

Original article

Mediterranean diet is associated with reduced asthma and rhinitis in Mexican children

Background: Diet during pregnancy and childhood has been suggested to play an important role in children's asthma risk. We assessed whether the adherence to a Mediterranean dietary pattern, for children in the last 12 months and their mothers during pregnancy, was associated with both childhood asthma and allergic rhinitis.

Methods: A cross-sectional study was conducted in 2004 using a random sample of 1476 children (6- to 7-year old) from the Mexicali region, Mexico. Dietary data of children's intake in the last 12 months and their mothers' intake during pregnancy was collected, through a parental food frequency questionnaire. A Mediterranean diet score was computed [Trichopoulou et al., *N Engl J Med* 348 (2003), 2599]. Data on seven asthma and rhinitis-related outcomes were obtained from the International Study of Asthma and Allergies in Childhood questionnaire.

Results: Adherence to a Mediterranean dietary pattern was inversely associated with asthma ever (OR = 0.60, 95% CI = 0.40–0.91), wheezing ever (0.64, 0.47–0.87), rhinitis ever (0.41, 0.22–0.77), sneezing ever (0.79, 0.59–1.07), current sneezing (0.71, 0.52–0.96) and current itchy-watery eyes (0.63, 0.42–0.95). No associations were found using the mothers' pregnancy diet score, except for current sneezing (0.71, 0.53–0.97).

Conclusions: Our findings suggest a protective effect of following a healthy dietary pattern on asthma and allergic rhinitis in Mexican children.

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The prevalence of asthma and allergies has been increasing worldwide during the last few decades, especially in children (1), although a plateau has been reached in some developed countries (2). Although the causes of this rise remain largely unexplained, lifestyle- and more specifically-diet habits are suggested to play an important role (3). The introduction of fast food and the westernization of many worldwide dietary patterns may be one of the underlying causes behind the rise in asthma and allergy prevalence (3). As reviewed elsewhere (4–6), previous studies have tried to find associations between foods or nutrients and asthma and allergies. However, although most studies explored the effects of a wide range of foods and/or nutrients, they could only find associations for some of them, and some of those associations could be partly attributed to the strong correlation of the different foods and nutrients among them. To unravel the potential role of foods and nutrients as risk or protective factors for asthma or allergies, new hypotheses have been generated, such as those focused on diet during pregnancy (4). Additionally, there is a need to explore new ways of diet assessment, such as the description of dietary patterns using cluster or factor analyses (7, 8), or the

utilization of diet scores (7), both of which aim to summarize the whole diet of an individual.

We examined the association between both children's diet in last 12 months and their mothers' diet during pregnancy, and asthma and allergic rhinitis prevalence in children. To do so, we used a dietary pattern approach analysis – based on a Mediterranean diet score (9) – on Mexican children from the International Study of Asthma and Allergies in Childhood (ISAAC) (10).

Material and methods

Study subjects

The study population consisted of a random selection of 3125 children, 6- to 7-year old, from all primary public and private schools registered in the Mexicali Public Education Secretary, in 2004. Recruitment was performed through schools, and a total of 2528 parents (81%) gave consent for participation. Five hundred and sixty-three children who did not fulfill age criteria were excluded from the database. For this study, we selected children who had available dietary data sufficient to compute their Mediterranean diet score and/or the score of their mothers, giving a total of 1476 children with at least one score (mothers' diet or children's

diet), and at least one available outcome variable. The study protocol was approved by the Ethics Committee of the Mexican National Public Health Institute, and written informed consent was obtained from the parents.

Study design

A cross-sectional prevalence study was conducted using ISAAC methodology (10) on Mexican children from Mexicali, in *Baja California*, Mexico. Parents were asked to complete the ISAAC questionnaire on respiratory and allergic symptoms (10), and seven outcome variables were selected: asthma ever, wheezing ever, current wheezing, allergic rhinitis ever, sneezing ever, current sneezing and current itchy-watery eyes. The exposure variables consisted of two Mediterranean diet scores that measured the adherence to the Mediterranean dietary pattern for children's diet in the last 12 months and their mothers' diet during pregnancy.

Methods

Outcome variables were defined as having a positive answer to the following questions: asthma ever: 'Have you ever been told by a doctor that your child has asthma?' or 'Have you ever been told by a doctor that your child has asthmatic bronchitis or reacting airways disease?'; wheezing ever: 'Has your child ever had wheezing or whistling in the chest?'; current wheezing: 'In the past 12 months, has your child ever had wheezing or whistling in the chest?'; allergic rhinitis ever: 'Has your child ever had allergic rhinitis?'; sneezing ever: 'Has your child ever had a problem with sneezing, or a runny, or blocked nose when he/she did not have a cold or the flu?'; current sneezing: 'In the past 12 months, has your child ever had nasal congestion or sneezing when he did not have cold or the flu?'; and current itchy-watery eyes: 'In the past 12 months, has this nose problem been accompanied by itchy-watery eyes?'. The questionnaire was self-administered and included questions about house conditions, tobacco exposure, medical history of asthma and allergic rhinitis in the family, and other exposures during pregnancy and early life, including diet.

Dietary information were collected using a food frequency questionnaire (FFQ) with 70 food items, asking about both the diet of children in the last 12 months and the diet of their mothers during pregnancy. The questionnaire was developed and validated for use in adult Mexican women (11) and includes foods eaten by Mexican children. Information were converted into a daily consumption frequency of each food, which was in turn converted into the daily consumption frequencies of eight food groups: vegetables (broccoli or cauliflower, carrot, tomato, potatoes, courgettes, lettuce, avocado, cladodes, green beans, chili or chili sauce), legumes (kidney beans, green peas, lentils), fruits and nuts (orange, grape, apple, banana, peach, watermelon, pineapple, papaya, pear, kiwi, mango, strawberry, prickly pears, plums, orange juice, grapefruit juice, almonds, walnuts, hazelnuts, peanuts), dairy products (milk, cheese, yogurt), cereals (cereals, pasta, rice, bread), meat (meat, chicken, ham, pork), fish (seafood, fish, canned fish, tuna, sardines), and junk food and fat (fast food, hamburgers, sweets, cakes, milk candy, chips, ice creams, cookies, popcorn, chocolate pastries, butter, cream, margarine).

A Mediterranean diet score, originally designed by Trichopoulos (9), was used to evaluate the adherence to the Mediterranean dietary pattern. The score was adapted as follows: (i) the moderate alcohol consumption component was *a priori* suppressed, as it was not applicable to children; (ii) the high monounsaturated:saturated fat ratio component could not be computed with the available data; and (iii) and a junk food and fat consumption component was

introduced, as previous literature suggested that fast food, snacks, and sweets should be included in Mediterranean diet scores (12–14). The final Mediterranean diet score included eight components that corresponded to the eight food groups previously described, and ranged from 0 (minimum adherence to Mediterranean diet) to 8 (maximum adherence). The median consumption of each score component was selected as the cut-off point, to have half of the subjects add +1 to the final score, and the other half add 0 to the final score. As in the original score (9), participants in the upper half of consumption of vegetables, legumes, fruits and nuts, cereals, and fish added +1, and participants in the lower half of consumption of dairy products, meat, and junk food and fat added +1, so a higher final score indicated higher adherence to the Mediterranean dietary pattern.

Analysis

Logistic regression analysis was used to estimate the association between the diet scores of children and mothers and the selected outcome variables: asthma ever, wheezing ever, current wheezing, allergic rhinitis ever, sneezing ever, current sneezing and current itchy-watery eyes. Both the children and mothers scores were categorized into tertiles, being the first (lower adherence to Mediterranean diet) the reference category in the logistic model. The following potential confounding factors were included in the final models only if they were related to both the Mediterranean diet score and the outcome, or were potentially relevant according to previous literature: gender, number of older sisters or brothers, birth weight, body mass index (BMI), maternal breastfeeding, parental educational level, children's exercise, smoking exposure (while in the womb, during the first year of life, or currently in the home), parental medical history of asthma and allergic rhinitis, animals at home during pregnancy, animals at home during first year of life, living in a ranch during pregnancy, premature birth, respiratory infections during early life, silhouette, changes from the silhouette they had at 4-year old, type of combustible used for cooking at home, sleeping alone in a room, and mould or dampness at home. Possible effect modification by gender, smoking, maternal education, and maternal asthma and allergic rhinitis was assessed through stratification of the final models. The goodness-of-fit of the statistical models was checked (15). Because of missing data on some variables, the sample size varied slightly between analyses. Data analysis was conducted using STATA 8.2 (StataCorp, College Station, TX, USA).

Results

We first compared data between children who were excluded from the present analyses because of lack of data on diet ($n = 489$) and those who were finally included (Table 1). Excluded subjects reported lower maternal education, higher maternal asthma, and lower current sneezing and current itchy-watery eyes. Only 3% of the mothers smoked during pregnancy, although 13% of the children were exposed to tobacco smoke during first year of life and up to 18% of them were currently exposed in their homes. Familial antecedents of asthma or allergic rhinitis ranged from 3% to 8%. Twelve percent of children had been diagnosed with asthma, 25% had ever had wheezing, 7% had ever had allergic rhinitis and 30% had ever had rhinitis-related symptoms.

Table 1. Characteristics of excluded and included children

	Excluded* (<i>n</i> = 489)	Included (<i>n</i> = 1476)	<i>P</i> -value (95% CI)
Body mass index, mean (SD)	18.8 (7.0)	18.8 (6.4)	0.945
Maternal education: less than primary	9 (2)	29 (2)	<0.001
Primary	143 (31)	148 (10)	
Secondary	228 (49)	638 (44)	
Preuniversity	67 (14)	379 (26)	
University	20 (4)	244 (17)	
Breast feeding	346 (81)	1077 (79)	0.459
Smoking during pregnancy	22 (5)	42 (3)	0.049
Smoking during first year of life	62 (16)	166 (13)	0.068
Early life respiratory infections	111 (28)	391 (30)	0.429
Home exposure to tobacco smoke	95 (23)	260 (19)	0.036
Sport hours per week: none or <2	103 (28)	339 (26)	0.208
2–5	130 (35)	420 (32)	
6 or more	138 (37)	556 (42)	
Maternal asthma†	39 (10)	56 (4)	<0.001
Paternal asthma†	15 (4)	59 (5)	0.589
Brother/sister with asthma†	33 (9)	100 (8)	0.609
Maternal rhinitis†	16 (4)	81 (6)	0.177
Paternal rhinitis†	6 (2)	38 (3)	0.175
Brother/sister with rhinitis†	14 (4)	53 (4)	0.824
Asthma ever	44 (10)	170 (12)	0.206
Wheezing ever	99 (22)	354 (25)	0.181
Current wheezing	45 (10)	147 (11)	0.794
Rhinitis ever	28 (7)	100 (7)	0.699
Sneezing ever	131 (30)	419 (30)	0.933
Current sneezing	96 (20)	370 (25)	0.013
Current itchy-watery eyes	31 (6)	166 (11)	0.002

Values are given as *n* (%).

*Subjects without any available dietary score or without any outcome variable were excluded.

†Doctor's diagnosis. A positive answer to the question: 'Have you ever been told by a doctor that a member of your family (mother, father, brother/sister) has asthma?'

Both mothers and children reported high consumption of fruits and nuts, vegetables, and junk food and fat (Table 2). The correlation between each component of the score in children and their mothers ranged from 0.42 to 0.64 ($P < 0.0001$ in all components). The mean Mediterranean diet score for children and mothers was 3.7 (SD = 1.3) and 3.9 (SD = 1.3) respectively, and the correlation between these scores was $r = 0.37$ ($P < 0.0001$).

The crude and adjusted associations between the diet of children (in the last 12 months) are shown in Tables 3 and 4. Associations with rhinitis-related outcomes are shown in Tables 5 and 6. After adjusting for confounding factors, being in the two higher tertiles of Mediterranean diet score was inversely associated with asthma ever (P -for trend = 0.034), wheezing ever (P -for trend = 0.001), allergic rhinitis ever (P -for trend = 0.046), current sneezing (P -for trend = 0.036) and current itchy-watery eyes (P -for trend = 0.084). Independent associations between each of the score components and asthma and allergic rhinitis were also assessed (data available from the authors). It is worth mentioning that children's junk food and fat consumption was positively

associated with most of the outcomes [1st tertile vs 3rd tertile OR (95% CI): asthma ever 3.53 (1.73–7.17), current wheezing 2.65 (1.30–5.42), sneezing ever 1.85 (1.15–2.91), current sneezing 1.67 (1.04–2.68), and current itchy-watery eyes 2.32 (1.26–4.29)]. On the other hand, cereals consumption was inversely associated with most of the outcomes [1st vs 3rd tertile OR (95% CI): wheezing ever 0.37 (0.21–0.63), current wheezing 0.22 (0.09–0.50), sneezing ever 0.51 (0.31–0.86), current sneezing 0.58 (0.34–0.99), and current itchy-watery eyes 0.47 (0.23–0.94)]. Stratification of the final models by gender, smoking, maternal education, maternal asthma, and maternal allergic rhinitis did not suggest any effect modification (data available from the authors).

Adjustment for BMI in children with available data ($n = 384$) also showed inverse associations between being in the two higher tertiles of the Mediterranean diet score and most outcomes. Although the magnitude of the point estimates remained generally unchanged, most of the associations were not statistically significant probably because of lack of statistical power: OR for asthma ever 0.78 ($P = 0.417$), wheezing ever 0.77 ($P = 0.266$), current wheezing 1.63 ($P = 0.125$), allergic rhinitis ever 0.19 ($P = 0.001$), sneezing ever 0.83 ($P = 0.415$), current sneezing 0.88 ($P = 0.581$) and current itchy-watery eyes 0.47 ($P = 0.016$).

No associations were found between mothers' diet score during pregnancy and asthma or allergic rhinitis outcomes in children in the crude or adjusted analyses, except for current sneezing. Adjusted OR, when comparing the second and third to the first tertiles of mothers' diet score during pregnancy, were: for asthma ever 1.03 (95% CI: 0.67–1.56), wheezing ever 0.74 (95% CI: 0.55–1.01), current wheezing 1.02 (95% CI: 0.65–1.60), rhinitis ever 0.64 (95% CI: 0.36–1.15), current rhinitis 0.87 (95% CI: 0.65–1.18), current sneezing 0.71 (95% CI: 0.53–0.97) and current itchy-watery eyes 0.96 (95% CI: 0.64–1.45).

Discussion

This study shows that a greater adherence to a Mediterranean dietary pattern – characterized by a high intake of vegetables, fruits and nuts, legumes, fish and cereals, and a low intake of dairy products, meat and junk food and fat – is associated with having less asthma, wheezing, allergic rhinitis, current sneezing and current itchy-watery eyes, in Mexican children. No associations were found when studying the mothers' adherence to a Mediterranean dietary pattern during pregnancy.

Our results are consistent with previous literature, as the Mediterranean diet score we used contains most of the food components that previous studies pointed out as relevant for asthma or allergies (4–6). Being in the upper half of consumption of food groups suggested to be protective in previous studies added +1 to the score. Likewise, for food groups suggested to be detrimental,

Table 2. Distribution of food consumption by study children and their mothers during pregnancy

		Mothers diet during pregnancy		Children's diet in the past 12 month	
		<i>n</i>	Mean intake (95% CI) (portions per day)	<i>n</i>	Mean intake (95% CI) (portions per day)
Vegetables	1st tertile	463	1.73 (1.68–1.78)	494	0.97 (0.93–1.01)
	2nd tertile	462	3.59 (3.54–3.64)	462	2.18 (2.15–2.21)
	3rd tertile	455	6.17 (6.04–6.31)	469	4.35 (4.22–4.47)
Legumes	1st tertile	532	0.35 (0.33–0.36)	551	0.25 (0.24–0.26)
	2nd tertile	403	0.83 (0.81–0.84)	418	0.72 (0.71–0.73)
	3rd tertile	440	1.67 (1.62–1.72)	433	1.51 (1.46–1.57)
Fruits and nuts	1st tertile	452	2.11 (2.04–2.19)	472	1.55 (1.50–1.60)
	2nd tertile	451	4.83 (4.74–4.92)	459	3.56 (3.50–3.62)
	3rd tertile	451	9.77 (9.50–10.05)	465	7.77 (7.52–8.02)
Dairy products	1st tertile	496	0.68 (0.65–0.71)	586	0.82 (0.79–0.85)
	2nd tertile	487	1.62 (1.60–1.64)	421	1.57 (1.56–1.59)
	3rd tertile	395	2.52 (2.49–2.56)	430	2.35 (2.32–2.39)
Cereals	1st tertile	497	0.88 (0.86–0.91)	483	0.96 (0.93–0.98)
	2nd tertile	442	1.81 (1.78–1.83)	509	1.97 (1.94–2.00)
	3rd tertile	443	2.92 (2.87–2.96)	447	3.10 (3.05–3.15)
Meat	1st tertile	496	0.66 (0.64–0.68)	496	0.60 (0.59–0.62)
	2nd tertile	469	1.31 (1.30–1.33)	522	1.26 (1.24–1.28)
	3rd tertile	418	2.14 (2.10–2.18)	443	2.14 (2.11–2.18)
Fish	1st tertile	502	0.21 (0.20–0.22)	675	0.19 (0.19–0.20)
	2nd tertile	417	0.57 (0.56–0.58)	410	0.57 (0.56–0.58)
	3rd tertile	417	1.36 (1.29–1.43)	348	1.28 (1.21–1.35)
Junk food and fat	1st tertile	465	0.93 (0.89–0.96)	469	1.25 (1.21–1.30)
	2nd tertile	434	2.13 (2.10–2.17)	468	2.65 (2.61–2.69)
	3rd tertile	444	4.92 (4.75–5.08)	465	5.55 (5.38–5.73)

n varies from 1273 to 1476 within the dietary exposure variables.

Table 3. Association between children's current diet and asthma

		Asthma ever	
		Crude OR (95% CI)	Adjusted† OR (95% CI)
<i>n</i> *	<i>n</i> (%)		
Children score	1326		
1st tertile (0–3)	588 60 (14.74)	1	1
2nd tertile (4)	367 24 (9.06)	0.58 (0.35–0.95)	0.59 (0.35–0.98)
3rd tertile (5–8)	371 24 (9.52)	0.61 (0.37–1.01)	0.61 (0.36–1.02)
1st tertile (0–3)	588 60 (14.74)	1	1
2nd & 3rd tertiles (4–8)	738 48 (9.28)	0.59 (0.36–0.89)	0.60 (0.40–0.91)

*The following variables had missing values: asthma ever (402).

†All models have been adjusted for: gender, maternal education, physical exercise, current tobacco smoking at home, maternal asthma, and maternal rhinitis.

being in the lower half of consumption added +1. Previous studies have suggested a protective effect of dairy products in asthma (5). However, it has also been suggested that they could be detrimental for allergic rhinitis (16). Therefore, we decided to treat dairy products as in the original Trichopoulou score (+1 to subjects in the lower half of consumption). The adjusted analysis of the individual components of the score showed that junk food and fat consumption were the stronger

components among the detrimental components of the score. This finding is consistent with previous literature suggesting that both junk food and fat consumption are risk factors for asthma (16, 17). Cereals consumption was its counterpart among the protective components of the score. Surprisingly, our results suggest that neither vegetables nor fruits and nuts were playing a major role in our final score, probably because of the high consumption of both of them in our study population (see Table 2). Our results are partially consistent with two previous ISAAC cross-sectional studies, which also assessed the association between a high level of adherence to a Mediterranean diet and several outcomes of asthma and allergic rhinitis in children. One of them found a reduction only in the risk of allergic rhinitis, but no association with other outcomes, which could be explained by the small sample size (18). The other study found a reduced risk of severe asthma in girls, but no association in boys or with other outcomes (19). Misclassification caused by the use of a very short FFQ could be an explanation for their partial lack of associations.

Our study found no significant associations when assessing the mothers' adherence to Mediterranean diet during pregnancy and asthma and allergy in children, except for current sneezing. Actually, despite previous

Table 4. Association between children's current diet and wheezing

	<i>n</i> *	<i>n</i> (%)	Wheezing ever		<i>n</i> (%)	Current wheezing	
			Crude OR (95% CI)	Adjusted† OR (95% CI)		Crude OR (95% CI)	Adjusted† OR (95% CI)
Children score	1326						
1st tertile (0–3)	588	126 (30.96)	1	1	40 (10.13)	1	1
2nd tertile (4)	367	64 (24.06)	0.71 (0.50–1.00)	0.76 (0.53–1.09)	29 (11.11)	1.11 (0.67–1.84)	1.22 (0.73–2.05)
3rd tertile (5–8)	371	47 (19.03)	0.52 (0.36–0.77)	0.52 (0.35–0.78)	20 (8.23)	0.80 (0.45–1.40)	0.80 (0.45–1.42)
1st tertile (0–3)	588	126 (30.96)	1	1	40 (10.13)	1	1
2nd & 3rd tertiles (4–8)	738	111 (21.64)	0.62 (0.46–0.83)	0.64 (0.47–0.87)	49 (9.72)	0.96 (0.62–1.48)	1.01 (0.64–1.58)

*The following variables had missing values: wheezing ever (406), current wheezing (427).

†All models have been adjusted for: gender, maternal education, physical exercise, current tobacco smoking at home, maternal asthma, and maternal rhinitis.

Table 5. Association between children's current diet and having ever reported rhinitis and sneezing

	<i>n</i> *	<i>n</i> (%)	Rhinitis ever		<i>n</i> (%)	Sneezing ever	
			Crude OR (95% CI)	Adjusted† OR (95% CI)		Crude OR (95% CI)	Adjusted† OR (95% CI)
Children score	1326						
1st tertile (0–3)	588	39 (10.13)	1	1	134 (33.00)	1	1
2nd tertile (4)	367	9 (3.46)	0.32 (0.15–0.67)	0.29 (0.12–0.67)	71 (26.89)	0.75 (0.53–1.05)	0.79 (0.55–1.13)
3rd tertile (5–8)	371	15 (6.15)	0.58 (0.31–1.08)	0.55 (0.27–1.13)	70 (27.78)	0.78 (0.55–1.10)	0.79 (0.55–1.14)
1st tertile (0–3)	588	39 (10.13)	1	1	134 (33.00)	1	1
2nd & 3rd tertiles (4–8)	738	24 (4.76)	0.44 (0.26–0.75)	0.41 (0.22–0.77)	141 (27.33)	0.76 (0.58–1.01)	0.79 (0.59–1.07)

*The following variables had missing values: rhinitis ever (483), sneezing ever (404).

†All models have been adjusted for: gender, maternal education, physical exercise, current tobacco smoking at home, maternal asthma, and maternal rhinitis.

Table 6. Association between children's current diet and reported current sneezing and itchy-watery eyes

	<i>n</i> *	<i>n</i> (%)	Current sneezing		<i>n</i> (%)	Current itchy-watery eyes	
			Crude OR (95% CI)	Adjusted† OR (95% CI)		Crude OR (95% CI)	Adjusted† OR (95% CI)
Children score	1326						
1st tertile (0–3)	588	122 (29.26)	1	1	60 (14.46)	1	1
2nd tertile (4)	367	61 (22.43)	0.70 (0.49–1.00)	0.73 (0.50–1.06)	24 (8.92)	0.58 (0.35–0.96)	0.58 (0.35–0.97)
3rd tertile (5–8)	371	57 (21.84)	0.68 (0.47–0.97)	0.68 (0.47–1.00)	28 (10.73)	0.71 (0.44–1.15)	0.69 (0.42–1.12)
1st tertile (0–3)	588	122 (29.26)	1	1	60 (14.46)	1	1
2nd & 3rd tertiles (4–8)	738	118 (22.14)	0.69 (0.51–0.92)	0.71 (0.52–0.96)	52 (9.81)	0.64 (0.43–0.96)	0.63 (0.42–0.95)

*The following variables had missing values: current sneezing (376), current itchy-watery eyes (381).

†All models have been adjusted for: gender, maternal education, physical exercise, current tobacco smoking at home, maternal asthma, and maternal rhinitis.

suggestions (4), the few longitudinal studies regarding maternal food consumption during pregnancy and children's asthma could not find a consistent role of dietary patterns or specific foods in children's asthma, except for fish intake (20–23). Unfortunately, although maternal fish consumption could truly play a role in this issue, its proposed biological mechanism of action (through ω -3 fatty acids) is still controversial, as there is at least one study measuring umbilical cord ω -3 and ω -6 fatty acids, which concluded that it is unlikely that those fatty acids play an important role in early childhood asthma (24).

Whether our lack of associations is because of real lack of effect or recall bias (as the information was collected > 6 years after pregnancy), cannot be determined.

The use of a Mediterranean diet score is new and considered to be a strength of this study. It allows for an easy description of a dietary pattern with a semi-quantitative FFQ, without calculating the grams of each food or nutrient consumed per day, as required in other scores (25). Moreover, the calculation of the score takes into account the synergic effects or interactions between foods or nutrients (26), and overrides the correlation between

different foods, as diet scores are designed to reflect the whole dietary pattern instead of specific nutrients or foods. Finally, use of the score improved statistical power, which is a concern when studying single nutrients or foods that account for small effects. Therefore, we recommend the use of scores in future studies, in addition to classical nutritional analyses with foods and nutrients as exposures.

Both experimental and epidemiological data support the biological plausibility of our findings (5). Mediterranean dietary pattern is rich in antioxidants that can protect against endogenous and exogenous oxidative damage in the airways (27). Additionally, maternal and early life dietary antioxidants play a role in the child's immune system development, which in turn plays a role in chronic inflammatory processes such as asthma. The relatively high consumption of fish, source of ω -3 fatty acids, combined with low ω -6 consumption from dietary fats is typical in a Mediterranean diet. This high ω -3/ ω -6 fatty acid ratio reduces the levels of pro-inflammatory cytokines [that are increased in asthmatic subjects (28)] and influences the differentiation of T-helper lymphocytes (29, 30). This mechanism could also explain the predominant role of the junk food and fat component in the score. Additionally, it is known that junk food (especially fast food and snacks) has a high salt content, which has also been suggested to have a detrimental effect on asthma (31).

Several limitations of our study need to be considered. Although the cross-sectional design makes determining the direction of causality impossible, we consider unlikely that asthmatic children changed their dietary pattern because of an asthma diagnosis. Although some outcome variables (e.g. asthma ever) may have happened before the exposure (children's last 12-month diet), this is not identified by the authors as a limitation. Actually, children's diet in the last 12 month was correlated with their mothers' diet during pregnancy, suggesting that their dietary patterns have most likely been unchanged during whole life. Information bias could arise from the use of parental auto-administered questionnaires for assessing both outcome and exposures. However, assessing dietary data with auto-administered questionnaires is generally considered a reliable method for ranking subjects according to food intake (32, 33), and 6- to 7-year old children are too young to answer the questionnaires themselves. Parent-reported respiratory symptoms and doctor's diagnosed asthma are also commonly used in epidemiologic studies (10). The role of recall bias as a potential explanation for the lack of association between the mothers' diet and the children's outcomes has already been mentioned. With regard to nonresponse bias, some differences in maternal education and exposure to tobacco smoke were found between children with Mediterranean diet score (included) and those without (excluded). The lack of differences in the association

between diet and the outcomes, when stratifying according to maternal education or exposure to tobacco smoke, makes it unlikely that nonresponse has led to biased results. Confusion by total caloric intake could also be a concern. Adjusting for energy intake is a standard procedure in nutritional epidemiology (34), as it allows standardizing of food and nutrient intake according to total food intake, while avoiding confusion on the effects of specific foods or nutrients and considering energy intake by itself as a possible primary determinant of disease. As available dietary data did not allow for the calculation of daily energy intake, we used an alternative approach, making additional adjustments for BMI where data were available. By doing so, we obtained similar associations, although not statistically significant probably because of the lack of statistical power. Dietary patterns are strongly related to lifestyle patterns, which need to be accounted for in the analyses. Nevertheless, as the analyses in this study were adjusted for gender, maternal education, physical exercise, tobacco exposure and maternal asthma and allergic rhinitis, we believe it unlikely that all the observed associations could be as a result of residual confounding. Finally, in relation to the choice of the diet score, we could not use a children's specific healthy diet score, such as the KIDMED score (12), because of limited data. The original Trichopoulou's Mediterranean diet score (9) was designed to be used in adult Greek population and had to be partially adapted for use in Mexican children. Nevertheless, we consider that it provides a fairly accurate description of the adherence to Mediterranean dietary pattern in the study participants.

In conclusion, our findings suggest a potential protective effect of following a Mediterranean dietary pattern (especially with a high consumption of cereals and a low consumption of junk food and fat) on asthma and allergic rhinitis in Mexican children. These results, if confirmed, provide additional evidence of the benefits of healthy dietary habits and support the need for public health measures to promote a healthy diet among children.

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References

1. Braman SS. The global burden of asthma. *Chest* 2006;**130**(Suppl.):4–12.
2. Braun-Fahrlander C, Gassner M, Grize L, Takken-Sahli K, Neu U, Stricker T et al. No further increase in asthma, hay fever and atopic sensitisation in adolescents living in Switzerland. *Eur Respir J* 2004;**23**:407–413.
3. Seaton A, Godden DJ, Brown K. Increase in asthma: a more toxic environment or a more susceptible population? *Thorax* 1994;**49**:171–174.
4. Devereux G, Seaton A. Diet as a risk factor for atopy and asthma. *J Allergy Clin Immunol* 2005;**115**:1109–1117.
5. Tricon S, Willers S, Smit HA, Burney PG, Devereux G, Frew AJ et al. Nutrition and allergic disease. *Clin Exp Allergy Reviews* 2006;**6**:117–188.
6. McKeever TM, Britton J. Diet and asthma. *Am J Respir Crit Care Med* 2004;**170**:725–729.
7. Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol* 2002;**13**:3–9.
8. Wirfalt E, Mattisson I, Gullberg B, Berglund G. Food patterns defined by cluster analysis and their utility as dietary exposure variables: a report from the Malmo Diet and Cancer Study. *Public Health Nutr* 2000;**3**:159–173.
9. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med* 2003;**348**:2599–2608.
10. Asher MI, Keil U, Anderson HR, Beasley R, Crane J, Martinez F et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;**8**:483–491.
11. Hernandez-Avila M, Romieu I, Parra S, Hernandez-Avila J, Madrigal H, Willett W. Validity and reproducibility of a food frequency questionnaire to assess dietary intake of women living in Mexico City. *Salud Publica Mex* 1998;**40**:133–140.
12. Serra-Majem L, Ribas L, Ngo J, Ortega RM, Garcia A, Perez-Rodrigo C et al. Food, youth and the Mediterranean diet in Spain. Development of KIDMED, Mediterranean Diet Quality Index in children and adolescents. *Public Health Nutr* 2004;**7**:931–935.
13. Goulet J, Lamarche B, Nadeau G, Lemieux S. Effect of a nutritional intervention promoting the Mediterranean food pattern on plasma lipids, lipoproteins and body weight in healthy French-Canadian women. *Atherosclerosis* 2003;**170**:115–124.
14. Ciccarone E, Di Castelnuovo A, Salcuni M, Siani A, Giacco A, Donati MB et al. A high-score Mediterranean dietary pattern is associated with a reduced risk of peripheral arterial disease in Italian patients with type 2 diabetes. *J Thromb Haemost* 2003;**1**:1744–1752.
15. Hosmer DW, Lemeshow S. Applied logistic regression. New York: Wiley, 1989.
16. Huang SL, Pan WH. Dietary fats and asthma in teenagers: analyses of the first Nutrition and Health Survey in Taiwan (NAHSIT). *Clin Exp Allergy* 2001;**31**:1875–1880.
17. Wickens K, Barry D, Friezema A, Rhodius R, Bone N, Purdie G et al. Fast foods – are they a risk factor for asthma? *Allergy* 2005;**60**:1537–1541.
18. Chatzi L, Apostolaki G, Bibakis I, Skypala I, Bibaki-Liakou V, Tzanakis N et al. Protective effect of fruits and vegetables and the Mediterranean diet on asthma and allergies among children in Crete. *Thorax* 2007;**62**:677–683.
19. Garcia-Marcos L, Canflanca IM, Garrido JB, Varela AL, Garcia-Hernandez G, Guillen Grima F et al. The relationship of asthma and rhinoconjunctivitis with obesity, exercise and Mediterranean diet in Spanish school-children 6–7 years old. *Thorax* 2007;**62**:503–508.
20. Martindale S, McNeill G, Devereux G, Campbell D, Russell G, Seaton A. Antioxidant intake in pregnancy in relation to wheeze and eczema in the first two years of life. *Am J Respir Crit Care Med* 2005;**171**:121–128.
21. Salam MT, Li YF, Langholz B, Gilliland FD. Maternal fish consumption during pregnancy and risk of early childhood asthma. *J Asthma* 2005;**42**:513–518.
22. Willers SM, Devereux G, Craig LC, McNeill G, Wijga AH, Abou El-Magd W et al. Maternal food consumption during pregnancy and asthma, respiratory and atopic symptoms in 5-year-old children. *Thorax* 2007;**62**:773–779.
23. Romieu I, Torrent M, Garcia-Esteban R, Ferrer C, Ribas-Fitó N, Antó JM et al. Maternal fish intake during pregnancy and atopy and asthma in infancy. *Clin Exp Allergy* 2007;**37**:518–525.
24. Newson RB, Shaheen SO, Henderson AJ, Emmett PM, Sherriff A, Calder PC. Umbilical cord and maternal blood red cell fatty acids and early childhood wheezing and eczema. *J Allergy Clin Immunol* 2004;**114**:531–537.
25. Bach A, Serra-Majem L, Carrasco JL, Roman B, Ngo J, Bertomeu I et al. The use of indexes evaluating the adherence to the Mediterranean diet in epidemiological studies: a review. *Public Health Nutr* 2006;**9**:132–146.
26. Kant AK. Dietary patterns and health outcomes. *J Am Diet Assoc* 2004;**104**:615–635.
27. Bowler RP, Crapo JD. Oxidative stress in airways: is there a role for extracellular superoxide dismutase? *Am J Respir Crit Care Med* 2002;**166**:38–43.
28. Broide DH, Lotz M, Cuomo AJ, Coburn DA, Federman EC, Wasserman SI. Cytokines in symptomatic asthma airways. *J Allergy Clin Immunol* 1992;**89**:958–967.
29. Black PN, Sharpe S. Dietary fat and asthma: is there a connection? *Eur Respir J* 1997;**10**:6–12.
30. Simopoulos AP. Essential fatty acids in health and chronic disease. *Am J Clin Nutr* 1999;**70**(Suppl.):560–569.
31. Pistelli R, Forastiere F, Corbo GM, Dell'Orco V, Brancato G, Agabiti N et al. Respiratory symptoms and bronchial responsiveness are related to dietary salt intake and urinary potassium excretion in male children. *Eur Respir J* 1993;**6**:517–522.
32. Ocke MC, Bueno-de-Mesquita HB, Pols MA, Smit HA, van Staveren WA, Kromhout D. The Dutch EPIC food frequency questionnaire. I. Description of the questionnaire, and relative validity and reproducibility for food groups. *Int J Epidemiol* 1997;**26**(Suppl.):37–48.
33. Byers T, Trieber F, Gunter E, Coates R, Sowell A, Leonard S et al. The accuracy of parental reports of their children's intake of fruits and vegetables: validation of a food frequency questionnaire with serum levels of carotenoids and vitamins C, A, and E. *Epidemiology* 1993;**4**:350–355.
34. Willett WC. Nutritional epidemiology, 2nd edn. New York: Oxford University Press, 1998.