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Article type : Original Article

Title page

Mediterranean diet and lung function, sensitization, and asthma at school age: the PARIS cohort

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This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version of Record](#). Please cite this article as [doi: 10.1111/PAI.13527](https://doi.org/10.1111/PAI.13527)

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Running title

Mediterranean diet and allergy in children

Abstract: 254 words

Text: 2899 words

Tables and Figures: 1 table, 2 figures

Supplemental Material: 4 tables, 1 figure

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i. Potential conflict of interest

Ms Amazouz has nothing to disclose. Dr Roda has nothing to disclose. Dr Beydon has nothing to disclose. Dr Lezmi reports personal fees from Novartis Pharma, personal fees from Astra Zeneca, personal fees from YSSUP research, during the conduct of the study; personal fees from DBV technologies, personal fees from Aimmune therapeutics, outside the submitted work. Dr Bourgoïn-Heack reports personal fees from Stallergene, personal fees from ALK, outside the submitted work; personal fees and nonfinancial support from Stallergene, personal fees and nonfinancial support from ALK, nonfinancial support from Astra Zeneca, outside the submitted work. Prof. Just reports grants and personal fees from Novartis, grants and personal fees from Astra Zeneca, personal fees from ALK, personal fees from Thermo Fisher, outside the submitted work. Prof. Momas has nothing to disclose. Dr Rancière reports a grant from Fondation Nestlé France during the conduct of the study.

ii. Financial support

This work was supported by the Paris Municipal Department of Social Action, Childhood, and Health (DASES), the European collaborative program MeDALL (FP7-261357), the French Nestlé Foundation through its 2018 research call and Paris Descartes University. Hélène Amazouz benefited from a PhD grant funded by the French Ministry for Higher Education, Research, and Innovation.

iii. Abstract and keywords

Background: The Mediterranean diet (MD) has known health benefits but its specific impact on allergy development is unclear. As part of the PARIS birth cohort follow-up, we aimed to investigate the adherence of 8 years old children to the MD and its association with allergic/respiratory morbidity at school age.

Methods: Diet was assessed using a food frequency questionnaire completed by the parents. Adherence to the MD was assessed based on two scores: the KIDMED index and the Mediterranean Diet Score (MDS). Current allergic diseases (asthma, rhinitis, eczema), lung function indices (FEV₁ and FVC), FeNO and specific IgE levels were determined during a health check-up at 8 years. Associations between levels of adherence to the MD and respiratory/allergic morbidity were studied using multivariable logistic and linear regression models adjusted for potential confounders.

Results: A total of 975 children were included in the present study, 35.6% with low adherence to the MD, 55.7% with moderate adherence, and 8.7% with high adherence according to the KIDMED index. High family socioeconomic status, any breastfeeding at 6 months, and consumption of organic food were associated with higher adherence to the MD. Compared to low adherence, high adherence was associated with lower risk of asthma and sensitization at 8 years, as well as higher FEV₁ and FVC.

Conclusion: This study suggests a protective effect of high adherence to the MD on allergic and respiratory morbidity at school age. These results need to be confirmed by further longitudinal analyses. A healthy diet may prevent allergic and respiratory morbidity in school-aged children.

Key Message

Higher adherence to the Mediterranean diet was associated with higher lung function indices and lower risk of current asthma and sensitization in French school-aged children from a population-based birth cohort. Using two recognized scores, this study is the first to examine the adherence to the Mediterranean diet in relation to lung function indices at school age in a population-based

setting. Results suggest that a healthy diet may help prevent respiratory and allergic morbidity in childhood.

Keywords

Allergic diseases, Birth cohort, Mediterranean diet, Lung function, Sensitization.

i. Main text

Introduction

For several decades, the prevalence of asthma and allergic diseases has increased, especially in industrialized countries. The World Health Organization (WHO) considers allergy as the most frequent chronic disease in children and childhood is a critical period for the development of respiratory function. In 2016, the Global Burden of Disease Study estimated that more than 339 million people suffered from asthma¹.

Many changes in lifestyle, including diet, and environmental exposure have occurred in recent decades and may explain this rise. The adoption of a Western lifestyle has dramatically changed people's dietary habits. Modern diet includes more processed food, less fresh fruit and vegetables as well as more imported foods which may lose their nutritional qualities.²

Among the dietary patterns, the Mediterranean diet (MD) is known for its many health benefits. The MD is characterized by a high intake of fruit, vegetables, legumes, nuts, unrefined cereals, bread, fish and olive oil.³ The main beneficial substances in the MD include a balanced ratio of n-6/n-3 essential fatty acids, fibre, antioxidants, vitamins E and C.⁴

Two meta-analyses^{5,6} and several reviews^{2,7,8} showed that a high level of adherence to the MD in children seems to be protective of asthma and wheezing symptoms. A recent meta-analysis suggested that higher adherence during childhood has short-term protective effects on wheezing but did not confirm the significant association with asthma.⁹

Concerning objective measurements of respiratory health, Romieu et al found that fruit and vegetable intake and higher adherence to the MD have a beneficial effect on lung function (forced expiratory volume in one second [FEV₁], forced vital capacity [FVC]) in asthmatic children but not in healthy children.¹⁰ In adults with asthma, high adherence to the MD improved the asthma control as measured by symptoms, lung function and fractional exhaled nitric oxide (FeNO).¹¹

Thus, as part of the PARIS (Pollution and Asthma Risk: an Infant Study) birth cohort, our aim was to study the adherence of children to the MD and to investigate the relationship between the level of MD adherence and respiratory health/allergy at school age.

Methods

Study design and population

In the PARIS population-based study including 3,840 healthy babies¹², data were prospectively collected using self-administered health, environmental and food questionnaires, and during health check-ups. The present study deals with children participating in the 8-year health check-up whose parents filled in the food frequency questionnaire (FFQ). The French ethics committees approved the PARIS study (permission nos. 031153, 051289, and ID-RCB 2009-A00824-53). All parents gave written informed consent.

Diet data and exposure assessment

Current food consumption was collected with a FFQ including 30 items with the question: “By the age of 8, how often does your child eat the following foods in a usual week, including meals at home and away from home, such as in the canteen?”. Parents were able to choose seven frequencies from “never“ to “more than once per day”. Two scores of adherence to the MD were computed.

An adapted KIDMED index was used to assess the quality of adherence to the MD in children.^{13,14} Unavailable information or different consumption frequency justified minor adaptations (Table S1). We used 14 items and categorised the index using the same thresholds: ≤ 3 low, 4-7 moderate, ≥ 8 high.

In addition, we used a Mediterranean Diet Score (MDS) originally developed for adults^{3,15} and adapted for children.¹⁶ The authors presumed dairy products are not detrimental for children and removed alcohol consumption. We included seven beneficial items: “Vegetables”, “Legumes”, “Fruit and nuts”, “Cereal”, “Fish”, “Dairy product and milk”, “Proportion of unsaturated fat” ; and one deleterious item: “Meat and meat products”. The MDS relies on the food frequency of eight items (i.e. the number of times a month the food was consumed).³ Thus, the consumption more than once a day was multiplied by 60, once per day by 30, 4-6 times per week by 20, 1-3 times per week by 8, 1-3 times per month by 2, < 1 time per month by 0.5, and a value of 0 was assigned to food items never consumed.

Health data

The health check-up at 8 years took place in two asthma and allergy reference centres in Paris (Necker and Trousseau hospitals). Current symptoms and medications, ever doctor-diagnosed asthma, eczema, and hay fever were collected by a paediatrician. Current asthma, eczema and rhinitis were defined according to the MEDALL consortium, as previously described.¹⁷ In addition, children performed spirometry tests (FEV₁ and FVC) and FeNO was measured (NIOX MINO®, Circassia Pharmaceuticals Inc., Chicago, USA). Weight and height at 8 years were measured during the health check-up and children were deemed as “overweight or obese” according to body mass index (BMI) for age and sex based on the WHO child growth standards. IgE sensitization to common food and inhalant allergens was assessed in sera with ImmunoCAP Trophatop® (fx26, fx27, fx28) and Phadiatop®, respectively (Phadia, Thermo Fisher Scientific, Uppsala, Sweden). Children were considered as sensitized if they were positive to at least one Trophatop® or Phadiatop® and the detection limit was set at 0.35 kUi/L. Ever doctor-diagnosed food allergy was documented at 6 years.

Covariates

Information such as child’s sex, mother's date of birth, geographic origin of parents, parental occupation, presence of older siblings, maternal smoking during pregnancy and parental history of allergy were collected at the maternity hospital. Family socioeconomic status (SES) was based on the highest position among the two parents and categorized as low, medium or high. Any breastfeeding at 6 months was ascertained using questionnaire at 6 months. Information was gathered about place of residence, exposure to environmental tobacco smoke (ETS) at home, sports and other physical activities, consumption of organic foods and dietary restrictions (for medical reasons or not) using a questionnaire completed by parents at 8 years. Physical activity was categorized as moderate or vigorous based on the frequency of participation in active sporting activities.¹⁸

Statistical methods

The main characteristics of participants and non-participants were described and compared using chi-squared tests. The associations between groups of adherence to the MD and sociodemographic, environmental, behavioural, and health variables were examined using multivariable multinomial logistic regression models. Correlation between KIDMED index and

MDS (as continuous variables) was investigated using Spearman test and a rank correlation coefficient (ρ) was calculated.

Associations of groups of adherence to the MD with respiratory indices (FEV_1 [mL], FVC [mL], FeNO >20 ppb) and respiratory/allergic morbidity in 8 year-olds were studied using multivariable linear and logistic regression models adjusted for potential confounding factors. Covariates included in the statistical models were selected based on the literature and a directed acyclic graph. The groups with the lowest adherence were considered as reference.

All analyses used Stata/SE 15.1 (StataCorp, College Station, Texas, USA) and results were expressed as adjusted beta coefficient (β) and odds ratio (aOR), with their 95% confidence intervals (95% CI). The significance level was 0.05. STROBE guidelines were followed.

Results

Participants

This study is based on 975 children with available data to compute the KIDMED index or MDS (Figure 1). Participating children came more often from a family with high SES, with an older mother and were less frequently exposed to maternal smoking during pregnancy than non-participating children. However, no differences were observed regarding sex, older siblings, place of residence at birth, parental history of asthma or allergy and exposure to ETS at birth (Table 1). Of the children, 47.5% were girls, 8.6% of children suffered from asthma, 7.9% suffered from allergic rhinitis, and 13.7% suffered from eczema. Also, 36.9% were sensitised to any allergen, 32.0% were sensitised to inhalant allergen and 16.7% were sensitised to food allergen.

Identification and description of scores

The KIDMED index was available for 968 children and ranged from -2 to 11, with a median (25th-75th percentile) of 4 (3-6). The “low adherence” group consisted of 345 children (35.6%) with a very low quality diet, the “moderate adherence” group consisted of 539 children (55.7%) with improvement needed to adjust intake to Mediterranean patterns, and the “high adherence” group consisted of 84 children (8.7%) with optimal MD. The distributions of the two scores are shown in Figure S1. The MDS was available for 822 children, ranged from 0 to 8 with a median (25th-75th percentile) of 3 (2-4). Tertile 1 consisted of 277 children (33.7%), Tertile 2, 348 children (42.3%), and Tertile 3, 197 children (24.0%). The concordance between KIDMED and MDS (n=815) is shown in Table S2 and the correlation was $\rho=0.68$ ($p<0.001$).

Factors associated with diet scores

Higher family SES, longer breastfeeding duration, and consumption of organic foods at 8 years of age were positively related to a higher adherence using the KIDMED index in a dose-response manner, while negative association was observed with the presence of older siblings (Table S3). Similar associations were found between breastfeeding and the consumption of organic foods and adherence to the MD assessed using the MDS (Table S4).

Adherence to the MD and respiratory/allergic morbidity at 8 years old

Regarding the KIDMED index, compared to the “low adherence” group, children with “high adherence” had significantly higher FEV₁ ($\alpha\beta=52.3$ mL, 95% CI: 5.5 to 99.1) and FVC ($\alpha\beta=67.4$

mL, 95% CI: 11.6 to 123.3), and a lower risk of current asthma (aOR=0.19, 95% CI: 0.04 to 0.85). The “high adherence” group had a lower risk of being sensitized to any allergens (aOR=0.56, 95% CI: 0.32 to 0.99), to inhalant allergens (aOR=0.60, 95% CI: 0.33 to 1.08) and to food allergens (aOR=0.38, 95% CI: 0.15 to 0.94). No significant association was found with FeNO, current rhinitis and current eczema (Figure 2).

Similar results were observed for the MDS. Compared to the first tertile group, children from the third tertile group, with higher adherence, had higher FEV₁ (aβ=49.9 mL, 95% CI: 15.1 to 84.6) and FVC (aβ=69.7 mL, 95% CI: 27.9 to 111.6). They also had a lower risk of current asthma (aOR=0.28, 95% CI: 0.12 to 0.64), FeNO >20 ppb (aOR=0.52, 95 CI: 0.29 to 0.91), sensitization to any allergens (aOR=0.59, 95% CI: 0.39 to 0.90), and to inhalant allergens (aOR=0.53, 95% CI: 0.34 to 0.82), with a significant trend across the tertile groups (all p for trend<0.05). No significant association was found with sensitization to food allergens, current rhinitis, and current eczema (Figure 2).

Discussion

Key results

Among a French population-based birth cohort, more than half of children had a moderate adherence to the MD and almost 9% of children followed an optimal MD. Children with higher adherence to the MD were more likely to be breastfed at 6 months and to consume organic food at 8 years. Compared to children with lower adherence to the MD, children with higher adherence had higher lung function indices and lower risk of current asthma and sensitization.

Strengths and limitations

Our study has several strengths, notably the quality and regularity of data collection from the PARIS participants. Health data was prospectively collected using standardized questionnaires and objective parameters were measured during a health check-up. Although based on a prospective cohort study, this research is limited by its cross-sectional design, and is not able to investigate the timing between diet and morbidity. However, it is unlikely that children would modify their adherence to the MD due to allergic or respiratory disorders.¹⁹ Dietary habits are established early in life^{20,21} and a questionnaire at 8 years is likely to reflect the diet during childhood. Food list was adapted to our French population, although the FFQ has not been validated in this population. As frequently observed in cohort follow-up, our study population shows an over-representation of high SES families but adjusting for family SES should avoid confounding bias regarding the association between adherence to the MD and respiratory/allergic morbidity.

The adherence to the MD was assessed using two existing scores. These comprehensive approaches are more relevant in studying the overall effects of dietary habits on health than studying each food or nutrient separately.^{2,10} The KIDMED index, first published in 2004¹⁴, is widely used to assess food habits regarding MD quality in children.²² Two KIDMED food items were not included in our FFQ (whole cereals/breakfast) and frequency thresholds were slightly different. These minor modifications were unlikely to impact the interpretation of the score. The KIDMED index was relevant in describing and comparing the adherence of our French population to the “optimal” MD using predefined frequency of consumption, while the adherence groups obtained for the MDS³ are based on dietary habits within our population, limiting the possibilities of comparison between studies.

Interpretation

Nearly two-thirds of the children had at least a moderate adherence in our Parisian study although PARIS children did not live near the Mediterranean Sea. Among studies evaluating the associations between KIDMED index and respiratory/allergic outcomes in children^{16,23,24}, Arvaniti et al²³ reported a similar distribution in urban Greek children. The adherence to the MD was higher in a Cretan study¹⁶, where 28% of the children had an optimal MD. The adherence was even higher in Menorca, Spain, where a high index was found for 37% of children.²⁴ Thus, the adherence of the PARIS children was consistent with a weaker adherence to the MD observed in urban populations compared to Mediterranean islands.^{16,23,24}

In urban Greek children, no significant association was found between the level of adherence to the MD and physical activity, BMI and obesity status²³ and in Crete, there were no significant associations with sex, parental education status, number of siblings, reported parental asthma and current parental farming.¹⁶ These findings are consistent with our results except for parental SES and older siblings.¹⁶ This could be explained by the difference in population settings (urban city vs. island) or geographical area (France vs. Greece).

In our population of French school-aged children, the KIDMED index and MDS led to similar results, suggesting that not only an optimal MD adherence but also the highest adherence based on the MDS distribution was beneficial for respiratory health and allergy. These results are consistent with previous studies^{16,19,23–26} showing a lower risk of asthma in school-aged children with higher adherence to the MD. In the literature, different outcomes have been studied such as asthma-like symptoms (mainly wheezing) reported by parental questionnaire^{16,19,23–26}, ever reported asthma by a physician¹⁹, score of asthma control with symptoms, and lung function indices. Some of these results are not statistically significant¹⁶ or found only in girls.²⁵ Three meta-analyses concluded that there were inverse associations between high adherence to the MD and the risk of current wheeze^{5,6,9}, but only two reported significant associations with asthma.^{5,6} Furthermore, associations between MD and eczema were examined in only one Spanish study which did not find any association.²⁷ A review of the association between MD and allergic rhinitis was inconclusive, which is consistent with our findings.⁷

Regarding associations with lung function, our results are consistent with the very few prior studies. Romieu et al showed that higher MDS was significantly related to higher lung function indices in asthmatic but not in non-asthmatic children, and not related to FeNO.¹⁰ Among Spanish adults, participants with a high adherence to the MD had both higher FVC and FEV₁ than participants with low adherence.²⁸ Interestingly, a high vegetable diversity consumption was beneficial regarding asthma and FeNO levels in school-aged Portuguese children.²⁹ In our study, higher adherence to the MD was significantly associated with FeNO levels <20 ppb when using the MDS but not the KIDMED index. This may be due to the smaller number of children in the KIDMED group with higher adherence.

Our findings shed a new light on the inverse associations between adherence to the MD and allergic sensitization. Four previous studies^{16,24,26,30} have investigated MD adherence during childhood in relation to allergic sensitization to common aeroallergens assessed by skin prick test^{16,24,26} or IgE measurements.³⁰ No studies found significant associations although two teams reported inverse associations: OR=0.54, 95% CI: 0.21 to 1.99¹⁶ and OR=0.49, 95% CI: 0.18 to 1.32²⁴ for high vs low KIDMED index. A recent review concluded on a very low level of evidence regarding the association between adherence to the MD and atopy.⁷

Biological evidence supports the potential beneficial effect of the MD on allergic and respiratory morbidity. Fresh fruit and vegetables are rich in vitamin C, E and β -carotene as well as flavonoids and polyphenolic compounds which are antioxidant and may be beneficial for asthma and lung function. An intervention study examined the effect of withdrawal of antioxidant-rich foods (in particular fruit and vegetables) from the diet, and found an increase in airway neutrophils in adults, thus disrupting asthma control and damaging lung function.³¹ Fish are rich in n-3-polyunsaturated fatty acids²⁶ and cereals (particularly whole grains) are rich in vitamin E, phenolic acids and phytic acid and had a protective effect during childhood against asthma.^{7,24} A balanced ratio of 5/1 omega-6/omega-3 fatty acid ratio was found to have a beneficial effect on patients with asthma, whereas a ratio of 10/1 had adverse consequences.³² Increased β -carotene intake was associated with a lower risk of allergic sensitization and IgE levels in children from the MAAS birth cohort.³³ Antioxidants may have a beneficial effect on the inflammatory response during childhood and appear to modulate immune reactions that play a role in chronic inflammatory processes such as asthma.^{7,20}

In conclusion, our findings suggest that a high adherence to the MD has a protective effect on current asthma, sensitization, and lung function in French school-aged children. Although more longitudinal studies and in other populations are required to confirm and generalise these results. These findings support evidence that public health messages promoting healthy dietary habits among children may also be beneficial to respiratory health and allergy.

ii. Acknowledgments

The authors are grateful to all children and parents of the PARIS birth cohort and to the administrative staff (Dominique Viguier, Marianne Bijou, and Bruno Metivier) for their involvement in the PARIS cohort follow-up. We thank the physicians (Dr Michèle Boulé, Dr Bernard Boutin, Dr Mathieu Pellan, Dr Rym Belmir, Dr Michaela Semeraro, Dr Isabelle Haegy, Dr Wajed Aljundi, Dr Candice Meyzer, Dr Eric Daireaux, Dr Anne-Marie Le Marec, Dr Sofia Kalaboka), the nurses (Eve Thioux, Patricia Laskowsky, Dorothée Nguyen Van Suong, Charlotte Pellerin), and the lung function test technicians, Dr Stephan Gabet for IgE measurements at 8 years old.

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iv. Table

Table 1. Characteristics of the PARIS cohort children included and not included in the present study.

	Not included N=2865	Included N=975	p†
Sex			
Male, n (%)	1458 (50.9)	512 (52.5)	0.38
Female, n (%)	1407 (49.1)	463 (47.5)	
Family socioeconomic status			
High, n (%)	1732 (60.5)	662 (67.9)	<0.001
Medium, n (%)	823 (28.7)	257 (26.4)	
Low, n (%)	310 (10.8)	56 (5.7)	
Older siblings			
None, n (%)	1654 (57.7)	525 (53.8)	0.10
One, n (%)	934 (32.6)	342 (35.1)	
Two or more, n (%)	277 (9.7)	108 (11.1)	
Place of residence at birth			
Paris city, n (%)	1828 (63.8)	605 (62.1)	0.33
Paris suburbs, n (%)	1037 (36.2)	370 (37.9)	
Maternal age at birth above 35 years old, n (%)	670 (23.4)	275 (28.2)	<0.01
Parental history of asthma, n (%)	570 (20.0)	194 (20.0)	0.99
Parental history of asthma, allergic rhinitis or eczema, n (%)	1504 (52.6)	524 (54.0)	0.47
Maternal smoking during pregnancy, n (%)	340 (11.9)	93 (9.5)	0.05
Exposure to ETS at home at birth, n (%)	596 (21.6)	201 (20.7)	0.56

ETS: environmental tobacco smoke. † Chi-squared test.

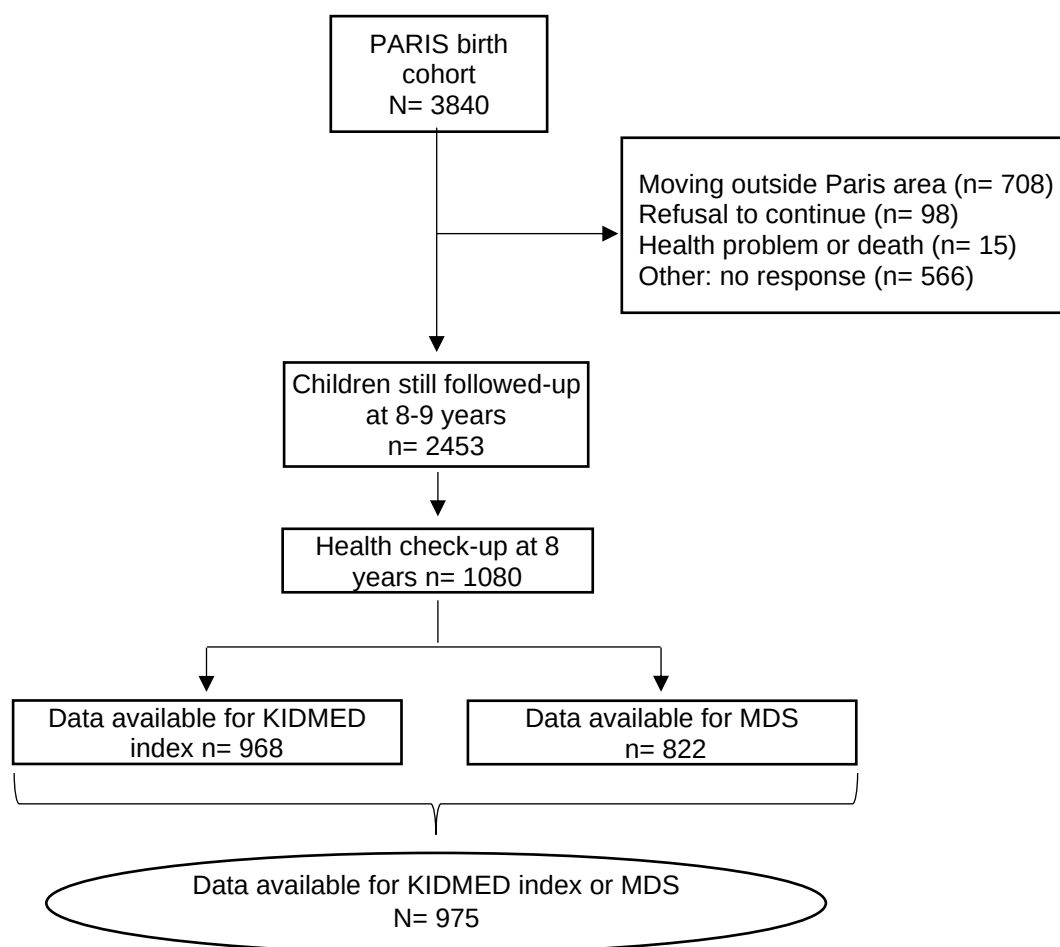
v. Figures legends

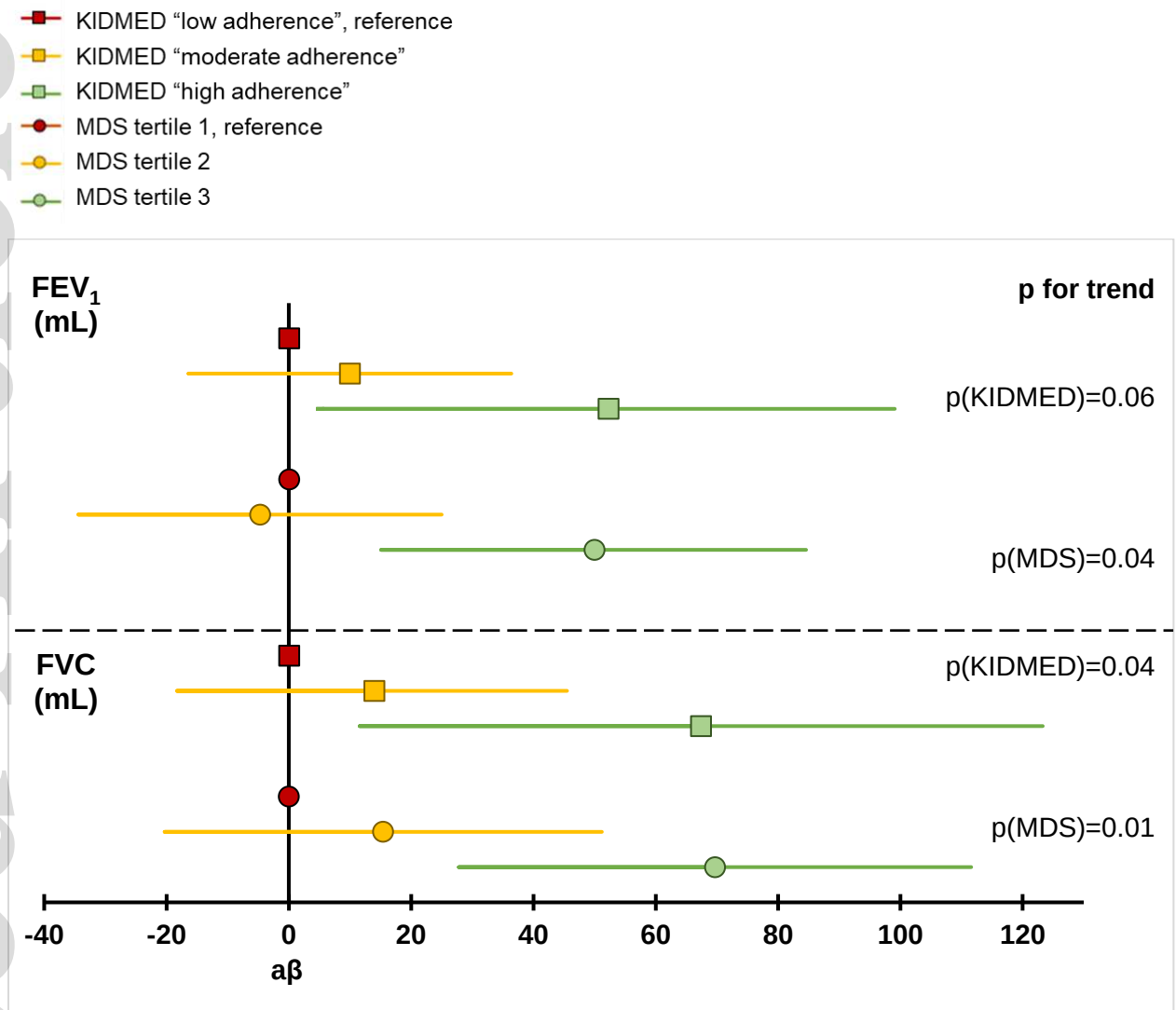
Figure 1. Flow chart of the PARIS cohort children participating in the present study.

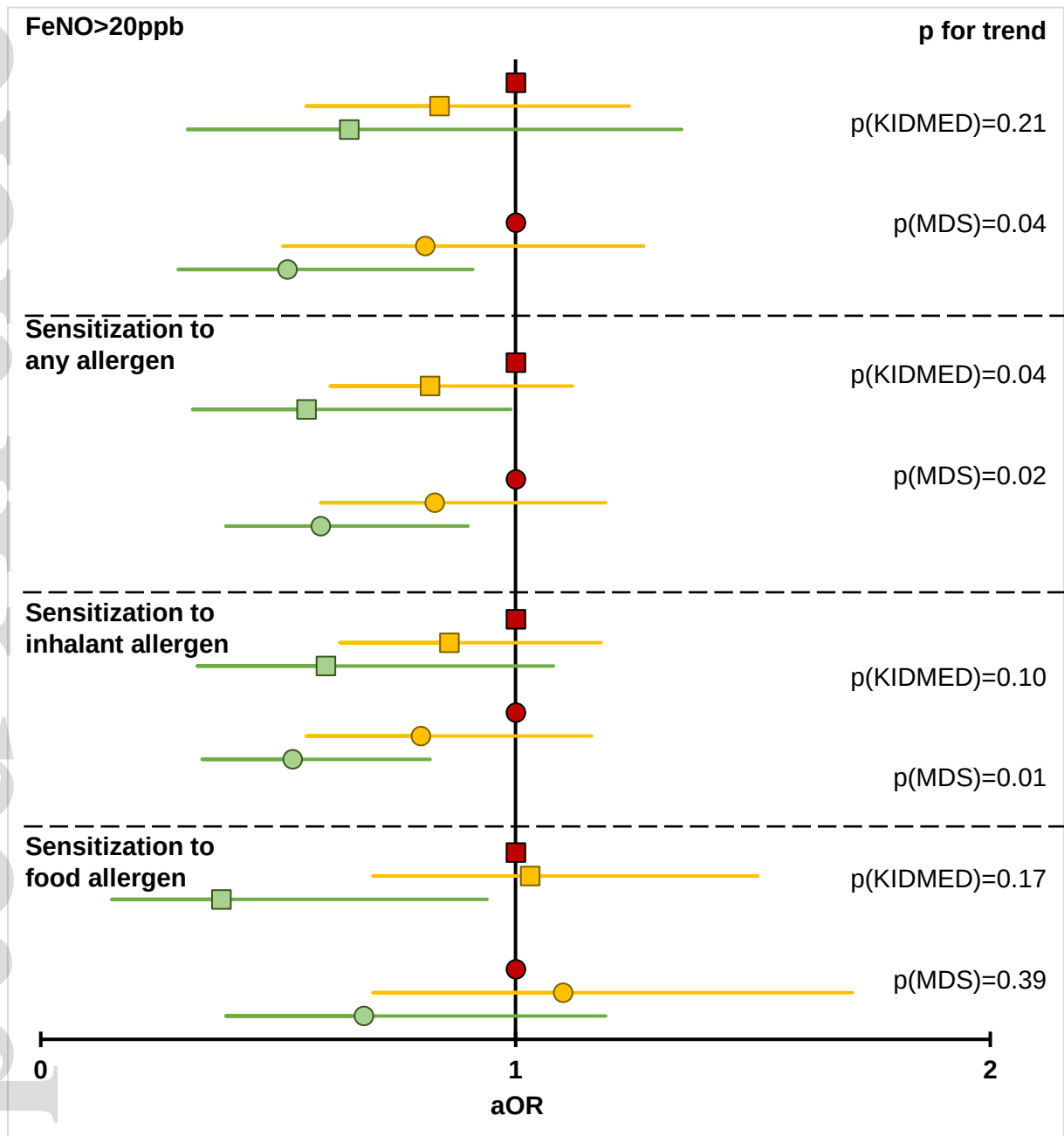
Legend: MDS: Mediterranean Diet Score.

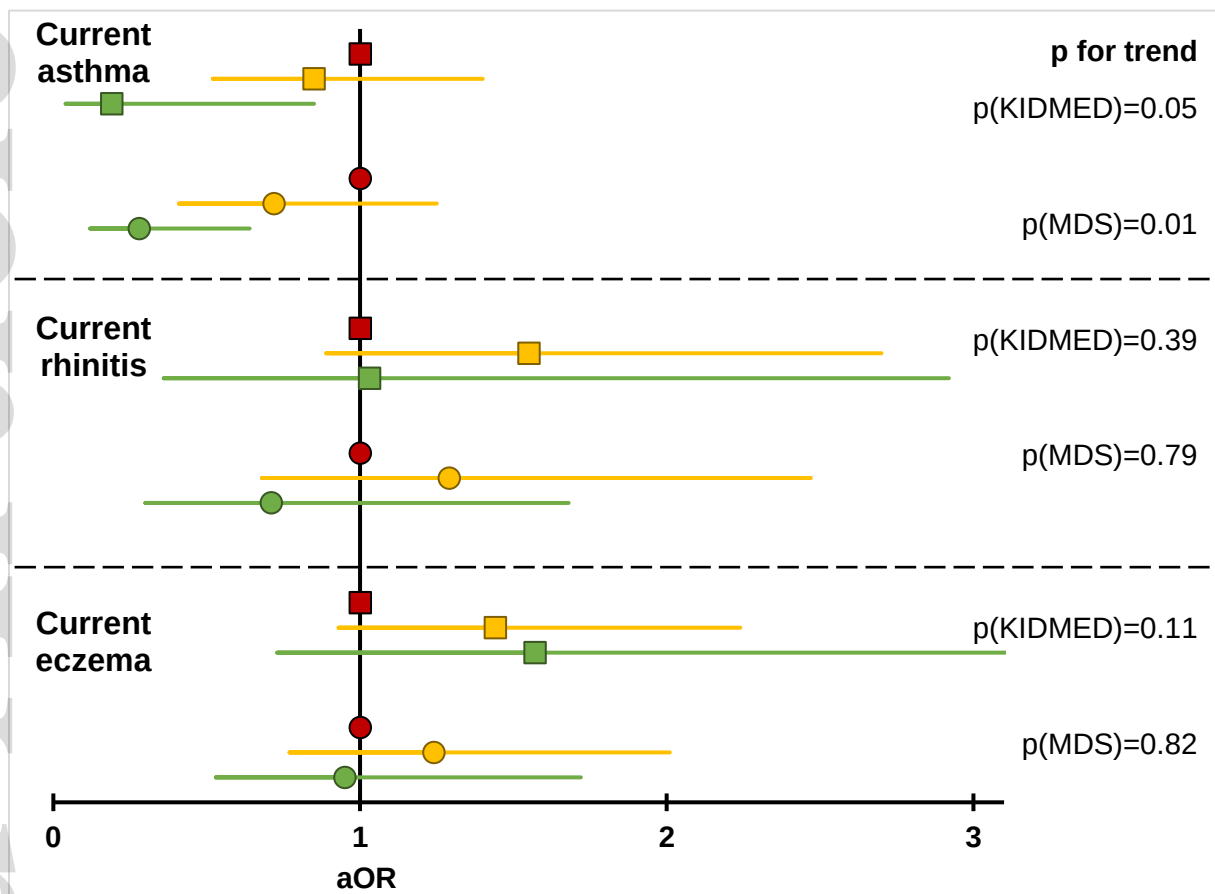
Figure 2. Adjusted associations for Mediterranean diet adherence groups (KIDMED index and MDS) with (a) lung function indices, (b) FeNO and allergic sensitization and (c) current allergic diseases at 8 years of age in children from the PARIS birth cohort.

Legend: β : adjusted regression coefficient, aOR: adjusted odds ratio, 95% CI: 95% confidence interval, FEV1: forced expiratory volume in one second, FVC: forced vital capacity, FeNO: fraction of exhaled nitric oxide, MDS: Mediterranean Diet Score. All models were adjusted for the following variables: maternal smoking during pregnancy, parental socioeconomic status at birth, parental history of allergies, older siblings at birth, child's sex, child's ethnicity (FEV1, FVC) or continent of maternal origin (FeNO, IgE and current allergic diseases models), any-breastfeeding at 6 months, exposure to environmental tobacco smoke at 8 years old, consumption of organic food at 8 years old, moderate or vigorous physical activity at least once a week at 8 years old, overweight or obese according to body mass index for age and sex at 8 years old based on the WHO child growth standards, season of food frequency questionnaire. FEV1 and FVC were also adjusted for age and height at health check-up.









Supporting information

Mediterranean diet and lung function, sensitization, and asthma at school age: the PARIS cohort

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Table S1. Assessment of the adherence to the Mediterranean diet in school-age children from the PARIS birth cohort using criteria adapted from the original KIDMED questionnaire.

Criteria of original KIDMED	Score	Criteria in the present study	Score
Similar criteria to Altavilla and Caballero-Pérez, 2019, <i>Public Health Nutrition</i>.			
Takes a fruit every day	+1	Takes a fruit every day	+1
Has a second fruit every day	+1	Has a second fruit every day	+1
Has fresh or cooked vegetables regularly once per day	+1	Has fresh or cooked vegetables regularly once per day	+1
Has fresh or cooked vegetables more than once per day	+1	Has fresh or cooked vegetables more than once per day	+1
Uses olive oil at home	+1	Uses olive oil at home	+1
Slightly modified criteria			
Consumes fish regularly (at least 2-3 times per week)	+1	Consumes fish regularly (at least 1-3 times per week)	+1
Likes pulses and eats them more than once per week	+1	Consumes pulses at least once per week	+1
Consumes nuts regularly (at least 2-3 times per week)	+1	Consumes nuts regularly (at least 1-3 times per week)	+1
Consumes whole-grain pasta or whole-grain rice almost every day (5 or more times per week)	+1	Consumes pasta, rice or semolina almost every day (4 or more times per week) †	+1
Has a dairy product for breakfast (yoghurt, milk, etc.)	+1	Has a dairy product (yoghurt, milk, cheese, etc.) every day	+1
Takes two yoghurts and/or some cheese (40 g) daily	+1	Takes second dairy products (yoghurt, milk, cheese, etc.) every day	+1
Has commercially baked goods or pastries for breakfast	-1	Has baked goods or pastries every day	-1
Goes to a fast-food (hamburger) restaurant more than once per week	-1	Consumes “fries” and “soda or light soda” at least once per week	-1
Takes sweets and candy several times every day	-1	Takes sweets and candy every day	-1
Removed criteria			
Has whole cereals or whole-grains (whole-meal bread, etc.) for breakfast	+1	Not available	-
Skips breakfast	-1	Not available	-

† Our question does not include the term “whole-grain” similarly to the first version of the KIDMED index (Serra-Majem, et al. 2004, *Public Health Nutrition*).

Figure S1. Description of the distribution of (a) KIDMED index (n= 968) and (b) MDS (n= 822) in children from the PARIS cohort.

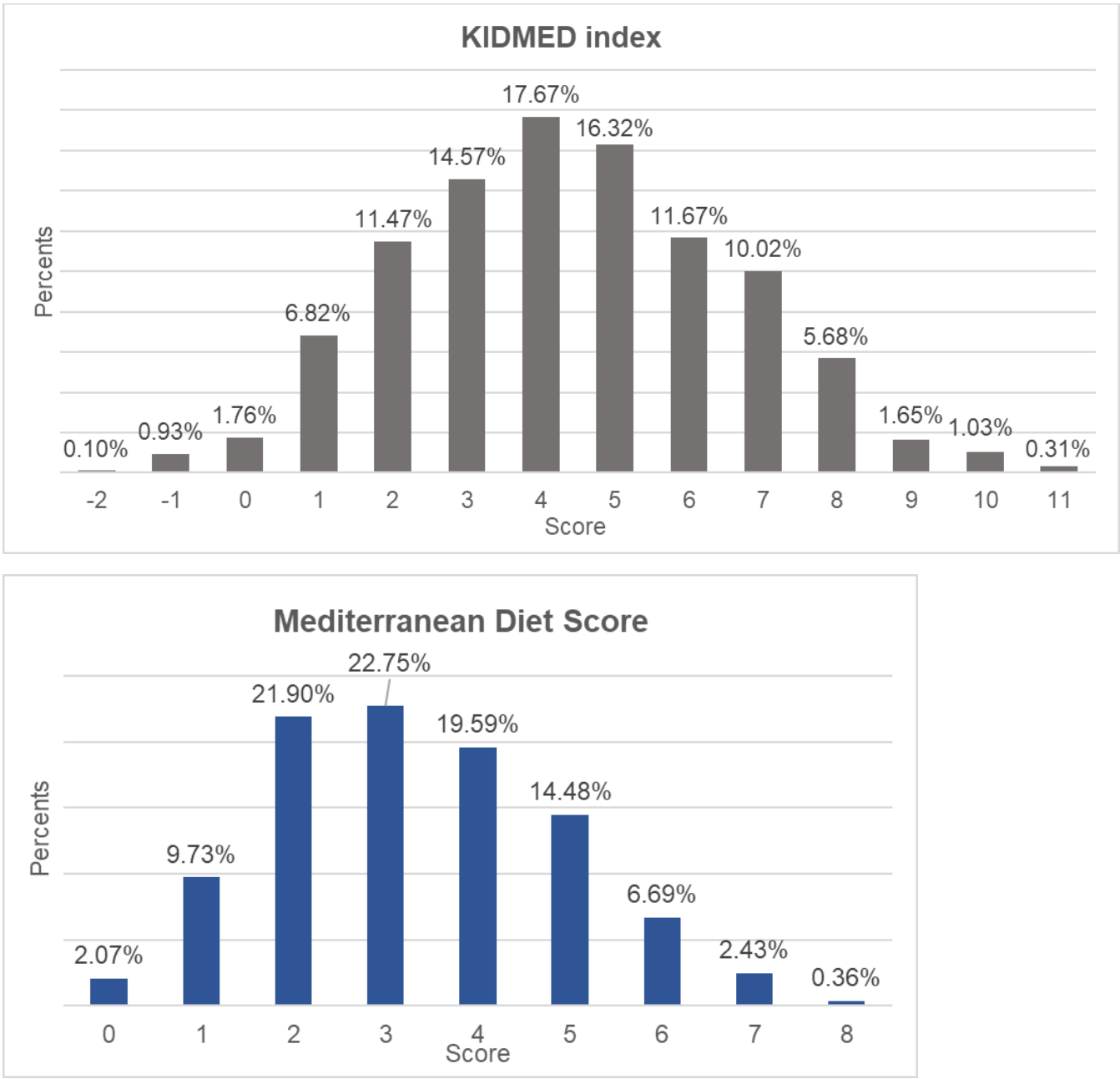


Table S2. The agreement between the KIDMED score and MDS in children from the PARIS cohort with both scores available (n=815)

Agreement		KIDMED score			
		Low	Moderate	High	Total
MDS	Tertile 1	195	79	0	274
	Tertile 2	96	230	19	345
	Tertile 3	13	130	53	196
	Total	304	439	72	815

MDS: Mediterranean Diet Score

Table S3. Factors associated with Mediterranean diet adherence groups (KIDMED index): multivariable multinomial regression model in children from the PARIS birth cohort.

KIDMED Group	“Low adherence” n= 287	“Moderate adherence” n= 478	“High adherence” n= 71
	Ref.	aOR (95% CI)	aOR (95% CI)
Environment and lifestyle			
Maternal smoking during pregnancy (yes vs. no)	Ref.	0.76 (0.44 to 1.31)	0.66 (0.21 to 2.07)
Continent of maternal origin:			
Europe	Ref.	Ref.	Ref.
Africa	Ref.	1.37 (0.62 to 3.01)	1.21 (0.31 to 4.76)
North & south America	Ref.	1.45 (0.50 to 4.21)	0.67 (0.07 to 6.10)
Asia/Australia/Oceania	Ref.	1.27 (0.49 to 3.34)	0.63 (0.07 to 5.45)
Parental SES at birth (high vs. low, medium)	Ref.	1.56 (1.12 to 2.16)	2.02 (1.07 to 3.83)
Maternal age at birth (≥median vs. <median) [†]	Ref.	0.86 (0.62 to 1.19)	0.66 (0.37 to 1.16)
Older siblings (yes vs. no)	Ref.	0.66 (0.48 to 0.91)	0.59 (0.33 to 1.05)
Any-breastfeeding at 6 months (yes vs. no)	Ref.	1.54 (1.09 to 2.19)	2.33 (1.32 to 4.10)
Consumption of organic food at 8 years old (yes vs. no)	Ref.	1.82 (1.33 to 2.50)	2.63 (1.39 to 4.99)
Exposure to ETS at 8 years old (yes vs. no)	Ref.	1.06 (0.73 to 1.54)	0.72 (0.34 to 1.53)
Place of residence at 8 years old:			
Paris city	Ref.	Ref.	Ref.
Paris inner suburbs	Ref.	0.89 (0.65 to 1.22)	0.77 (0.43 to 1.35)
Paris outer suburbs	Ref.	0.82 (0.45 to 1.49)	1.12 (0.42 to 2.98)
Child’s characteristics			
Parental history of allergy (yes vs. no)	Ref.	1.05 (0.77 to 1.43)	1.12 (0.64 to 1.95)
Sex (girl vs. boy)	Ref.	0.93 (0.68 to 1.26)	1.02 (0.59 to 1.75)
Food allergy at 6 years old (yes vs. no)	Ref.	1.27 (0.53 to 3.01)	0.93 (0.22 to 3.97)
Dietary restrictions at 8 years old (yes vs. no)	Ref.	0.79 (0.28 to 2.20)	1.50 (0.37 to 6.10)
BMI at 8 years old (overweight, obese vs. normal)	Ref.	0.90 (0.59 to 1.37)	0.99 (0.47 to 2.09)
Moderate/vigorous physical activity at 8 years old (yes vs. no)	Ref.	1.13 (0.72 to 1.79)	1.36 (0.56 to 3.29)
Season of FFQ (fall-winter vs. spring-summer)	Ref.	1.06 (0.78 to 1.44)	1.37 (0.79 to 2.38)

aOR: adjusted odds ratio, 95% CI: 95% confidence interval, BMI: body mass index, ETS: environmental tobacco smoke, FFQ: food frequency questionnaire, SES: socioeconomic status. [†] The median of maternal age at birth is 32 years old. The odds ratios in bold differ significantly from the reference (p<0.05).

Table S4. Factors associated with tertiles of Mediterranean diet adherence (MDS): multivariable multinomial regression model in children from the PARIS birth cohort.

	Tertile 1 n= 235	Tertile 2 n= 305	Tertile 3 n= 174
	Ref.	aOR (95% CI)	aOR (95% CI)
Environment and lifestyle			
Maternal smoking during pregnancy (yes vs. no)	Ref.	0.73 (0.40 to 1.35)	0.82 (0.40 to 1.65)
Continent of maternal origin:			
Europe	Ref.	Ref.	Ref.
Africa	Ref.	1.26 (0.51 to 3.10)	1.30 (0.47 to 3.59)
North & south America	Ref.	1.31 (0.31 to 5.53)	1.63 (0.34 to 7.81)
Asia/Australia/Oceania	Ref.	1.20 (0.40 to 3.58)	0.49 (0.09 to 2.54)
Parental SES at birth (high vs. low, medium)	Ref.	1.37 (0.94 to 2.01)	1.17 (0.75 to 1.81)
Maternal age at birth (≥median vs. <median) [†]	Ref.	0.95 (0.65 to 1.38)	0.82 (0.54 to 1.27)
Older siblings (yes vs. no)	Ref.	0.80 (0.55 to 1.16)	0.84 (0.55 to 1.28)
Any-breastfeeding at 6 months (yes vs. no)	Ref.	1.70 (1.13 to 2.57)	2.25 (1.42 to 3.56)
Consumption of organic food at 8 years old (yes vs. no)	Ref.	1.54 (1.07 to 2.21)	1.82 (1.18 to 2.81)
Exposure to ETS at 8 years old (yes vs. no)	Ref.	1.05 (0.68 to 1.63)	1.08 (0.65 to 1.78)
Place of residence at 8 years old:			
Paris city	Ref.	Ref.	Ref.
Paris inner suburbs	Ref.	0.79 (0.55 to 1.14)	0.72 (0.47 to 1.10)
Paris outer suburbs	Ref.	1.13 (0.55 to 2.34)	1.26 (0.56 to 2.83)
Child's characteristics			
Parental history of allergy (yes vs. no)	Ref.	1.05 (0.74 to 1.51)	0.97 (0.64 to 1.47)
Sex (girl vs. boy)	Ref.	0.74 (0.52 to 1.04)	0.77 (0.52 to 1.16)
Food allergy at 6 years old (yes vs. no)	Ref.	0.83 (0.33 to 2.12)	0.58 (0.18 to 1.87)
Dietary restrictions at 8 years old (yes vs. no)	Ref.	2.78 (0.70 to 11.03)	1.78 (0.36 to 8.87)
BMI at 8 years old (overweight, obese vs. normal)	Ref.	1.17 (0.72 to 1.92)	1.11 (0.63 to 1.95)
Moderate/vigorous physical activity at 8 years old (yes vs. no)	Ref.	0.95 (0.56 to 1.62)	0.89 (0.48 to 1.65)
Season of FFQ (fall-winter vs. spring-summer)	Ref.	0.94 (0.66 to 1.34)	1.37 (0.91 to 2.07)

aOR: adjusted odds ratio, 95% CI: 95% confidence interval, BMI: body mass index, ETS: environmental tobacco smoke, FFQ: food frequency questionnaire, MDS: Mediterranean diet score, SES: socioeconomic status. [†] The median of maternal age at birth is 32 years old. The odds ratios in bold differ significantly from the reference (p<0.05).