**Supplementary file 5:**

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| **Supplementary table S5 Mediterranean diet and dietary patterns in infancy and childhood** | | | |
| **Single studies on Mediterranean Diet** | | | |
| **KIDMED Mediterranean score** | | | |
| **Calatayud-Saez et al. 2016** **78**  prospective (cohort) study  Spain  **Sample Size**:  Baseline N: 104 asthmatic children (1-5 year old)  Sample Size Calculation:  a significance level of 0.05 and a power of 85% were used, assuming a decrease in the mean number of childhood asthma attacks of 1 unit/patient/yr, with a standard deviation of 4 units, adjusted for a 25% loss. The resulting sample size was 115 patients.  **Sex:** 50 girls and 54 boys  **Atopic Disease Risk Status**: | **Intervention/Exposure:**  Definition of mediterrean diet (MD)  Characterized by a high intake of unrefined plant-based foods such as fruits and fresh vegetables, whole grains, legumes, olive oil and nuts; low to moderate consumption of foods of animal origin such as fermented milk, fish, eggs and lean meats; and by a low intake of sugar, refined flour and fast food  **Assessment Methods of MD**:  At start of 1-year program ‘‘Learning to Eat from the Mediterranean’’: 7-day recall questionnaire, KIDMED test  Nutritional counselling, after 4 months KIDMED test  1-year follow-up: adherence to MD by KIDMed test | **Outcomes studied:**  Asthma control  Adherence to MD improved during programme, but not statistically analysed  The adoption of a traditional Mediterranean diet could contribute significantly to the improvement of patients diagnosed with childhood asthma. | **Confounders taken into account:**  **Limitations:**  Inappropriate statistical analysis  (comment in ref 50: “suffered from inappropriate statistical analysis and  Lack of consideration of potential bias such as nonresponse and dropout bias that led to unreliable results and ambiguity in study population characteristics which made it difficult to compare the results against other studies.”) |
| **Grigoropoulou et al. 2011 79**  Cross-sectional survey, same cohort (extended PANACEA study)  Greece  **Sample Size**:  Baseline N: 1125 children 10 to 12 years old  Partician rate: 83,5%  The total number of enrolled children (*n* = 1125) was deemed adequate to evaluate odds ratios (ORs) between various groups of study equal to 1.20, at probability  level < 0.05, and achieving statistical power equal to 77%  **Sex:** m 529, 596 f  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**: | **Intervention/Exposure:**  Definition of mediterrean diet (MD): KIDMED  **Assessment Methods of MD**:  KIDMED food frequency questionnaire | **Outcomes studied:**  Asthma by standardized ISAAC questionnaire  Any asthmatic symptom 23.7% urban-residing children vs 14.6% living in rural areas (p<0.001)  Mean adherence to MD 5.3% rural vs 4.7% urban  High adherence to MD 4,8 % rural vs 2,4 % urban (different from ref 36 13,4 vs 11,6)  The analysis showed that 1-unit increase in the KIDMED score was associated with 16% lower likelihood of having asthma symptoms  greater adherence to MD was inversely associated with ever had wheeze (OR \_ 0.88; 95% CI, 0.78, 0.98) and exercise wheeze (OR \_ 0.79; 95% CI, 0.67, 0.93). | **Confounders taken into account:**  Adjusted for age, sex, BMI, physical activity status, and energy intake  **Limitations:**  Cross-sectional study, limitations such as recall bias and reverse causality bias |
| **Chatzi et al. 2008 80**  Birth cohort, prospective  Spain  **Sample Size**:  460 children included at follow-up at age 6.5 years  Analytic N: 412 for SPT  **Sex:** NR 228 f, 232 m  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**:  General population | **Intervention/Exposure:**  Mediterrean diet (MD) assessed by modified KidMed index  **Assessment Methods of MD**: Semiquantitative FFQs of 96 food items based on KidMed index, modified  ≥ 7 optimal MD  ≤ 3 low level MD | **Outcomes studied:**  Persistent wheeze (≥1 episode over past 12 months or preceding years) 13,8%  atopic wheeze (current wheeze and atopy) 5.8%  Atopy (sensitization to ≥1/6 common aeroallergens) 17%  Adherence to MD  9.3% low level  53.7% medium level  37 % high level  High adherence to MD was negatively associated with persistent wheeze OR 0.46 (0.10 – 2.17) and atopy =R 0.49 (0.18 – 1.32), but did not reach statistical significance  Atopic wheeze OR 0.64 (0.10 – 4.06) | **Confounders taken into account:**  Gender, maternal age at pregnancy, maternal social class and education, maternal smoking during pregnancy, supplement use during pregnancy, breastfeeding, lower track resp. infection at 1 year, birth weight, gestational age, birth order, number of siblings, BMI at 6.5 years  Control for energy intake  **Limitations:**  Variability in choosing cut-off points  Different distribution of selected foods in different populations |
| **Alphantonogeorgos et al. 2014 81**  Cross-sectional study (extended PANACEA study ref 37)  Greece, urban (Athens, n = 700) or rural environment (n = 425)  **Sample Size**:  Baseline N: 1125 children 10 to 12 years old  Partician rate: 83,5%  Sample Size Calculation: NR  **Sex:** m 529, 596 f  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**:  Parental atopy 34% urban vs 27,3 rural | **Intervention/Exposure:**  Hypothesis: living environment could affect asthma prevalence, with MD and physical activity as mediators  Definition of mediterrean diet (MD): KIDMED  **Assessment Methods of MD**:  KIDMED food frequency questionnaire | **Outcomes studied:**  Asthma by standardized ISAAC questionnaire  Any asthmatic symptom 23.7% urban-residing children vs 14.6% living in rural areas (p<0.001)  Mean adherence to MD 5.3% rural vs 4.8% urban  High adherence to MD 12,3% (13.4% rural vs 11.6% urban) different from ref 46 (4,8% rural vs 2,4% urban) data concerning diet more detailed in Grigoropoulou et al.79  Adherence to the Mediterranean diet was related negatively with asthma symptoms (standardized beta = -0.224, p<0.001). An inverse mediating effect of the Mediterranean diet was observed for the urban environment – asthma relation (standardized beta=-0.029, p<0.001) while physical activity had no significant contribution (p=0.62), adjusted for several confounders | **Confounders taken into account:**  Adjusted for several confounders  **Limitations:**  Cross-sectional study, limitations such as recall bias and reverse causality bias |
| **Arvaniti et al. 2011 82**  Cross-sectional study (PANACEA study)  Athen, Greece  **Sample Size**:  Baseline N: 700 (10-12 years old)  Partician rate 83,5%  **Sex:** m 323, f 377 | **Intervention/Exposure:**  MD adherence measured by KidMed sore  **Assessment Methods of MD**: semi-Quantitative FFQ on consumption of 63 food items on daily or weekly basis completed by parents during face-to-face interviews  Assessment of dietary pattern of breakfast, but answers not different between asthma and no asthma | **Outcomes studied:**  Asthma acc. to ISAAC II criteria 23.7%  Adherence to MD (mean 4.8)  Low n=213, Moderate n=413, high n=74  Greater adherence to MD inversely associated:   |  |  |  |  |  | | --- | --- | --- | --- | --- | |  | Bad (0-3) | Moderate (4-7) | Good  (8-12) | p | | N | 213 | 413 | 74 |  | | Ever had wheeze (%) | 29 | 19 | 8 | 0.001 | | Exercise wheeze (%)) | 11 | 7 | 0 | 0.004 | | Night cough (%) | 17 | 11 | 6 | 0.07 | | Ever had diagn. Asthma (%) | 16 | 9 | 3 | 0.002 | | Any asthma symptoms (%) | 34 | 22 | 5 | <0.001 |   One-unit increase in KidMed score was associated with 14% lower likelihood of having asthma  Pattern:  No sign. associations with single food groups except fish and meat (increased intake, less asthma symptoms) | **Confounders taken into account:**  Various factors considered as potential confounders and effect mediators  **Limitations:**  Cross-sectional study  Recall bias not excluded |
| **Arvaniti et al. 2011 83**  Cross-sectional study (PANACEA study)  Athen, Greece  **Sample Size**:  Baseline N: 700 (10-12 years)  Partician rate 83,5%  **Sex:** m 323, f 377 | **Intervention/Exposure:**  MD adherence measured by KidMed sore  **Assessment Methods of MD**: see Arvaniti et al. 82  Including salty-snack consumption (pattern) | **Outcomes studied:**  Asthma acc. to ISAAC II criteria 23.7%  Pattern:  48% reported salty-snack consumption (SSC) ≥1 times/week  SSC was inversely associated with the KidMed score.  SSC >3 times/ week vs never was associated with a 4.8 times higher likelihood of having asthma symptoms | **Confounders taken into account:**  see Arvaniti et al. 82  **Limitations:**  see Arvaniti et al. 82 |
| **Chatzi et al. 2007 84**  Cross-sectional survey  Crete, Greece  **Sample Size**:  Baseline N: 690 (age: 7-18 years)  Analytic N: 537 (incl. information about allergic manifestations)  **Sex:** m 331, f 359  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**:  6.8% parental asthma | **Intervention/Exposure:**  Adherence to MD measured by modified KidMed score (left out questions on fast food, sweets and legumes, optimum reduced from 8 to 6)  **Assessment Methods of MD**: FFQ (58 items) usual weekly food consumption during previous 12 months with a 6-level-scale (never, <1 times per week, 1-2 times, 3-4 times, once per day, > once per day)  ≥ 6 optimal MD  ≤ 3 low level MD  Degree of adherence based on KidMed index, modified + MD Sore (EPIC), modified  Definition of meditterean diet (MD)  KidMed Index, more red than white meat per week -1, margarine more than once a week -1 | Questionnaires on respiratory and allergic symptoms over the past 12 months by parents, SPT 10 aeroallergens  Any wheezing in the past 16.8%, atopic wheeze 5.4%, current wheezing 4.6%, nocturnal dry cough (last 12 months) 10.9%  Any rhinitis in the past 18.7% (atopic rhinitis 6.7%, current AR 13.3, current seasonal AR 5.1)  Atopy 22.3%  adherence to MD  27.9 % low level  43.8 % medium level  28.3 % high level  After multivariate logistic regression analysis high level of adherence to MD was inversely related to  AR ever OR 0.34 (0.18 – 0.64) p<0.01  AR with atopy OR 0.39 (0.13-0.97)  Current AR OR 0.49 (0.24 – 0.99) p<0.05  Nocturnal cough apart from cold in the last 12 months OR 0.49 (0.23-0.96)  Protective but not sign. for wheezing and atopy  Pattern:  Nuts ≥3 times/w reduced wheezing ever OR 0.54 (0.34-0.86) and current wheeze OR 0.46 (0.20-0.98)  Margarine > once/w increased current wheezing OR 2.19 (1.01-4.82), AR ever OR 1.99 (1.32-3.00), current AR OR 2.10 (1.31-3.37) | **Confounders taken into account:**  Age, sex, BMI, parental asthma number of older siblings  **Limitations:**  Cross sectional design  Self-administered questionnaire  Non-validated FFQ |
| **Chatzi et al. 2007**  **85**  Birth cohort, prospective  Spain  **Sample Size**:  460 children included at follow-up at age 6.5 years  Analytic N: 412 for SPT  **Sex:** NR 228 f, 232 m  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**:  General population Attrition:  Sample Size Calculation: NR  **Sex:** NR  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**: | **Intervention/Exposure:**  Mediterrean diet (MD) assessed by modified KidMed index (questions regarding breakfast left out, optimum reduced from 8 to 7)  **Assessment Methods of MD**: Semiquantitative FFQs of 96 food items based on KidMed index, modified  ≥ 7 optimal MD  ≤ 3 low level MD | **Outcomes studied:**  prevalence of current wheeze, atopic wheeze, and atopy at age 6.5 yr were 8.7%, 5.8%, and 17.0%  pattern:  A high consumption (>40 g/day) of fruity  vegetables were found to have beneficial effect on current wheeze (OR, 0.38; 95% CI, 0.15–0.95, p < 0.05), and atopic wheeze with a significant decreasing trend with increasing intake (OR, 0.19; 95% CI, 0.04–0.95, p for trend = 0.04). Atopy was negatively associated with a high fish intake (>60.5 g) (OR, 0.43; 95% CI, 0.21–0.90, p < 0.05). | **Confounders taken into account:**  Gender, maternal and parental  asthma, maternal and paternal atopy, maternal smoking, BMI at age 6.5 yr, maternal and paternal education and social class, breastfeeding, fish intake during pregnancy, and number of siblings at age 6.5 yr.  In addition, analyses including specific food intake were adjusted for total energy intake using the standard multivariate method  **Limitations:** |
| **Adult EPIC score/ Mediterranean diet pattern** | | | |
| **Castro-Rodriguez et al. 2017 86**  Cross-sectional  Spain  **Sample Size**:  Baseline N: 2922 pre-school children invited  Analytic N: 1784 (mean age 4.08 ± 0.8) completed questionnaire, 1757 answered questions regarding current wheezing  **Sex:** male cw 53.3, cnw 51.1  **Race/Ethnicity**: caucasian cw 91.5, cnw 94.3  **Atopic Disease Risk Status**:  General population,  Paternal asthma cw 6.3, cnw 3.1, maternal asthma cw 8.0, cnw 4.0 | **Intervention/Exposure:**  Definition of meditterean diet (MD)  Pro: Fruit, fish, vegs, legumes, cereals, pasta, rice, potatoes  Anti: meat, milk, fast food  3 answers (0-2 and 2-0 pts, respectively)  Based on score used in adults (EPIC) with regard to cardiovascular risk (Trichopoulou/ Psaltopoulou)87  Range in study group 14-36, adherence by quartiles  **Assessment Methods of MD**: Environmental questionnaires including questions on consumption and allergic manifestations (based on ISAAC phase III) | **Outcomes studied:**  Current wheezing cw (episodes over the past 12 months) 20%  Highest quartile of MD cw 42.9, cnw 53.2  After multivariate analysis: highest quartile of MD aOR 0.54 (0.33 – 0.88) | **Confounders taken into account:**  Children with current wheeze were more often born by cesarean section, lower birth weight, lower proportion of breast-feeding, higher antibiotic and acetaminophen consumption in first year of life, more acetaminophen consumption in previous 12 months,  More parental asthma, more smoking, heavier truck traffic in front of house, more cat owners, lower rate of vigorous physical activity, significantly more margarine consumption  **Limitations:**  Questionable MD score,  Adherence by quartiles not by cut-off values – highest quartile does not mean high adherence (e.g. only 30% of children ate vegs more than 3 times per week) |
| **de Batlle et al. 2008 88**  Cross sectional study  Mexico  **Sample Size**:  Baseline N: random sample of 3125 children  Analytic N: 1476 children (6-7 years)  Attrition:  Sample Size Calculation: NR  **Sex:** NR  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**:  General population | **Intervention/Exposure:**  Mediterranean diet (MD)  Based on score used in adults (EPIC) with regard to cardiovascular risk (Trichopoulou/ Psaltopoulou) 87  **Assessment Methods of MD**:  Parental FFQ with 70 food items, usual diet in the last 12 months (8 food groups: vegs (+) , legumes (+), fruit and nuts (+), dairy products (-), cereals (+), meat (-), fish (+), junk food and fat (-) with minimum (0) to maximum (8)  Adherence measure in tertiles | **Outcomes studied:**  Asthma/rhinitis related outcomes by ISAAC questionnaire  Asthma ever 170 (12%)  Wheezing ever 354 (25%)  Current wheezing n=147 (11%)  Rhinitis ever n=100 (7%)  Sneezing ever n=419 (30%)  Current sneezing n=370 (25%)  Current itchy-watery eyes n=166 (11%)  high consumption of fruits and nuts, vegetables, and junk food and fat -> mean MD 3.7 (!)  Adherence to MD (2nd and 3rd tertile compared with 1st tertile) inversely associated with  Asthma ever OR 0.60 (0.40-0.91)  Wheezing ever OR 0.64 (047-0.87)  Sneezing ever OR 0.79 (0.59-1.07), current Sneezing OR 0.71 (0.52-0.96)  Current itchy-watery eyes OR 0.63 (0.42-0.95) | **Confounders taken into account:**  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.  **Limitations:**  Cross-sectional study  Adherence to MD by tertiles not cut-offs,  Diet score questionable |
| **Garcia-Marcos L et al. 200789**  Cross sectional study  Spain  **Sample Size**:  Baseline N: 20106 children (6-7 years old)  Mean participation rate: 78.7%  Complete data on consumption: 17145 children  **Sex:** NR  **Race/Ethnicity**: only Spanish children  **Atopic Disease Risk Status**:  General population | **Intervention/Exposure:**  Relationship of MD with asthma/ rhinoconjunctivitis adjusting for obesity and exercise  Based on score used in adults (EPIC) with regard to cardiovascular risk (Trichopoulou/ Psaltopoulou)87  Definition of mediterrean diet (MD):  fruit, fish, vegetables, pulses, cereals, pasta, rice and potatoes were considered ‘‘pro-Mediterranean’’ foods and rated 0, 1 or 2 points from less frequent to more frequent intake.  Meat, milk and fast food were considered ‘‘anti-Mediterranean’’ foods and rated 0, 1 or 2 points from more frequent to less frequent consumption | **Outcomes studied:**  Asthma/ rhinoconjuncitivitis acc. to ISAAC questionnaire  Current occasional asthma (COA) 1379 (8%)  Current severe asthma (CSA) 390 (2.3%)  Rhinoconjunctivitis 1446 (8.4%)  Independent of the amount of exercise, each Mediterranean score unit had a small but protective effect on CSA in girls (adjusted OR 0.90, 95% CI 0.82 to 0.98).  Diet Pattern  Protective factor for COA: frequent intake of nuts (1–2 times/week and >3 times/week vs never/occasionally) aOR 0.82 (0.73-0.94) and aOR 0.68 (0.51-0.90) p<0.001  protective factors for CSA: of seafood (adjusted ORs 0.63 (95% CI 0.44 to 0.91) and 0.53 (95% CI 0.35 to 0.80)) and cereals (adjusted OR 0.56 (95% CI 0.30 to 1.02) and 0.39 (95% CI 0.23 to 0.68)), trend for meat, fruit, vegs, cereal, milk)  risk factor for CSA: fast food (adjusted ORs 1.64 (95% CI 1.28 to 2.10) and 2.26 (95% CI 1.09 to 4.68))  protective factors for rhinoconjunctivitis: seafood (adjusted ORs 0.74 (95% CI 0.60 to 0.92) and 0.67 (95% CI 0.53 to 0.85)) and fruit (adjusted ORs 0.76 (95% CI 0.60 to 0.97) and 0.71 (95% CI 0.57 to 0.88)), trend for meat | **Confounders taken into account:**  **Limitations:**  No adjustment of food consumption to energy intake  Questionable MD score |
| **Suarez-Varela et al. 2010** **90**  Cross-sectional study  ISAAC phase III Spain  **Sample Size**:  Baseline N: 20106 (6-7 years of age)  Analytic N: 13153  Participation rate 76.5%  **Sex:** m 6621, f 6512  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**: | **Intervention/Exposure:**  Definition of mediterrean diet (MD) based on91 which was again based on score used in adults (EPIC) with regard to cardiovascular risk (Trichopoulou/ Psaltopoulou)87  Range 0-22  **Assessment Methods of MD**:  FFQ on 16 foods and food groups with 3 answers (never, 1-2 times/ wk, ≥3 times/wk) | **Outcomes studied:**  Atopic dermatitis assessed acc. to ISAAC questionnaire 5.92%  Mean MDS 13.26  Good adherence 9.43%  Bad adherence 90.57%  No association between MDS and AD  Pattern Milk was negatively associated with AD (aOR 0.42 (0.22-0.79) when eaten 1-2 times/wk, aOR 0.50 (0.33-0.75) when consumed ≥3 times/wk).  Butter aOR 0.70 (0.50-0.97) when consumed ≥3 times/wk)  Nuts aOR 0.51 (0.33-0.80) when consumed ≥3 times/wk) | **Confounders taken into account:**  Gender, obesity, exposure to tobacco smoke in the first year of life, younger and older siblings, and exercise.  **Limitations:**  Questionable MD Definition, especially with regard to outcome |
| **Tamay et al. 2014 92**  Cross-sectional study  Turkey  **Sample Size**:  Baseline N: 11483 (6-7 years of age)  Analytic N: 9875  Attrition:  Sample Size Calculation: NR  **Sex:** m 50.7%, f 49.3%  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**: | **Intervention/Exposure:**  Definition of mediterrean diet (MD)  MDS based on91 which again was based on score used in adults (EPIC) with regard to cardiovascular risk (Trichopoulou/ Psaltopoulou) 87  Range: 0 to 22  **Assessment Methods of MD**:  Semiquantitative FFQ with 30 food items assessing diet in the past 12 months completed by parents  Consumption of protective foods such as potatoes, rice, cereals, pasta, vegetables, tomatoes, broad bean fish and other sea foods, fruits, nuts, olive oil, fish oil, and some traditional foods made from grapes and mulberries, fermented drinks made from millets and various seeds, pickle; aggravating foods including fast-food, potato chips and crackers, chocolates, lollipops and candies, cookies and muffins, margarine; and other foods including eggs, animal fats, milk and dairy products, meat, polyunsaturated fatty acids (butter), sun-flower oil, corn oil, tea, and olive were asked. (3 answers possible) | **Outcomes studied:**  Allergic rhinitis acc. to ISAAC protocoll  Lifetime rhinitis 44.3%  Current rhinitis 29.2%  Current rhinoconjunctivitis 8.5%  Physician-diagnosed AR 8.1%  No protective effect of MD  Pattern physician-diagnosed allergic rhinitis: Consumption of rice, and cereals ≥3 times/wk protective effect (aOR = 0.53, 95% CI = 0.32-0.87 and aOR = 0.58,  95% CI = 0.36-0.92).  current rhinoconjunctivitis: pasta, and Chocolates ≥3 times/ wk protective effect (aOR = 0.45, 95% CI = 0.25-0.79 and aOR = 0.50, 95% CI = 0.29-0.86).  current rhinoconjunctivitis Eating lollipops, candies and animal fats ≥3 times per week was positively associated with (aOR = 1.47, 95% CI = 1.00-2.17 and aOR = 2.25, 95% CI = 1.11-4.56). | **Confounders taken into account:**  Gender, parental education level and exercise  **Limitations:**  Questionable MDS |
| **Akcay et al. 2014 93**  Cross-sectional study  Turkey  **Sample Size**:  Baseline N: 10894 adolescens (13-14 years of age)  Analytic N: 9991  Response rate: 91.7%  Sample Size Calculation: NR  **Sex:** 4746 boys (47.9%)and 5166 girls (52.1%)  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**: | **Intervention/Exposure:**  Definition of mediterrean diet (MD): MD score based on the work of García-Marcos et al. 2016 et al. which again was based on score used in adults (EPIC) with regard to cardiovascular risk (Trichopoulou/ Psaltopoulou) 87  Ranging from 0 to 22  **Assessment Methods of MD**:  Dietary intake was estimated by a semi-quantitative food frequency questionnaire. Consumption of foods including potatoes, rice, cereal, pasta, vegetables, fish, other sea foods, fruits, tomatoes, nuts, olive oil, fish oil, boiled grape juice, fermented drinks made from millets and various seeds, hamburger, potato chips, crackers, chocolates, lollipops, candies, cookies, muffins, margarine, eggs, animal fats, milk and dairy products, meat, PUFAs (butter), sun-flower oil, corn oil, tea, broad bean and olives were asked. (3 answers possible) | **Outcomes studied:**  Wheeze ever 17.4%, wheezing in last 12 months 9.0%, and lifetime doctor diagnosed asthma prevalence 11.8%  The mean MD scores for children with asthma and children without asthma were 12.51 and 12.53  The Mediterranean-style diet was not associated with the prevalence of asthma.  Pattern: Asthma prevalence in children consuming fruits and animal fats ≥3 times a week was lower than in those with these foods consumed never or occasionally (aOR = 0.66, 95% CI = 0.48-0.93; and aOR = 0.58, 95% CI = 0.35-0.93, respectively. When animal fats or olive were consumed three or more times a week, asthma prevalence was lower than it was in those who consumed these foods once or twice per week (aOR = 0.48, 95%CI = 0.28-0.84; and aOR = 0.79, 95% CI = 0.66-0.94, respectively). When fermented drinks made from millets and various seeds, mix pickles and margarine were consumed ≥3 times a week, asthma prevalence was higher than it was in those who consumed these foods never or occasionally, or once to twice per week. When meat was consumed three or more times a week, asthma prevalence was higher than it was in those who consumed these foods once to twice per week (aOR = 1.26, 95% CI = 1.04---1.52) | **Confounders taken into account:**  **Limitations:**  Asthma based on a questionnaire, without confirming the diagnosis according to their medical histories or to lung function tests. Another limitation of this study was that ISAAC protocol questions have not been validated in Turkey. |
| **Rice et al. 2015 94**  Case-control study  Peru  **Sample Size**:  Baseline N: 287 asthmatic (physician diagnosed) children (9-19 years of age, mean 13.5) + 96 controls without asthma  **Sex:** m 165, f 112 (controls m 40, f 56)  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**:  No information on parental allergy | **Intervention/Exposure:**  Definition of mediterrean diet (MD): MDS based on score used in adults (EPIC) with regard to cardiovascular risk (Trichopoulou/ Psaltopoulou) 87, except milk (+)  range 0-22  **Assessment Methods of MD**:  FFQ with 170 food items assessed usual dietary intake over previous 2 weeks (6 answers possible) | **Outcomes studied:**  Asthma status (asthma control, FEV1), AR, atopy  86% with controlled asthma  Being above the median MDS scores was associated with decreased odds of asthma [OR = 0.55, 95 % CI (0.33, 0.92), p = 0.02]. Among children whose mothers completed secondary education, being above the median MDS significantly decreased the odds of asthma [OR = 0.31, 95 % CI (0.14, 0.71), p\0.01], whereas among those whose mothers did not complete secondary education there was no protective effect [OR = 0.86, 95 % CI (0.43, 1.7), p = 0.66].  No association between MDS scores and asthma control, FEV1, allergic rhinitis, or atopic status | **Confounders taken into account:**  Maternal education, age, sex, BMI  **Limitations:**  No correction for energy intake  Questionalbe MDS, but better than in other studies |
| **Silveira et al. 2015 95**  Cross-sectional study  Brazil  **Sample Size**:  Baseline N: 268 (3-12 years of age) with persistent asthma, 126 age-matched controls with intermittend asthma  **Sex:** m 159, f 109 (controls m 61, f 65)  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**:  FA asthma 59.5% (controls 56%)  FA AR 72.8% (controls 67.2%) | **Intervention/Exposure:**  Definition of mediterrean diet (MD)  (Criteria adapted from the literature)  pro-MD pattern (fruit, vegetables, fish,  fruit juices, root vegetables and tubers and grains) and a contra-MD diet (milk, meat, eggs, processed foods, soft drinks, butter). The Mediterranean diet was classified as “yes” when intake of at least 5 foods in each group was frequent (≥3 times per week)  **Assessment Methods of MD**:  Interview with parents/ guardians using a pre-coded questionnaire several outcomes including dietary habits food consumption over the past 12 months assessing frequent and infrequent consumption (never or <3 times/week) | **Outcomes studied:**  No significant association between frequency of consumption of specific foods, food groups or dietary pattern (pro- vs anti-MD) and severity of asthma (not risk!) | **Confounders taken into account:**  Multivariate analysis was applied to control for potential confounding  factors, with inclusion of variables according to the preestablished  hierarchical levels as follows: level 1: gender, skin color, maternal schooling, income, paternal schooling, and smoking during pregnancy; level 2: allergens in the home, gestational age, birth weight, family history of allergic rhinitis, exposure to passive smoking; level 3: dietary variables; and level 4: obesity. Only the variables with *P* ≤0.20 remained in the model.  **Limitations:**  Statistical power insufficient  Brought range of age – food consumption varies with age |
| **Romieu et al. 2009 96**  Cohort study  Mexico  **Sample Size**:  Baseline N: 158 asthmatic children (6-14 years of age), 50 non-asthmatic children  Analytic N:  Attrition:  Sample Size Calculation: NR  **Sex:** NR  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**: | **Intervention/Exposure:**  Definition of mediterrean diet (MD) based on score used in adults (EPIC) with regard to cardiovascular risk (Trichopoulou/ Psaltopoulou) 87  **Assessment Methods of MD**:  Dietary intake was evaluated using a 108-item validated quantitative FFQ completed by mothers with 8 possible answers regarding frequency and a fruit and vegetable index (FVI) and a Mediterranean diet index (MDI) were constructed.  FVI: based on intake of fruits and vegetables and the consumption of vitamins or supplements reported on the questionnaire and were scored on a scale of 0 to 3  MDI adapted from that by Trichopoulou/ Psaltopoulou used in adults (EPIC) 87 with regard to cardiovascular risk modifications: 1) without alcohol ii) without high monounsaturated/saturated consumptions iii) introduction of junk food  In the case of fruits, vegetables, cereals, legumes, dairy products and fish, a value of 1 was assigned if consumption was above of the median value and 0 otherwise. For meat and junk food, the scoring was reversed. | **Outcomes studied:**  Pulmonary function was measured and nasal  lavage collected and analyzed every 2 weeks  The impact of these indices on lung function and interleukin-8 (IL-8) and their interaction with air pollutants were determined using mixed regression models with random intercept and random slope.  No significant difference between the asthmatic and the non-asthmatic children.  We observed a high frequency of intake of fruit or fruit juices, vegetables and dairy products as well as junk food, while the intake of fish was low  FVI was inversely related to IL-8 levels in nasal lavage (p < 0.02) with a significant inverse trend (test for trend p < 0.001), MDI was positively related to lung function (p < 0.05), and children in the highest category of MDI had a higher FEV1 (test for trend p < 0.12) and FVC (test for trend  p < 0.06) than children in the lowest category. A significant interaction was observed between FVI and ozone for FEV1 and FVC as was with MDI and ozone for FVC. No effect of diet was observed among healthy children. | **Confounders taken into account:**  5-day accumulated moving average O3 (ppb), 5-day accumulated average (maximum) PM2.5 (μg/m3),  Previous day minimum temperature, gender, body mass index, calories and chronological time  **Limitations:** |
| **Nagel et al. 2010** **97**  Cross-sectional studies of 29 centres in 20 countries  ISAAC  **Sample Size**:  Baseline N: 50004 schoolchildren (8-12 years)  Analytic N: 29579 with SPT  Attrition:  Sample Size Calculation: NR  **Sex:** NR  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**: | **Intervention/Exposure:**  Definition of mediterrean diet (MD)  “score of MD derived according to consumption frequency of food items”  Selected food items: meat (-), fish (+), fresh fruit (+), raw green vegs (+), cooked green vegs (+), burgers (-), fruit juice (+), fizzy drinks (-)  **Assessment Methods of MD**: FFQ  When was dietary intake assessed and how often? E.g. twice during pregnancy at 24 and 36 weeks. | **Outcomes studied:**  Effect on current wheeze: Fruit intake (ORadj 0.86, 95% CI 0.73 to 1.02) and consumption of fish (ORadj 0.85, 95% CI 0.74 to 0.97) was associated with low prevalence in affluent countries.  Burger consumption aOR 0.76 (0.61-0.95), fruit (ORadj 0.71, 95% CI 0.57 to 0.88) and fruit juice intake aOR 0.80 (068-0.94) and consumption of cooked green vegetables (ORadj 0.78, 95% CI 0.65 to 0.95) was associated with a lower prevalence of current wheeze in non-affluent countries.  Association with lower lifetime prevalence of asthma: more frequent consumption of fruit, vegetables and fish  Association with higher lifetime asthma prevalence asthma: high burger consumption ≥3 times/week aOR 1.42 (1.08-1.87) (comment: obviously driven by affluent countries - in non-affluent countries, an inverse relationship was found between burger consumption and wheeze aOR 0.76 (0.61-0.95).  allergic sensitisation: no sign. association of any food item  atopic wheeze no sign. associations  “Food selection according to the ‘Mediterranean diet’ was associated with a lower prevalence of current wheeze and asthma ever (ptrend=0.03).” | **Confounders taken into account:**  Age, sex, environmental tobacco smoke, parental atopy, exercise, number of siblings  **Limitations:**  Questionable def of MD  No adjustment for total energy intake and BMI |
| **Gonzalez et al. 2010 98**  cross-sectional study  Spain  **Sample Size**:  Baseline N: 14700  Analytic N: 7454 children (6-7 years of age), 7391 adolescents (13- to 14-yr olds)  Response rate: 75% in the 6- to 7-yr age group and 85% in the 13- to 14-yr-old age group  **Sex:** NR  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**:  Not assessed | **Intervention/Exposure:**  Definition of mediterrean diet (MD):  Fruit, fish, vegetables, pulses, cereals, pasta, rice and potatoes were considered pro-Mediterranean foods and rated 0, 1 or 2 points from less frequent to more frequent intake (0 points = never or occasionally; 1 point = 1 or 2 times/  wk; 2 points = ≥3 times/wk).  Meat, milk and fast food were considered anti-Mediterranean foods and rated 0, 1 or 2 points from more frequent to less frequent consumption (0 points  = ≥3 times/wk; 1 point = 1 or 2 times/wk; 2 points = never or occasionally).  MDS developed by Garcia-Marcos91 to be added based on score used in adults (EPIC) with regard to cardiovascular risk (Trichopoulou/ Psaltopoulou) 87 | **Outcomes studied:**  Based on ISAAC questionnaire  The prevalence of asthma in children was 39.9%, current asthma 13.8%, severe asthma 4.7% and exercise-induced asthma 6.5%. In adolescents, this prevalence was  22.2%, 12.4%, 5.2% and 19.5%, respectively  MDS range 3-21 (mean 13.1) in children and 4-20 (mean) 12 in adolescents  Greater adherence to the MD is associated with a higher risk of severe asthma (odds ratios = 2.26, 95% CI: 1.21–4.22 in the 2nd quartile, but not in the 3rd and 4th) in girls of 6–7 yr.  There was no significant relationship for the other asthma categories in the population studied. | **Confounders taken into account:**  **Limitations:**  Questionable MDS  “As regards individual foods, it was noted that in the lower age group, more than 2/3 of the children ate meat (-), fruit, cereals, potatoes and milk (-) more than three times per week.”  Adherence by quartiles not by cut-off values – highest quartile does not mean high adherence |
| **Other dietary patterns** |  |  |  |
| **de Cassia et al. 2014 99**  Cross-sectional study  Brazil  **Sample Size**:  Baseline N: 1500 children (6-12 year old)  Analytic N: 1187  Attrition:  Sample Size Calculation: NR  **Sex:** male 53.3%  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**: | **Intervention/Exposure:**  Dietary pattern: Western Diet vs prudent  **Assessment Methods of MD**:  Validated quantitative food frequency questionnaire of 97 food items adapted to take local dishes into account administered to mothers by nutritionists  The frequency of consumption of these  items were divided into the following 4 categories: never consumes = 0; consumed 1–3 times a month = 1; once a week = 2; 2–4 times a week = 3; and ‡ 4 times in weeks = 4.  Afterward, the scores of the frequency of consumption were calculated as weighed proportion consumption where the  numerator is the sum of the categories of all food items into in food cluster multiplied by 4 and the denominator the number of food items into food cluster multiplied by 4. This score or weighed proportion consumption represents a summary measure of the food consumption | **Outcomes studied:**  Asthma by ISAAC questionnaire 10.6%  From this analysis, 2 components (patterns) were extracted that accounted for 45.7% of the total variance. The eating patterns that were extracted were named as Western and Prudent.  The first component was positively correlated with the intake of sugars, typical Brazilian dishes, pastries, fast food, oils, milk, cereals, cakes, and sauces. The  second component was positively correlated with roots, legumes, fruits, and leafy vegetables. The indices relating to internal consistency (a > 0.60) ensured an acceptable level of accuracy of measurement for the 2 patterns, ensuring internal  consistency for the dimensions of the questionnaire.  Certain foods and food groups were not considered in the analysis due to the low communality presented (h2 < 0.30): soft drinks, beef, chicken, fish, eggs, processed meat products, bread, baked beans, and artificial sweeteners.  We found a positive statistically significant association of the Western  pattern with wheeze (odds ratio = 1.77, 95% confidence interval: 1.10–2.84) after adjustment for total energy intake and controlling for potential confounders | **Confounders taken into account:**  BMI, physical activity, pubertal development, gender  (male, female reference category), age (< 10 years, ‡ 10 years  reference category), education of caregiver (£ 4th grade, 5th  grade ‡ reference category), household location (urban, rural  reference category), per capita income [as minimum salary  (MS); £ 1 MS, > 1 MS reference category], number of people  living in the household (> 3, £ 3 reference category), and  presence of smokers in the house (no reference category, Yes)  **Limitations:** |
| **Lee et al. 2012 100**  Cross-sectional study  Taiwan  **Sample Size**:  Baseline N: 2,419 schoolchildren  Analytic N: 2082  Response rate: 78.8%.  Sample Size Calculation: NR  **Sex:** m 1111, f 971  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**:  Parental asthma: 3,7% | **Intervention/Exposure:**  Dietary pattern identified by reduced rank regression (RRR)  **Assessment Methods of DP**:  FFQ with 21 food groups to assess dietary intake (at home)  Average intake in days/wk in the past month  Food groups included vegetables, fruits, milk, yogurt, Yakult (lactic acid beverages with low dairy protein and high sugar), cheese, meat, fish, shellfish, organ meat (e.g. heart, liver, kidney and stomach of poultry and livestock), soybean milk, soy products, eggs, fast foods (e.g. hamburgers, pizza, French fries, fried chicken, and fried Asian delicacies), high-fat snacks (e.g. potato chips, flour based and rice flour-based crisps), sweet drinks (e.g. cola and soda), candy (e.g. chocolate and candy), desserts (e.g. cakes, cookies and sweet pastries), instant noodles, rice and flour. | **Outcomes studied:**  Asthma assessed by ISAAC questionnaire by face-to-face interviews  Asthma ever 5.4%  Current asthma 3.5%  Current severe asthma 2.3%  Exercise-induced wheeze 3.1%  Nocturnal cough 6.9%  More prevalent in boys  The RRR derived dietary pattern was characterized by high consumption of fast foods, high-fat snacks, candy, and cheese; and low consumption of fruit, vegetables and rice. The RRR-derived dietary pattern was associated with an increased risk of current asthma (OR [95% CI]) (2.42 [1.19-4.93] for Q4/Q1, *p-*for-trend=0.01), current severe asthma (3.21 [1.11-9.25] for Q3/Q1, 4.45 [1.59-12.5] for Q4/Q1; *p*-for-trend=0.003), and nocturnal cough (1.79 [1.06-3.05] for Q2/Q1, 1.74 [1.02-2.97] for Q3/Q1, 1.82 [1.07-3.11] for Q4/Q1; *p*-for-trend=0.049). | **Confounders taken into account:**  Age, sex, BMI z-score, older  sibling number (0, 1 and 2+), parental education level  (<high school, high school, and college+), parental asthma  status (yes and no), ambient NOx concentration and  Seasonal effect (spring and summer versus fall and winter)  **Limitations:**  Cross-sectional design -> no causal relationship |
| **Jonsson et al. 2016 101**  Birth cohort  Sweden  **Sample Size**:  Baseline N: 65 children, 28 living on a farm, 37 controls from a rural area but not farm (10-14 months of age)  **Sex:** farm: m 36%, f 64%  Control: m 62%, f 38%  **Atopic Disease Risk Status**:  Farm: mother 25%, father 4%  Controls mother 30%, father 32% | **Intervention/Exposure:**  Dietary differences in relation to allergy outcomes  **Assessment Methods of MD**:  24-h dietary recall by pre-decided interview protocol + 24-h food diary at 1 year of age | **Outcomes studied:**  AR, asthma, FA, AD (pediatrician diagnosed at year 1.5 and 3): 1 farm child with eczema (4%), 10 controll children (32%): 6 AD, 4 A, 2 FA, 1 AR  Farm children had a higher intake of farm milk (comment: median intake was 0g), whole cream (comment: median intake was 1g, energy-adjusted 0g), cholesterol, saturated fat, and fat in total and tended to eat more butter, while controls consumed more carbohydrates and poultry (comment: median intake was 0g) and tended to eat more margarine (comment: median intake was 2g, energy-adjusted 0g). Farm children also had higher intakes of homemade porridge/gruel (comment: median intake was 0g), oily fish (comment: median intake was 0g), and iodine.  A weak negative association was found between seafood intake and allergy development, while allergy was positively associated with the intake of pork as well as zinc in the control group; these intakes also correlated with each other. | **Confounders taken into account:**  **Limitations:**  Numbers too small for statistical analysis |
| **Loo et al. 2017** **102**  cohort study (GUSTO study)  Singapore  **Sample Size**:  Baseline N: 486 infants  Analytic N:  Attrition:  Sample Size Calculation: NR  **Sex:** NR  **Race/Ethnicity**: Chinese, Malays and Indians  **Atopic Disease Risk Status**: | **Intervention/Exposure:**  Influence of infant dietary pattern on allergic outcomes until 5 yr of age  **Assessment Methods of DP**:  Analysis of dietary data  from 6-12 months revealed 4 patterns:  *Predominantly breastmilk—*mainly breastmilk  and less formula milk;  *according to Guidelines—*rice porridge, vegetables, fruits and low-fat fish and meat;  *Easy-to-prepare foods—*infant cereals, juices, cake and biscuits;  *Noodles (in soup) and seafood*—rice and wheat noodles and common accompaniments such as fish  and shellfish.  A fifth pattern emerged at age 12 months: *Pulses and*  *grains—*characterized by high intake of nuts and seeds, grains, legumes and lentils and high energy-dense confectionaries | **Outcomes studied:**  Allergic outcomes (sensitization, eczema, rhinitis, wheeze with use of nebulizer) by modified ISAAC questionnaire at 3,6,9,12,18,24,36,48,60 months  “*Noodles and seafood*” dietary pattern at month 12 which consists of consumption of rice and wheat noodles, prawn, scallop and cuttlefish was associated with reduced odds of developing allergen sensitization at ages 18 months [adjusted OR (95% CI): 0.5 (0.3-0.98) and at 60 months [adjusted OR (95% CI): 0.7 (0.4-0.98)  Further analysis showed that a “*Noodles and seafood*” dietary pattern at month 12 was also associated with reduced odds of developing house dust mite allergen sensitization at ages 18 months [adjusted OR (95% CI): 0.4 (0.2-0.9) and 60 months [adjusted OR (95% CI): 0.7 (0.4-0.99). There were no associations between a “*Noodles and seafood*” dietary pattern at month 12 and development of food allergen sensitization at 18, 36 and 60 months. In addition, no associations were observed between  a “*Noodles and seafood*” dietary pattern at month 12 and eczema, rhinitis and wheeze with use of nebulizer.  “Predominantly Breastmilk” dietary pattern at months 6 and 9 was associated with increased odds of developing allergen sensitization at 18 months [adjusted OR (95% CI): 1.6 (1.01-2.5) and adjusted OR (95% CI): 1.5 (1.01-2.1) after adjusting for sex, ethnicity, maternal education levels, family history of allergy and eczema. There were no changes in trend upon performing sensitivity analysis. | **Confounders taken into account:**  Sex, ethnicity, maternal education level, FA, eczema  **Limitations:**  Regular collection of information at multiple time points. The collection  of infant dietary patterns  also reduces recall and  response bias as this information is collected prior to the assessment  of infant allergic outcomes. To further reduce misrepresentation of  day-to- day variation of infant diet, a high correlation of dietary pattern  scores across the 3 days of the food diaries was observed, signifying good reproducibility of 1-day dietary records |
| **Nguyen et al. 2017103**  Population-based cohort (Generation R) see also Tromp 2012 **104**  Netherlands  **Sample Size**:  Baseline N: 5225  Analytic N: 2796 at infancy, 4066 at childhood for diet assessment  **Sex:** m 49.2%, f 50.8%  **Race/Ethnicity**: 63.7% Dutch background  **Atopic Disease Risk Status**:  Maternal history of atopic disease 40.5% | **Intervention/Exposure:**  Impact of diet quality on allergic outcomes  **Assessment Methods of DP**:  Diet assessed during (pregnancy)\*, infancy (mean age 12.9 months), childhood (mean age 8.1 yr) by validated semi-quantitative FFQ filled out by parents  \*not relevant in this table  Food-based diet quality scores reflecting adherence to guidelines with 10 components representing a healthy diet | **Outcomes studied:**  Sensitization with 10 years of age by SPT 26%  Information on physician-diagnosed inhalant (10.6%) and food allergies (1.9%), eczema 20%, asthma (8.3%) by questionnaires  Max diet quality score not reached by any participant diet quality in infancy (mean 4.3 of 10) or childhood (4.5 of 10) were not associated with atopic outcomes in childhood in any of the models. The findings did not support the hypothesis that a healthy dietary pattern in early life is associated with a lower risk of allergic sensitization or atopic diseases in childhood | **Confounders taken into account:**  All associations were analyzed in three models with stepwise adjustment for potential confounders based on previous evidence.  1. Model: adjusted for child’s ethnic background, sex, age at outcome assessment, and total energy intake.  2. Model: additionally, adjusted for several socioeconomic and lifestyle factors, including maternal BMI at enrolment, maternal educational level, household income, parity, prenatal pet exposure, alcohol intake during pregnancy, smoking during pregnancy, folic acid supplements during pregnancy, and maternal history of atopic disease.  3. Model: associations of diet quality in pregnancy, infancy, or childhood with allergic sensitization and atopic diseases were independent of diet at the other two time points by additionally adjusting them for each other. Breastfeeding, child’s sex, child’s ethnic background, and maternal history of atopic diseases were separately examined as potential effect modifiers by including interaction terms in the models  **Limitations:** |
| **Grimshaw et al. 2015105**  nested, case-control within a cohort study (PIFA)  UK  **Sample Size**:  Baseline N: 41 food-allergic infants (DBPCFC+), 82 controlls  **Sex:** FA: male 58.5%  Control: male 52.4%  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**:  Maternal asthma 26.8% (FA), 13.4 % (controls), maternal allergy 53.7% (FA), 37.8% (controls) | **Intervention/Exposure:**  Characterization of a DP related with diagnosed FA  **Assessment Methods of DP**:  Food diary sets of 4weekly sheets about infant nutrition without amounts were sent out every 2 months for the 1st year of life (prospectively collected)  The first PCA looked at characteristics of the early infant diet, such as duration and exclusivity of breast-feeding, infant formula use, and timing and types of solid food introduced into the infant diet.  The second PCA looked at the diet from solid introduction to 1 year of life and was termed the ongoing infant diet (not including foods, the child was allergic to). | **Outcomes studied:**  No difference between the study groups for the early infant diet pattern, but significant difference for the ongoing diet pattern (P = .001).  PCA for ongoing infant diet finally produced a  pattern in which the first 3 components accounted for 50% of the variance, with the first component accounting for 32% of the variance.  Component 1 depicted a dietary pattern, with high positive values associated with fruit, vegetable, fish, and poultry consumption, “predominantly home cooked”. Highly processed adult foods and commercial baby foods were not important in the component. It was named “healthy infant diet”.  Component 2 was a pattern defined by finger foods. The highest positive values were allocated to healthy finger foods, and the low/negative values were allocated to pureed baby foods and  unhealthy finger foods.  The third component had high values allocated to highly processed adult foods.  The PCA assigned a score to each infant in the analysis according to how his or her diet corresponded to each of the dietary components.  These scores were significantly different between the symptomatic and control infants (P = .002) for component 1 but not for components 2 or 3.  Control infants having a significantly higher healthy infant diet dietary pattern score than children who had a food allergy. | **Confounders taken into account:**  Infant guidance score from PCA analysis, age at solid introduction, maternal asthma, maternal allergy, maternal smoking, maternal education, maternal age, pet ownership, female sex, any siblings  **Limitations:** |
| **Grimshaw et al. 2014 106**  Nested, case-control within a cohort study (PIFA)  UK  **Sample Size**:  Baseline N: 41 food-allergic infants (DBPCFC+), 82 controls  **Sex:** FA: male 58.5%  Control: male 52.4%  **Race/Ethnicity**: NR  **Atopic Disease Risk Status**:  Maternal asthma 26.8% (FA), 13.4 % (controls), maternal allergy 53.7% (FA), 37.8% (controls) | **Intervention/Exposure:**  Timing of solid food introduction  **Assessment Methods of DP**:  Food diary sets of 4weekly sheets about infant nutrition without amounts were sent out every 2 months for the 1st year of life  Descriptive analysis of baseline characteristics | **Outcomes studied:**  Infants who were diagnosed with food allergy by the time they were 2 years of age were introduced to solids earlier (≥16 weeks of age) and were less likely to be receiving breast milk when cow’s milk protein was first introduced into their diet | **Confounders taken into account:**  **Limitations:** |
| **Tromp et al. 2012 104**  Prospective cohort study (Generation R)  Netherlands  **Sample Size**:  Baseline N: 5088 mothers received FFQ  Analytic N: 2173 preschool children (≤4 years of age)  Attrition:  Sample Size Calculation: NR  **Sex:** NR  **Race/Ethnicity**: only  children of Dutch origin were included in the analyses (n=2443). Siblings within the  Generation R cohort were randomly selected and excluded (n =270)  **Atopic Disease Risk Status**: | **Intervention/Exposure:**  Dietary patterns related to asthma-related symptoms  **Assessment Methods of DP**:  Validated quantitative FFQs at 14 months of age  The frequency of consumption of a food item was to be recorded per day, per week, or per month over the past 4 weeks.  Prinzipal component analysis (PCA) | **Outcomes studied:**  Asthma-related symptoms by ISAAC questionnaire at age 2,3 and 4  Questionnaire regarding respiratory tract infections at age 2,3 and 4  2 dietary patterns (DP) identified:  DP 1 was associated with starchy foods, fruit, vegetables, potatoes, vegetable oils, fish, legumes and meat. This pattern is referred to here as the “Health conscious” DP. Comment: very similar to MD  DP 2 was associated with refined grains, soups and sauces, savoury and snacks,  other fats, sugar containing beverages and meat. This pattern will be referred to as the “Western” dietary pattern.  high adherence to the “Western” dietary pattern was significantly associated with frequent wheeze at 3 years of age (RR: 1.39; 95% CI: 1.02-1.89) and frequent shortness of breath (RR: 1.44; 95% CI: 1.03-2.01) and respiratory tract infections (RR: 1.54; 95% CI: 1.08-2.19) at 4 years of age. However, this association was partially explained by energy intake After adjustment for total energy intake, high adherence to the “Western” dietary pattern remained significantly associated with frequent wheeze (≥ 4) (aRR: 1.47, 95% CI: 1.04-2.07) at 3 years of age and frequent respiratory tract infections (≥ 3) (aRR: 1.46, 95% CI: 1.00-2.13) at 4 years of age, but no longer significantly associated with  shortness of breath up to 4 years of age. Adherence to the “Western” dietary pattern remained not significantly associated with any respiratory symptom at age 2 years or short-term respiratory symptom up to 4 years of age.  Adherence to the “Health  conscious” diet was not significantly associated with respiratory symptoms up to 4 years of age, even after adjustment for total energy intake. Therefore, it does not support a protective effect of a “Health conscious” diet on respiratory outcomes in children younger than 4 years of age. | **Confounders taken into account:**  Gender, gestational age and birth weight, maternal age, maternal socioeconomic status (SES), maternal smoking during pregnancy,  Multiple parities and parental history of atopy  **Limitations:**  Several arbitrary decisions are involved in identifying dietary  patterns by PCA. Decisions on combining food items into food groups, the number of factors  to extract, the method of rotation, and the labelling of the components may influence the  reproducibility of the findings. [ Although we adjusted for potential confounders residual  confounding cannot be fully excluded thereby precluding final conclusions regarding the causality of the study results. |

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