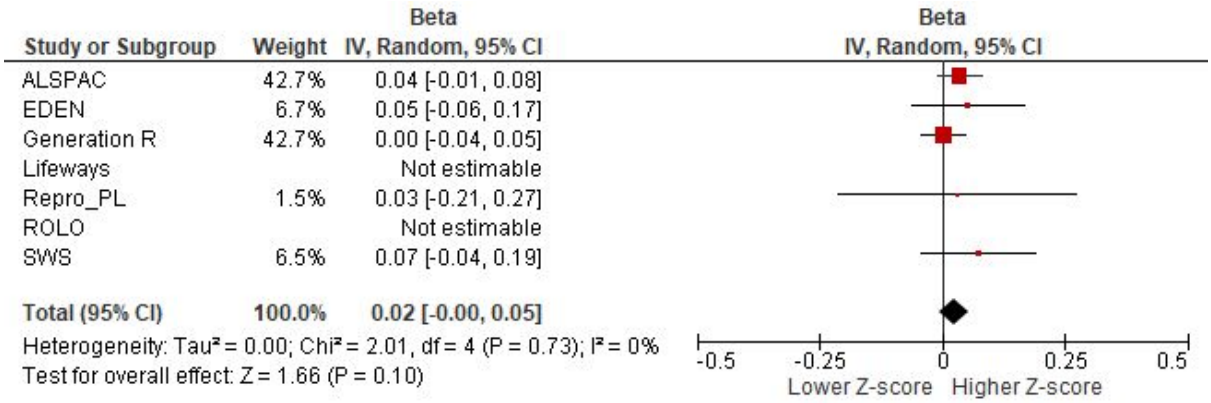
C. FEV_1



D. FVC



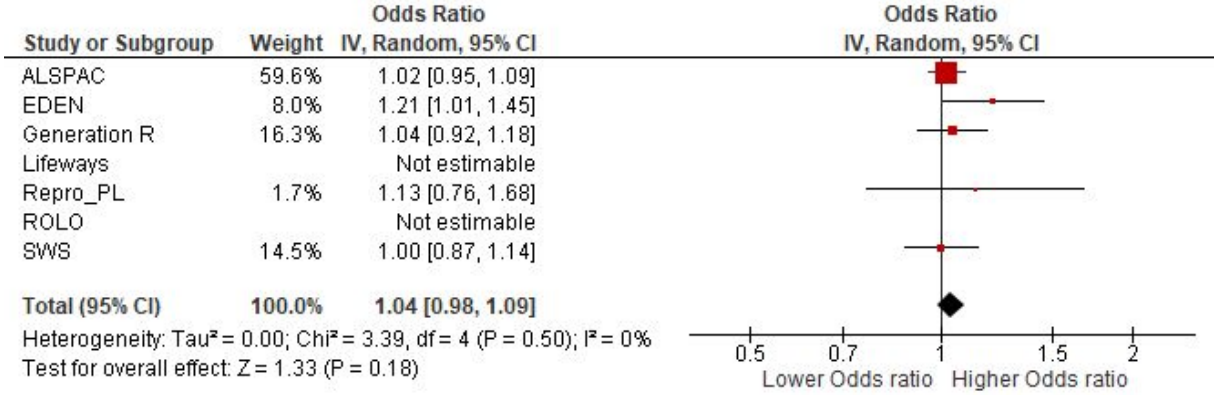
E. FEV_1/FVC



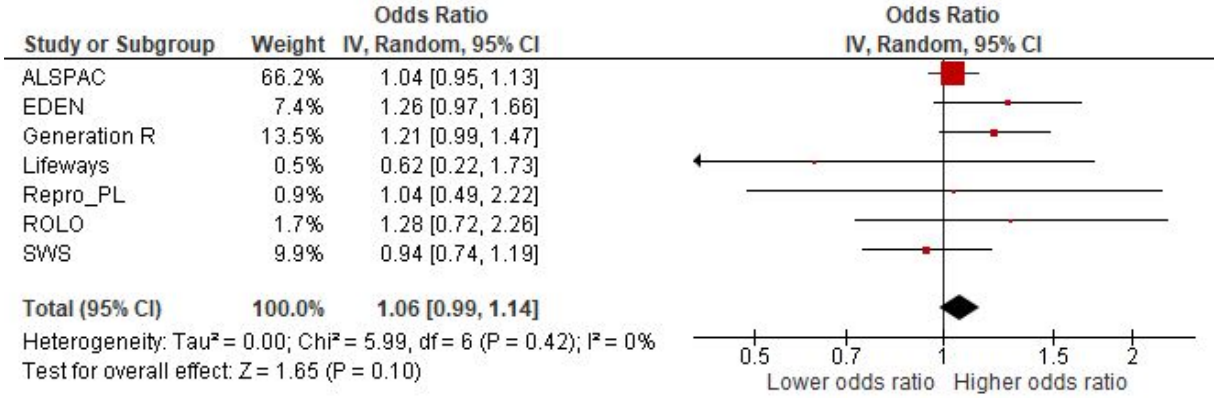
Values are derived from logistic or linear regression models and reflect Odds ratios or changes in Z-scores with their corresponding 95% confidence interval (95% CI) per inter quartile range (IQR) increase in the E-DII score. Forced Expiratory Flow in 1 second (FEV_1), and Forced Vital Capacity (FVC). The cohorts for which no estimate is provided had no data available on that specific outcome. The models are adjusted for maternal BMI, education, birthplace/ethnic background, smoking during pregnancy and parity, and child's sex and breastfeeding.

Figure E3. Associations of maternal DASH score with child's respiratory outcomes assessed by a two-stage individual participant data meta-analysis

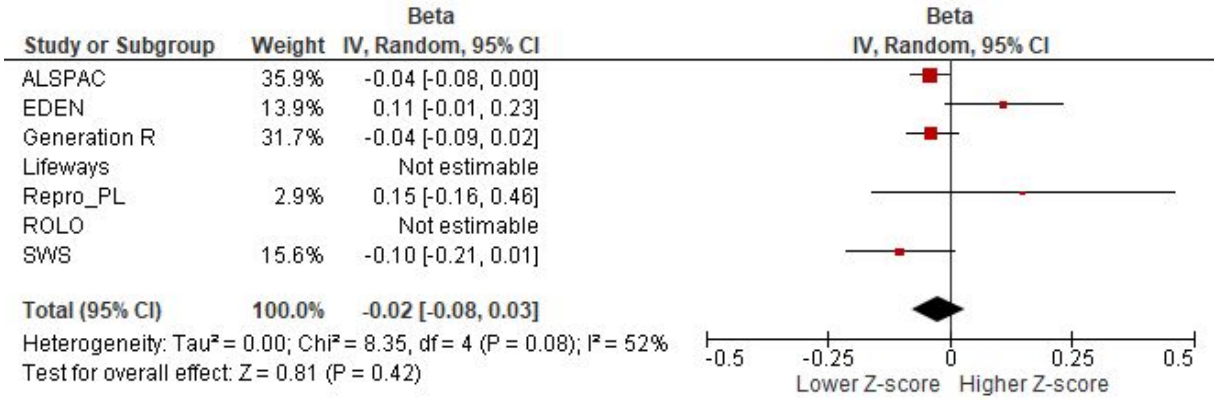
A. Preschool wheezing



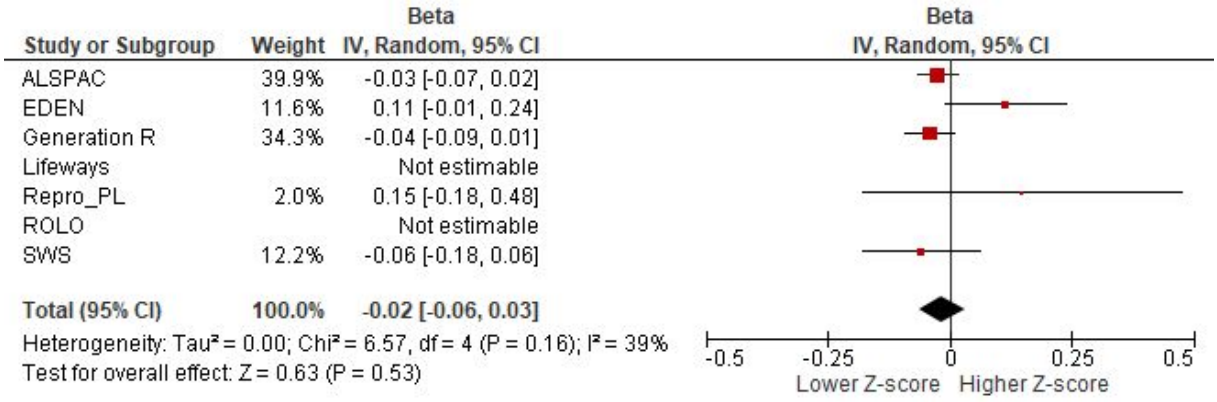
B. School-age asthma



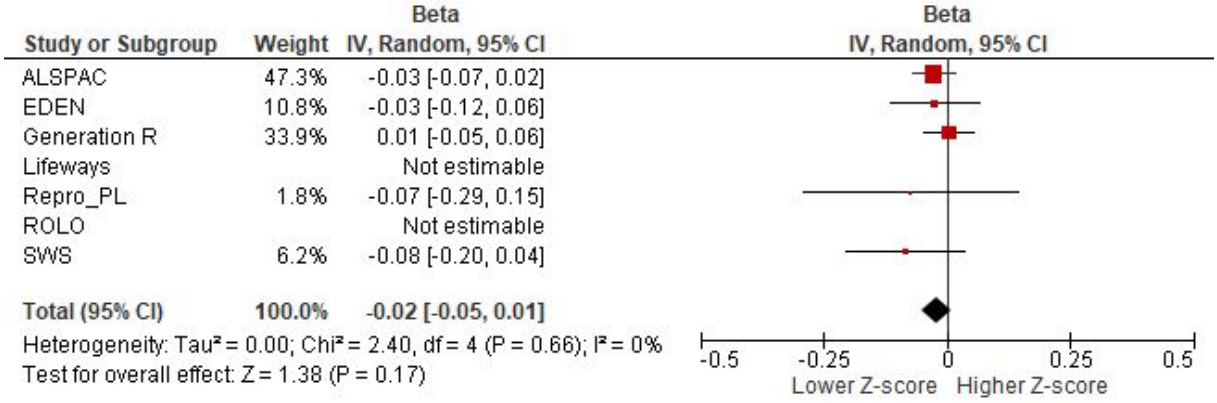
C. FEV_1



D. FVC



E. FEV_1/FVC



Values are derived from logistic or linear regression models and reflect Odds ratios or changes in Z-scores with their corresponding 95% confidence interval (95% CI) per inter quartile range (IQR) decrease in the DASH score. Forced Expiratory Flow in 1 second (FEV_1), and Forced Vital Capacity (FVC). The cohorts for which no estimate is provided had no data available on that specific outcome. The models are adjusted for maternal energy intake, BMI, education, birthplace/ethnic background, smoking during pregnancy and parity, and child's sex and breastfeeding.