Dietary patterns at 6, 15 and 24 months of age are associated with IQ at 8 years of age

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ABSTRACT

Diet supplies the nutrients needed for the development of neural tissues that occurs over the first 2 years of life. Our aim was to examine associations between dietary patterns at 6, 15 and 24 months and intelligence quotient (IQ) scores at 8 years. Participants were enrolled in an observational birth cohort (ALSPAC study, n=7097). Dietary data was collected by questionnaire and patterns were extracted at each time using principal component analysis. IQ was measured using the Wechsler Intelligence Scale for Children at 8 years. Associations between dietary patterns and IQ were examined in regression analyses adjusted for potential confounding and by propensity score matching, with data imputation for missing values. At all ages, higher scores on a *Discretionary* pattern (characterized by biscuits, chocolate, sweets, soda, crisps) were associated with 1-2 point lower IQ. A *Breastfeeding* pattern at 6 months and *Home-made contemporary* patterns at 15 and 24 months (herbs, legumes, cheese, raw fruit and vegetables) were associated with 1-to-2 point higher IQ. A *Home-made traditional* pattern (meat, cooked vegetables, desserts) at 6 months was positively associated with higher IQ scores, but there was no association with similar patterns at 15 or 24 months. Negative associations were found with patterns characterized by *Ready-prepared baby foods* at 6 and 15 months and positive associations with a *Ready-to-eat foods* pattern at 24 months. Propensity score analyses were consistent with regression analyses. This study suggests that dietary patterns from 6-24 months may have a small but persistent effect on IQ at 8 years.

KEYWORDS:

Dietary patterns, infant, toddler, intelligence quotient, ALSPAC

ABBREVIATIONS:

ALSPAC	Avon longitudinal study of parents and children
CSE	Certificate of secondary education
FSIQ	Full scale intelligence quotient
HM	Home-made
IQ	Intelligence quotient

45	PCA	Principal component analysis
46	PIQ	Performance intelligence quotient
47	RM	Ready-prepared
48	VIQ	Verbal intelligence quotient
49	WISC	Wechsler intelligence scale for children

50 **Introduction**

51 Infant diets supply the nutritional substrate for the rapid growth and brain development that
52 occurs in the first years of life. Evidence from observational studies and randomized trials
53 suggests that the postnatal diet may have a lasting influence on child development, even in the
54 absence of overt nutritional deficiencies. For example, prolonged breastfeeding is thought to
55 lead to a higher intelligence quotient (IQ) scores in childhood [1, 2], while supplementing
56 infants with iron-enriched formula may influence cognitive and behavioral outcomes in
57 childhood [3]. In addition to iron, other nutrients have been linked to child development or
58 cognition [4, 5].

59

60 Nutrient intakes are correlated and one of the limitations of examining associations between
61 single nutrients and cognitive outcomes is that the synergistic effect of the entire diet is not
62 examined. Although multivariate methods exist to examine whole diets, there is a paucity of
63 studies linking whole diets of infants to cognitive development [6]. One small study (n=241)
64 has shown that a dietary pattern characterised by breastfeeding and consumption of fruits,
65 vegetables and home-made foods at 1 year of age was associated with a ~2.7 point increase in
66 full scale IQ measured by the Wechsler Preschool and Primary Scale of Intelligence at 4 years
67 of age [7]. Northstone *et al* showed that dietary patterns at 3 years of age had stronger
68 associations with IQ at 8, than patterns at 4, 7 or 8 years [8], supporting the concept that the
69 cognitive development of younger children may be more sensitive to diet.

70

We have previously characterized dietary patterns of 6- and 15-month old children participating in a large population-based birth cohort called the Avon Longitudinal Study of Parents and Children (ALSPAC) [9]. Four patterns were extracted at both ages and three of these patterns were similar. The first pattern common to both ages was characterized by home-cooked meat, vegetables and desserts (henceforth referred to as '*Homemade traditional*' pattern). The second pattern was characterized by discretionary foods such as biscuits, sweets and crisps ('*Discretionary*' pattern), and the third pattern was characterised by and named *Ready-prepared baby foods*. At 6 and 15 months of age, a fourth pattern was characterised by breastfeeding ('*Breastfeeding*') and by contemporary-style foods including herbs, legumes, nuts, raw fruit and vegetables (*Home-prepared contemporary*'), respectively. The aim of this study is to characterize dietary patterns at 24 months of age and examine whether patterns at 6, 15 and 24 months are associated with IQ scores at 8 years of age.

Subjects and Methods

ALSPAC cohort

ALSPAC is a longitudinal birth cohort study designed to investigate the determinants of health and development [10]. All pregnant women residing in the former county of Avon, UK who were expected to deliver between April 1991 and December 1992 were invited to participate. The core ALSPAC sample consists of 14,541 pregnancies and 13988 infants who survived to 1 year of age. The study sample is broadly representative of the population living in Avon at the time although ethnic minorities, single parents and unmarried couples were slightly underrepresented when compared with the 1991 National Census of women with infants under 1 year residing in Avon. Ethical approval for the study was obtained from the ALSPAC Law and Ethics Committee and local Research Ethics Committees. All participants gave informed consent.

Dietary data and pattern analysis

Child food and beverage intake data was collected by caregiver-completed postal questionnaire when the study child was 6, 15 and 24 months of age. To maintain the response rate, postal reminders were sent if questionnaires were not returned within one month. Caregivers were asked to document the frequency of consumption of foods and beverages commonly fed to infants and toddlers. The questionnaire included 43 food and beverage items at 6 months, 70 items at 15 months and 72 items at 24 months of age. The food items included in the questionnaires were determined by an experienced nutritionist (PE). Questionnaires included specific items on the frequency of consuming foods prepared in the home and ready-prepared retail foods manufactured for infants and toddlers. Participants were asked how old the child was when an item was first introduced and how many times per week they fed their child each food item. Infants who had never been fed an item were given an intake of zero. Only questionnaires with complete information on all diet questions were used for principal component analysis (PCA).

PCA analysis of dietary data from the questionnaire at 24 months of age is currently under review (K Northstone personal communication, 2011). However, we conducted a separate PCA analysis to ensure consistency with the procedure we applied at 6 and 15 months. Briefly, non-standardised food and beverage data collected at 24 months of age were entered into PCA analysis with Oblimin rotation. Thirty-one food items with low communalities that made almost no contribution to the PCA solution were removed from the analysis to aid statistical convergence. Four patterns were extracted based on the Scree plot, interpretability and consistency with dietary patterns at 6 and 15 months. Dietary pattern scores were computed by summing the product of a standardized frequency of consumption for each food item by its factor loading. Patterns were approximately normally distributed, had a mean of

zero and standard deviation of one. Patterns were named based on foods with loadings $\geq |0.3|$. PCA analysis was conducted using PASW software (Version 17.0, Chicago Illinois).

IQ data

At 8 years of age, all ALSPAC children were invited to attend a clinic where their cognitive ability was assessed using an adapted form of the Wechsler Intelligence Scale for Children (WISC) Version III [11]. WISC assessments were administered by trained psychologists. To reduce participant burden, alternate items from each of the 10 WISC subtests was administered (5 verbal and 5 performance subtests), except for the coding subtest which was administered in full. To be comparable with administration of the full WISC assessment, raw scores were calculated by summing the individual items on each subtest and multiplying by 2 for picture completion, information, arithmetic, vocabulary, comprehension and picture arrangement, multiplying by 1.67 for similarities and multiplying by 1.5 for object assembly and block design. Raw scores were converted to age-standardized scores and combined to determine Full Scale IQ (FSIQ) and subscales of Verbal (VIQ) and Performance IQ (PIQ).

Covariables

Covariables were decided *a priori* based on a causal model of influences on infant feeding, nutritional status at birth and IQ. Covariables included; maternal age, education, social class, marital status, tobacco smoking, family income, parity, ethnicity and number of children (<16 years old) living in the family home. These data were collected by postal questionnaires sent to the mother. Maternal education was reported as the highest completed level on five categories from Certificate of Secondary Education (CSE), Vocational training, O-levels, A-levels and degree or higher. The CSE, O- and A-levels are completed at secondary school. O-levels are usually studied at age 16 and A-levels at 18 years. Social class was categorized according to maternal occupation using standard UK classifications of occupation, ranging from class I (highest), II, III-non-manual, III-manual, IV, and V (lowest) [12]. Marital status

was categorized into the following four categories; first marriage, subsequent marriage/s, formerly married (now divorced, widowed or separated) and never married. Tobacco smoking was divided into three categories; never, quit or smoked in the last 2 months of pregnancy. Family income was divided into five £100 categories ranging from £<100 to £>400/week. Categories for the number of children living in the family home were none, 1, 2, 3 and ≥ 4 . Infant covariables including sex, gestational age at birth, birth weight and singleton/multiple birth information was collected by ALSPAC staff at delivery, from medical records or from birth notification. Stimulation in the home environment was measured by an adaptation of the HOME questionnaire at 18 months of age [13].

Statistical analyses

Linear regression analysis was used to examine associations between dietary pattern scores and FSIQ, subscales of VIQ and PIQ. The first regression model included the four PCA patterns scores extracted at one time point, with subsequent models adjusting for perinatal (sex, gestational age, birth weight, ethnicity, singleton/twin, maternal age and parity) and sociodemographic variables (maternal education, social class, smoking, marital status, family income, HOME score and other children). The final model at 15 and 24 months of age included all covariables and dietary pattern scores at younger ages (i.e. the model at 15 months of age included 6 month dietary pattern scores; the model at 24 months of age included 6 and 15 month dietary pattern scores). The beta coefficient in the final model is indicates the independent effect of the current dietary patterns after accounting for past dietary patterns. Regression coefficients (β) and 95% confidence intervals were used to evaluate the strength and precision of the associations between dietary patterns and IQ scores. The primary analysis examined the effect of dietary patterns scores at 6, 15 and 24 months of age on FSIQ, with concurrent adjustment for other patterns, perinatal and sociodemographic variables. Secondary analyses included the effect of dietary patterns on Performance and Verbal

subscale of IQ, with adjustment for confounders and other dietary patterns. Statistical analyses were conducted using STATA (IC11.0, StataCorp TX, USA).

Multiple Imputation

Multiple imputation was used to address missing data [14]. Imputed datasets were generated using Multiple Imputation by Chained Equations under the missing at random assumption. Missing at random is the probability that a missing value does not depend on itself after accounting for other observed explanatory variables [15]. The imputation model included the four dietary patterns at 6, 15 and 24 months of age (i.e. 12 dietary pattern scores in total), all covariables listed above and scores on all three measures of IQ (FSIQ, VIQ, PIQ). Dietary pattern scores and covariables were imputed for those with at least one of the IQ subscales measured at 8 years of age. Twenty imputed datasets were generated, using 50 cycles of regression switching [16]. The distribution of imputed variables was comparable with the non-missing data (data not shown). Regression coefficients for the 20 imputed datasets were combined using Rubin's rules [17]. We report the imputed analyses rather than complete case analyses to address possible non-response bias as some of the potentially confounding variables differed between respondents and non-respondents.

Propensity score

Propensity score matching offers an alternative method for adjusting for confounding [18-20]. As a sensitivity analysis, we evaluated the average treatment effect (ATE) of dietary pattern scores on FSIQ, VIQ and PIQ by propensity score matching. Using probit regression, the propensity score was calculated as the probability of being in the highest versus the lowest tertile of dietary pattern scores, conditional on the covariates listed above. Probabilities of being in the highest versus lowest tertile were then matched across the area of common support (where the distribution of propensity scores overlap) using the nearest neighbor matching method with callipers set to $0.2 \times SD$ [21]. This method matches participants with

high and low dietary pattern scores on their probability of being in the highest versus lowest tertile of dietary pattern score, conditional on all covariables. Other methods of propensity score matching showed similar results, such as matching by radius (at 0.01) and greedy matching with ratios of high: low pattern scores at 1:2 and 1:5. Propensity scores were matched within each of the imputed dataset, then an overall estimate of ATE and the between-dataset variance was computed using Rubin's rules [17]. Propensity score analyses were conducted using STATA's PSMATCH2 command.

Results

Fig. 1 shows the number of participants at each stage of the study and **Table 1** shows the sociodemographic characteristics of ALSPAC participants who had IQ measured at 8 years. Of the eligible cohort (n=13988), dietary pattern analysis was conducted on 7052 (50.5%), 5610 (40.1%) and 6366 (45.5%) participants at 6, 15 and 24 months of age respectively and IQ measurements were conducted on 7097 (50.8%) participants. Of the participants with IQ measurements, those with complete information for all dietary pattern scores and covariables was n=1366. This group differed from participants with one or more data items missing (n=5731). Those with complete data included higher proportions of children of white ethnicity, mothers of higher social classes, higher educational qualifications and fewer mothers who smoked during pregnancy and were unmarried. Family income and social class comprised the two variables with the biggest proportion of missing socio-demographic data (24.1% and 20.3%, respectively).

Dietary patterns

Dietary patterns at 6 and 15 months have been described previously [9]. At 24 months of age, four dietary patterns were extracted and are named *Home-made traditional*, *Contemporary*, *Discretionary* and *Ready-to-eat foods*. Foods with loadings ≥ 0.3 on the *Home-made traditional* pattern included potatoes (loading 0.76), other vegetables (0.692), meat products

(0.667), gravy/soy sauce (0.574), green beans (0.531). Foods loading on the *Contemporary* pattern included legumes (0.592), raw apple (0.488), other raw fruit (0.557), herbs (0.486), cheese (0.461), apple juice (0.394), other fruit juice (0.357) and egg (0.373). Foods loading on the *Discretionary* pattern included crisps (0.642), sweets (0.597), fizzy drink (0.557), chocolate (0.544), cola (0.536), tomato ketchup (0.488), savoury snacks (0.414), baked beans (0.347) and biscuits (0.304). Finally, food loadings for the *Ready-to-eat foods* pattern included biscuits (0.650), bread/toast (0.617), breakfast cereal (0.565), yoghurt (0.333), milk pudding (0.330) and cola (-0.304). A complete list of loadings for each dietary pattern and all food items entered into the PCA are provided in **Online Resource 1**.

Regression analysis: effect of dietary patterns at 6, 15 and 24 months of age on IQ at 8 years

Results from imputed analyses are reported because participants with complete data differed from those with missing data on one or more potentially confounding variables. **Table 2** shows the association between dietary pattern scores at 6 months of age and IQ at age 8 years after adjusting for other pattern scores at 6 months (model 1) and potentially confounding covariables (model 2). Higher scores on the *Home-made traditional* pattern and the *Breastfeeding* patterns were associated with higher IQ scores, whereas *Ready-prepared baby foods* and *Discretionary* patterns were associated with lower IQ scores at 8 years. Adjustment for potentially confounding variables attenuated the association between dietary patterns and IQ, except for *Ready-prepared baby foods* pattern, which remained stable. Although confidence intervals are wide, the association between dietary patterns and FSIQ and VIQ was consistent. For example, a one-standard deviation increase in the *Discretionary Foods* pattern score was associated with approximately 1-point lower FSIQ score (β coefficient -1.15 (95%CI -1.80, -0.50) as well as lower scores on the Verbal (-1.23 (-1.93, -0.54)) and Performance (-0.77 (-1.42, -0.12)) subscales.

The association between dietary pattern scores at 15 months of age and IQ (**Table 3**) was consistent with the 6-month data in that patterns were associated with IQ at 8 years (model 1) and effects were attenuated after adjustment for potential confounding (model 2). Because dietary patterns may track over time [22-24], we undertook a third model in which we examined the effect of dietary patterns at 15 months while adjusting for earlier diet at 6 months (model 3). In the fully adjusted model, a 1 SD higher score on the *Home-made contemporary* patterns was positively associated with IQ at age 8 while the *Discretionary* and *Ready-prepared* pattern scores were negatively associated, but the effect was somewhat weaker after adjustment. The *Home-made traditional* pattern at 15 months of age was not an independent predictor of IQ at 8 years after adjustment for potential cofounders and diet at 6 months.

At 24 months of age, the *Contemporary* pattern had a positive association and the *Discretionary* and *Home-made traditional* patterns had weak negative associations with FSIQ, VIQ and PIQ. The fourth *Ready-to-eat foods* pattern at 24 months was different from patterns at earlier ages and after adjustment for potential confounding and other dietary patterns, there was some evidence of a positive association with FSIQ (0.76 (0.23, 1.29)) and VIQ scores (0.90 (0.36, 1.44)), but no association with PIQ (0.37 (-0.18, 0.92)). **Table 4** shows that after adjustment for potentially confounding covariables and for diet at 6 and 15 months, all observed effects of diet pattern at 24 months on IQ were less than one IQ point.

Propensity score analysis: effect of dietary patterns at 6, 15 and 24 months on IQ at 8 years

The direction of the effect in the highest compared with the lowest tertiles of dietary pattern scores (**Table 5**) was consistent with the findings from the regression analyses. In sensitivity analysis, different ways of categorizing dietary pattern scores to obtain a “high” versus a “low” category of diet for generating the propensity score were explored. Dividing dietary

pattern scores into tertiles retained the greatest sample while attaining the clearest separation of scores (compared with the highest versus lowest quintiles or dichotomizing pattern scores). Checks of the matching process showed that covariables were well balanced after matching, with standardized differences in covariables between the high versus low tertiles were generally <10%. The effect size estimated from imputed datasets was more conservative than the complete case analysis. The effect of dietary pattern appears consistently lower on PIQ compared with FSIQ and VIQ. However, the overall effect for dietary pattern scores on IQ was in the range of 1 to 2 IQ points which is similar to the multivariable regression analyses. For example, being in the highest compared with the lowest tertile of *Contemporary* pattern scores at 24 months of age was associated with an average treatment effect of 2.08 points on FSIQ, given other dietary pattern scores (at 6, 15 and 24 months) and covariables.

Tertiles of Dietary Pattern scores and Adjustment for Propensity Scores in Regression Analyses

Effect sizes estimated by regression and propensity scores are not directly comparable. To aid interpretation between these methods of controlling for confounding we conducted regression analyses in the imputed datasets, in which tertiles of dietary pattern scores at 6 months were treated as a continuous diet exposure variables on FSIQ and adjusted for either 1) all other dietary patterns and covariables in their natural units or 2) the propensity score. Tertiles of *Home-made traditional* pattern scores at 6 months were associated with 0.81 (95% CI 0.19, 1.43) and 0.77 (0.13, 1.41) higher FSIQ scores at age 8 years after adjustment for all covariables and for propensity scores, respectively. Associations between tertiles of other pattern scores at 6 months and FSIQ were as follows: *Discretionary* (adjusted for; all covariables -1.06 (-1.66, -0.45), propensity scores -1.05 (-1.69, -0.42)), *Ready-prepared baby foods* (all covariables -0.53 (-1.04, -0.03), propensity scores -0.54 (-1.09, 0.004)) and *Breastfeeding* patterns (all covariables 1.12 (0.53, 1.71) propensity scores 1.19 (0.57, 1.81)).

Discussion

Our analyses suggest that dietary patterns at 6, 15 and 24 months of age make a small contribution to IQ at 8 years of age. The association between dietary patterns and IQ is confounded by sociodemographic factors that differ between participants with complete versus missing data. Therefore multiple imputation was conducted to reduce the risk of non-response bias due to missing data, while propensity score matching was performed as a sensitivity analysis to the regressions and to address possible selection bias. The findings from the regression analysis and propensity scores are consistent. A positive association between the *Breastfeeding* and *Contemporary* dietary patterns and IQ, and a negative association between the *Discretionary* dietary pattern and IQ were consistent across age groups and analysis methods. The effect size from each method is similar when compared on similar scales. The propensity scores are calculated using the outermost tertiles of the dietary pattern distribution, the boundaries of which are ± 2 SD from the mean and therefore the effect size in propensity score-based regressions should be halved when comparing with the effect size in regression analysis. Thus, the effect of a 1 SD higher score in *Discretionary* pattern at 6 months is associated with lower FSIQ scores of 1.15 (95%CI 1.8, 0.5, Table 2) in regression and 1.11 (Table 5) in propensity analyses. For illustration, a 1 SD increase in *Discretionary* scores at 6 months from 1.0 to 2.0 is equivalent to increasing intake of chocolate from <1 to 1.5 times/wk, biscuits from 1.5 to 2.5 times/wk and tea from <1 to 1.5 times/wk, although it must be remembered that diet pattern scores reflect simultaneous intake of all foods.

The *Discretionary* and *Home-made traditional* patterns were present at all ages suggesting that certain styles of diet emerge and persist throughout the first 2 years. However, associations between patterns and IQ differed over time. In the fully adjusted models, the *Discretionary* pattern at all ages was negatively associated with IQ, but the *Home-made*

traditional pattern at 6 months was positively associated, 15 months was not associated and 24 months was negatively associated with IQ. The *Breastfeeding* pattern at 6 months and the *Contemporary* patterns at 15 and 24 months appear to reflect healthier-style diets and are favourably associated with IQ. The *Ready-prepared baby foods* patterns at 6 and 15 months and the *Ready-to-eat foods* pattern at 24 months are characterised by foods that require little cooking or preparation, but despite this similarity, higher scores on the *Ready-made baby foods* pattern was associated with poorer IQ but the *Ready-to-eat foods* pattern was associated with better IQ. This may be because the *Ready-to-eat foods* pattern is characterised by nutrient-rich foods including bread, breakfast cereal, yoghurt and milk pudding.

The concept that infant diet influences cognitive ability has been demonstrated for breastfeeding [1] but there is only one study examining dietary patterns in infancy and IQ [6]. Gale *et al* reported that dietary patterns characterized by fruit, vegetables and home-made foods at 6 and 12 months of age were associated with around a 0.18 standardized increase in IQ scores at 4 years (~2 points), but no association was found with a dietary pattern characterised by breads, savoury snacks, biscuits, pasta and breakfast cereals [7]. Analyses were adjusted for a range of confounders, but the study is limited by the small sample selected from a larger cohort (n=241/1981) and complete case analysis. Despite this, effect sizes of our study are consistent with Gale *et al*. Furthermore, our large sample (n=7097), use of imputation and outcomes based at 8 years provide more convincing evidence of the effect of early life dietary patterns, particularly with respect to effects being sustained into childhood.

Our results suggest that the effect of dietary patterns on FSIQ appear to be driven by VIQ rather than PIQ, which is similar to other studies involving infants [7] and 3-year-old children [8]. It may be argued that that since VIQ is more dependent on knowledge and experience,

the effect of dietary patterns might indicate unmeasured confounding, such as a more nurturing environment or parenting practices. However, it is difficult to explain how the effect of dietary patterns on IQ may differ over time if the effect is solely due to confounding. Whether the effects of dietary patterns on IQ outcomes are due to chance, the nutrient profile of dietary patterns, other factors associated with IQ or limitations of these analyses is not clear.

One of the ongoing difficulties facing nutritional epidemiologists is how to model diet over time. Repeated measures analysis is designed to model repeated outcomes rather than repeated exposures and a further complexity with paediatric nutrition studies is that the exposure (diet) changes considerably from a milk-based diet at 6 months to family foods at 24 months. Thus, it should be noted that a potential limitation of these analyses is that we have not adjusted for the repeated nature of individuals' dietary pattern scores. In the absence of more parsimonious methods for modelling repeated dietary exposures, we adjusted for dietary pattern scores at earlier ages to ascertain the independent contribution of dietary patterns at 15 and 24 months. Adjustment for earlier diet did attenuate the effect of current dietary patterns (model 3, Tables 3 and 4). This is supported by other studies suggesting that dietary patterns may track over time [23, 22, 24]. Even with adjustment for previous diet, most current dietary patterns remained associated with IQ and this contributes evidence of a cumulative effect of dietary patterns on IQ.

Propensity score analyses are an efficient way of addressing systematic differences in the distribution of covariables between exposed and unexposed participants in observational studies. Differences in covariables between the highest and lowest tertiles of dietary pattern scores were large but became well-balanced after matching, thereby allowing us to compare

the average treatment effect of diet patterns on IQ in a non-experimental setting. The highest and lowest tertiles of pattern scores resulted in a clear separation in diet exposure while maximising sample size. There is very little literature utilising propensity score methods in paediatric nutrition as we found only 2 studies on breastfeeding and IQ [25, 26], indicating that propensity score matching is underutilised in paediatric nutritional epidemiology.

Despite using sophisticated techniques to account for non-response and selection bias, there is no perfect method for controlling residual and unmeasured confounding in observational studies of complex socially patterned exposures and outcomes like diet and IQ. In regression analyses, the effect of dietary pattern scores on IQ was considerably reduced after adjustment for other covariables, indicating substantial confounding and raising the possibility that residual confounding remains. Imputation of missing data was important because participants with complete data were different from those with incomplete data on many covariables that are associated with dietary patterns in early life (Table 1) [27, 24]. Imputation was conducted on the sample who had IQ measured and it is not possible to know the effect of diet in the cohort who did not have IQ measured. A potential limitation of these analyses is that we did not adjust for effect of current diet at age 8 or for parental IQ (data not available), which is thought to account for a small effect of confounding beyond maternal education [28]. In addition, dietary patterns are likely to be specific to the population from which they were derived and therefore caution is needed in extrapolating these findings to other populations.

The present study provides some of the strongest evidence to date that dietary patterns from 6 to 24 months have a small but robust effect on IQ at 8 years of age, after taking into account a range of potential confounding factors (using traditional regression analysis and propensity score matching) and accounting for bias (using multiple imputation) due to missing data.

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Table 1: Characteristics of participants with an IQ measurement at 8 years (n=7097) according to completeness of dietary pattern score and covariable data^a

	Complete diet and covariable data n=1366	One or more pieces of missing diet or covariables data n=5731		Mean difference (95% CI), [P value]
		Missing n (%)		
Infant characteristics				
Birth weight (kg)	3.43 ± 0.51 ^b	85 (1)	3.41 ± 0.56	-0.02 (-0.05, 0.01) [0.216]
Gestational age (wk)	39.5 ± 1.6	0 (0)	39.4 ± 2.0	-0.2 (-0.3, -0.1) [0.005]
Male [n (%)]	699 (51.2)	(0)	2848 (49.7)	[0.327]
Singleton [n (%)]	1326 (97.1)	(0)	5578 (97.3)	[0.598]
White ethnicity [n (%)]	1324 (96.9)	30 (0.6)	5448 (95.6)	[0.024]
Maternal characteristics				
Age at child's birth (y)	29.3 ± 4.2	0 (0)	29.1 ± 4.6	-0.2 (-0.5, 0.1) [0.136]
Primiparous [n (%)]	711 (52.1)	246 (4.3)	2486 (45.3)	[<0.001]
Smoked during pregnancy	149 (10.9)	485 (8.5)	760 (14.5)	[0.001]

[n (%)]				
Never married [n (%)]	141 (10.3)	161 (2.8)	807 (14.5)	[<0.001]
Degree level education or higher [n (%)]	276 (20.2)	251 (4.4)	845 (15.4)	[<0.001]
Social class I or II [n (%)] ^c	610 (44.7)	1166 (20.3)	1890 (41.4)	[0.033]
Family income >£400/wk	411 (30.1)	1382 (24.1)	1217 (25.9)	[0.002]
HOME questionnaire ^d	8.2 ± 2.2	392 (6.8)	8.2 ± 2.2	-0.1 (-0.2, 0.1) [0.308]

Abbreviations: PCA, principal component analysis

^a Statistical tests were used to compare characteristics of participants who had complete data with those who had one or more pieces of covariable data missing. Continuous variables were compared by using independent t-test and categorical variables were compared by using χ^2 test.

^b Mean ± SD (all such values)

^c Social class was categorized according to maternal occupation using UK standard classifications of occupation [12].

^d Measured using an adaptation of the HOME observation [13].

Table 2: Associations between dietary pattern scores at 6 months of age and full scale, verbal and performance IQ at 8 years of age (n=7097)^a

	Full Scale IQ ^b			Verbal IQ ^b			Performance IQ ^b		
	β	95% CI	<i>P</i>	β	95% CI	<i>P</i>	β	95% CI	<i>P</i>
Model 1: adjusted for other dietary pattern at 6 months of age^c									
6 mo HM traditional	1.80	1.27, 2.32	<0.001	1.68	1.11, 2.26	<0.001	1.48	0.99, 1.98	<0.001
6 mo Discretionary	-3.34	-3.98, -2.70	<0.001	-3.47	-4.15, -2.79	<0.001	-2.35	-2.98, -1.73	<0.001
6 mo RM baby food	-0.65	-1.15, 0.15	0.011	-0.86	-1.37, -0.35	0.001	-0.23	-0.76, 0.31	0.409
6 mo Breastfeeding	2.54	2.08, 3.00	<0.001	2.70	2.23, 3.18	<0.001	1.69	1.19, 2.19	<0.001
Model 2: adjusted for dietary patterns at 6 months and other covariables^c									
6 mo HM traditional	0.69	0.18, 1.21	0.009	0.59	0.04, 1.15	0.037	0.63	0.13, 1.13	0.014
6 mo Discretionary	-1.15	-1.80, -0.50	0.001	-1.23	-1.93, -0.54	0.001	-0.77	-1.42, -0.12	0.021
6 mo RM baby food	-0.63	-1.06, -0.19	0.005	-0.84	-1.28, -0.39	<0.001	-0.20	-0.72, 0.32	0.442
6 mo Breastfeeding	0.97	0.49, 1.45	<0.001	1.13	0.65, 1.61	<0.001	0.51	0.04, 1.06	0.068

^a Abbreviations: HM, home-made; RM ready-made; IQ, intelligence quotient.

^b IQ was measured by using a short form of the Wechsler Intelligence Scale for Children version III (WISC-III).

^c Data were analyzed by multivariate linear regression. In model 1 data were adjusted only for other dietary pattern scores at 6 months. In model 2, data were adjusted for other dietary pattern scores and other potentially confounding variables including: sex, gestational age, birth weight, ethnicity, singleton/twin pregnancies, parity, maternal education, social class, marital status, family income, smoking and HOME questionnaire. Missing data were imputed by using chained equations. Twenty imputed datasets were created and regression coefficients of each imputed dataset were combined using Rubin's rules [17].

Table 3: Associations between dietary pattern scores at 15 months of age and full scale, verbal and performance IQ at 8 years of age (n=7097)^a

	Full Scale IQ ^b			Verbal IQ ^b			Performance IQ ^b		
	β	95% CI	<i>P</i>	β	95% CI	<i>P</i>	β	95% CI	<i>P</i>
Model 1: adjusted for other dietary patterns at 15 months of age^c									
15 mo Contemporary ³	3.36	2.88, 3.85	<0.001	3.36	2.84, 3.87	<0.001	2.56	2.09, 3.03	<0.001
15 mo Discretionary	-3.57	-4.10, -3.03	<0.001	-4.01	-4.54, -3.48	<0.001	-2.13	-2.66, -1.60	<0.001
15 mo RM baby food	-1.24	-1.93, -0.56	0.001	-1.27	-1.94, -0.60	<0.001	-0.88	-1.55, -0.20	0.012
15 mo Rev HM traditional	-0.87	-1.43, -0.32	0.003	-0.82	-1.39, -0.26	0.005	-0.73	-1.28, 0.18	0.009
Model 2: adjusted for dietary patterns at 15 months and covariables^c									
15 mo Contemporary	1.06	0.53, 1.59	<0.001	1.07	0.50, 1.63	<0.001	0.81	0.28, 1.34	0.003
15 mo Discretionary	-1.25	-1.81, -0.69	<0.001	-1.62	-2.19, -1.06	<0.001	-0.47	-1.04, 0.10	0.108
15 mo RM baby food	-1.24	-1.84, -0.63	<0.001	-1.32	-1.92, -0.73	<0.001	-0.79	-1.41, -0.18	0.012
15 mo Rev HM traditional	-0.23	-0.76, 0.30	0.387	-0.16	-0.70, 0.38	0.550	-0.27	-0.81, 0.27	0.322
Model 3: model 2 with further adjustments for dietary patterns at 6 months of age^c									
15 mo Contemporary	0.67	0.07, 1.26	0.029	0.63	0.004, 1.25	0.049	0.59	-0.03, 1.21	0.061

	Full Scale IQ ^b			Verbal IQ ^b			Performance IQ ^b		
	β	95% CI	<i>P</i>	β	95% CI	<i>P</i>	β	95% CI	<i>P</i>
15 mo Discretionary	-0.86	-1.52, -0.20	0.012	-1.20	-1.90, -0.50	0.001	-0.22	-0.86, 0.42	0.498
15 mo RM baby food	-1.11	-1.71, -0.50	0.001	-1.18	-1.78, -0.59	<0.001	-0.71	-1.34, -0.09	0.026
15 mo HM traditional	-0.30	-0.87, 0.27	0.301	-0.29	-0.89, 0.30	0.329	-0.24	-0.81, 0.33	0.404

^a Abbreviations: HM, home-made; mo, months; Rev, reverse; RM, ready-made; IQ, intelligence quotient.

^b IQ was measured by a short form of the Wechsler Intelligence Scale for Children version III (WISC-III).

^c Data were analyzed by multivariate linear regression. In model 1 data were adjusted only for other dietary pattern scores at 15 months. In model 2, data were adjusted for dietary pattern scores at 15 months and potentially confounding variables including: sex, gestational age, birth weight, ethnicity, singleton/twin pregnancies, parity, maternal education, social class, marital status, family income, smoking and HOME questionnaire. Model 3 included all variables described in model 2 as well as adjustment for earlier dietary pattern scores at 6 months of age. Missing data were imputed by using chained equations. Twenty imputed datasets were created and regression coefficients of each imputed dataset were combined using Rubin's rules [17].

Table 4: Associations between dietary pattern scores at 24 months of age and full scale, verbal and performance IQ at 8 years of age (n=7097)^a

	Full Scale IQ ^b			Verbal IQ ^b			Performance IQ ^b		
	β	95% CI	<i>P</i>	β	95% CI	<i>P</i>	β	95% CI	<i>P</i>
Model 1: adjusted for other dietary pattern at 24 months of age^c									
24 mo HM traditional	-0.77	-1.23, -0.32	0.001	-0.79	-1.30, -0.29	0.002	-0.52	-1.03, -0.02	0.041
24 mo Contemporary	3.01	2.55, 3.47	<0.001	3.04	2.57, 3.51	<0.001	2.23	1.73, 2.74	<0.001
24 mo Discretionary	-2.73	-3.24, -2.23	<0.001	-2.88	-3.40, -2.37	<0.001	-1.90	-2.43, -1.37	<0.001
24 mo Ready-to-eat foods	2.34	1.87, 2.81	<0.001	2.53	2.04, 3.01	<0.001	1.94	1.02, 1.96	<0.001
Model 2: adjusted for dietary patterns at 24 months and other covariables^c									
24 mo HM traditional	-0.37	-0.82, 0.08	0.104	-0.37	-0.85, 0.11	0.133	-0.24	-0.75, 0.27	0.349
24 mo Contemporary	1.19	0.74, 1.65	<0.001	1.21	0.73, 1.69	<0.001	0.88	0.34, 1.41	0.001
24 mo Discretionary	-1.12	-1.64, -0.61	<0.001	-1.24	-1.75, -0.74	<0.001	-0.73	-1.30, -0.16	0.013
24 mo Ready-to-eat foods	0.89	0.41, 1.37	<0.001	1.07	0.56, 1.57	<0.001	0.42	-0.08, 0.91	0.099
Model 3: model 2 with further adjustments for dietary patterns at 6 and 15 months of age^c									
24 mo HM traditional ³	-0.51	-1.03, 0.01	0.057	-0.41	-0.99, 0.17	0.163	-0.46	-1.05, 0.13	0.123

	Full Scale IQ ^b			Verbal IQ ^b			Performance IQ ^b		
	β	95% CI	<i>P</i>	β	95% CI	<i>P</i>	β	95% CI	<i>P</i>
24 mo Contemporary	0.90	0.13, 1.66	0.023	0.80	0.08, 1.52	0.029	0.78	-0.13, 1.69	0.09
24 mo Discretionary	-0.68	-1.36, -0.01	0.046	-0.56	-1.23, 0.11	0.098	-0.71	-1.44, 0.03	0.06
24 mo Ready-to-eat foods	0.76	0.23, 1.29	0.005	0.90	0.36, 1.44	0.001	0.37	-0.18, 0.92	0.191

^a Abbreviations: HM, home-made; mo, months; RM, ready-made; IQ, intelligence quotient.

^b IQ was measured by a short form of the Wechsler Intelligence Scale for Children version III (WISC-III).

^c Data were analyzed by multivariate linear regression. In model 1 data were adjusted for other dietary pattern scores at 24 months. In model 2, data were adjusted for dietary pattern scores at 24 months and potentially confounding variables including: sex, gestational age, birth weight, ethnicity, singleton/twin pregnancies, parity, maternal education, social class, marital status, family income, smoking and HOME questionnaire. Model 3 included all variables described in model 2 as well as adjustment for earlier dietary pattern scores at 6 and 15 months of age. Missing data were imputed by using chained equations. Twenty imputed datasets were created and regression coefficients of each imputed dataset were combined using Rubin's rules [17].

Table 5: Propensity score analysis: the average treatment effect of being in the highest compared with the lowest tertile of dietary pattern scores at 6, 15 and 24 months of age on full scale, verbal and performance IQ at 8 years of age^a

	Average treatment effect by complete case analysis				Average treatment effect in imputed datasets ^b		
	n used in match	FS IQ	V IQ	P IQ	FS IQ	V IQ	P IQ
6 mo HM traditional	961	1.60	0.72	2.23	1.46 (0.42)	1.24 (0.47)	1.33 (0.48)
6 mo Discretionary	889	-2.50	-2.21	-2.27	-2.21 (0.63)	-2.17 (0.69)	-1.68 (0.56)
6 mo RM baby foods	1003	-0.78	-1.02	-0.35	-1.08 (0.37)	-1.60 (0.35)	-0.17 (0.47)
6 mo Breastfeeding	971	3.25	3.24	2.52	2.25 (0.47)	2.53 (0.50)	1.30 (0.48)
15 mo Contemporary	367	2.02	0.65	3.73	1.02 (0.68)	1.02 (0.68)	0.90 (0.59)
15 mo Discretionary	432	0.22	-1.37	1.96	-1.95 (0.72)	-2.56 (0.84)	-0.68 (0.69)
15 mo RM baby foods	537	-0.52	-0.41	-0.64	-2.04 (0.59)	-1.96 (0.59)	-1.57 (0.66)
15 mo Rev HM traditional	543	0.13	-0.01	0.51	-0.44 (0.53)	-0.59 (0.57)	-0.12 (0.50)
24 mo HM traditional	358	-2.67	-2.64	-2.10	-1.44 (0.54) ³	-1.38 (0.56)	-1.09 (0.58)
24 mo Contemporary	240	4.57	6.46	0.93	2.08 (1.25)	2.60 (1.49)	0.88 (1.32)
24 mo Discretionary	223	-4.58	-5.31	-2.77	-1.48 (1.15)	-1.73 (1.15)	-0.86 (1.17)

24 mo Ready-to-eat foods	374	2.73	3.35	0.96	2.27 (0.56)	2.26 (0.50)	1.63 (0.61)
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^aAbbreviations: FSIQ full scale IQ; HM, home-made; PIQ, Performance IQ; Rev, reverse; RM, ready-made; VIQ, Verbal IQ. Propensity score calculated as the probability of being in the highest compared with the lowest tertile of dietary pattern scores given the following covariables; sex, gestational age, birth weight, ethnicity, singleton/twin pregnancies, parity, maternal education, social class, marital status, family income, smoking, HOME questionnaire and other dietary pattern scores at current and previous times. Propensity scores matched in the high- compared with the lowest tertile by nearest neighbor method with calipers set to 0.2*SD [21]. IQ was measured by a short form of the Wechsler Intelligence Scale for Children version III (WISC-III).

^bValues show average treatment effect and the between dataset standard deviation in parentheses for all 20 imputed datasets. Datasets were combined according to Rubin's rules [17]. The number of matches not shown as it differs for each of the 20 datasets, but is >2000 for all comparisons at 6 and 15 months and >1000 at 24 months.

FIG. 1 LEGEND & TITLE

TITLE: Participant data at each stage of study^a

Footnotes:

^a Abbreviations: ALSPAC, Avon longitudinal study of parents and children; IQ, intelligence quotient; WISC, Wechsler Intelligence Scale for Children version III

^b Triplets and quadruplets are excluded from all ALSPAC datasets to protect their identity

^c All participants who were part of the core cohort and survived to age 1 were invited to complete diet questionnaires at 6, 15, 24 months and assessments of IQ at 8 years. The current study was undertaken on participants who had at least one WISC IQ subscale measured at 8 years (n=7097).