Dietary influences on chronic obstructive lung disease and asthma: a review of the epidemiological evidence

Henriette A. Smit[1]*, Linda Grievink[1,2,3] and Cora Tabak[1,2,3]

[1]*Department of Chronic Disease and Environmental Epidemiology, National Institute of Public Health and the Environment (RIVM), Bilthoven, The Netherlands*
[2]*Environmental and Occupational Health Group, Wageningen Agricultural University, The Netherlands*
[3]*Netherlands Institute of Health Sciences (NIHES), Rotterdam, The Netherlands*

The epidemiological evidence for a relationship between diet and indicators of asthma and chronic obstructive pulmonary disease (COPD) is evaluated. The review focuses on the intake of Na, *n*-3 fatty acids, and antioxidant vitamins as well as fruit and vegetables. Experimental studies suggest that a high-Na diet has a small adverse effect on airway reactivity in asthma patients. However, observational studies provide no clear evidence that high Na intake has adverse effects on airway reactivity or asthma symptoms in open populations. *n*-3 Polyunsaturated fatty acids, which are present in fish oils, are metabolized into less broncho-constricting and inflammatory mediators than *n*-6 polyunsaturated fatty acids. Studies in the general adult population suggest that a high fish intake has a beneficial effect on lung function, but the relationship with respiratory symptoms and clinically-manifest asthma or COPD is less evident. Also, experimental studies in asthma patients have not demonstrated an improvement in asthma severity after supplementation with fish oil. Several studies showed a beneficial association between fruit and vegetable intake and lung function, but the relationship with respiratory symptoms and the clinically-manifest disease was less convincing. A similar pattern was found for vitamin C in relation to indicators of asthma and COPD, but there are still conflicting results with respect to vitamin E and β-carotene. In conclusion, the epidemiological evidence for a beneficial effect on indicators of asthma and COPD of eating fish, fruit and vegetables is increasing. However, the effectiveness of dietary supplementation in open-population samples is often not demonstrated. Several unresolved questions are raised, which should be addressed in future studies on the relationship between diet and respiratory disease.

Chronic obstructive pulmonary disease: Asthma: Sodium: *n*-3 Polyunsaturated fatty acids: Antioxidants: Fruit and vegetable consumption

Over the last few decades, the morbidity and mortality of asthma and chronic obstructive pulmonary disease (COPD) have been rising worldwide. Increasingly, it is believed that this rise is associated with the development of a 'Western lifestyle', accompanied by unfavourable changes in exposure to air pollution, tobacco smoke, and housing conditions and respiratory infections in early life (von Mutius *et al*. 1994). Diet is an important aspect of Western lifestyle. Changes in dietary habits, such as increasing salt intake, decreasing intake of fruits and vegetables, and changing fatty acid composition of the diet, were suggested to contribute to the rise in asthma and COPD mortality and morbidity (Burney, 1987; Chang *et al.* 1993; Seaton *et al*. 1994; Sridhar, 1995; Black & Sharpe, 1997).

Sodium, potassium and magnesium

Burney (1987) noted that geographical variations in asthma mortality across England and Wales were accompanied by similar regional differences in table salt consumption; high salt consumption was present in regions with high asthma mortality. He suggested that increasing dietary Na caused an increase in airway reactivity through potentiation of the electrogenic Na pump in the membrane of the airway smooth muscle.

Abbreviations: COPD, chronic obstructive pulmonary disease; EPA, eicosapentaenoic acid; FEV_1, forced expiratory volume in 1 s; NHANES, National Health and Nutrition Examination Survey.

***Corresponding author:** Dr H. A. Smit, fax +31 30 274 4407, email Jet.smit@rivm.nl

https://doi.org/10.1017/S0029665199000427 Published online by Cambridge University Press

The effect of changes in Na intake on airway reactivity and other respiratory end points has been investigated in human experimental studies. The first experimental study was performed in a small group of asthmatic patients and non-asthmatic subjects (Javaid *et al*. 1988). This study showed an increased bronchial reactivity to histamine in asthmatics, after doubling the salt intake for 1 month. No change was observed in non-asthmatics. Further studies were restricted to asthmatic patients and showed consistent evidence that increased airway reactivity was associated with high-Na diets (Burney *et al*. 1989; Medici & Vetter, 1991; Carey *et al*. 1993). The evidence of a relationship with other respiratory end points such as medication use and lung function variables was not consistent (Medici & Vetter, 1991; Lieberman & Heimer, 1992; Carey *et al*. 1993). Carey *et al*. (1993) noted that the difference in airway reactivity between asthmatic subjects on a low-salt diet and on salt supplementation was relatively small. They suggested that 'sodium restriction as a therapeutic intervention may only be of use in asthmatic patients with high daily sodium intakes'.

From the public health point of view the question arising is whether Na intake has adverse respiratory effects in non-asthmatics. In addition to the study by Javaid *et al*. (1988), which showed no effect in a small number of non-asthmatic patients, information may be derived from observational studies in open populations, as these populations consist mainly of non-asthmatics (Table 1). Burney *et al*. (1986) observed a positive association between Na excretion and airway reactivity, but this was not confirmed in later studies among population samples (Sparrow *et al*. 1991; Pistelli *et al*. 1993; Britton *et al*. 1994*a*). Possibly the positive association observed by Burney *et al*. (1986) was partly due to the over-representation of 'wheezers' in that study. The relationship between K excretion and airway reactivity was also inconsistent between these studies: Burney *et al*. (1986) observed no relationship, whereas Sparrow *et al*. (1991) and Pistelli *et al*. (1993) observed an increased airway reactivity in association with increasing K excretion in adult males and in boys respectively. In National Health and Nutrition Examination Survey (NHANES) II, a high Na:K value was associated with an increased risk of bronchitis, but not of wheeze (Schwartz & Weiss, 1990). This is not consistent with the proposed causal mechanism of increased airway reactivity. Pistelli *et al*. (1993) reported an increased risk of cough, phlegm and wheezing with increasing table salt use in boys only. The experimental study by Burney *et al*. (1989) had also shown that the adverse effect of Na was restricted to men. Some mechanistic explanations were suggested for these sex differences (Knox, 1993). However, since most studies were restricted to men because of these earlier observations, the evidence in women is not sufficient to evaluate whether a differential effect exists between sexes.

Mg has been shown to have broncho-dilating properties in experimental studies, but little epidemiological

Table 1. Sodium and potassium excretion in relation to airway reactivity or asthma symptoms in observational studies

Study	Study characteristics	Assessment of Na intake	Respiratory end point	Results	Gender difference observed?
Burney *et al.* (1986)	138 Men, 16–64 years, enhanced proportion of wheezers Subsample from cross-sectional study	24 h Urinary Na and K excretion	Airway reactivity to histamine (PD_{20})	Na: harmful association with airway reactivity, 10-fold difference in reactivity over 95 % of Na excretion K: no association	na
Morabia *et al.* (1989)	1510 Men and women, subsample of whites with usual diet, 25–74 years NHANES I Cross-sectional	Na intake 24 h Recall + FFQ	Airway obstruction: FEV_1:FVC ≤ 65 %	Na: no relationship with airway obstruction OR high *v.* low intake: 1·2 (NS)	No difference
Sparrow *et al.* (1991)	273 Men healthy at baseline, 44–82 years Normative Ageing Study Cross-sectional subsample	24 h Urinary Na and K excretion	Airway reactivity to metacholine (PD_{20})	Na: no association K: harmful association	na
Schwartz & Weiss (1990)	9074 Men and women, 30–70 years NHANES II Cross-sectional	Na : K 24 h Recall	Symptoms: bronchitis, wheeze	Na: harmful association with bronchitis No association with wheeze	Not reported
Pistelli *et al.* (1993)	2439 Boys and girls, 9–16 years Cross-sectional	Table salt use Na and K excretion (untimed sample)	Symptoms: cough, phlegm, wheeze Airway reactivity to metacholine (PD_{20})	Table salt: harmful association with symptoms in boys Na excretion: no relationship with symptoms or airway reactivity K: harmful association in boys	Relationship in boys only
Britton *et al.* (1994*a*)	1702 Men and women, 18–70 years Cross-sectional	24 h Urinary Na excretion	Airway reactivity to metacholine (PD_{20}) Atopic symptoms	No association with airway reactivity OR 1·18 per 10-fold increase in Na excretion No association with atopic symptoms	No relationship in either sex

na, Not applicable, study was restricted to men only; FFQ, food-frequency questionnaire; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; PD_{20}, provocative dose of histamine or metacholine precipitating a 20 % decrease in FEV_1; NHANES, National Health and Nutrition Examination Survey; OR, odds ratio.

https://doi.org/10.1017/S0029665199000427 Published online by Cambridge University Press

information on a possible beneficial association between Mg intake and airway reactivity is available. One large cross-sectional study reported a beneficial association between Mg intake and respiratory end points such as lung function, wheezing and airway reactivity (Britton *et al*. 1994*b*). These authors suggested that Mg intake may act as a confounder in the relationship between Na intake and airway reactivity in open populations, since refined and processed foods, characteristic of a Western lifestyle, are low in Mg and high in salt.

In conclusion, there is substantial evidence for an adverse effect of a high-Na diet on airway reactivity in asthma patients from experimental studies, although the effect was small. Observational studies provide no consistent evidence for an adverse effect of Na or K intake on airway reactivity or other asthma symptoms in open populations. Epidemiological evidence on the potential beneficial effect of Mg intake is not sufficient to draw firm conclusions.

Polyunsaturated fatty acids

Polyunsaturated fatty acids include *n*-6 and *n*-3 fatty acids. The *n*-6 fatty acids are more likely to stimulate the disease process in asthma and COPD, whereas *n*-3 fatty acids are thought to inhibit this process. Linoleic acid, an *n*-6 fatty acid which is present in animal fat, is metabolized to arachidonic acid, which generates potent inflammatory mediators and broncho-constricting agents. Consistent with this mechanism, Miedema *et al*. (1993) observed an increased risk of 25-year incidence of chronic non-specific lung disease with increasing intake of linoleic acid (relative risk 1·55; 95 % CI 1·11, 2·16). However, other studies have not confirmed this observation (Troisi *et al*. 1995; Hodge *et al*. 1996).

n-3 Fatty acids are abundantly present in fish, in particular in fatty fish, and are metabolized to eicosapentaenoic acid (EPA) and docosahexaenoic acid. EPA and docosahexaenoic acid may competitively inhibit the use of arachidonic acid as a substrate for the production of pro-inflammatory mediators such as prostaglandins and leukotrienes (Holtzman, 1991; Simopoulos, 1991). Mediators derived from EPA have diminished biological activity compared with the arachidonic acid-derived mediators. Several experimental studies, reviewed by Monteleone & Sherman (1997), have shown that supplementation of a Western diet (which is rich in *n*-6 fatty acids) with EPA and docosahexaenoic acid from fish led to increased docosahexaenoic acid and EPA content in cell membranes. However, often no improvement in the clinical manifestation of asthma was observed (Arm *et al*. 1988; Kirsch *et al*. 1988). No intervention studies have been published on the effect of fish oil supplementation in COPD patients or in symptom-free subjects.

Several observational studies (Table 2) showed no relationship between fish intake and respiratory symptoms or clinically-manifest respiratory disease as an outcome variable (Schwartz & Weiss, 1990; Miedema *et al*. 1993; Troisi *et al*. 1995; Fluge *et al*. 1998). However, Shahar *et al*. (1994*a*) showed a strong beneficial association between fish intake and the prevalence of COPD. This association was restricted to former and current smokers. A beneficial association between oily-fish intake and asthma was also observed in children (Hodge *et al*. 1996). NHANES I (Schwartz & Weiss, 1994*b*) and the Honolulu Heart Program (Sharp *et al*. 1994) were consistent in showing that the forced expiratory volume in 1 s (FEV_1) was higher in subjects with high levels of fish intake. In NHANES I, the magnitude of the effect was slightly higher after exclusion of smokers (Schwartz & Weiss, 1994*b*), whereas the relationship in the Honolulu Heart Program was only observed in smokers (Sharp *et al*. 1994). Some other points need to be raised before drawing conclusions relating to the true protective effect of fish intake in the general population. Thien *et al*. (1996) questioned whether a true protective effect may be expected at usual levels of intake. He pointed out that the level of fish intake in the general population of about one portion per week is equivalent to 0·2–0·8 g EPA/week. This is much lower than doses of 2–3 g EPA and docosahexaenoic acid/d, at which beneficial effects were observed in experimental studies. Britton (1995) pointed out that modification of the effect due to smoking habits was not only inconsistent between studies, but was also inconsistent between subgroups within studies. Thien *et al*. (1996) and Britton (1995) both argued that confounding by other aspects of a healthy diet or a healthy lifestyle may explain at least part of the observed beneficial effect. However, the study by Hodge *et al*. (1996) showed that the relationship in children was independent of other dietary habits.

In summary, the findings of several large studies in adults suggest that high fish intake has beneficial effects on lung function. It is not clear, however, whether smokers have more or less benefit from high fish intake than non-smokers. The relationship between fish intake and respiratory symptoms and clinical disease is less evident.

Antioxidants

Vitamins C and E and β-carotene are antioxidant (pro)vitamins that may protect the lungs from oxidative damage resulting from smoking or air pollution (Heffner & Repine, 1989). Vitamin C is a water-soluble vitamin mainly present in fruit and vegetables. It is an oxygen-radical scavenger, present in both extracellular and intracellular fluids in the lungs. Furthermore, vitamin C is able to regenerate oxidized vitamin E. Vitamin E is present in vegetable oils and margarines and comprises four lipid-soluble tocopherols (α-, β-, δ- and γ-tocopherol). α-Tocopherol is the most active antioxidant of the four tocopherols. It is present in the lipid membranes and in the extracellular fluids, where it converts oxygen radicals and lipid peroxyl radicals to less-reactive forms. β-Carotene (provitamin A) is mostly present in vegetables. It is a lipid-soluble antioxidant (free-radical scavenger) present in tissue membranes.

Several experimental studies have evaluated whether antioxidant (pro)vitamins are able to modulate the acute harmful effects of oxidative air pollution on the lungs (Hackney *et al*. 1981; Chatham *et al*. 1987; Mohsenin, 1987, 1991; Bucca *et al*. 1992; Grievink *et al*. 1998*a*; Romieu *et al*. 1998). These studies differed in many aspects, such as the experimental conditions (chamber or ambient air exposure), level and type of oxidative air pollution (O_3, NO_2, or a mixture of urban air pollution), dose and

https://doi.org/10.1017/S0029665199000427 Published online by Cambridge University Press

Table 2. Intake of polyunsaturated fatty acids (PUFA) in relation to indicators of asthma and chronic obstructive pulmonary disease (COPD) in observational studies

Study	Study characteristics	Level of PUFA intake	Respiratory end point	Results
Schwartz & Weiss (1990)	9074 White and black adults, 30–70 years NHANES II Cross-sectional	Fish intake 1 (SD 0·9) portions per week 24 h Recall	Symptoms: bronchitis and wheeze	Fish: no association with symptoms after adjustment for confounders
Miedema *et al.* (1993)	793 Men, 40–59 years Zutphen study 25 year follow-up	*n*-3 Fatty acids: > 230 *v.* 0 mg/d Linoleic acid: > 5·6 *v.* < 4·0 % dietary energy Cross-check dietary history	25-year incidence of chronic non-specific lung disease*	*n*-3 Fatty acids: no association with incidence of CNSLD Linoleic acid: harmful association with incidence of CNSLD, RR high *v.* low intake 1·55 (95 % CI 1·11, 2·16)
Schwartz & Weiss (1994*b*)	2526 Men and women, 30–70 years NHANES I Cross-sectional	Fish intake, > 1 *v.* < 1 portions per week 24 h Recall	FEV_1	Beneficial association with FEV_1; FEV_1 115 ml higher for high *v.* low fish intake
Shahar *et al.* (1994*a*)	8960 Former and current smokers, 45–64 years Atherosclerosis Risk in Communities study Cross-sectional	*n*-3 Fatty acids ≥ 2·5 *v.* ≤ 0·5 portions per week SFFQ	COPD based on symptoms and spirometry†	Fish: beneficial association with COPD OR high *v.* low intake 0·55 (95 % CI 0·43, 0·71) Association with FEV_1 and FVC (NS)
Sharp *et al.* (1994)	6346 Men, 45–68 years Honolulu Heart Program Cross-sectional	Fish intake < 2 *v.* ≥ 2 portions per week FFQ	FEV_1	*n*-3 Fatty acids: beneficial association with FEV_1 and COPD FEV_1 47 ml higher for high *v.* low fish intake in current smokers (95 % CI 16, 79) and FEV_1 21 ml higher in past smokers (NS)
Troisi *et al.* (1995)	77 886 Women, 34–68 years Nurses' Health Study 10 year follow-up	*n*-3 Fatty acid intake Medians of quintiles 0·36 *v.* 0·05 g/d Linoleic acid intake 11·1 *v.* 4·49 g/d SFFQ	10-year incidence of asthma	No association with 10 year incidence of asthma *n*-3 Fatty acids high *v.* low intake RR 0·85 (NS) Linoleic acids high *v.* low intake RR 0·74 (95 % CI 0·59, 0·93)
Hodge *et al.* (1996)	468 Australian children, 8–11 years Case–control study	Fish intake Former and current *v.* never consumption of fresh fish, oily fish, non-oily fish SFFQ	Current asthma‡	Fish: beneficial association with current asthma High *v.* low intake of oily fish OR 0·26 (95 % CI 0·09, 0·72)
Fluge *et al.* (1998)	4300 Men and women, 20–44 years European Community Respiratory Health Survey Cross-sectional study	Fish intake ≥ 150 *v.* < 150 g/week FFQ	Symptoms: wheeze, chest tightness, breathless at night, cough at night, asthma attack	Fish: no association with four of five symptoms OR high *v.* low intake 0·86 (95 % CI, 0·76, 0·97)

CNSLD, chronic non-specific lung disease; NHANES, National Health and Nutrition Examination Survey; RR, relative risk; OR, odds ratio; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; FFQ, food-frequency questionnaire; SFFQ, semi-quantitative food-frequency questionnaire.

* Defined as episodes of symptoms or specialist's diagnosis of asthma or COPD.

† Based on symptoms: (1) history of chronic productive cough, (2) doctor's diagnosed emphysema, (3) spirometrically-detected COPD (FEV_1 ≤ 65 % predicted value in the presence of a normal FVC ≥ 80 % predicted value).

‡ Presence of airway hyper-responsiveness (provocative dose resulting in 20 % decrease in FEV_1 after exercise) and recent wheeze (wheeze in the past 12 months with or without exercise).

duration of antioxidant supplementation (vitamins C or E or β-carotene or combinations of these vitamins), as well as outcome measures (from lipid peroxidation and inflammation markers to lung function, airway reactivity and symptoms). Despite the methodological differences, the results of these studies provide relatively consistent evidence that antioxidant supplementation has the potential to protect against the acute damage of oxidative air pollution. In addition to these experimental studies, two intervention studies have evaluated the potential protective effect of antioxidant supplementation on chronic respiratory end points under normal living conditions. The Alpha-Tocopherol Beta-Carotene Cancer Prevention Study investigated the effect of supplementation with α-tocopherol (50 mg/d) and β-carotene (20 mg/d) for 6 years among 29 133 smokers on the 5–8-year incidence of COPD symptoms: the results showed no effect of this form of supplementation (Rautalahti *et al.* 1997). The Beta-Carotene and Retinol Efficacy Trial investigated the effect of 11-year supplementation with β-carotene (30 mg/d) and vitamin A (7·5 mg/d) on lung function decline in 3056 subjects. The annual decline in lung function did not differ between the supplementation group and the placebo group (Balmes *et al.* 1998). Thus, large-scale intervention studies so far have shown no protective effect of antioxidant supplementation on chronic respiratory end points.

Observational studies in the open population provide information on the association between antioxidant intake at true levels of intake. Table 3 summarizes the design of the published observational studies.

https://doi.org/10.1017/S0029665199000427 Published online by Cambridge University Press

Table 3. Observational studies on antioxidants in relation to asthma and chronic obstructive pulmonary disease (COPD): study characteristics

Study	Study characteristics	Study population	Measure of antioxidant intake	Assessment of dietary intake	Respiratory end point
Morabia *et al.* (1989)	NHANES I Cross-sectional	1510 Men and women, whites with usual diet, 25–74 years	Vitamin A and C intake Fruits and vegetables	24 h Recall + FFQ	Airway obstruction: $FEV_1 : FVC \leq 65\%$
Schwartz & Weiss (1990)	NHANES II Cross-sectional	9074 White and black men and women, 30–70 years	Vitamin A and C intake Serum vitamin C	24 h Recall	Symptoms: bronchitis and wheeze
Strachan *et al.* (1991)	Health and Lifestyle Survey Cross-sectional	1502 Never smokers and 1357 current smokers, no history of chronic respiratory disease, 18–69 years	Fresh fruit intake	FFQ	FEV_1
Miedema *et al.* (1993)	Zutphen study 25-year follow-up	793 Men, 40–59 years	Fruit and vegetables intake Vitamin A and C and β-carotene	Cross-check dietary history	25-year incidence of chronic non-specific lung disease*
Schwartz & Weiss (1994*a*)	NHANES I Cross-sectional	2526 Men and women, 30–70 years	Vitamin C intake	24 h Recall + FFQ	FEV_1
Troisi *et al.* (1995)	Nurses' Health Study 10-year follow-up	77 886 Women, 34–68 years	Vitamin C and E, and carotene intake Intake of foods rich in antioxidant vitamins	SFFQ	10-year incidence of asthma
Britton *et al.* (1995)	Cross-sectional	2633 Men and women, 18–70 years	Vitamin C and E intake	SFFQ	FEV_1, FVC
Dow *et al.* (1996)	Cross-sectional	178 Men and women with high proportion of symptomatic subjects, 70–96 years	Vitamin C and E intake Fruits and vegetables intake	FFQ	FEV_1, FVC
Ness *et al.* (1996)	Cross-sectional	1860 Men and women in GP practices, 45–75 years	Plasma vitamin C		FEV_1, FVC
Soutar *et al.* (1997)	Case–control	Fifty-two cases with seasonal allergic symptoms *v.* thirty-eight controls Twenty-nine bronchial reactive cases *v.* fifty-eight non-reactors	Vitamin C and E and β-carotene intake	7 d dietary record	Allergic symptoms: recurrent eye, nasal or respiratory symptoms Airway reactivity PD_{20}
Cook *et al.* (1997)	Cross-sectional	278 Boys and girls, 8–11 years	Fresh fruit intake Plasma vitamin C	FFQ	FEV_1 Wheeze
LaVecchia *et al.* (1998)	Italian Household Multipurpose Survey Cross-sectional	22 560 Men and 24 133 women, ≥15 years	Vegetable intake	FFQ	Symptoms: chronic bronchitis or bronchial asthma
Rautalahti *et al.* (1997)	Alpha-Tocopherol Beta-Carotene Cancer Prevention Study Intervention	29 133 Smoking men, 50–69 years at baseline	Vitamin C and E and β-carotene intake	FFQ	COPD* symptoms: cough, phlegm, dyspnoea
Chuwers *et al.* (1997)	Beta-Carotene and Retinol Efficacy Trial Intervention	816 Asbestos-exposed men, 45–74 years	Serum β-carotene		FEV_1, FVC
Grievink *et al.* (1998*b*)	MORGEN study Cross-sectional	6555 Men and women, 20–59 years	Vitamin C and E and β-carotene intake	SFFQ	FEV_1, FVC Symptoms: cough, phlegm, productive cough, wheeze, shortness of breath, nocturnal attacks
Carey *et al.* (1998)	Health and Lifestyle Survey 7-year follow-up	2171 Men and women, 16–73 years at first survey	Fresh fruit intake	FFQ	FEV_1

FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; FFQ, food-frequency questionnaire; SFFQ, semi-quantitative food-frequency questionnaire; PD_{20}, provocative dose of histamine precipitating a 20 % decrease in FEV_1; NHANES, National Health and Nutrition Examination Survey.
* Defined as episodes of symptoms or specialist's diagnosis of asthma or COPD.

https://doi.org/10.1017/S0029665199000427 Published online by Cambridge University Press

Fruits and vegetables

The relationship between fruit and vegetable intake and respiratory symptoms or disease incidence is equivocal (Table 4). The Zutphen study observed a protective effect of fruit intake on the 25-year incidence of chronic non-specific lung disease (Miedema *et al*. 1993), but the Nurses' Health Study reported no relationship between total fruit intake and the 10-year incidence of asthma (Troisi *et al*. 1995). One cross-sectional study in children observed no relationship between fruit intake and wheeze (Cook *et al*. 1997). Another survey among adults demonstrated a beneficial association between vegetable consumption and chronic bronchitis or asthma (LaVecchia *et al*. 1998). Findings with respect to fruit intake and lung function (FEV_1 and forced vital capacity) give a more consistent picture. In NHANES I, no relationship was observed between fruit intake and airway obstruction (Morabia *et al*. 1989). Possibly the use of a dichotomous outcome resulted in a lack of power to detect a small effect. A beneficial association between fruit intake and lung function (in particular FEV_1) was observed in other cross-sectional surveys (Strachan *et al*. 1991; Cook *et al*. 1997; Carey *et al*. 1998). The estimates of the effect were of the same order of magnitude: FEV_1 for subjects with 'high' fruit intake (once per week or more) was about 80–100 ml higher than that for subjects with a 'low' fruit intake (less than once per week). Since these results were observed in cross-sectional studies only, one may argue that the association between fruit intake and FEV_1 was caused by another underlying factor, such as aspects of a healthy diet other than fruit intake, or more generally, a healthy lifestyle. Strachan *et al*. (1991) included several indicators of a healthy lifestyle (e.g. levels of passive smoking, alcohol consumption, physical activity) in the analysis and observed no change in the relationship between fruit intake and FEV_1. Although the effects of a healthy lifestyle cannot be completely accounted for in observational studies, these results suggest that factors associated with healthy lifestyle have no substantial impact on the relationship between fruit intake and lung function.

In conclusion, the relationship between fruit and vegetable intake and FEV_1 is more consistent than that with respiratory symptoms or respiratory morbidity. A possible explanation is that the observed changes in lung function are too small to result in clinically-manifest disease. Another explanation may be that the effects are reversible, and for that reason they do not result in clinically-manifest disease. The prospective study recently reported by Carey *et al*. (1998) sheds more light on the issue of reversibility. It was shown that a decreasing frequency of fresh fruit consumption over a period of 7 years was accompanied by a decrease in FEV_1. However, the average level of fruit intake over the 7-year period was not associated with a change in FEV_1. This suggests that the effect of fruit intake has a reversible effect on the lungs.

Vitamin C

Most studies observed no relationship between vitamin C and asthma or COPD symptoms (Table 5). Exceptions were NHANES II, which demonstrated a beneficial association between bronchitis or wheeze and serum vitamin C in the absence of a relationship with the intake of vitamin C

Table 4. Fruit and vegetable intake in relation to indicators of asthma and chronic obstructive pulmonary disease in observational studies

Study	Level of intake	Results
Morabia *et al.* (1989)	Fruit and vegetables, ≤ once per week *v.* > once per week	No association with airway obstruction (FEV_1:FVC ≤ 65 %) OR low *v.* high intake 2·2 (NS)
Strachan *et al.* (1991)	Fresh fruit in winter, < once per week *v.* ≥ once per week	Beneficial association with FEV_1 FEV_1 79 ml higher (95 % CI 24, 132 ml) for high *v.* low intake
Miedema *et al.* (1993)	Fruits, > 145 g/d *v.* < 50 g/d Vegetables mean 202 g/d	Fruit: beneficial association with 25-year incidence of CNSLD High *v.* low fruit intake RR 0·73 (95 % CI 0·53, 0·99), solid fruits stronger relationship Vegetables: no association with 25-year incidence of CNSLD
Schwartz & Weiss (1994*a*)	Vitamin C-rich vegetables in past 3 months, portions per week*	No association with FEV_1
Troisi *et al.* (1995)	Intake of fruit and fruit juice*	No association with 10-year incidence of asthma
Dow *et al.* (1996)	Total fruit and vegetable intake*	No association with FEV_1 and FVC
Cook *et al.* (1997)	Fresh fruit intake (summer + winter)	Fruit: beneficial association with FEV_1
	Green salad (summer + winter) and green vegetables, never *v.* > once per d	FEV_1 79 ml higher (95 % CI 22, 136) for high *v.* low intake Vegetables and salad: similar relationship but less pronounced Fruit and vegetables: no association with wheeze
La Vecchia *et al.* (1997)	Vegetable consumption, > once per d *v.* < once per d	Beneficial association with chronic bronchitis; high *v.* low vegetable intake OR 0·69 (95 % CI 0·61, 0·78) Beneficial association with bronchial asthma: high *v.* low vegetable intake OR 0·70 (95 % CI 0·61, 0·78)
Carey *et al.* (1998)	Fruit intake at HALS 1 and HALS 2 daily *v.* never	Cross-sectional: beneficial association with FEV_1 high *v.* low fruit intake HALS 1 105 ml higher FEV_1, HALS 2 188 ml higher FEV_1
	Average fruit intake of HALS 1 and HALS 2	Average FEV_1 of two surveys not related to annual change in FEV_1 Beneficial association of change in FEV_1 with change in fruit intake
	Change in fresh fruit intake over 7-years follow-up	Men and women with decrease in fruit consumption respectively lost 89 and 133 ml FEV_1/year more than those with no change in fresh fruit consumption

FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; OR, odds ratio; RR, relative risk; CNSLD, chronic non-specific lung disease; HALS, Health and Lifestyle Survey.
* No quantitative information on cut-off points of high *v.* low.

https://doi.org/10.1017/S0029665199000427 Published online by Cambridge University Press

Table 5. Vitamin C in relation to respiratory symptoms, lung function and bronchial reactivity in observational studies

Study	Level of intake*	Results
Morabia *et al.* (1989)	Vitamin C intake†	No association with airway obstruction
Schwartz & Weiss (1990)	Vitamin C Intake 98·5 (SD 94·9) mg/d† Serum 10·4 (SD 5·96) mg/l	Intake: no association with bronchitis and wheeze Serum: beneficial association bronchitis OR 0·65 (95 % CI 0·48, 0·88) for 2SD difference wheeze OR 0·71 (95 % CI: 0·58, 0·88) for 2SD difference
Miedema *et al.* (1993)	Vitamin C intake (mean) CNSLD cases *v.* controls 84·7 *v.* 87·4 mg/d	No association with 25-year incidence of CNSLD
Schwartz & Weiss (1994*a*)	Vitamin C intake (mean) 88·2 mg/d	Beneficial association with FEV_1; FEV_1 13·4 ml higher per 100 mg vitamin C intake/d
Troisi *et al.* (1995)	Vitamin C intake from diet only (median of highest *v.* lowest quintile) 209 *v.* 61 mg/d Vitamin C intake including supplements 705 *v.* 70 mg/d	Diet only: no association with 10-year incidence of asthma; high *v.* low intake RR 1·11 (NS) Including supplements: harmful association with 10-year incidence of asthma; high *v.* low intake RR 1·69 (95 % CI 1·28, 2·23)
Britton *et al.* (1995)	Vitamin C intake 99·2 (SD 40·2) mg/d	Beneficial association with FEV_1 and FVC FEV_1 25 ml higher (95 % CI 5·2, 44·8) and FVC 23 ml higher (95 % CI 1·3, 40·4), with vitamin C intake higher by 40·2 mg/d (1 SD)
Dow *et al.* (1996)	Vitamin C intake: median 49 (range 49–228) mg/d	No association with FEV_1 and FVC FEV_1 0·7 ml higher and FVC 1 ml higher, with vitamin C intake higher by 1 mg/d (NS)
Ness *et al.* (1996)	Non-fasting plasma vitamin C: men 46 μmol/l, women 58 μmol/l	Men: beneficial association with FEV_1 and FVC; FEV_1 220 ml higher (95 % CI 0·10, 0·33) and FVC 230 ml higher (95 % CI 0·09, 0·37) per 50 μmol/l Women: no association
Soutar *et al.* (1997)	Vitamin C intake (geometric mean): cases *v.* controls 97·3 *v.* 104·0 mg/d Reactors *v.* non-reactors 77·3 *v.* 115 mg/d	No association with symptoms Beneficial association with bronchial reactivity OR lowest *v.* highest tertile 7·13 (95 % CI 1·91, 26·71)
Cook *et al.* (1997) nested case–control	Plasma vitamin C (mean) cases v. controls: 64·1 *v.* 60·1 μmol/l	No association with wheeze
Grievink *et al.* (1998*b*)	Vitamin C intake 132·6 (SD 61·7) mg/d	No association with symptoms except for cough OR cough 0·66 (95 % CI 0·50, 0·87) for 90th *v.* 10th percentile (145 mg/d) Beneficial association with FEV_1, FVC FEV_1 53 ml higher (95 % CI 23, 82) and FVC 79 ml higher (95 % CI 42, 116) with vitamin C intake higher by 145 mg/d (90th *v.* 10th percentile)

OR, odds ratio; RR, relative risk; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; CNSLD, chronic non-specific lung disease.
* Mean values unless otherwise indicated.
† No quantitative information on cut-off points available.

(Schwartz & Weiss, 1990). In contrast to the hypothesis of a beneficial association, the Nurses' Health Study reported an increase in the 10-year incidence of asthma associated with increasing dietary vitamin C (Troisi *et al*. 1995). As a possible explanation the authors suggested that women with recurrent respiratory problems may have been more likely to take vitamin C supplements. A beneficial association between vitamin C and lung function (in particular FEV_1) was observed repeatedly. The effect was of similar magnitude throughout the studies: a 100 mg increase in vitamin C intake/d was associated with about 10–50 ml increase in FEV_1 (Schwartz & Weiss, 1990; Britton *et al*. 1995; Grievink *et al*. 1998*b*). Two studies observed no statistically significant relationship between vitamin C and airway obstruction (Morabia *et al*. 1989) or FEV_1 (Dow *et al*. 1996), but the effect in the latter relatively small study was of similar magnitude. A beneficial association was observed between vitamin C intake and bronchial reactivity (Soutar *et al*. 1997) and between non-fasting plasma vitamin C and lung function (FEV_1 and forced vital capacity) in men (Ness *et al*. 1996). In line with the hypothesis that antioxidants protect against oxidative damage, it would be expected that the protective effect would be larger in smokers than in non-smokers. However, none of the reported studies has demonstrated modification of the effect by smoking. Although the studies often had a large sample size, it is likely that after stratification for smoking habits, the sample size had become too small to detect a difference between effects in smokers and non-smokers, given that the effect is already small.

In summary, there is substantial evidence for a beneficial effect of vitamin C on lung function (in particular FEV_1). The effect of vitamin C on development of asthma or COPD derived from prospective studies and the relationship between vitamin C and respiratory symptoms in cross-sectional studies is less convincing.

Vitamin E

The evidence for a beneficial protective effect of vitamin E intake on symptoms of asthma or of COPD is still small (Table 6); a beneficial association was observed with the 10-year incidence of asthma in women (Troisi *et al*. 1995) and with the prevalence of COPD symptoms in men (Rautalahti

https://doi.org/10.1017/S0029665199000427 Published online by Cambridge University Press

Table 6. Vitamin E in relation to indicators of asthma and chronic obstructive pulmonary disease (COPD) in observational studies

Study	Dietary factor	Results
Morabia *et al.* (1990)	Serum vitamin E cases *v.* controls 12·5 *v.* 13·3 mg/l	No association with airway obstruction
Troisi *et al.* (1995)	Vitamin E intake from diet only: medians of highest *v.* lowest quintiles 6·9 *v.* 3·2 mg/d	Diet only: beneficial association with 10-year incidence of asthma, high *v.* low intake RR 0·53 (95 % CI 0·33, 0·86)
	Vitamin E intake including supplements: medians of quintiles 209·8 *v.* 3·3 mg/d	Including supplements: no association with 10-year incidence of asthma, high *v.* low intake RR 0·83 (NS)
Britton *et al.* (1995)	Vitamin E intake: 6·2 (SD 2·2) mg/d	Beneficial association with FEV_1 and FVC FEV_1 20 ml higher (95 % CI 1·3, 40·4) and FVC 23 ml (95 % CI 1, 45) higher with vitamin E intake 2·2 mg/d (1 SD) higher after adjusting for vitamin C (NS)
Dow *et al.* (1996)	Vitamin E intake: median 5·3 (range 1·1–15·7) mg/d	Beneficial association with FEV_1 and FVC FEV_1 42 ml/mg vitamin E per d higher (95 % CI 10, 74) and FVC 53 ml/mg vitamin E per d higher (95 % CI 18, 88)
Soutar *et al.* (1997)	Vitamin E intake (geometric mean): cases *v.* controls 7·0 *v.* 7·9 mg/d reactors *v.* non-reactors 6·6 *v.* 7·7 mg/d	No association with symptoms OR lowest *v.* highest tertile 1·50 (NS) No association with bronchial reactivity OR lowest *v.* highest tertile 1·89 (NS)
Rautalahti *et al.* (1997)	Vitamin E intake at baseline: > 12·4 mg/d *v.* < 8·6 mg/d	Intake: beneficial association with COPD symptoms OR chronic bronchitis high *v.* low intake 0·87 (95 % CI 0·0·82, 0·93)
	Serum vitamin E at baseline: > 12·8 mg/l *v.* < 10·3 mg/l	Serum: beneficial association with symptoms, OR chronic bronchitis, high *v.* low intake 0·76 (95 % CI 0·71, 0·80); similar for cough, phlegm, dyspnoea
Grievink *et al.* (1998*b*)	Vitamin E intake: 16·3 (SD 5·9) mg/d	No association with symptoms except for cough OR productive cough 1·26 (95 % CI 1·02, 1·56) with vitamin E intake 14·4 mg/d higher (90th *v.* 10th percentile) No association with FEV_1 and FVC FEV_1 27·9 ml higher (NS) and FVC 18·2 ml higher (NS) with vitamin E intake 14·4 mg/d higher (90th *v.* 10th percentile)

RR, relative risk; OR, odds ratio; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity.

et al. 1997). Troisi *et al*. (1995) suggested that recent intake was more important for the beneficial association with vitamin E than past intake, based on the observation in the Nurses' Health Study that baseline vitamin E intake was not associated with a beneficial effect, whereas the vitamin E intake re-assessed after 4 and 6 years was associated with a beneficial effect. A higher FEV_1 associated with higher vitamin E intake was reported by Britton *et al*. (1995) and Dow *et al*. (1996), although the relationship in the latter study disappeared after adjustment for vitamin C. Other studies observed no associations between vitamin E and indicators of asthma or COPD. Thus, the evidence for a protective effect of vitamin E intake on respiratory symptoms and lung function is equivocal. Given the biological interaction between vitamin C and vitamin E, the extent to which the protective effect of vitamin E is related to vitamin C is unresolved.

β-Carotene

Most of the studies in Table 7 showed no relationship between β-carotene intake and respiratory symptoms (Soutar *et al*. 1997; Grievink *et al*. 1998*b*), the 25-year incidence of chronic non-specific lung disease (Miedema *et al*. 1993), or the 10-year incidence of asthma (Troisi *et al*. 1995), although the beneficial association was of borderline significance in the latter study. Only the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study showed a beneficial association between (serum and dietary) β-carotene and COPD symptoms (Rautalahti *et al*. 1997). FEV_1 and forced vital capacity were not associated with dietary β-carotene in the study among male asbestos workers (Chuwers *et al*. 1997), but a beneficial association was observed with serum β-carotene in the same study and with dietary β-carotene in the MORGEN study (Grievink *et al*. 1998*b*). As for vitamin E, it is concluded that the available evidence from observational studies is insufficient and too conflicting to draw conclusions as to a potential protective effect of β-carotene on asthma or on COPD. In addition to β-carotene, other carotenoids have antioxidant activity, such as α-carotene and lycopene. These carotenoids are not investigated separately in observational studies. The intake of total carotene was not associated with FEV_1 and forced vital capacity in a cross-sectional study (Shahar *et al*. 1994) or with the 10-year incidence of asthma (Troisi *et al*. 1995). Although β-carotene is a provitamin A and has antioxidant properties, preformed vitamin A (retinol) has no antioxidant properties (McLaren *et al*. 1993). Retinol is assumed to repair damage from inflammation to the lung epithelium cells. In NHANES I (Morabia *et al*. 1989, 1990) a beneficial association was observed between retinol and airway obstruction and also the prevalence of dyspnoea, but not bronchitis (Rautalahi *et al*. 1997). Using the same methodology as in NHANES I, the analysis of the Atherosclerosis Risk in Communities study (with a larger study sample) showed no relationship between total carotene or retinol and airway obstruction (Shahar *et al*. 1994). In other studies, such as the Nurses' Health Study, the Zutphen study and NHANES II, no beneficial association was observed between vitamin A and the incidence of asthma, chronic non-specific lung disease or the prevalence of bronchitis and wheeze (Schwartz & Weiss, 1990; Miedema *et al*. 1993;

https://doi.org/10.1017/S0029665199000427 Published online by Cambridge University Press

Table 7. β-Carotene in relation to indicators of asthma and chronic obstructive pulmonary disease in observational studies

Study	Level of β-carotene intake	Results
Miedema *et al.* (1993)	β-Carotene intake: CNSLD cases *v.* non-cases 3·4 *v.* 3·4 mg/d	No association with 25-year incidence of CNSLD
Troisi *et al.* (1995)	Carotene intake: median of highest *v.* lowest quintiles 14 558 *v.* 2935 IU/d	No association with 10-year incidence of asthma; high *v.* low intake: RR 0·82 (95 % CI 0·65, 1·05)
Soutar *et al.* (1997)	β-Carotene intake: Cases *v.* controls: 1951 *v.* 2107 μg/d Reactors *v.* non-reactors: 1673 *v.* 1099 μg/d	No association with symptoms OR lowest *v.* highest tertile* 0·92 (NS) No association with bronchial reactivity OR lowest *v.* highest tertile 3·43 (95 % CI 0·97, 12·11)
Rautalahti *et al.* (1997)	β-Carotene intake at baseline: > 2·3 mg/d *v.* < 1·2 mg/d Serum β-carotene at baseline: > 225 μg/d *v.* < 129 μg/d	Intake and serum: beneficial association with symptoms OR chronic bronchitis low *v.* high tertile 0·78 (95 % CI 0·73, 0·83); similar for cough, phlegm, dyspnoea
Chuwers *et al.* (1997)	β-Carotene intake: values not given Serum β-carotene at baseline: 201 (SD 276) ng/ml	Intake β-carotene: no association with FEV_1 and FVC Serum β-carotene beneficial association with FEV_1 and FVC FEV_1, 90 ml higher and FVC 82 ml higher with serum β-carotene 155 ng/ml higher (75th *v.* 25th percentile)
Grievink *et al.* (1988*b*)	β Carotene intake: 2·3 (SD 1·1) mg/d	No association with symptoms Beneficial association with FEV_1 and FVC FEV_1 60 ml higher (95 % CI 31,89) and FVC 75·2 ml higher (95 % CI 40, 111) with β-carotene 2·5 mg/d higher (90th *v.* 10th percentile)

CNSLD, chronic non-specific lung disease; RR, relative risk; OR, odds ratio; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity.
* No quantitative information on cut-off points available

Troisi *et al*. 1995). Thus, no firm conclusion on the relationship between vitamin A and asthma or COPD can be drawn from the available evidence.

Concluding remarks

There is increasing evidence from observational studies that diet is related to respiratory disease. For Na intake an unfavourable association is observed in asthmatics, but the intake of fruit and vegetables and fish is more likely to be beneficial. However, the effectiveness of dietary supplementation in open-population samples has not been demonstrated. A possible explanation is that beneficial effects of dietary supplementation may be restricted to subjects with respiratory symptoms or to patients with clinical diagnosis of asthma or COPD.

After evaluation of the available studies, some aspects remain unresolved and deserve further investigation in future studies (for example, see Strachan *et al*. 1991; Britton, 1995; Carey *et al*. 1998):

which disease entity is related to diet? End points in observational studies are often lung function variables or self-reported respiratory symptoms, which are not specific enough to distinguish between asthma and COPD. Bronchial reactivity as an end point already provides more information, but this method is applicable only to a limited extent in large-scale studies.

is a beneficial effect of diet persistent, or short term and reversible?

is a healthy diet more likely to have a beneficial effect in children than in adults?

are beneficial effects restricted to subgroups such as smokers only or patients only?

is a beneficial effect of fruit and vegetable intake due to the presence of antioxidants only, or do any other bioactive nutrients play a role?

The most important question, however, is whether the relationship between diet and respiratory disease is a causal one. Although the relationship cannot be easily explained by other lifestyle factors in observational studies, it cannot be excluded that other underlying factors related to a 'healthy diet' are responsible for potential beneficial effects of diet.

References

Arm JP, Horton CE, Mencia-Huerta JM, House F, Eiser NM, Clark TJ, Spur BW & Lee TH (1988) Effect of dietary supplementation with fish oil lipids on mild asthma. *Thorax* **43**, 84–92.

Balmes J, Ngo L, Keogh J, Cullen M, Brodkin CA, Williams J, Redlich CA, Omenn G & Barnhart S (1998) Effect of supplemental β-carotene and retinol on rate of decline in lung function. *American Journal of Respiratory and Critical Care Medicine* **157**, A46 Abstr.

Black PN & Sharpe S (1997) Dietary fat and asthma: is there a connection? *European Respiratory Journal* **10**, 6–12.

Britton J (1995) Dietary fish and airways obstruction. *Thorax* **50**, S11–S15.

Britton JR, Pavord ID, Richards KA, Knox AJ, Wisniewski AF, Lewis SA, Tattersfield AE & Weiss ST (1995) Dietary antioxidants on lung function in the general population. *American Journal of Respiratory and Critical Care Medicine* **151**, 1383–1387.

Britton JR, Pavord ID, Richards KA, Knox AJ, Wisniewski AF, Weiss ST & Tattersfield AE (1994*a*) Dietary sodium intake and the risk of airway hyperreactivity in a random adult population. *Thorax* **49**, 875–880.

Britton JR, Pavord ID, Richards KA, Wisniewski AF, Knox AJ, Lewis SA, Tattersfield AE & Weiss ST (1994*b*) Dietary

https://doi.org/10.1017/S0029665199000427 Published online by Cambridge University Press

magnesium, lung function, wheezing, and airway hyperreactivity in a random adult population sample. *Lancet* **344**, 357–362.
Bucca C, Rolla G & Farina JC (1992) Effect of vitamin C on transient increase of bronchial responsiveness in conditions affecting the airways. *Annals of the New York Academy of Sciences* **669**, 175–187.
Burney P (1987) A diet rich in sodium may potentiate asthma: epidemiologic evidence for a new hypothesis. *Chest* **91**, 143S–148S.
Burney PGJ, Britton JR, Chinn S, Tattersfield AE, Platt HS, Papacosta AO & Kelson MC (1986) Response to inhaled histamine and 24 hour sodium excretion. *British Medical Journal* **292**, 1483–1486.
Burney PGJ, Neild JE, Twort CHC, Chinn S, Jones TD, Mitchell WD, Bateman C & Cameron IR (1989) Effect of changing dietary sodium on the airway response to histamine. *Thorax* **44**, 36–41.
Carey IM, Strachan DP & Cook DG (1998) Effect of changes in fresh fruit consumption on ventilatory function in healthy British adults. *American Journal of Respiratory and Critical Care Medicine* **158**, 728–733.
Carey OJ, Locke C & Cookson JB (1993) Effect of alterations of dietary sodium on the severity of asthma in men. *Thorax* **48**, 714–718.
Chang CC, Phinney SD, Halpern GM & Gershwin ME (1993) Asthma mortality: another opinion – is it a matter of life and . . . bread? *Journal of Asthma* **30**, 93–103.
Chatham MD, Eppler JH Jr, Saunder LR, Green D & Kulle TJ (1987) Evaluation of the effects of vitamin C on ozone induced bronchoconstriction in normal subjects. *Annals of the New York Academy of Sciences* **498**, 269–279.
Chuwers P, Barnhart S, Blanc P, Brodkin CA, Cullen M, Kelly T, Keogh J, Omenn G, Williams J & Balmes JR (1997) The protective effect of beta-carotene and retinol on ventilatory function in an asbestos-exposed cohort. *American Journal of Respiratory and Critical Care Medicine* **155**, 1066–1071.
Cook DG, Carey IM, Whincup PH, Papacosta O, Chirico S, Bruckdorfer KR & Walker M (1997) Effect of fresh fruit consumption on lung function and wheeze in children. *Thorax* **52**, 628–633.
Dow L, Tracey M, Villar A, Coggon D, Margetts BM, Campbell MJ & Holgate ST (1996) Does dietary intake of vitamins C and E influence lung function in older people? *American Journal of Respiratory and Critical Care Medicine* **154**, 1401–1404.
Fluge O, Omenaas E, Eide GE & Gulsvik A (1998) Fish consumption and respiratory symptoms among young adults in a Norwegian community. *European Respiratory Journal* **12**, 336–340.
Grievink L, Jansen SMA, van 't Veer P & Brunekreef B (1998*a*) Acute effects of ozone on pulmonary function of cyclists receiving antioxidant supplements. *Occupational and Environmental Medicine* **55**, 13–17.
Grievink L, Smit HA, Ocke MC, van 't Veer P & Kromhout D (1998*b*) Dietary intake of antioxidant (pro)-vitamins, respiratory symptoms and pulmonary function: The MORGEN-study. *Thorax* **53**, 166–171.
Hackney JD, Linn WS, Buckley RD, Jones MP, Wightman LH & Karusa SK (1981) Vitamin E supplementation and respiratory effects of ozone in humans. *Journal of Toxicological and Environmental Health* **7**, 383–390.
Heffner JE & Repine JE (1989) Pulmonary strategies of antioxidant defense. *American Review of Respiratory Disease* **140**, 531–554.
Hodge L, Salome CM, Peat JK, Haby MM, Xuan W & Woolcock AJ (1996) Consumption of oily fish and childhood asthma risk. *Medical Journal of Australia* **164**, 137–140.
Holtzman MJ (1991) Arachidonic acid metabolism. Implications of biological chemistry for lung function and disease. *American Journal of Respiratory Disease* **143**, 188–203.
Javaid A, Cushley MJ & Bone MF (1988) Effect of dietary salt on bronchial reactivity to histamine in asthma. *British Medical Journal* **297**, 454.
Kirsch CM, Payan DG, Wong MYS, Dohlman JG, Blake VA, Petri MA, Offenberger J, Goetzl EJ & Gold WM (1988) Effect of eicosapentaenoic acid in asthma. *Clinical Allergy* **18**, 177–187.
Knox AJ (1993) Salt and asthma: a high salt diet may make asthma worse in men. *British Medical Journal* **307**, 1159–1160.
LaVecchia C, Decarli A & Pagano R (1998) Vegetable consumption and risk of chronic disease. *Epidemiology* **9**, 208–210.
Lieberman D & Heimer D (1992) Effect of dietary sodium on the severity of bronchial asthma. *Thorax* **47**, 360–362.
McLaren DS, Loveridge N, Duthie G & Bolton-Smith C (1993) Fat-soluble vitamins. In *Human Nutrition and Dietetics*, pp. 208–238 [JS Garrow, WPT James and A Ralph, editors]. Edinburgh: Churchill Livingstone.
Medici TC & Vetter W (1991) Bronchialasthma und Kochsalz. *Schweizerische Medizinische Wochenschrift* **121**, 501–508.
Miedema I, Feskens EJM, Heederik D & Kromhout D (1993) Dietary determinants of long-term incidence of chronic nonspecific lung diseases: the Zutphen study. *American Journal of Epidemiology* **138**, 37–45.
Mohensin V (1987) Effect of vitamin C on NO_2-induced airway hyperresponsiveness in normal subjects. *American Review of Respiratory Disease* **136**, 1408–1411.
Mohensin V (1991) Lipid peroxidation and antielastase activity in the lung under oxidant stress: role of antioxidant defenses. *Journal of Applied Physiology* **70**, 1456–1462.
Monteleone CA & Sherman AR (1997) Nutrition and asthma. *Archives of Internal Medicine* **157**, 23–34.
Morabia A, Menkes MJS, Comstock GW & Tockman MS (1990) Serum retinol and airway obstruction. *American Journal of Epidemiology* **132**, 77–82.
Morabia A, Sorenson A, Kumanyika SK, Abbey H, Cohen BH & Chee E (1989) Vitamin A, cigarette smoking, and airway obstruction. *American Review of Respiratory Disease* **140**, 1312–1316.
Ness AR, Khaw KT, Bingham S & Day NE (1996) Vitamin C status and respiratory function. *European Journal of Clinical Nutrition* **50**, 573–579.
Pistelli R, Forastiere F, Corbo GM, Dell'Orco V, Brancato G, Agabiti N, Pizzabiocca A & Perucci CA (1993) Respiratory symptoms and bronchial responsiveness are related to dietary salt intake and urinary potassium excretion in male children. *European Respiratory Journal* **6**, 517–522.
Rautalahti M, Virtamo J, Haukka J, Heinonen OP, Sundvall J, Albanes D & Huttunen JK (1997) The effect of alpha-tocopherol and beta-carotene supplementation on COPD symptoms. *American Journal of Respiratory and Critical Care Medicine* **156**, 1447–1452.
Romieu I, Meneses F, Ramirez M, Ruiz S, Perez Padilla R, Sienra JJ, Gerber M, Grievink L, Dekker R, Walda I & Brunekreef B (1998) Antioxidant supplementation and respiratory functions among workers exposed to high levels of ozone. *American Journal of Respiratory and Critical Care Medicine* **158**, 226–232.
Schwartz J & Weiss ST (1990) Dietary factors and their relation to respiratory symptoms: the second national health and nutrition examination survey. *American Journal of Epidemiology* **132**, 67–76.
Schwartz J & Weiss ST (1994*a*) Relationship between dietary vitamin C intake and pulmonary function in the first national health and nutrition examination survey (NHANES 1). *American Journal of Clinical Nutrition* **59**, 110–114.

Schwartz J & Weiss ST (1994*b*) The relationship of dietary fish intake to level of pulmonary function in the first national health and nutrition examination survey (NHANES 1). *European Respiratory Journal* **7**, 1821–1824.

Seaton A, Godden DJ & Brown K (1994) Increase in asthma: a more toxic environment or a more susceptible population? *Thorax* **49**, 171–174.

Shahar E, Folsom AR, Melnick SL, Tockman MS, Comstock GW, Gennaro V, Higgins MW, Sorlie PD, Ko W-J & Szklo M (1994*a*) Dietary n-3 polyunsaturated fatty acids and smoking-related chronic obstructive pulmonary disease. *New England Journal of Medicine* **331**, 228–233.

Shahar E, Folsom AR, Melnick SL, Tockman MS, Comstock GW, Shimakawa T, Higgins MW, Sorlie PD & Szklo M (1994*b*) Does dietary vitamin A protect against airway obstruction? *American Journal of Respiratory and Critical Care Medicine* **150**, 978–982.

Sharp DS, Rodriguez BL, Shahar E, Hwang L-J & Burchfiel CM (1994) Fish consumption may limit the damage of smoking on the lung. *American Journal of Respiratory and Critical Care Medicine* **150**, 983–987.

Simopoulos AP (1991) Omega-3 fatty acids in health and disease and in growth and development. *American Journal of Clinical Nutrition* **54**, 438–463.

Soutar A, Seaton A & Brown K (1997) Bronchial reactivity and dietary antioxidants. *Thorax* **52**, 166–170.

Sparrow D, O'Connor GT, Rosner B & Weiss ST (1991) Methacholine airway responsiveness and 24-hour urine excretion of sodium and potassium. The Normative Aging Study. *American Review of Respiratory Diseases* **144**, 722–725.

Sridhar S (1995) Nutrition and lung health: should people at risk of chronic obstructive lung disease eat more fruit and vegetables? *British Medical Journal* **310**, 75–76.

Strachan DP, Cox BD, Erzinclioglu SW, Walters DE & Whichelow MJ (1991) Ventilatory function and winter fresh fruit consumption in a random sample of British adults. *Thorax* **46**, 624–629.

Thien FCK, Woods RK & Walters EH (1996) Oily fish and asthma: A fishy story? – Further studies are required before claims can be made of a beneficial effect of oily fish consumption on asthma. *Medical Journal of Australia* **164**, 135–136.

Troisi RJ, Willett WC, Weiss ST, Trichopoulos D, Rosner B & Speizer FE (1995) A prospective study of diet and adult-onset asthma. *American Journal of Respiratory and Critical Care Medicine* **151**, 1401–1408.

von Mutius E, Fritzsch C, Weiland SK, Röll G & Magnussen H (1992) Prevalence of asthma and allergic disorders among children in united Germany: a descriptive comparison. *British Medical Journal* **305**, 1395–1399.

https://doi.org/10.1017/S0029665199000427 Published online by Cambridge University Press