



## Original article

# Predictors of maternal dietary quality and dietary inflammation during pregnancy: An individual participant data meta-analysis of seven European cohorts from the ALPHABET consortium



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## SUMMARY

**Background & aims:** Maternal diet during pregnancy is a modifiable behaviour which plays an important role in maternal, neonatal and child health outcomes. Thus, knowledge of predictors of dietary quality and dietary inflammatory potential in European countries may contribute to developing maternal diet-related public health policies that target specific at-risk populations in Europe.

**Methods:** We used harmonised data from >26,000 pregnant women enrolled in the ALSPAC, EDEN, Generation R, Lifeways, REPRO\_PL, ROLO and SWS cohorts, as part of the ALPHABET consortium. Maternal dietary quality and inflammatory potential were assessed using the Dietary Approaches to Stop

**Abbreviations:** ALSPAC, Avon Longitudinal Study of Parents and Children; BMI, Body Mass Index; CI, Confidence Interval; DASH, Dietary Approaches to Stop Hypertension; DOHaD, Developmental Origins of Health and Disease; EDEN, the study on the pre- and early postnatal determinants of child health and development; E-DII, Energy-adjusted Dietary Inflammatory Index; FFQ, Food Frequency Questionnaire; Generation R, The Generation R study; Lifeways, Lifeways Cross-Generation Cohort Study; REPRO\_PL, Polish Mother and Child Cohort; ROLO, Randomised cOntrol trial of LOw glycaemic index diet during pregnancy study; SD, Standard Deviation; SWS, Southampton Women's Survey.

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Pregnancy  
Risk factors  
DASH  
E-DII

Hypertension (DASH) and the energy-adjusted Dietary Inflammatory Index (E-DII). We conducted an individual participant data meta-analysis to investigate the maternal sociodemographic, health and behavioural predictors of maternal diet before and during pregnancy.

**Results:** DASH and E-DII scores were moderately correlated: from  $-0.63$  (95% CI:  $-0.66, -0.59$ ) to  $-0.48$  (95% CI:  $-0.49, -0.47$ ) across cohorts. Higher maternal age, education, household income, and physical activity during pregnancy were associated with a better dietary quality and a more anti-inflammatory diet. Conversely, multiparity and smoking during pregnancy were associated with a poorer dietary quality and a more proinflammatory diet. Women with obesity had a poorer pregnancy dietary quality than women with a normal body mass index range.

**Conclusions:** The results will help identify population subgroups who may benefit from targeted public health strategies and interventions aimed at improving women's dietary quality during pregnancy.

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## 1. Introduction

The Developmental Origins of Health and Disease (DOHaD) paradigm postulates that environmental exposures during the periconceptional period may alter later health in childhood and adulthood [1,2]. Maternal dietary quality, even before pregnancy, may influence both pregnancy and child outcomes [1,3]. Indeed, several studies have highlighted its potential impact on pregnancy complications (e.g., risk of pre-eclampsia), birth outcomes (e.g., risk of preterm birth and low birth weight) and offspring physical and mental health and development (e.g., obesity, neurocognitive development) [4–7]. The quality of diet during pregnancy varies considerably between women [8,9], and especially according to age, education and income, however the evidence regarding parity, ethnicity or other factors are less clear [10].

Pregnancy is a period of life when changes in dietary habits may occur [11,12]. It is considered as a window of opportunity for interventions to improve dietary quality and maternal, neonatal and child health outcomes [5,7]. The development of public health strategies aimed at promoting a healthy diet during pregnancy should rely on evidence-based knowledge regarding the predictors of a healthy diet in the population, to target specific at-risk populations and develop more effective tailored interventions [13].

To investigate maternal diet, the ALPHABET consortium derived two scores: the Dietary Approaches to Stop Hypertension (DASH) [14] and the energy-adjusted Dietary Inflammatory Index (E-DII) [15] within its seven European cohorts. These scores rely on two different approaches to examine diet: the former considers the diet as a whole, while the latter uses a primarily nutrient-based approach to estimate pro- or anti-inflammatory dietary potential. Both scores have been associated with a wide range of health outcomes and markers throughout the life course [16,17], but also specifically on pregnancy, its outcomes and child health and development [17–21].

Using data from >26,000 women from seven European cohorts and combined in an individual participant data meta-analysis, this study aims to i) describe and compare maternal DASH and the E-DII indexes; and ii) examine maternal sociodemographic, health and behavioural predictors associated with dietary quality and dietary inflammatory potential before and during pregnancy across cohorts. In this second aim, we adopted the framework put by Schooling and Jones [22], and Hernán et al. [23], where the term “predictor” is used, as a synonym of “factors associated with”, for variables that statistically predict women's dietary quality, regardless of whether it implies causation. Conducting an individual participant data meta-analysis based on harmonized data is a strategy method which reduces clinical heterogeneity and yields more robust evidence than the more traditional aggregate data meta-analysis [24].

## 2. Methods

### 2.1. Study design and participants

The European ALPHABET consortium, created specifically to investigate early-life nutritional programming of childhood health [17], comprised seven longitudinal mother-offspring cohort studies: the Avon Longitudinal Study of Parents and Children (ALSPAC) [25,26], the study on the pre- and early postnatal determinants of child health and development (EDEN) [27], the Generation R study (Generation R) [28], the Lifeways Cross-Generation Cohort Study (Lifeways) [29], the Polish Mother and Child Cohort (REPRO\_PL) [30], the Randomised Control Trial of Low Glycaemic Index Diet study (ROLO) [31], and the Southampton Women's Survey (SWS) [32].

The main characteristics of each cohort included for current analysis are presented in Table 1. In brief, out of the seven studies, two were based in Ireland, two in the United Kingdom, and the last three were from Poland, the Netherlands and France. ALSPAC was the first launched study (enrolment in 1990–1992), whereas REPRO\_PL and ROLO (enrolment in 2007–2011) were the most recent. The sample size ranged from 759 (ROLO) to 14,541 (ALSPAC).

All participating cohorts have obtained relevant institutional ethical approvals and research to date has been conducted according to the guidelines laid down in the Declaration of Helsinki (Supplementary materials).

### 2.2. Dietary data collection and indices of dietary quality and inflammatory potential

**Maternal dietary assessment:** Dietary information was collected by self-administered semi-quantitative (EDEN, Generation R, Lifeways, ROLO) [33–36], and non-quantitative (ALSPAC, REPRO\_PL, SWS) [30,37,38] Food Frequency Questionnaires (FFQs) (except SWS which used nurse-administered FFQs). Maternal diet was assessed in pre-pregnancy in two studies (EDEN and SWS) and during pregnancy in all studies. Of note, maternal diet was assessed twice during pregnancy in SWS: early and late pregnancy measures were averaged to reflect overall pregnancy diet.

**Maternal dietary quality – Dietary Approaches to Stop Hypertension (DASH) score:** As previously described in detail [14], the DASH score was adapted to the data collected within the cohorts of the ALPHABET consortium (Supplemental Table S1), using eight food components (seven food groups and one nutrient) combined into a score based on cohort-quintile rankings [39]. For intakes of total grains, vegetables (excluding potatoes and condiments), fruits, non-full-fat dairy products, and nuts/seeds/legumes, women received a score from 1 (lowest quintile) to 5 (highest quintile).

**Table 1**  
Characteristics of the cohorts part of the ALPHABET consortium.

Cohort	Location, Country	Enrolment period	Number of recruited women	Food Frequency Questionnaires		
				Period of assessment	Target period	n <sup>a</sup>
ALSPAC	Bristol, The United Kingdom	1990–1992	14,541	around 32 WG	late pregnancy	11,964
EDEN	Nancy and Poitiers, France	2003–2006	2002	24–28 WG birth	pre-pregnancy late pregnancy	1964 1849
Generation R	Rotterdam, The Netherlands	2002–2006	9778	<24 WG	early pregnancy	6246
Lifeways	Multicentric, Republic of Ireland	2001–2003	1132	12–16 WG	early pregnancy	1121
REPRO_PL	Multicentric, Poland	2007–2011	1451	20–24 WG	early pregnancy	1314
ROLO	Dublin, Republic of Ireland	2007–2011	759	≤28 WG	early pregnancy	631
SWS	Southampton, The United Kingdom	1998–2002	12,583	pre-pregnancy 11 WG 34 WG	pre-pregnancy early pregnancy late pregnancy	3,156 <sup>b</sup> 2222 2642

Abbreviations: WG, Weeks of Gestation.

<sup>a</sup> Women included in these analyses.

<sup>b</sup> 12,572 women had available dietary information in pre-pregnancy but only 3158 pregnant women delivered a live singleton baby and were included in the present study.

Inversely, for intakes of red and processed meats, sugar-sweetened beverages/sweets/added sugars, and sodium, women received a score from 5 (lowest quintile) to 1 (highest quintile). Finally, component scores were summed up and an overall DASH score for each participant was calculated, ranking from 8 to 40 points with a higher score characterizing a higher dietary quality.

Maternal dietary inflammatory potential – energy-adjusted Dietary Inflammatory Index (E-DII): A complete description of the method used to build the E-DII is available elsewhere [15,40]. Briefly, a total of 1943 articles were peer-reviewed and scored. Scoring for each food parameter was based on its inflammatory potential on six inflammatory biomarkers including C-reactive protein, IL-1 $\beta$ , IL-4, IL-6, IL-10, and tumor necrosis factor- $\alpha$ . The dietary information on each participant was first linked to food consumption data sets from 11 countries around the world to estimate the average and standard deviation for each of the 45 food parameters. Z scores were calculated by subtracting the global standard average from the amount reported and dividing by the global standard deviation. To limit influence from highly skewed data each Z score was converted to proportions (i.e., with values ranging from 0 to 1). These proportions were then “centered” on zero by multiplying each by 2 and subtracting 1 [40]. Each obtained value was multiplied by the corresponding food parameter effect score. All of the food parameter-specific E-DII scores were summed to obtain the overall E-DII score. In ALPHABET, the E-DII score was generated from 24 to 28 dietary parameters (out of the 44 possible excluding energy intake; as the E-DII has been intrinsically adjusted for energy intake, it is not considered as a distinct parameter) in all cohorts except for Generation R, which included 20 dietary parameters (Supplemental Table S1). Positive scores indicated a more proinflammatory diet, whereas negative scores indicated a more anti-inflammatory diet.

### 2.3. Maternal predictors

Information on maternal sociodemographic, health and behavioural predictors was collected by questionnaires (self- or interviewer-administered) or abstracted from obstetrical and birth records during pregnancy and after childbirth. Concerning maternal sociodemographic predictors, we considered age at childbirth (continuous), educational level (low:  $\leq$ lower secondary; medium: upper secondary or post-secondary non-tertiary; high:  $\geq$ tertiary) (adapted from the International Standard Classification of Education – 2011 levels) [41], household income (low; medium; high, defined as cohort-specific tertiles), parity (primiparous; multiparous) and birthplace/maternal ethnicity (European-born/White; non-European-born/non-White). We also investigated

maternal health and behavioural predictors including pre-pregnancy Body Mass Index (BMI) (underweight [ $<18.5$  kg/m<sup>2</sup>]; normal range [18.5–24.9 kg/m<sup>2</sup>]; overweight [25–29.9 kg/m<sup>2</sup>]; obesity [ $\geq 30$  kg/m<sup>2</sup>]) [42], smoking status during pregnancy (non-smoker; smoker), alcohol consumption during pregnancy (no; yes), and physical activity during pregnancy (low; medium; high, defined as cohort-specific tertiles).

### 2.4. Statistical analyses

We present means and standard deviations (SD) and proportions to describe the maternal factors for continuous variables or categorical variables, respectively. We examined the rank correlations between DASH and E-DII scores using Spearman's correlation coefficients.

The associations between predictors and DASH and E-DII scores were analysed by a two-stage individual participant data meta-analysis: first, cohort-specific effect estimates were obtained by multiple linear regression (mutually controlling for all other predictors), then, the effect estimates were pooled using random-effects meta-analysis, which considers both within- and between-study variability [24,43]. Because of different missing/available data patterns between predictors and cohorts (Supplemental Table S2), we organized analyses of associations into two parts: i) a main analysis on the seven predictors available for all cohorts (age, educational level, parity, birthplace/maternal ethnicity, pre-pregnancy BMI, smoking status and alcohol consumption during pregnancy) (Fig. 2A–G); ii) a secondary analysis additionally looking at household income and physical activity during pregnancy with adjustment for the seven predictors of the main analysis (Fig. 3A–B). We additionally realized a sensitivity analysis restricted to the three cohorts with the nine predictors available throughout a model adjusted for all the nine predictors (ALSPAC, EDEN, and Lifeways) (Supplemental Tables S3–4). Another sensitivity analysis was conducted with both adjustment for energy intake (kcal/day) for models with DASH (to follow the same logic as for the E-DII intrinsically adjusted for energy intake) and the exclusion of participants with likely implausible energy intake ( $<500$  or  $>3500$  kcal/day) which could induce extreme misreporting (Supplemental Tables S5–6) [44,45]. Statistical heterogeneity among included studies was assessed using the Cochran Q test and  $I^2$ -statistic [46,47]. Data are presented alongside study weight (%),  $I^2$  statistics, and expressed as standardized regression coefficient ( $\beta$ ) changes in DASH and E-DII scores and their 95% confidence intervals (CI). All analyses were carried out using the statistical software Stata version 15.1 (StataCorp, College Station, TX, USA).

### 3. Results

Characteristics of the 26,410 participants are summarised in Table 2. The mean (SD) maternal age at delivery ranged from 28.3 (4.9) (ALSPAC) to 32.2 (4.1) (ROLO) years. Differences in education levels were observed: from 26.2% (Generation R) to 78.1% (ROLO) of women had tertiary education. With the exception of ROLO where second gravida was an inclusion criterion, 44.6% (EDEN) to 58.9% (REPRO\_PL) were nulliparous. In Generation R, 34.3% of women were non-European-born/non-white. Most women in the

other cohorts were European-born/white: i.e., from 95.1% (ALSPAC) to 97.8% (ROLO) (100% for Lifeways and REPRO\_PL where it was an inclusion criterion). Household income was not available in three cohorts, namely REPRO\_PL, ROLO and SWS. The prevalence of women with pre-pregnancy BMI in the normal range varied from 43.4% (ROLO) to 72.6% (REPRO\_PL); 3.6% (ROLO) to 26.9% (EDEN) of women were smokers, and 6.4% (REPRO\_PL) to 68.9% (ROLO) consumed alcohol during pregnancy. Data on physical activity during pregnancy were available for all cohorts except Generation R.

**Table 2**

Characteristics of participants of the ALPHABET cohort studies overall and by cohort (n = 26,410).

	ALPHABET 26,410	ALSPAC 11,964	EDEN 1978	Generation R 6246	Lifeways 1121	REPRO_PL 1314	ROLO 631	SWS 3156
<b>Maternal dietary indices</b>								
Pre-pregnancy DASH	24.0 (4.4)	n.a.	24.0 (4.3)	n.a.	n.a.	n.a.	n.a.	24.1 (4.4)
Pregnancy DASH	24.0 (4.2)	24.0 (4.0)	23.9 (4.3)	24.0 (4.5)	23.7 (4.6)	24.1 (4.4)	24.0 (4.1)	24.1 (4.1)
Pre-pregnancy E-DII	0.2 (1.7)	n.a.	0.5 (1.7)	n.a.	n.a.	n.a.	n.a.	0.0 (1.7)
Pregnancy E-DII	0.3 (1.7)	0.6 (1.8)	0.9 (1.7)	−0.3 (1.1)	0.4 (1.8)	−1.1 (1.5)	0.2 (1.7)	0.5 (1.4)
<b>Maternal sociodemographic factors</b>								
Age (years)	29.2 (4.9)	28.3 (4.9)	29.5 (4.9)	30.1 (5.1)	29.8 (5.9)	29.0 (4.2)	32.2 (4.1)	30.2 (3.9)
Educational level								
Low	22.3 (5779)	29.8 (3543)	7.6 (144)	22.7 (1355)	18.3 (200)	8.4 (110)	5.3 (33)	12.5 (394)
Medium	51.3 (13,307)	57.3 (6818)	38.9 (742)	51.1 (3054)	32.3 (353)	28.4 (373)	16.6 (104)	59.2 (1863)
High	26.5 (6867)	12.9 (1533)	53.5 (1021)	26.2 (1562)	49.5 (541)	63.2 (831)	78.1 (488)	28.3 (891)
Missing	1.7 (457)	0.6 (70)	3.6 (71)	4.4 (275)	2.4 (27)	0.0 (0)	1.0 (6)	0.3 (8)
Household income								
Low	32.2 (5563)	33.7 (3101)	46.7 (892)	21.1 (1091)	47.6 (479)	n.a.	n.a.	n.a.
Medium	28.2 (4877)	33.0 (3041)	26.2 (501)	19.5 (1008)	32.5 (327)	n.a.	n.a.	n.a.
High	39.6 (6856)	33.3 (3062)	27.1 (517)	59.4 (3077)	19.9 (200)	n.a.	n.a.	n.a.
Missing	34.5 (9114)	23.1 (2760)	3.4 (68)	17.1 (1070)	10.3 (115)			
Parity <sup>a</sup>								
Primiparous	48.4 (12,505)	44.9 (5181)	44.6 (847)	58.0 (3605)	45.3 (489)	58.9 (771)	0.0 (0)	51.1 (1612)
Multiparous	51.6 (13,317)	55.1 (6347)	55.4 (1054)	42.0 (2615)	54.7 (591)	41.1 (537)	100.0 (631)	48.9 (1542)
Missing	2.2 (588)	3.6 (436)	3.9 (77)	0.4 (26)	3.7 (41)	0.5 (6)	0.0 (0)	0.1 (2)
Birthplace/ethnicity <sup>b,c</sup>								
European-born/White	88.7 (22,818)	95.1 (11,019)	95.5 (1714)	65.7 (4018)	100.0 (1121)	100.0 (1314)	97.8 (617)	95.5 (3015)
Non-European-born/Non-White	11.3 (2909)	4.9 (573)	4.5 (80)	34.3 (2101)	0.0 (0)	0.0 (0)	2.2 (14)	4.5 (141)
Missing	2.6 (683)	3.1 (372)	9.3 (184)	2.0 (127)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)
<b>Maternal health and behavioural factors</b>								
Pre-pregnancy BMI <sup>d</sup>								
Underweight	7.3 (1779)	11.5 (1185)	8.6 (163)	3.8 (230)	3.4 (31)	8.9 (115)	0.5 (3)	1.7 (52)
Normal range	65.8 (15,933)	68.0 (7002)	64.8 (1225)	67.5 (4075)	68.2 (627)	72.6 (942)	43.4 (273)	57.0 (1789)
Overweight	18.3 (4421)	14.0 (1439)	17.7 (335)	19.6 (1183)	19.7 (181)	14.9 (193)	37.7 (237)	27.2 (853)
Obesity	8.6 (2078)	6.5 (670)	8.8 (167)	9.2 (553)	8.8 (81)	3.7 (48)	18.4 (116)	14.1 (443)
Missing	8.3 (2199)	13.9 (1668)	4.5 (88)	3.3 (205)	17.9 (201)	1.2 (16)	0.3 (2)	0.6 (19)
Smoking status during pregnancy								
Non-smoker	77.1 (19,424)	75.0 (8724)	73.1 (1400)	74.7 (4211)	78.4 (876)	86.5 (1101)	96.4 (608)	83.8 (2504)
Smoker	22.9 (5762)	25.0 (2903)	26.9 (515)	25.3 (1423)	21.6 (242)	13.5 (172)	3.6 (23)	16.2 (484)
Missing	4.6 (1224)	2.8 (337)	3.2 (63)	9.8 (612)	0.3 (3)	3.1 (41)	0.0 (0)	5.3 (168)
Alcohol consumption during pregnancy								
Non-consumer	51.8 (12,770)	42.3 (5059)	73.9 (1461)	59.3 (3355)	51.4 (565)	93.6 (1230)	31.1 (189)	44.4 (911)
Consumer	48.3 (11,908)	57.7 (6905)	26.1 (517)	40.8 (2307)	48.6 (535)	6.4 (84)	68.9 (419)	55.6 (1141)
Missing	6.6 (1732)	0.0 (0)	0.0 (0)	9.4 (584)	1.9 (21)	0.0 (0)	3.7 (23)	35.0 (1104)
Physical activity level during pregnancy								
Low	37.6 (6349)	36.6 (3628)	50.3 (964)	n.a.	37.3 (345)	36.6 (318)	33.6 (212)	33.4 (882)
Medium	33.8 (5714)	34.1 (3381)	28.4 (545)	n.a.	31.5 (291)	42.2 (367)	34.5 (218)	34.5 (912)
High	28.7 (4845)	29.4 (2914)	21.3 (408)	n.a.	31.2 (289)	21.3 (185)	31.9 (201)	32.1 (848)
Missing	36.0 (9502)	17.1 (2041)	3.1 (61)		17.5 (196)	33.8 (444)	0.0 (0)	16.3 (514)

Abbreviations: DASH, Dietary Approaches to Stop Hypertension. E-DII, energy-adjusted Dietary Inflammatory Index. BMI, Body Mass Index. n.a., not available.

Values are mean (SD) for continuous variables and % [excluding missing values] (n) for categorical variables.

<sup>a</sup> Second gravida was a recruitment criterion for ROLO.

<sup>b</sup> For EDEN, maternal ethnicity was proxied by place of birth using the question “Are you born in Europe? Outside Europe?”, because specific question on ethnicity was not allowed.

<sup>c</sup> “White Irish” and “European white” were recruitment criteria for Lifeways and REPRO\_PL, respectively.

<sup>d</sup> Weight measured or reported at inclusion or during early pregnancy follow-up has been used, when available, to impute missing values: EDEN: 9 cases (Gestational age (GA) = 12.6 ± 1.1 [mean ± sd]), Generation R: 575 cases (GA = 14.1 ± 1.6), REPRO\_PL: 5 cases (GA = 10.3 ± 1.7), ROLO: 629 cases (all the sample) (GA = 12.8 ± 2.3), SWS: 8 cases (GA = 12.2 ± 1.1).



### 3.1. DASH & E-DII scores

Mean (SD) of DASH scores ranged from 23.7 (4.6) to 24.1 (4.4) depending on cohorts and periods, as expected by construction. ALPHABET's average E-DII scores were 0.2 (1.7) and 0.3 (1.7) for the pre-pregnancy and pregnancy periods, respectively; some differences between cohorts and periods were observed, however, with a range from  $-1.1$  (1.5) (REPRO\_PL, pregnancy) to  $0.9$  (1.7) (EDEN, pregnancy) (Table 2). Spearman correlations between DASH and E-DII scores (Fig. 1) were negative and mostly moderate, with small variations depending on cohorts and periods; it ranged from  $-0.63$  (95% CI:  $-0.66$ ,  $-0.59$ ) and  $-0.63$  ( $-0.65$ ,  $-0.60$ ) for Lifeways and SWS, respectively, to  $-0.48$  ( $-0.49$ ,  $-0.47$ ) for ALSPAC.

### 3.2. Maternal predictors associated with DASH and E-DII scores

Regarding maternal sociodemographic predictors, older age (Fig. 2A) and higher educational level (Fig. 2B) were consistently associated with a better dietary quality and an anti-inflammatory diet during both pre-pregnancy and pregnancy periods. Indeed, associations of older maternal age with the DASH were found in all cohorts but REPRO\_PL, and associations of medium (vs high) educational level with both the DASH and E-DII scores were found in all cohorts but ROLO. Overall, multiparity was associated with a lower dietary quality and a more proinflammatory diet (Fig. 2C), although not in SWS in pre-pregnancy and REPRO\_PL during pregnancy. Maternal birthplace/ethnicity was not associated with neither dietary quality nor inflammatory potential (Fig. 2D). In analyses restricted to the four cohorts with information on household income (Fig. 3A), low (vs high) household income was associated with a lower dietary quality during pregnancy, whereas both low and medium household income were associated with a more proinflammatory diet before and during pregnancy.

Examining maternal health and behavioural predictors, obese women before pregnancy had lower pregnancy DASH score than women with normal BMI in two cohorts only (ALSPAC and Generation R) (Fig. 2E). E-DII scores did not differ significantly by pre-pregnancy BMI. Women who smoked during pregnancy had poorer dietary quality and more proinflammatory dietary scores

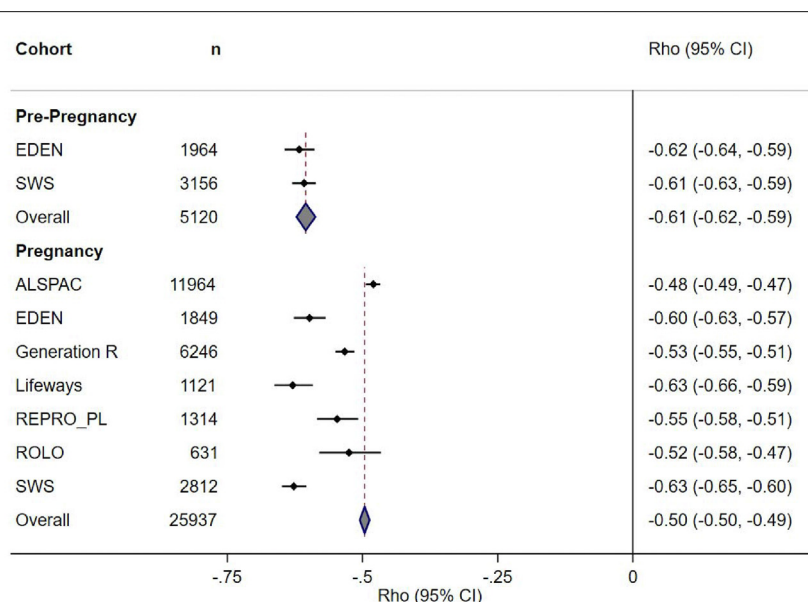
before and during pregnancy (Fig. 2F). Maternal alcohol consumption during pregnancy was associated with a more anti-inflammatory diet during the pre-pregnancy period, but a more proinflammatory diet during the pregnancy period (Fig. 2G). Maternal alcohol consumption was not related to dietary quality before or during pregnancy. Finally, low physical activity level during pregnancy was associated with a lower dietary quality and a more proinflammatory diet during pregnancy (Fig. 3B).

Sensitivity analyses accounting for the nine predictors (including household income and physical activity) available only in three cohorts (ALSPAC, EDEN, and Lifeways) yielded similar results and conclusions than the main analyses accounting for only the seven predictors available in all cohorts (Supplemental Tables S3–4). In models with the DASH as the outcome, sensitivity analysis with further adjustment for energy intake and exclusion of participants with implausible energy intake also yielded similar results, overall (Supplemental Table S5). Two slight changes should be noted (Supplemental Table S6). Parity remained associated with the pre-pregnancy DASH in one out of two studies but became non-significant, overall. Maternal birthplace/ethnicity remained not associated with the pregnancy DASH in three out of five studies but the overall effect became significant. In both cases, we did not observe changes in the other periods and scores.

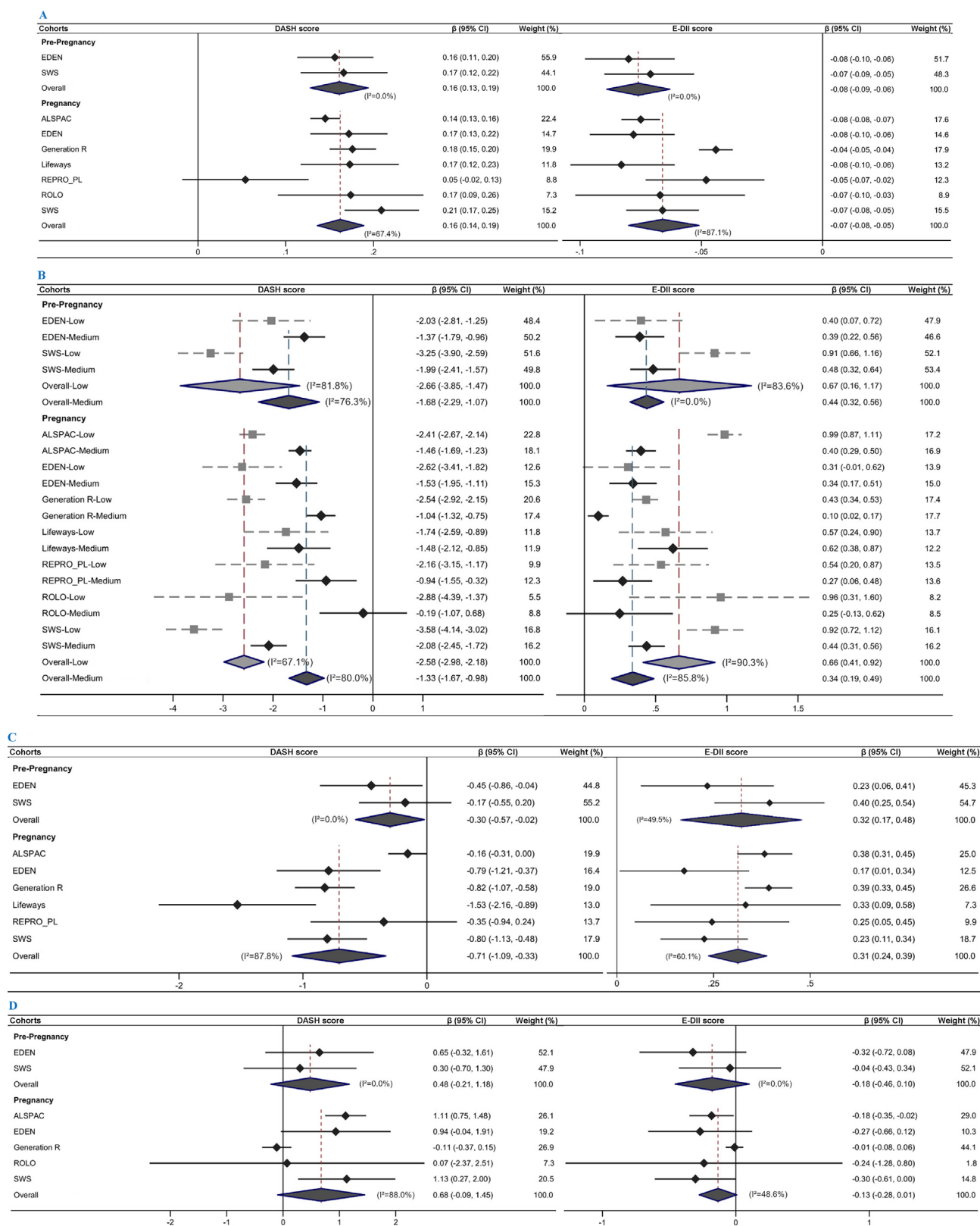
## 4. Discussion

### 4.1. Findings summary

Using dietary data from seven European pregnancy cohorts, we report that DASH scores (higher values indicating better dietary quality) and E-DII scores (lower values indicating less inflammatory diets) were moderately and negatively correlated with each other. We identified consistent associations between older maternal age, higher educational level, higher household income, and higher physical activity level during pregnancy with a greater dietary quality and anti-inflammatory potential. Conversely, multiparity and smoking during pregnancy were associated with a lower dietary quality and a more proinflammatory diet. Maternal obesity was related to poorer dietary quality during pregnancy but not to dietary inflammatory potential; while maternal alcohol



**Fig. 1.** Forest plot of Spearman's correlation coefficients between DASH and E-DII scores by cohort and period in ALPHABET. Abbreviations: DASH, Dietary Approaches to Stop Hypertension. E-DII, energy-adjusted Dietary Inflammatory Index. Mean score of early pregnancy and late pregnancy when both available for SWS.



**Fig. 2.** Forest plots of the adjusted associations of seven predictors (panels A–G) with maternal dietary quality (DASH) and dietary inflammatory potential (E-DII). Predictors are as follows: age (in years; panel A), educational level (reference = high; panel B), parity (reference = primiparous; panel C), birthplace/ethnicity (reference = European-born/White; panel D), pre-pregnancy BMI (reference = normal; panel E), smoking status during pregnancy (reference = non-smoker; panel F) and alcohol consumption during pregnancy (reference = non-consumer; panel G). Values are standardized regression coefficients ( $\beta$ ), and their 95% confidence intervals (CI), study weights (%) and  $I^2$  statistics. Models were mutually adjusted for the seven predictors available in all cohorts: age, educational level, parity, ethnicity/birthplace, pre-pregnancy BMI, smoking status during pregnancy, and alcohol consumption during pregnancy. Panel A: Regression coefficients are expressed as changes in standardized DASH/E-DII scores per 1 year increment in maternal age. Panel B: Regression coefficients are expressed as changes in standardized DASH/E-DII scores per category of educational (low category – gray square or medium

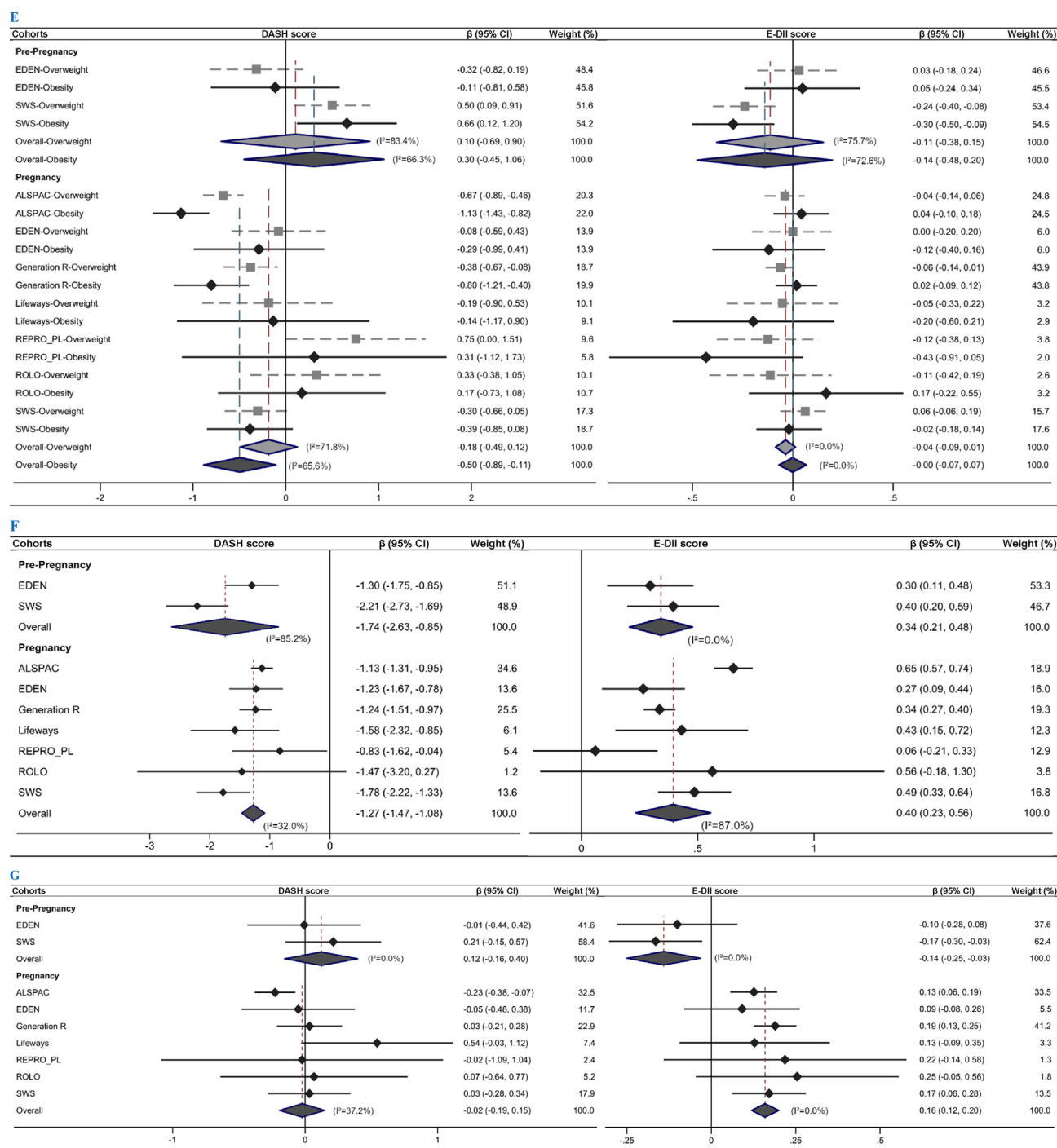
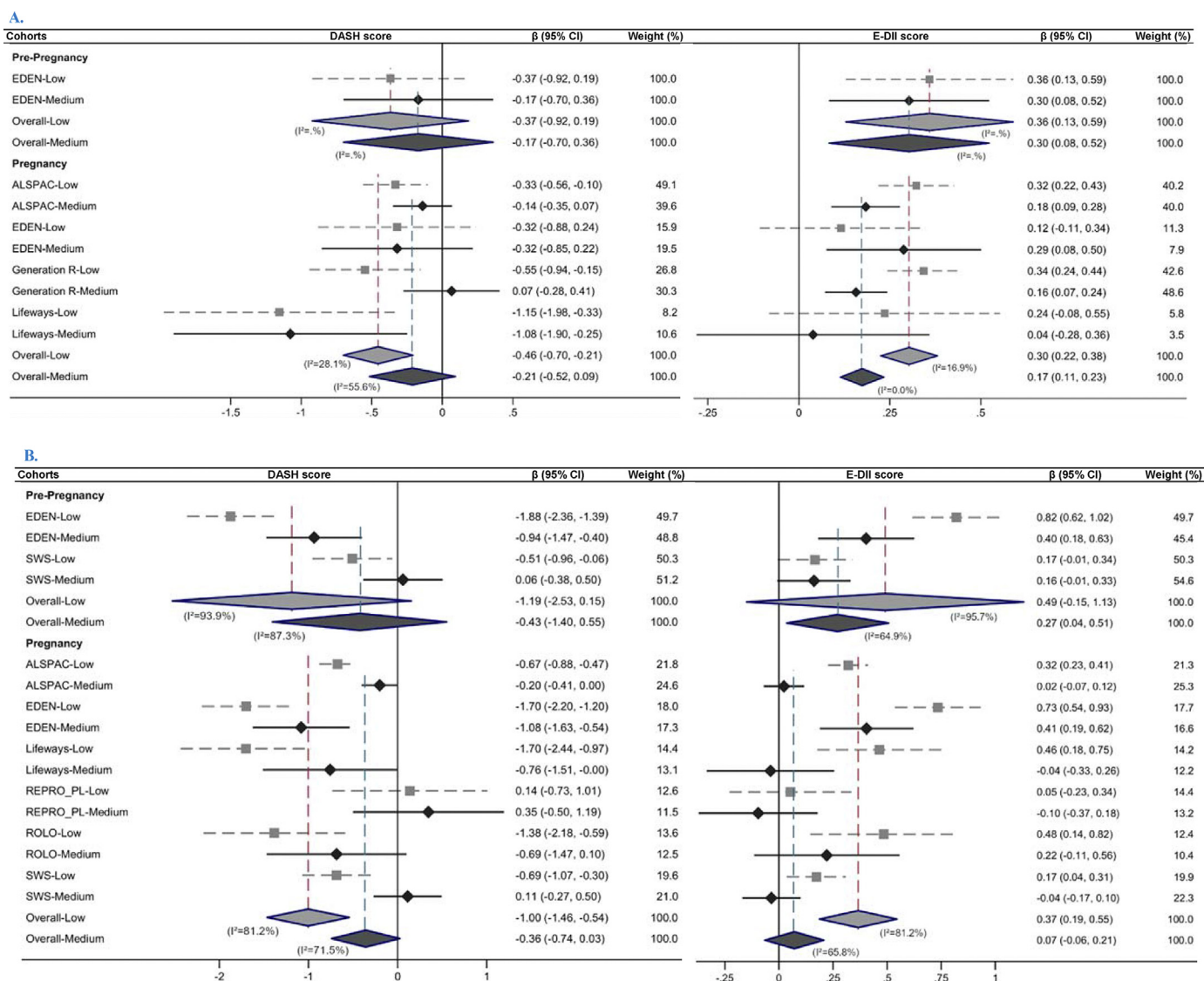


Fig. 2. (continued).

category – black lozenge, in comparison with the high category – reference category). Panel C: Regression coefficients are expressed as changes in standardized DASH/E-DII scores for multiparous mothers in comparison to primiparous mothers (reference category). Second gravida was a recruitment criterion for ROLO. Panel D: Regression coefficients are expressed as changes in standardized DASH/E-DII scores for Non-European-born/Non-White mothers in comparison to European-born/White mothers (reference category). For EDEN, maternal ethnicity was proxied by place of birth using the question “Are you born in Europe? Outside Europe?”, because specific question on ethnicity was not allowed. “White Irish” and “European white” were recruitment criteria for Lifeways and REPRO\_PL, respectively. Panel E: Regression coefficients are expressed as changes in standardized DASH/E-DII scores per category of pre-pregnancy BMI (overweight category – gray square or obesity category – black lozenge, in comparison with the normal range category – reference category). Because the first category of BMI “underweight” was not significantly associated and with small frequencies in most cohorts, it is not represented in this forest plot for the sake of readability. Weight measured or reported at inclusion or during early pregnancy follow-up has been used, when available, to impute missing values: EDEN: 9 cases (Gestational age =  $12.6 \pm 1.1$  [mean  $\pm$  SD]), Generation R: 575 cases ( $14.1 \pm 1.6$ ), REPRO\_PL: 5 cases ( $10.3 \pm 1.7$ ), ROLO: 629 cases (all the sample) ( $12.8 \pm 2.3$ ), SWS: 8 cases ( $12.2 \pm 1.1$ ). Panel F: Regression coefficients are expressed as changes in standardized DASH/E-DII scores for smoker mothers in comparison to non-smoker mothers (reference category). Panel G: Regression coefficients are expressed as changes in standardized DASH/E-DII scores for alcohol consumer mothers in comparison to non-consumer mothers (reference category). Abbreviations: DASH, Dietary Approaches to Stop Hypertension; E-DII energy-adjusted Dietary Inflammatory Index; BMI, body mass index.



**Fig. 3.** Forest plots of the adjusted associations of two predictors with cohort-specific missing data (panels A and B), with maternal dietary quality (DASH) and dietary inflammatory potential (E-DII). Predictors are as follows: household income (available for ALSPAC, EDEN, Generation R, and Lifeways only; reference = higher tertile; panel A) and physical activity level during pregnancy (not available for Generation R only; reference = higher tertile; panel B). Values are standardized regression coefficients ( $\beta$ ), and their 95% confidence intervals (CI), study weights (%) and  $I^2$  statistics. All models were adjusted for the seven predictors available in all cohorts: age, educational level, parity, ethnicity/birthplace, pre-pregnancy body mass index, smoking status during pregnancy, and alcohol consumption during pregnancy. Panel A: Regression coefficients are expressed as changes in standardized DASH/E-DII scores per category of household income (defined as cohort-specific tertiles) (low category – gray square or medium category – black lozenge, in comparison with the high category – reference category). Panel B: Regression coefficients are expressed as changes in standardized DASH/E-DII scores per category of physical activity level during pregnancy (defined as cohort-specific tertiles) (low category – gray square or medium category – black lozenge, in comparison with the high category – reference category). Abbreviations: DASH, Dietary Approaches to Stop Hypertension. E-DII, energy-adjusted Dietary Inflammatory Index.

consumption during pregnancy was associated with E-DII score only (with an anti-inflammatory potential pre-pregnancy and proinflammatory potential in the pregnancy period).

#### 4.2. Dietary data and predictors of dietary quality and dietary inflammatory potential

Correlations between DASH and E-DII scores observed in our study (from  $-0.63$  to  $-0.48$ ) are in concordance with the literature. A previous study comparing the DII with other diet scores reported a similar correlation with DASH ( $r = -0.52$ ) [48]. Collectively, this suggests that both scores are complementary for assessing the complexity of diet [48].

We found that maternal age, education level and household income were consistently and positively associated with dietary

quality and anti-inflammatory potential. These results reinforce findings already described in the literature [10,49,50]. In our study, multiparity was mostly associated with a lower dietary quality and more proinflammatory potential. This association has been suggested in some studies (e.g., with “Alternate Healthy Eating Index” or “Western diet”) [8,51] but seems inconsistent overall [10]. We report null findings for maternal birthplace/ethnicity and both dietary scores before and during pregnancy, except with the DASH during pregnancy after adjustment for energy intake and exclusion of participants with likely implausible energy intake. This sensitivity analysis changed slightly the effect for Generation R (remaining not associated in three out of five studies) and resulted in an overall effect which became significant. The literature is inconsistent in this regard [49,52,53], and our finding may be explained by the adjustment for other sociodemographic factors including maternal age,



educational level or parity [10]. Moreover, the “non-European-born/non-white” group is not homogenous in the ALPHABET consortium and probably constituted of various ethnic groups. Last and already discussed in another article of the consortium [19], the FFQs were mainly validated in European-born/White women (e.g., in Generation R), introducing potential heterogeneity and measurement error for non-European-born/non-White women.

Obesity, but not overweight, was associated with poorer dietary quality during pregnancy but not with the dietary inflammatory potential. In the literature, the association between diet and BMI categories has already been presented as inconsistent [52,54,55]. Indeed, the relation between pre-pregnancy BMI and prenatal diet is difficult to interpret because BMI could be a determinant but also a consequence of dietary quality [10]. In addition, anthropometric measures were assessed at different times depending on the cohort and self-reported weight is known to be subject to misestimation [56], which could affect associations. Detrimental behaviours such as smoking during pregnancy has been associated with poorer dietary quality in several studies [49,57,58]. We also found smoking during pregnancy associated with poorer dietary quality and a more proinflammatory score, for both periods. Less commonly examined [10], maternal alcohol consumption was associated with the E-DII, but not the DASH score, and in different directions depending on the period (positively at pre-pregnancy and negatively during pregnancy). These discrepancies might be explained by the methodological variations of when/how the behaviour was assessed, the inconsistency of association between alcohol consumption during pregnancy and socio-demographic variables [59], and the differences of consumption between countries and periods [60–62]. Last, alcohol consumption was dichotomized and these results could be different with information on the quantity. Physical activity during pregnancy, already found to be positively associated with diverse dietary quality scores [57,63], was associated in this study with a better dietary quality and a higher anti-inflammatory potential during pregnancy. Indeed, associations of low (vs high) physical activity level with dietary scores during pregnancy were found in all cohorts (excluding Generation R without this information) but REPRO\_PL.

Our dietary score-specific findings (e.g., parity, maternal alcohol consumption during pregnancy) highlight potential benefits of using complementary tools to characterize diet in nutritional epidemiological studies. Furthermore, differences between dietary scores could also explain between-study discrepancies in determinants of dietary patterns and dietary quality, as revealed by the systematic review of Doyle et al. [10]. Three main points could explain the high heterogeneity of some of the presented results. First, the cohorts represent different generational cohorts because recruitment periods ranged from 1990 to 2011; some behaviours including smoking status and alcohol consumption have evolved importantly over decades in some countries [60,62]. Second, differences in maternal sociodemographic characteristics including age, educational level or birthplace/ethnicity between cohorts highlight diverse populations. Finally, some of the variability between cohorts can be explained by the methodological recall of some covariates. Harmonisation of certain variables (e.g., educational level) [41] is straightforward, whereas other maternal health and behavioural factors may differ between cohorts, depending on timing and how the questions were worded (e.g., smoking status asked during the 1st or the 2nd trimester of pregnancy). However, using an individual participant data meta-analysis process in two-steps permits adjustment for cohort effect and limits the impact of such variability on our results.

#### 4.3. Strengths and limitations

The main strengths of this study include its large sample size of >26,000 pregnant women from seven cohorts conducted in five

European countries, the availability of individual data which permits to proceed to an individual participant data meta-analysis with several common covariates, and the consistency of the main results. Despite its strengths, the study has limitations. Dietary quality has been measured based on self-reported FFQs, which are subject to recall biases. However, most tools were validated within each cohort and, as highlighted by Olsen et al. [60] (when merging dietary data from the world's two largest pregnancy cohorts), tool differences could lead to some differences in food and nutrient intake estimates. However, these variations would be systematic within each cohort and adjustment for this “cohort effect” in analyses might (at least partially) offset disparities. In addition, our overall population is mainly composed of European-born/White women; so, our results may only partly be generalizable to other populations. A final limitation is the observational design and measurement of the different predictors at the same time as dietary quality.

This work may open important perspectives for research and in public health. Since our objective was to identify predictors of maternal dietary quality, and not to determine causality,<sup>23</sup> future observational and interventional studies are needed to better decipher whether some of the identified predictors may be causal, and understand the causal cascade at play. Still, the estimates reported in our study are clinically meaningful: we found that low (vs high) education was associated with a 2.58-point decrease (i.e., 0.61-SD) and 0.66-point increase (i.e., 0.39-SD) in maternal pregnancy DASH and E-DII scores, respectively. Taking previous results from the ALPHABET consortium as an illustration, a 1-SD increase in the DASH (4.2 points) or decrease in the E-DII (1.7 points) has been found to be associated with a 13% and 18% lower risk of small-for-gestational risk, respectively [18]. However, some of the potential causal predictors may not be directly modifiable, reason why the most important perspective derived from our study is not about determining causality. Indeed, our work identifies commonly available predictors consistently associated with maternal dietary quality and dietary inflammation across European countries, which paves the way for large-scale dietary interventions targeting the women the most at-risk of having poorer diet before and during pregnancy. Because the different cohort studies included in the ALPHABET consortium have been selected *a priori* to specifically investigate maternal dietary quality and inflammatory potential, and associations with child health and development [17], results must not be seen as deriving from a systematic review of the literature. Last, the use of an individual participant data meta-analysis based on harmonized data yields more reliable and robust evidence than aggregate data meta-analysis [24].

#### 5. Conclusion

To our knowledge, this study is the largest meta-analysis of the predictors of dietary quality conducted in pregnant women enrolled in European mother-child cohorts. Our findings may help health professionals and policy makers identify specific population subgroups who could benefit from targeted public health messages and to design interventions to improve maternal nutrition quality before and during pregnancy. It could subsequently translate into improved clinical outcomes for the mothers and their offspring given the importance of nutrition over the first 1000 days of life.

#### Ethical approvals

Specific cohort approvals are as follows: **ALSPAC**: ALSPAC Ethics and Law Committee (IRB00003312) and Local Research Ethics

Committees; **EDEN**: Ethics Committee (CCPRB) and CNIL (Commission Nationale Informatique et Liberté), the French data privacy institution; **Generation R**: Medical Ethical Committee of the Erasmus Medical Center, Rotterdam; **Lifeways**: University College Dublin Research Ethics Committee and St. Vincent's University Hospital Research Ethics Committee; **REPRO\_PL**: Ethical Committee of the Nofer Institute of Occupational Medicine, Łódź, Poland (Decision No. 7/2007); **ROLO**: Ethics Committee of the National Maternity Hospital, Dublin, Ireland; **SWS**: Southampton and South West Hampshire Research Ethics Committee, ALSPAC Law and Ethics Committee, and the Local Research Ethics Committees.

## Author contributions

Adrien M. Aubert: Conceptualization, Data curation, Formal analysis, Methodology, Software, Visualization, Writing – original draft, Writing – review and editing.

Ling-Wei Chen: Conceptualization, Software, Validation, Writing – review and editing.

Nitin Shivappa: Conceptualization, Validation, Writing – review and editing.

Cyrus Cooper: Writing – review and editing.

Sarah R. Crozier: Writing – review and editing.

Liesbeth Duijts: Funding acquisition, Investigation, Resources, Writing – review and editing.

Anne Forhan: Conceptualization, Data curation, Formal analysis, Methodology, Software, Writing – review and editing.

Wojciech Hanke: Data curation, Funding acquisition, Investigation, Resources, Writing – review and editing.

Nicholas C. Harvey: Funding acquisition, Investigation, Resources, Writing – review and editing.

Agnieszka Jankowska: Data curation, Writing – review and editing.

Cecily C. Kelleher: Writing – review and editing.

Blandine de Lauzon-Guillain: Data curation, Writing – review and editing.

Fionnuala M. McAuliffe: Writing – review and editing.

Sara M. Mensink-Bout: Writing – review and editing.

Kinga Polanska: Data curation, Funding acquisition, Investigation, Resources, Writing – review and editing.

Caroline L. Relton: Funding acquisition, Investigation, Resources, Writing – review and editing.

Matthew Suderman: Data curation, Funding acquisition, Investigation, Resources, Writing – review and editing.

Catherine M. Phillips: Conceptualization, Funding acquisition, Investigation, Project administration, Resources, Writing – review and editing.

James H. Hebert: Conceptualization, Validation, Writing – review and editing.

Jonathan Y. Bernard: Conceptualization, Methodology, Project administration, Software, Supervision, Validation, Writing – original draft, Writing – review and editing.

Barbara Heude: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Writing – original draft, Writing – review and editing.

Jonathan Y. Bernard and Barbara Heude contributed and supervised equally the work of this article.

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## Conflicts of interest

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 smartphone applications for patient counselling and dietary intervention in clinical settings. Dr. Nitin Shivappa is an employee of CHI. All other authors declare no support from any organisation for the submitted work other than those described above; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clnu.2022.06.042>.

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