High Adherence to a Mediterranean Diet at Age Four Reduces Overweight, Obesity and Abdominal Obesity Incidence in Children at the Age of Eight

Leyre Notario-Barandiaran*, Desirée Valera-Gran*, Sandra Gonzalez-Palacios, Manuela Garcia-de-la-Hera, Silvia Fernández-Barrés, Eva Pereda-Pereda, Ana Fernández-Somoano, Mònica Guxens, Carmen Iñiguez, Dora Romaguera, Martine Vrijheid, Adonina Tardón, Loreto Santa-Marina, Jesús Vioque, Eva Mª Navarrete-Muñoz, on behalf of the INMA Project**

*LNB and DVG these authors contributed equally to this work.

** For a complete list of INMA project researchers:

http://www.proyectoinma.org/presentacion-inma/listado-investigadores/en_listado-investigadores.html)

Running title: Adherence to a Mediterranean Diet and Child Obesity

Author Affiliations

Department of Public Health, History of Medicine and Gynaecology, Universidad Miguel Hernández, Alicante (LNB, SGP, MGH, JV, EMNM)

Institute for Health and Biomedical Research (ISABIAL - FISABIO Foundation), Alicante, Spain (LNB, DVG, SGP, MGH, JV, EMNM)

Department of Pathology and Surgery, Universidad Miguel Hernández, Alicante (DGV, EMNM)

Spanish Consortium for Research on Epidemiology and Public Health (CIBERESP), Instituto de Salud Carlos III, Madrid, Spain (MGH, SFB, AFS, MG, CI, MV, AT, LSM, JV, EMNM)

ISGlobal, Barcelona, Spain (SFB, MG, DR, MV)

Universitat Pompeu Fabra (UPF), Barcelona, Spain (SFB, MG, DR, MV)

Faculty of Psychology, University of the Basque Country (UPV/EHU), Donostia-San Sebastián, Spain (EPP)

Biodonostia Health Research Institute, Donostia-San Sebastián, Spain (EPP, LSM)

IUOPA-Departamento de Medicina, University of Oviedo, Oviedo, Spain (AFS, AT)

Department of Child and Adolescent Psychiatry/Psychology, Erasmus University Medical Centre–Sophia Children's Hospital, Rotterdam, The Netherlands (MG)

Departamento de estadística e I.O. Universitat de València (CI)

Balearic Islands Health Research Institute (IdISBa), Palma, Spain (DR)

CIBER Physiopathology of Obesity and Nutrition (CIBEROBN), Spain (DR)

Department of Health, Basque Government, Donostia-San Sebastián, Spain (LSM)

Corresponding author: Jesús Vioque. Department of Public Health, History of Medicine and Gynecology, Universidad Miguel Hernández, Campus San Juan. Ctra. Nacional 332 s/n 03550-Sant Joan d'Alacant, Spain. vioque@umh.es

+34 965919517

Financial support

This study was funded by grants from Instituto de Salud Carlos III and the Spanish Ministry of Health (Red INMA G03/176; CB06/02/0041; FIS 97/0588; 00/0021-2; PI061756; PS0901958; FIS-FEDER 03/1615; 04/1509; 04/1112; 04/1931; 05/1079; 05/1052; 06/1213; 07/0314; 09/02647; FIS-PI041436; FIS- PI081151; FIS-PI06/0867; FIS-PS09/00090; FIS-PI04/2018; FIS-PI09/02311; FIS PI11/01007; FIS-PI13/02429; MS13/00054, CPII18/00018; PI12/01890; CP13/00054; PI18/00825) University of Oviedo, Conselleria de Sanitat Generalitat Valenciana, Generalitat de Catalunya-CIRIT 1999SGR 00241, Generalitat de Catalunya-AGAUR 2009 SGR 501 and 2014 SGR 822. Department of Health of the Basque

Government (2005111093, 2009111069 and 201311089) the Provincial Government of Gipuzkoa (DFG06/004 and DFG08/001), annual agreements with the municipalities of the study area of Gipuzkoa (Zumarraga, Urretxu, Legazpi, Azkoitia y Azpeitia y Beasain), Fundació Marató TV3 (20162210 and 090430). ISGlobal is a member of the CERCA Programme, Generalitat de Catalunya. Spanish Ministry of Economy and Competitiveness (SAF2012-32991 incl. FEDER funds), Agence Nationale de Securite Sanitaire de l'Alimentation de l'Environnement et du Travail (1262C0010), EU Commission (261357, 308333, 603794 and 634453). The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

ABSTRACT

Background/Objectives: A higher adherence to a Mediterranean diet has been shown to be protective against obesity in adults, but the evidence is still inconclusive in children at early ages. Our objective was to explore the association between adherence to Mediterranean Diet at the age of four and the prevalence of overweight, obesity and abdominal obesity at four years of age, and incidence at the age of eight.

Subjects/Methods: We analysed data from children of the INMA cohort study who attended follow-up visits at age four and eight years (n=1801 and n=1527, respectively). Diet was assessed at the age of four using a validated food frequency questionnaire. The adherence to MD was evaluated by the relative Mediterranean diet (rMED) score, and categorized as low (0-6), medium (7-10) and high (11-16). Overweight and obesity were defined according to the age-sex specific BMI cut-offs proposed by the International Obesity Task Force, and abdominal obesity as waist circumference >90th percentile. We used Poisson regression models to estimate prevalence ratios at four years of age, and Cox regression analysis to estimate hazard ratios (HR) from four to eight years of age.

Results: In cross-sectional analyses at the age of four no association was observed between adherence to MD and overweight, obesity, or abdominal obesity. In longitudinal analyses, a high adherence to MD at age four was associated with lower incidence of overweight (HR=0.38; 95%CI: 0.21-0.67; p=0.001), obesity (HR=0.16; 95%CI: 0.05-0.53; p=0.002), and abdominal obesity (HR=0.30; 95%CI: 0.12-0.73; p=0.008) at the age of eight.

Conclusion: This study shows that a high adherence to MD at the age of four is associated with a lower risk of developing overweight, obesity, and abdominal

obesity at age eight. If these results are confirmed by other studies, MD may be recommended to reduce the incidence of obesity at early ages.

INTRODUCTION

Childhood obesity is one of the most crucial health challenges of this century. According to the latest global estimates from a pooled analysis of 2 416 studies with 128.9 million participants aged five years and older, the trends in mean body mass index (BMI) and obesity prevalence increased worldwide from 1975 to 2016 (1). In European countries, Spain presented one of the highest rates of childhood obesity in 2016, with prevalence of 10.5% for obesity and 33.7% for overweight, in children and adolescents aged five to 19 years (2).

Obesity at early ages is characterized by an increase in the number and size of adipocytes (adipose tissue cells); a process known as hyperplasia. By contrast, in adults, the most common obesity process is hypertrophy, which is distinguished by a large accumulation of fat in the adipocytes without an increment in the number of cells (3). Importantly, the massive formation of adipocytes in infancy may become an irreversible process that results in obesity in adulthood, increasing the potential risk of developing multiple concomitant health problems such as glucose tolerance, hyperlipidaemia, cardiovascular diseases and certain types of cancer (4–6). Since obesity in adolescence and adulthood is very difficult to reverse, it is important to identify modifiable environmental factors such as diet, at early ages, in order to prevent obesity and non-communicable diseases later in life.

Few studies have explored the relationship between diet and childhood obesity, and the main findings suggest that a greater consumption of vegetables and a lower intake of sugary drinks are associated with a lower risk of childhood obesity (7–9). An alternative to studying the effect of specific foods and nutrients is to explore dietary patterns such as the traditional Mediterranean diet (MD), which has shown a beneficial effect on many chronic diseases and longevity in adults (10). The traditional MD is a dietary pattern characterized by abundance of plant-based foods such as vegetables, legumes, fruits, nuts and cereals, the use of olive oil as main source of dietary fat, moderate to high intake of fish, low or moderate intake of dairy products, and a low consumption of meat (11). Regarding nutrients, MD is characterized by a high intake of carbohydrates of low glycemic index, dietary fibre and antioxidants, monounsaturated fatty acids, vegetable proteins and a balanced ratio between omega-6 and -3 fatty acids (11,12). Thus, MD has high antioxidant and anti-inflammatory properties that play a preventive role against overweight and obesity (13–15), as corroborated by several systematic reviews mostly in adult populations (16–18). However, the evidence of potential beneficial effects of MD on child health is still insufficient and not fully consistent. In a recently published systematic review based on 17 studies, an inverse association was reported between adherence to MD and BMI in children or adolescents, although there were differences by sex and age (19). More prospective cohort studies may better elucidate the relationship of the MD adherence in the obesity in children.

In the light of the research cited above, this study had the following aims: first, to explore the cross-sectional association between adherence to MD and its components at age four and the prevalence of overweight, obesity and abdominal obesity at the age of four; and, second, to examine the prospective association between adherence to MD at age four and the incidence of overweight, obesity, and abdominal obesity at the age of eight.

METHODS

The INfancia y Medio Ambiente [Environment and Childhood] project (INMA, www.proyectoinma.org) is a population-based multi-center prospective birth cohort study established in seven Spanish regions that uses a common protocol (20). For the present analysis, we used the data from the INMA study areas of Valencia, Sabadell, Asturias, and Gipuzkoa collected between 2003 and 2008. At the outset, there were 2 644 women who agreed to participate, of which 2 506 delivered a live infant. At the four-year follow-up assessment 1 801 children participated and 1 527 children participated at the eight-year interview. Figure 1 shows the flow chart of the population sample in our study. All participant parents provided informed consent, and the ethical committees of the centers (Hospital La Fe, Valencia; Sabadell Hospital, Sabadell; Central University Hospital of Asturias, Asturias; Zumarraga Hospital, Gipuzkoa) involved in the study approved the research protocol.

Dietary Assessment

A semi-quantitative food frequency questionnaire (FFQ) of 105 food items was used to assess the child's usual daily intake of foods and nutrients (available at: http://epinut.edu.umh.es/cfa-105-inma-infancia/) (22). The FFQ was derived from an adult version of FFQ previously validated among the mothers from the Valencia-INMA cohort (21). The FFQ was modified to include food items and portion sizes appropriate for children ages four to five. It was validated in a sample of 169 children from the INMA study and showed moderately good reproducibility with an average correlation coefficient of 0.41 for nutrients and 0.43 for food groups. The average correlation coefficients for validity of daily nutrient intakes, as compared to three 24-hour dietary recalls and blood concentration of vitamins, were 0.44 and 0.21 respectively (22).

Parents were asked to report the dietary intake of their children as the average frequency of consumption for the specified serving or portion size of each food item over a previous nine-month period. The questionnaire included nine possible frequencies of consumption, ranging from "never, once or less than once a month" to "six or more times a day". Nutrient values and total energy intake were obtained from the United States Department of Agriculture food composition tables (23) and other published sources as cultural reference for specific Spanish food and portion sizes (24,25). In order to calculate average daily nutrient intakes from the diet for each child, we multiplied the frequency of consumption of each food item by the nutrient content of the portion indicated in the FFQ and added the results across all foods.

Adherence to a Mediterranean Diet

Adherence to MD was measured by the relative Mediterranean Diet Score (rMED) after excluding alcohol consumption, since our study population was made up of children (16). This dietary index was composed of eight components of MD, and the total score range was from 0 (minimal adherence) to 16 (maximum adherence). The rMED components were: vegetables (excluding potatoes), fruit (including nuts, seeds and fruit juices), legumes, cereals (including whole grains and bread), fish (including seafood), meat (including processed meat), dairy products (including low-fat and high-fat products) and olive oil. Each rMED component was calculated in grams per 1 000 kcal/day and divided into tertiles of intake. A score of 0, 1 and 2 was assigned to the first, second and third tertiles of intake, respectively; higher intakes scored positively, with the exception of meat and dairy products for which the scoring was inverted. The rMED scores were categorized into low (0-6 points), medium (7-10 points) and high (11-16 points) adherence to MD based on Buckland's cut-off points after excluding the score for alcohol (16).

Anthropometric Measures

The body weight, height, and waist circumference (WC) of children were measured at the age four- and age eight- interviews by trained personnel using standard protocols (in light clothing and without shoes). BMI was obtained as weight in kilograms divided by the square of height in meters, and we calculated BMI according to the specific cut-offs proposed by the International Obesity Task Force (IOTF) (26). WC in centimeters was measured using an inelastic tape (SECA 201) at the midpoint between the lower rib margin and the superior anterior iliac spine, in a standing position and after a gentle expiration. The values of WC within the 90th percentile or above of the sample distribution were used to determine abdominal obesity (27). Since the Gipuzkoa-INMA cohort did not perform this follow-up assessment, the analyses of WC results did not include data from this study area.

Incident cases of overweight, obesity, and abdominal obesity were defined as those participants without that condition at age four and were classified as having overweight, obesity, and abdominal obesity at the age of eight using the aforementioned criteria.

Other Variables

Mother's socio-demographic and lifestyle factors considered were age (years), study area (Asturias; Gipuzkoa; Sabadell; Valencia), social class (I/II, high; III, medium; IV/V, low), pre-pregnancy BMI (normal weight; overweight; obesity), smoking during pregnancy (no; yes), second-hand smoking (no; yes), parity (0; ≥1), breastfeeding duration (<4 months; ≥4 months). We also collected information about children. At birth: sex (female; male), small for gestational age by weight (no; yes); and at four-year follow-up interview: age (years), sleep (hours per day), television watching (hours per day) and sweetened beverages consumption (<1 drink/week; ≥1 drinks/week). The sweetened beverages consumption were estimated from the data collected by the FFQ.

Statistical analysis

The distribution of socio-demographics and lifestyle characteristics by the rMED score categories were compared using the chi-square test for categorical variables and ANOVA for continuous variables.

To evaluate the association between adherence to MD at four years as measured by rMED and prevalence of overweight, obesity, and abdominal obesity at the age of four, we used multiple Poisson regression models with robust variance based on the Huber sandwich estimate (28,29) to obtain prevalence ratios (PR) and their 95% Confidence Interval (CI). A robust Poisson regression model was used instead of log-binomial regression model due to it did not converge (30). We used Cox regression analysis to estimate hazard ratios (HR) to evaluate the association between adherence to MD at four years and incidence of the overweight, obesity, and abdominal obesity from age four to eight. Both the cross-sectional and longitudinal analyses were also performed using the rMED as a continuous variable to explore the associations per two-point increase in the rMED score. Furthermore, to explore the associations in more detail, we replicated these analyses for each component of the rMED per one-point increase in the component score.

We fitted several models, initially adjusting for location, age (continuous), and sex, and secondly, adjusting for maternal characteristics (social class, BMI, smoking, second-hand smoking, parity) and child characteristics (breastfeeding duration, small for gestational age by weight, television watching, sleep and sweetened beverage consumption at age four). When we carried out the analysis of the components of the rMED, we also included the variable rMED score in the adjusted model excluding the component specifically assessed. All of the covariates with $P < 0.20$ and those that changed the magnitude of the main effects by 10 percent after a backward elimination procedure were included in the multiple model.

We also analyzed the associations separately for each study area to quantify the heterogeneity using I^2 statistics (31). Due to the fact that all I^2 values for the outcome associations were <50 percent, we performed the analyses adjusting all the models for the study area.

Statistical analyses were conducted with R statistical software version 3.4.2 (R Foundation for Statistical Computing).

RESULTS

Table 1 presents the baseline characteristics of mothers and children according to categories of adherence to MD. Mothers whose children had the highest scores of rMED (i.e. high adherence to MD) tended to be older, belonged to a high social class, and were also more likely to be non-smokers. Regarding children's characteristics, a greater adherence to MD was observed in girls, children with a longer mean sleep time per day, those who had lower energy intake on average, and those who consumed <1 drink/week of sweetened beverages. The mean rMED score at age four was 8 points, 29.9% of children were classified as low adherence and 19.3% as high adherence to MD.

Table 2 presents the results of the association between adherence to MD at age four and overweight, obesity, and abdominal obesity prevalence at the age of four, and incidence of overweight, obesity, and abdominal obesity at the age of eight. The prevalence of overweight, obesity, and abdominal obesity in the children in our study at age four was 14.5 percent, 6 percent and 9 percent, respectively. Regarding incidence from four to eight years, 15 percent of children with normal weight at age four became overweight at age eight and six percent who were not obese at age four (normal weight or overweight) developed obesity at age eight. Overall, no association was observed in cross-sectional analyses between adherence to MD and overweight, obesity, or abdominal obesity in children at the age of four. By contrast, in the longitudinal analyses, those children who had high adherence to MD at the age of four showed lower risk of developing overweight (HR=0.38; 95% CI, 0.21 to 0.67), obesity (HR=0.16; 95% CI, 0.05 to 0.53), and abdominal obesity (HR=0.30; 95%CI, 0.12 to 0.73) at the age of eight, compared to those children with a low adherence to MD. When exploring the incidence at the age of eight per every two-point increase in rMED at age four, we observed a lower risk of overweight (HR=0.88; 95%CI, 0.78 to 1.00), obesity (HR=0.80; 95% CI, 0.66 to 0.97), and abdominal obesity (HR=0.82; 95%CI, 0.68 to 0.99).

The results of the association between the consumption of rMED components at the age of four and overweight and obesity prevalence at four years and the incidence at the age of eight are shown in **Table 3**. Regarding overweight, no association was observed in the cross-sectional analysis for the prevalence at age four. In longitudinal analysis for overweight at age eight, a lower risk was observed for a one-point increase in rMED score of fruits (HR=0.79; 95% CI, 0.64 to 0.97) and olive oil (HR=0.65; 95% CI, 0.52 to 0.82). A lower risk of overweight was observed for a lower consumption of meat (HR=0.70; 95% CI, 0.56 to 0.87). On the other hand, we observed a higher risk of overweight for a higher intake of fish (HR=1.23; 95% CI, 1.00 to 1.51) and for a lower intake of dairy products (HR= 1.38; 95% CI, 1.11 to 1.70). Regarding obesity, no association was observed for the prevalence at age four. A one-point increase in the rMED score of fish (HR=1.49; 95% CI, 1.08 to 2.06) was associated with a higher risk of obesity at the age of eight, while a lower intake of meat (HR=0.63; 95% CI, 0.46 to 0.88) was associated with a lower risk of obesity at this age.

The associations between rMED components and the abdominal obesity prevalence at age four and the abdominal obesity incidence at age eight are displayed in **Table 4**. Lower risks of abdominal obesity were observed for a one-point increase in the score of vegetables (HR=0.70; 95% CI, 0.52 to 0.95) and meat (HR=0.61; 95% CI, 0.44 to 0.83), whereas a higher incidence of abdominal obesity at the age of eight was found for one-point increase in the score of fish (HR=1.62; 95% IC, 1.19 to 2.20).

DISCUSSION

This study supports that higher adherence to MD in children at the age of four is associated with a lower risk of overweight, obesity, and abdominal obesity at the age of eight. The analysis of the specific rMED components revealed that the protective effect of overweight, obesity and abdominal obesity was mainly due to a greater intake of vegetables and olive oil, as well as a reduction in the consumption of meat. We also observed a lower risk of overweight due to a greater intake of fruits. Our findings are consistent with those from previous prospective studies in adults and may also suppose good evidence to reinforce the role of MD in preventing overweight and obesity in children at early ages.

On the balance of the available evidence, the role of adherence to MD in child adiposity indicators still remains controversial (19). As far as we know, only three studies have explored the association between adherence to MD and adiposity markers in children aged four or younger (32–34), and only one study found no association between adherence to MD and prevalence of childhood overweight and obesity (32).

The results of the cross-sectional analyses showed no associations between adherence to MD and prevalence of adiposity outcomes at four years of age. A possible explanation may be attributed to the fact that early childhood is a critical period of adaptation in feeding style and eating habits, in which children are especially responsive to changes in dietary intake (35). However, although eating habits during childhood may vary resulting in different dietary patterns, it has been suggested that they tend to be stable throughout this stage (36). This may indicate that the absence of an association with adherence to MD at age four could be likely due to the lack of time to produce an effect on child adiposity at this age, whereas the maintenance of the MD pattern for several years could explain the detectable effect that we observed on adiposity outcomes at age eight. Thus, although in the present study we did not track the changes in the diet from age four to eight, the association observed between a high adherence to MD at age four and a lower incidence of overweight, obesity, and abdominal obesity at age eight might be understood as indicative of a potential stability in healthy eating habits over this period of time. Nevertheless, we are aware that this association should be not interpreted as a result of a cumulative effect of children's diet on the risk of adiposity outcomes.

To date, only one prospective study has reported that adherence to MD was inversely associated with overweight and obesity among children at early ages (34). As suggested in adult populations (37,38), our findings also support that MD may exert a long-term protective effect against overweight, obesity, and abdominal obesity throughout childhood. The beneficial effect of MD on obesity has been explained by the potential influence of some components of this dietary pattern, such as dietary fiber, dietary fat and energy density, on satiation and satiety (14). Dietary fiber has been associated with reduced risks of obesity, overweight, and high waist-to-hip ratio (39), which may be particularly due to its effect on the regulation of the short-term subjective appetite and acute energy intake, and the long-term energy intake and body weight (40). Hence, our results suggest that foods rich in dietary fiber such as fruits and vegetables may be associated with a lower incidence risk of overweight and abdominal obesity at eight years of age.

Contrary to expectations, a higher intake of fish at age four was associated with higher incidence of obesity at the age of eight. A recent randomized controlled trial conducted in Spain showed that fish consumption could be a protective factor for obesity in children aged seven to eight (41). Although our findings seem to contradict the beneficial effects of fish, the observed inverse association might be explained by the fact that the fish intake in the children of our study could indicate a different pattern of food consumption within a context of a healthy diet such as MD. In fact, children at these ages commonly consume breaded or battered fried fish from frozen coated fish products, which could lead to excess weight gain (42).

One of the main features of MD is low consumption of meat. Our results would support that a lower consumption of meat would prevent weight gain. Although weight gain is the result of a very complex process, specific foods such as red and processed meats have been suggested to play an important role in metabolic syndrome in adults, particularly in the incidence of central obesity (43). Actually, a recent systematic review and meta-analysis of observational studies with adult populations established that red and processed meat consumption were directly associated with the risk of obesity, higher BMI, and higher WC (44). Importantly, in our study, we observed that children with overweight, obesity and abdominal obesity had an overall higher intake of meat, especially of red and processed meats, compared with normal-weight children.

Regarding dairy food products, a recently published meta-analysis suggested that its consumption might have a protective effect on childhood adiposity (45), although the accumulated evidence remains still insufficient and inconclusive. On the basis of the available data, it may be hypothesized that dairy food products may exert a beneficial effect on adiposity through lipolysis, lipogenesis and fatty acid absorption, suggesting a positive impact on appetite regulation and food intake (46). Our results showed that lower dairy consumption at age four was associated with a higher incidence of overweight at the age of eight, which would support the assumption accepted so far about the potential beneficial impact of dairy on disease prevention. However, in light of the apparently controversial results, further prospective research is recommended to clarify the role of the different types of dairy in child adiposity markers and obesity risk.

Unlike the rest of rMED components, olive oil is recognized as the hallmark of the traditional MD. Our results of a beneficial effect of olive oil on childhood overweight are consistent with the strong evidence available from prospective studies in adults (47). To the best of our knowledge, only one small clinical trial among Spanish children ages 1 to 13 (n=92) has shown that the consumption of olive oil reduced the risk of weight gain over 1-year follow-up (48).

The present study has limitations. We adjusted for a wide range of potential confounding factors, although the effect of unmeasured variables, residual confounding, or modifiers cannot be ruled out. In terms of the scoring system to measure adherence to MD, the rMED score has not been previously developed for the child population; however, supported by strong evidence from prospective studies (49), we confirmed our hypothesis that adherence to MD as measured by rMED categories and several of their components are related to a protective effect on the development of obesity at early ages in childhood. Another potential limitation might be that parents' and children's caregivers may misreport a child's diet, particularly in children with obesity, thereby causing a potential differential bias. Although some under-reporting of diet has been described among adults and elderly populations with obesity, it seems more unlikely to occur in younger parents with children at age 4 when reporting their children diet by the nutritional status. Thus, if any misclassification of diet occurred, it should be non-differential, which would reinforce the associations found in our study. Also, the FFQ used in our study was previously validated and showed acceptable reproducibility and validity for assessing dietary intake among children ages four to five in the same study (22).

Strengths of this study include the accuracy of the data on child anthropometry, which was measured by trained personnel using standard protocols and not self-reported. Moreover, the multi-center structure of this population-based cohort study located in different Mediterranean areas of Spain ensured the representativeness of the results. These results can be extrapolated to a wide range of situations with similar characteristics. The longitudinal design of the study permitted us to detect a long-term effect in children age eight through specific assessments conducted at the age of four, thereby confirming the strength of our findings. The prospective follow-up of the INMA project study should enable us to analyze the persistence of the effects on child and adolescent health outcomes and to identify potential changes over time in further assessments.

In summary, this observational prospective study shows that having a higher adherence to MD at age four may prevent overweight, obesity, and abdominal obesity at the age of eight. Our findings also suggest that the associations observed in terms of high adherence to MD in children at age 4 can be attributed to a greater intake of vegetables and olive oil, as well as to a reduction in the consumption of meat. Taking into account that the current diet of children in Spain is most likely affected by the phenomenon known as “Westernization” (50), or an abandonment of the traditional Mediterranean dietary pattern, further research efforts are required to ascertain potential determinants of adherence to MD and to explore the association with child health outcomes. Our findings may be of help for developing dietary recommendations and designing public health programs to enhance healthy lifestyle habits at early ages.

Acknowledgment: We like to acknowledge Emily Felt for providing assistance with the English revision of the manuscript; she received compensation.

Competing Interests: All authors have no conflicts of interest to declare.

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Figure 1. Flowchart of the study population describing the selection process.

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Table 1. Baseline participants' characteristics of mothers and their children from the INMA study according to adherence to MD as assessed by relative Mediterranean Diet Score (rMED) at the age of four years

	All	rMED categories			p-value[1]
		Low (0-6)	**Medium (7-10)**	**High (11-16)**	
% (n)	1801	29.9 (539)	50.8 (915)	19.3 (347)	
Maternal characteristics					
Age at delivery, mean (SD)	30.1 (4.08)	30.3 (4.25)	31.1 (4.04)	31.6 (3.95)	<0.001
Region, % (n)					
Asturias	21.5 (387)	9.5 (51)	24.3 (222)	32.9 (114)	<0.001
Gipuzkoa	22.2 (399)	21.7 (117)	21.9 (200)	23.6 (82)	
Sabadell	24.2 (435)	23.7 (128)	24.7 (226)	23.3 (81)	
Valencia	32.2 (580)	45.1 (243)	20.2 (267)	20.2 (70)	
Social class, % (n)					
I/II, high	24.0 (433)	17.8 (96)	25.2 (231)	30.5 (106)	<0.001
III, medium	27.0 (486)	24.1 (130)	27.1 (248)	31.1 (108)	
IV/+V, low	49.0 (882)	58.1 (313)	47.7 (436)	38.3 (133)	
Pre-pregnancy BMI, % (n)					
Normal weight	73.7 (1327)	77.6 (418)	70.7 (647)	75.5 (262)	0.018
Overweight	18.8 (338)	14.7 (79)	21.2 (194)	18.7 (65)	
Obesity	7.6 (136)	7.8 (42)	8.1 (74)	5.8 (20)	
Smoking in pregnancy, % (n)					
No	69.8 (1234)	63.1 (332)	72.4 (651)	73.0 (251)	<0.001
Yes	30.2 (535)	36.9 (194)	27.6 (248)	27.0 (93)	
Second hand smoking[2], % (n)					
No	39.1 (688)	32.6 (170)	39.3 (351)	48.7 (167)	<0.001
Yes	60.9 (1071)	67.4 (352)	60.7 (543)	51.3 (176)	
Parity, % (n)					
0	57.8 (1040)	54.3 (292)	59.5 (544)	58.8 (204)	0.136
≥1	42.2 (759)	45.7 (246)	40.5 (370)	41.2 (143)	
Child characteristics					
Age at 4 years, mean (SD)	4.42 (0.18)	4.40 (0.15)	4.42 (0.18)	4.44 (0.20)	0.018
Age at 8 years, mean (SD)	7.58 (0.63)	7.50 (0.60)	7.59 (0.64)	7.67 (0.63)	<0.001
Sex, % (n)					
Female	48.0 (864)	44.3 (239)	47.9 (438)	53.9 (187)	0.021
Male	52.0 (937)	55.7 (300)	52.1 (477)	46.1 (160)	
SGA according to weight, % (n)					
No	90.1 (1620)	89.1 (480)	89.6 (818)	93.1 (322)	0.115
Yes	9.9 (178)	10.9 (59)	10.4 (95)	6.9 (24)	
Breastfeeding duration, % (n)					
< 4 months	53.8 (929)	59.0 (306)	53.2 (468)	47.0 (155)	0.003
≥ 4 months	46.2 (799)	41.0 (213)	46.8 (411)	53.0 (175)	
Sleep (h/d), mean (SD)	10.4 (0.90)	10.2 (0.99)	10.4 (1.01)	10.6 (0.87)	<0.001
Television viewing (h/d), % (n)					
<1	29.7 (534)	24.7 (133)	28.5 (261)	40.3 (140)	<0.001
1-2	52.1 (938)	49.7 (268)	54.3 (497)	49.9 (173)	
>2	18.3 (329)	25.6 (138)	17.2 (157)	9.8 (34)	
Energy intake (kcal/d), mean (SD)	1582 (339.0)	1648 (346.8)	1589 (353.7)	1458 (316.6)	<0.001
Sweetened beverages, % (n)					
<1 drink/week	34.7 (625)	28.4 (153)	34.6 (317)	44.7 (155)	<0.001
≥ 1 drinks/week	65.3 (1176)	71.6 (386)	65.4 (598)	55.3 (192)	

MD: Mediterranean diet; rMED: Relative Mediterranean Diet Score; SD: Standard Deviation; BMI: Body Mass Index; SGA: small for gestational age.

[1]p-value was calculated by Chi-square for categorical variables, and ANOVA for continuous variables.

[2] Second-hand Smoking was defined as being exposed to tobacco at least twice a week in any of the following environments: at work, at home or in leisure time.

Table 2. Association between adherence to MD at age four using rMED score and overweight, obesity and abdominal obesity prevalence at the age of four and incidence risk at age eight in children from the INMA cohort study

Prevalence at 4 years		Low (0-6)	Medium (7-10) PR (95% CI)	Medium (7-10) p-value	High (11-16) PR (95% CI)	High (11-16) p-value	2-unit increase PR (95% CI)	2-unit increase p-value
Overweight	**cases/total**	76/539	128/915		57/347		261/1801	
	Model 1	Ref.	1.00 (0.97-1.03)	0.926	1.02 (0.97-1.06)	0.462	1.00 (0.99-1.01)	0.758
	Model 2	Ref.	0.99 (0.96-1.02)	0.549	1.01(0.96-1.05)	0.806	1.00(0.99-1.01)	0.995
Obesity	**cases/total**	35/539	54/915		17/347		106/1801	
	Model 1	Ref.	0.99 (0.97-1.01)	0.401	0.98 (0.95-1.01)	0.118	0.99 (0.98-1.00)	0.055
	Model 2	Ref.	0.99 (0.97-1.02)	0.451	0.99 (0.96-1.02)	0.493	1.00(0.99-1.00)	0.412
Abdominal obesity[1]	**cases/total**	47/515	60/719		21/150		128/1384	
	Model 1	Ref.	0.97 (0.95-1.00)	0.079	1.01 (0.95-1.06)	0.807	0.99 (0.98-1.00)	0.192
	Model 2	Ref.	0.98 (0.95-1.01)	0.403	1.01 (0.96-1.08)	0.686	0.99 (0.98-1.01)	0.320
Incidence from 4 to 8 years		**Low (0-6)**	**Medium (7-10) HR (95% CI)**	**p-value**	**High (11-16) HR (95% CI)**	**p-value**	**2-unit increase HR (95% CI)**	**p-value**
Overweight	**Incident cases**	56	91		36		183	
	Person-years	1087.36	1994.99		784.38		3866.73	
	Model 1	Ref.	0.86 (0.61-1.22)	0.398	0.37 (0.21-0.65)	<0.001	0.87 (0.78-0.98)	0.025
	Model 2	Ref.	0.79 (0.55-1.13)	0.200	0.38 (0.21-0.67)	0.001	0.88 (0.78-1.00)	0.047
Obesity	**Incident cases**	28	45		10		83	
	Person-years	1270.14	2332.79		952.51		4555.44	
	Model 1	Ref.	0.85 (0.52-1.39)	0.514	0.08 (0.02-0.31)	<0.001	0.74 (0.62-0.88)	<0.001
	Model 2	Ref.	0.92 (0.53-1.59)	0.776	0.16 (0.05-0.53)	0.002	0.80 (0.66-0.97)	0.026
Abdominal obesity[1]	**Incident cases**	24	54		19		97	
	Person-years	922.99	1689.58		662.40		3274.97	
	Model 1	Ref.	0.93 (0.56-1.55)	0.795	0.26 (0.12-0.59)	0.001	0.78 (0.66-0.92)	0.004
	Model 2	Ref.	1.01 (0.58-1.73)	0.982	0.30 (0.12-0.73)	0.008	0.82 (0.68-0.99)	0.041

MD: Mediterranean diet; rMED: relative Mediterranean Diet Score; PR: prevalence ratio. HR: hazard ratio; 95% CI = 95% confidence interval.
Model 1 was adjusted for region (Asturias; Guipuzkoa; Sabadell; Valencia), child age (in years) and sex (female; male). Model 2 was adjusted with the same variables than model 1 plus maternal social class (I/II, high; III, medium; IV/+V, low), mother's pre-pregnancy body mass index (normal-weight; overweight; obesity), smoked during pregnancy (no; yes), second hand smoking (no; yes), parity (0; ≥1), breastfeeding duration (< 4 months; ≥ 4 months), small child for gestational age according to weight (no; yes), child television watching at 4 years (hours per day), sleep at 4 years (hours per day) and child sweetened beverages consumption at 4 years (<1 drinks/week; ≥1 drinks/week).
[1]Children from Gipuzkoa were excluded because the information on the waist circumference was not collected.

Table 3. Association between 1-point increase in the components of the rMED score and overweight and obesity prevalence at four years and incidence risk

Components of rMED (1-point increase)		Overweight				Obesity			
		Prevalence at 4y Cases= 261 Total=1801		Incidence risk until 8y Incident cases=183 Person-years= 3866.73		Prevalence at 4y Cases=106 Total= 1801		Incidence risk until 8y Incident cases=83 Person-years= 4555.44	
		PR (95% CI)	**p-value**	**HR (95% CI)**	**p-value**	**PR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**
Vegetables	Model 1	1.00 (0.98-1.02)	0.779	0.76 (0.62-0.93)	0.007	1.00 (0.99-1.02)	0.609	0.63 (0.47-0.85)	0.003
	Model 2	1.00 (0.98-1.02)	0.825	0.78 (0.64-0.96)	0.020	1.01 (0.99-1.02)	0.359	0.72 (0.53-0.99)	0.428
	Model 3	1.00 (0.98-1.02)	0.800	0.80 (0.65-1.00)	0.048	1.01 (0.99-1.02)	0.201	0.76 (0.55-1.06)	0.106
Fruits	Model 1	1.00 (0.99-1.02)	0.687	0.82 (0.68-1.00)	0.048	1.00 (0.99-1.01)	0.958	0.89 (0.67-1.18)	0.427
	Model 2	1.00 (0.98-1.02)	0.939	0.78 (0.63-0.95)	0.015	1.00 (0.99-1.02)	0.541	0.88 (0.65-1.18)	0.401
	Model 3	1.00 (0.98-1.02)	0.935	0.79 (0.64-0.97)	0.025	1.01 (0.99-1.02)	0.399	0.92 (0.68-1.25)	0.605
Legumes	Model 1	0.99 (0.98-1.01)	0.492	0.91 (0.74-1.12)	0.387	0.98 (0.97-0.99)	0.006	0.83 (0.61-1.14)	0.254
	Model 2	1.00 (0.98-1.02)	0.825	0.97 (0.78-1.20)	0.766	0.99 (0.97-1.00)	0.039	0.94 (0.68-1.31)	0.729
	Model 3	1.00 (0.98-1.02)	0.816	0.99 (0.80-1.23)	0.954	0.99 (0.97-1.00)	0.040	1.00 (0.72-1.40)	0.984
Fish	Model 1	1.02 (1.00-1.03)	0.082	1.18 (0.98-1.43)	0.087	1.00 (0.99-1.01)	0.827	1.16 (0.87-1.55)	0.321
	Model 2	1.02 (1.00-1.03)	0.092	1.17 (0.96-1.44)	0.122	1.01 (0.99-1.02)	0.296	1.35 (0.99-1.84)	0.060
	Model 3	1.02 (1.00-1.04)	0.065	1.23 (1.00-1.51)	0.047	1.01 (1.00-1.02)	0.197	1.49 (1.08-2.06)	0.014
Cereals	Model 1	0.99 (0.98-1.01)	0.409	1.05 (0.86-1.27)	0.643	0.98 (0.97-0.99)	0.003	0.66 (0.49-0.89)	0.007
	Model 2	0.99 (0.97-1.01)	0.383	1.12 (0.91-1.37)	0.275	0.99 (0.98-1.00)	0.068	0.78 (0.57-1.06)	0.114
	Model 3	0.99 (0.97-1.01)	0.369	1.13 (0.92-1.38)	0.248	0.99 (0.98-1.00)	0.072	0.77 (0.57-1.06)	0.111
Meat[1]	Model 1	1.00 (0.98-1.02)	0.843	0.68 (0.55-0.83)	<0.001	1.00 (0.99-1.02)	0.456	0.71 (0.53-0.96)	0.028
	Model 2	1.00 (0.98-1.02)	0.851	0.72 (0.58-0.89)	0.002	1.00 (0.99-1.02)	0.468	0.66 (0.48-0.92)	0.014
	Model 3	1.00 (0.98-1.02)	0.854	0.70 (0.56-0.87)	0.001	1.00 (0.99-1.02)	0.541	0.63 (0.46-0.88)	0.007
Dairy products[1]	Model 1	1.00 (0.98-1.02)	0.926	1.29 (1.06-1.57)	0.012	0.98 (0.97-1.00)	0.015	0.89 (0.67-1.20)	0.449
	Model 2	1.00 (0.98-1.02)	0.766	1.27 (1.03-1.55)	0.024	0.99 (0.97-1.00)	0.037	0.93 (0.68-1.26)	0.647
	Model 3	1.00 (0.98-1.02)	0.740	1.38 (1.11-1.70)	0.002	0.99 (0.97-1.00)	0.037	1.01 (0.74-1.38)	0.953
Olive oil	Model 1	1.00 (0.98-1.02)	0.888	0.68 (0.55-0.85)	<0.001	1.00 (0.99-1.02)	0.915	0.72 (0.52-1.01)	0.055
	Model 2	1.00 (0.98-1.02)	0.789	0.65 (0.51-0.81)	<0.001	1.00 (0.98-1.01)	0.909	0.77 (0.55-1.07)	0.118
	Model 3	1.00 (0.98-1.02)	0.775	0.65 (0.52-0.82)	<0.001	1.00 (0.99-1.02)	0.980	0.82 (0.58-1.16)	0.262

rMED: relative Mediterranean Diet Score; y: years; PR: prevalence ratio; HR: hazard ratio; 95% CI = 95% confidence interval.
Model 1 was adjusted for region (Asturias; Gipuzkoa; Sabadell; Valencia), child age (in years) and sex (female; male). Model 2 was adjusted for the variables in the model 1 plus maternal social class (I/II, high; III, medium; IV/+V, low), mother's pre-pregnancy body mass index (normal-weight; overweight; obesity), smoked during pregnancy (no; yes), second hand smoking (no; yes), parity (0; ≥1), breastfeeding duration (< 4 months; ≥ 4 months), small child for gestational age according to weight (no; yes), child's television watching at 4 years (hours per day), sleep at 4 years (hours per day) and child sweetened beverages consumption at 4 years (<1 drinks/week; ≥1 drinks/week). Model 3 was adjusted for the variables included in the model 2 plus total rMED score excluding the component assessed.
[1]In Meat and Dairy products, a higher score indicates lower consumption

Table 4. Association between 1-point increase in the components of rMED score and abdominal obesity at four years and incidence risk from four to eight years in children from the INMA cohort study

Components of rMED (1-point increase)		Abdominal obesity[1] Prevalence at 4y Cases=128 Total= 1384		Abdominal obesity[1] Incidence risk until 8y Incident cases= 97 Person-years= 3274.97	
		PR (95% CI)	**p-value**	**HR (95% CI)**	**p-value**
Vegetables	Model 1	1.03 (0.99-1.06)	0.565	0.61 (0.46-0.81)	<0.001
	Model 2	1.02 (0.99-1.05)	0.630	0.69 (0.51-0.92)	0.012
	Model 3	1.03 (1.00-1.06)	0.366	0.70 (0.52-0.95)	0.022
Fruits	Model 1	1.00 (0.98-1.02)	0.923	0.81 (0.62-1.06)	0.129
	Model 2	1.00 (0.98-1.02)	0.802	0.80 (0.60-1.06)	0.122
	Model 3	1.00 (0.99-1.02)	0.643	0.82 (0.62-1.09)	0.175
Legumes	Model 1	0.99 (0.97-1.01)	0.203	0.88 (0.66-1.19)	0.411
	Model 2	0.99 (0.97-1.01)	0.345	0.96 (0.70-1.31)	0.787
	Model 3	0.99 (0.97-1.01)	0.399	0.99 (0.72-1.35)	0.940
Fish	Model 1	1.00 (0.98-1.02)	0.945	1.47 (1.12-1.94)	0.005
	Model 2	1.00 (0.99-1.02)	0.583	1.50 (1.11-2.04)	0.008
	Model 3	1.01 (0.99-1.02)	0.430	1.62 (1.19-2.20)	0.002
Cereals	Model 1	0.98 (0.97-1.00)	0.055	0.77 (0.59-1.02)	0.066
	Model 2	0.99 (0.97-1.01)	0.220	0.88 (0.65-1.18)	0.388
	Model 3	0.99 (0.97-1.01)	0.233	0.88 (0.65-1.19)	0.410
Meat[2]	Model 1	0.99 (0.98-1.01)	0.506	0.62 (0.47-0.81)	<0.001
	Model 2	0.99 (0.97-1.01)	0.462	0.63 (0.46-0.86)	0.004
	Model 3	0.99 (0.97-1.01)	0.395	0.61 (0.44-0.83)	0.002
Dairy products[2]	Model 1	0.98 (0.97-1.00)	0.030	1.14 (0.87-1.48)	0.343
	Model 2	0.98 (0.96-1.00)	0.017	1.11 (0.83-1.48)	0.476
	Model 3	0.98 (0.96-1.00)	0.017	1.18 (0.89-1.58)	0.252
Olive oil	Model 1	1.01 (0.99-1.02)	0.525	0.73 (0.54-0.98)	0.035
	Model 2	1.01 (0.99-1.02)	0.558	0.73 (0.53-1.01)	0.060
	Model 3	1.01 (0.99-1.03)	0.432	0.77 (0.55-1.07)	0.115

rMED: relative Mediterranean Diet Score; y: years; PR: prevalence ratio; HR: hazard ratio; 95% CI = 95% confidence interval.

Model 1 was adjusted for region (Asturias; Gipuzkoa; Sabadell; Valencia), child age (in years) and sex (female; male). Model 2 was adjusted for the variables in the model 1 plus maternal social class (I/II, high; III, medium; IV/+V, low), mother's pre-pregnancy body mass index (normal-weight; overweight; obesity), smoked during pregnancy (no; yes), second hand smoking (no; yes), parity (0; ≥1), breastfeeding duration (< 4 months; ≥ 4 months), small child for gestational age according to weight (no; yes), child's television watching at 4 years (hours per day), sleep at 4 years (hours per day) and child sweetened beverages consumption at 4 years (<1 drinks/week; ≥1 drinks/week). Model 3 was adjusted for the variables included in the model 2 plus total rMED score excluding the component assessed.

[1]Children from Gipuzkoa were excluded because the information on the waist circumference was not collected.

[2]In Meat and Dairy products, a higher score indicates lower consumption

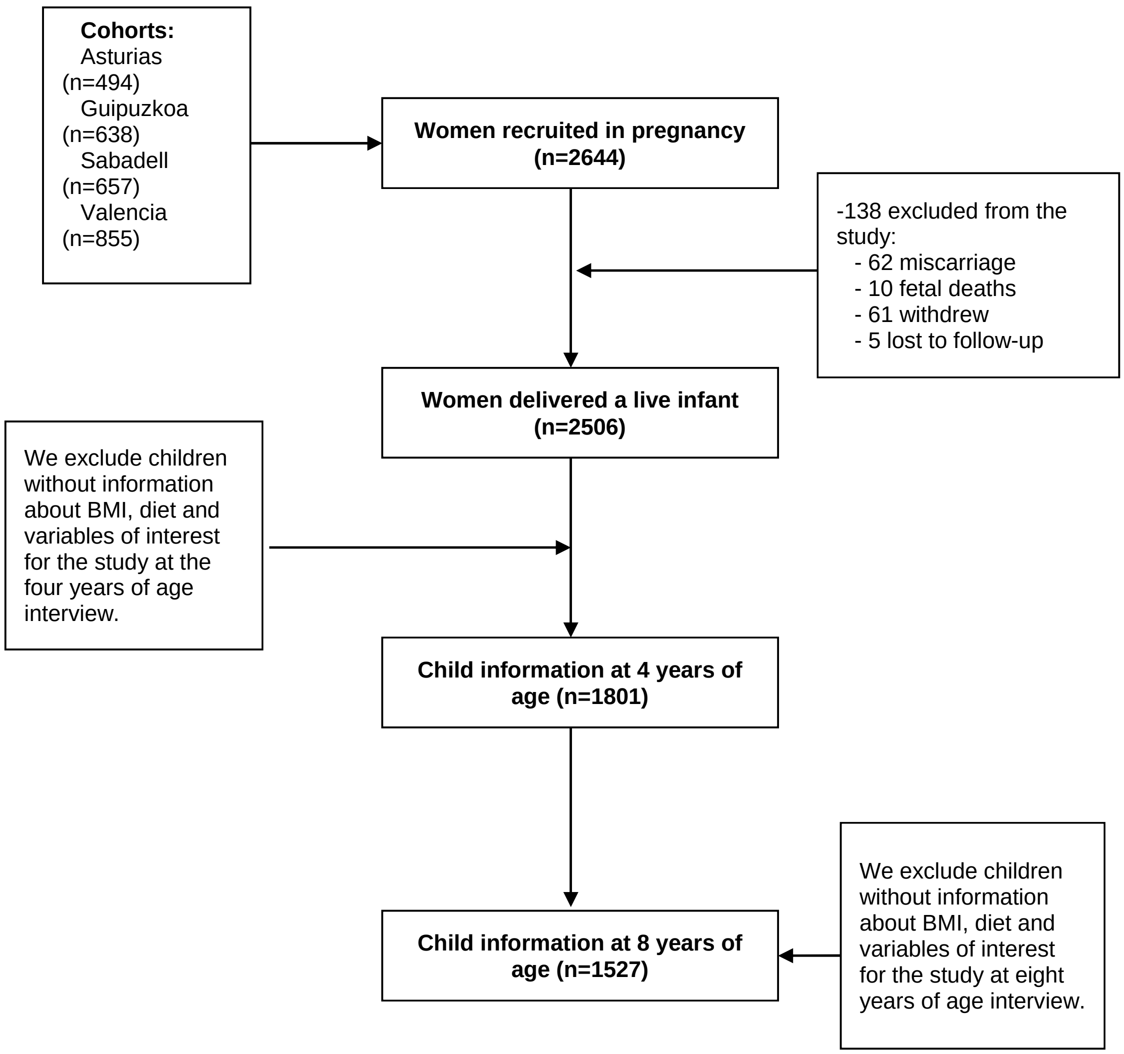

Figure 1. Flowchart of the study population describing the selection process.