

# Dietary Antioxidants and Asthma in Adults

## Population-based Case–Control Study

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A protective role for dietary antioxidants in asthma has been proposed. However, epidemiological evidence to implicate antioxidant vitamins is weak, and data on the role of flavonoid-rich foods and antioxidant trace elements are lacking. We carried out a population-based case–control study in South London, UK, to investigate whether asthma is less common and less severe in adults who consume more dietary antioxidants. Participants were aged 16–50 yr and registered with 40 general practices. Asthma was defined by positive responses to a standard screening questionnaire in 1996, and complete information about usual diet was obtained by food frequency questionnaire from 607 cases and 864 controls in 1997. After controlling for potential confounding factors and total energy intake, apple consumption was negatively associated with asthma (odds ratio [OR] per increase in frequency group 0.89 [95% confidence interval [CI]: 0.82 to 0.97];  $p = 0.006$ ). Intake of selenium was also negatively associated with asthma (OR per quintile increase 0.84 [0.75 to 0.94];  $p = 0.002$ ). Red wine intake was negatively associated with asthma severity. The associations between apple and red wine consumption and asthma may indicate a protective effect of flavonoids. The findings for dietary selenium could have implications for health policy in Britain where intake has been declining.

**Keywords:** antioxidants; adult asthma; diet; selenium; apples

One hypothesis to explain the rising prevalence of asthma in Britain is that a falling dietary intake of antioxidants has led to an increased vulnerability of the pulmonary airways to reactive oxygen species (1). However, epidemiological evidence to support this hypothesis in adults is weak. Two studies have suggested that a higher intake of fresh fruit (2) and vegetables (3) may protect against asthma, but neither could determine which specific foods or nutrients were responsible. Other studies have focused on the possible role of antioxidant vitamins. However, evidence for a protective effect of a higher dietary intake of vitamin C is unconvincing. Three large studies of asthma symptoms (4, 5) and incident asthma (6) found no association, although small studies have reported a protective effect of vitamin C intake on bronchial hyperresponsiveness (BHR) (7) and, in smokers, on wheeze (8). There is conflicting evidence that vitamin E may protect against asthma in adults (4, 6–8). It is possible that other dietary antioxidants, including flavonoids and trace elements required for antioxidant en-

zyme function, such as selenium, are more important in asthma, but data are lacking. We carried out a population-based case–control study to investigate whether asthma was less common and less severe in adults who have a higher intake of dietary antioxidants.

## METHODS

### Asthma and Dietary Surveys

The study was based on 9,709 individuals who responded to an asthma survey in a random sample of adults aged 16–50, registered with 40 general practices in Greenwich, South London, UK, in autumn 1996 (9, 10). Asthma was defined by positive responses to any of three screening questions, which have been used previously in adults of this age (11) and predict BHR (12), and “nonasthma” by negative responses to all three questions (*see* online data supplement). We measured severity of disease among cases using an asthma quality of life score (13) and defined early- versus late-onset asthma according to age at first attack (*see* online data supplement). We selected 1,438 (15%) individuals with asthma and a random sample of 2,000 without and mailed them a dietary and lifestyle questionnaire in September 1997. Of these, 720 (50.1%) cases and 980 (49.0%) controls replied. After allowing for likely wrong addresses, the overall response rate was 55% (14).

### Assessment of Diet

We assessed usual diet (previous 12 mo) using a food frequency questionnaire (FFQ), based on one used previously (15), which included over 200 items of food and drink. We used additional cross-check questions on total number of servings of fruit and vegetables eaten per week to correct for overreporting and to adjust estimates of vitamin C and carotene intake (15). Prior to coding, we excluded 76 individuals for whom information on 46 or more food items (equivalent to two pages) was missing. In the remainder, items were coded as “never eaten” if a frequency of consumption was not specified. We estimated weekly intake (grams) of foods and food groups by multiplying frequency of consumption by the weight of standard portion sizes, and daily nutrient intake in the same way, using British food composition tables (16). We could not estimate total nutrient intake among supplement users as information on dose of nutrients in supplements was incomplete. We estimated total energy intake and used Schofield equations to estimate basal metabolic rate (BMR) (17). Implausibly low intakes were defined by a ratio of energy intake to BMR of  $< 1.2$  (18). Three months later, we sent a repeat FFQ to a random sample of 200 respondents, of whom 99 replied with complete information. The repeat data allowed us to estimate repeatability of estimates of flavonoid-rich food intakes (*see* online data supplement) and to adjust nutrient effect estimates for attenuation arising from measurement error when dietary intake is assessed on a single occasion (19, 20). Prior to the main study, we compared the estimates of intake of key foods and nutrients obtained from the FFQ with those obtained from a 7-d weighed record, in 61 individuals (for correlation coefficients, *see* online data supplement).

### Analyses

All analyses were done using Stata. Primary exposures of interest were intakes of fruit, vegetables, flavonoid-rich items (apples, onions, tea, and red wine [21]), antioxidant vitamins (C, E, and carotene), and trace elements with antioxidant enzyme function (selenium, manganese, copper, and zinc). Secondary exposures of interest included to-

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mato-rich products (a source of lycopene), chocolate (rich in flavonoids), fish (especially oily), magnesium, and n3/n6 fatty acids. We used logistic regression to analyze dietary associations with asthma, and linear regression to examine associations with the asthma quality of life score (square root transformed), controlling for total energy intake, body mass index (self-reported weight/height<sup>2</sup>), and other potential confounders (*see* online data supplement).

## RESULTS

The main analyses were restricted to 1,471 individuals (607 cases and 864 controls) with complete information on diet and confounders. Table 1 shows the distribution of background and selected dietary characteristics of cases and controls.

After controlling for total energy intake and potential confounding factors, total fruit and total vegetable consumption were weakly negatively associated with asthma (odds ratio [OR] per quintile, 0.92 [95% confidence interval [CI]: 0.84 to 1.00],  $p = 0.048$ , and 0.92 [0.84 to 1.00],  $p = 0.056$ , respectively). Table 2 shows the association between asthma and consumption of flavonoid-rich foods and drinks. There was a negative association with apple intake (OR per increase in frequency group 0.89 [0.82 to 0.97]), after controlling for potential confounders. The clearest effect was seen in individuals who ate apples twice a week or more. Intakes of tea (with or without milk), onions, and red wine were not related to asthma, after controlling for confounders.

Table 3 shows the association between asthma and dietary intake of antioxidant trace elements. Selenium intake was negatively associated with asthma. The OR, after controlling for potential confounders, was 0.84 per quintile increase (95% CI: 0.75 to 0.94). Excluding 38 individuals taking selenium supplements made little difference to this estimate (OR 0.85 [0.76 to 0.95]). When we used repeat data on selenium intake from 94 individuals to adjust for measurement error in the whole sample, the OR per doubling of selenium intake decreased from 0.69 (0.53 to 0.89) to 0.50 (0.33 to 0.78), after controlling for confounders. Zinc intake was weakly associated with asthma, but intakes of copper and manganese were not, after controlling for confounders. The effect of zinc intake disappeared, however, after controlling for selenium intake.

There was no evidence for an association between asthma and dietary intake of vitamin C and vitamin E, but there was weak evidence for a positive association with carotene intake, after controlling for confounding factors (Table 4). These findings did not change substantially when we restricted the

analyses to individuals who were not taking relevant supplements (data not shown).

The main findings for apple consumption and selenium intake were not altered when we controlled additionally for frequent acetaminophen use (14), family size, family history of atopic disease, years of full-time education, and frequent use of steroid inhalers. Nor did they change when we controlled additionally for potential confounders related to the prenatal and postnatal environment, including number of older siblings, young maternal age at birth, low birth weight, maternal smoking in pregnancy or childhood, being breastfed as a baby, and attendance at preschool nursery or kindergarten (data not shown). Similarly, they did not change when we controlled the apple and selenium effects for each other (OR per group increase in apples 0.91 [0.84 to 0.99]; OR per quintile increase in selenium 0.86 [0.77 to 0.96]). Furthermore, exclusion of 161 cases (27%) and 207 controls (24%) who reported implausibly low energy intakes, or 109 vegetarians, or 187 nonwhite individuals, or 132 cases (22%) and 62 controls (7%) who said they avoided foods or took supplements because of asthma or allergy, made little difference to the main effect estimates (data not shown). The effects of apple and selenium intake and the other antioxidants on asthma were not modified by smoking. When we examined associations between asthma and other dietary factors of interest, we found no association with intake of tomato products or chocolate. There was some evidence for negative effects of magnesium, fish, and n3 fatty acid intake, but these relations were no longer apparent after controlling for selenium intake. Intakes of other fruits (citrus, pears, bananas) were not related to asthma after controlling for intake of apples and selenium.

When we carried out a subsidiary analysis of early- and late-onset asthma (first attack before or after 15 yr of age, respectively), we found some evidence to suggest that apple intake, but not selenium intake, was more strongly associated with early-onset than with late-onset asthma (data not shown).

In linear regression analyses among cases, we found no association between the asthma quality of life score and intake of any of the nutrients or foods of interest, with the exception of red wine, which was negatively associated (mean difference in score per group increase in wine intake  $-0.05$  [ $-0.09$  to  $-0.01$ ],  $p = 0.0058$ , after controlling for confounding factors), indicating a reduction in severity with increasing consumption. This effect was diminished when we excluded individuals who reported avoiding foods because of asthma or allergy (difference per group  $-0.03$  [ $-0.07$  to  $0.00$ ];  $p = 0.071$ ).

**TABLE 1. BACKGROUND AND SELECTED DIETARY CHARACTERISTICS OF CASES AND CONTROLS**

	Cases (n = 607)	Controls (n = 864)
Mean (SD) age in years	34.1 (9.8)	36.3 (9.2)
Number (%) female	375 (61.8)	507 (58.7)
Number (%) of current smokers	216 (35.6)	280 (32.4)
Number (%) nonwhite	77 (12.7)	110 (12.7)
Number (%) obese (BMI $\geq$ 30)	85 (14.0)	91 (10.5)
Number (%) unemployed	158 (26.0)	166 (19.2)
Number (%) manual social class	194 (32.0)	240 (27.8)
Mean (SD) portions of fruit and vegetables/day*	2.3 (1.5)	2.4 (1.5)
Number (%) taking any supplement	231 (38.1)	328 (38.0)
Number (%) of low energy reporters†	161 (26.5)	207 (24.0)
Number (%) of vegetarians	47 (7.7)	62 (7.2)
Number (%) avoiding foods because of asthma/allergy	123 (20.3)	55 (6.4)

Definition of abbreviation: BMI = body mass index.

\* Includes fruit juice and excludes potatoes.

† Defined in METHODS section.

## DISCUSSION

In this population-based study, we have found that asthma was less common in adults who consumed more apples and who had a higher intake of selenium. There was also some evidence that asthma was less severe among individuals with asthma who drank more red wine. We were investigating these associations a priori, and the  $p$  values were small, even after controlling for confounding factors. A strength of our study is that there is a wide degree of social inequality across Greenwich (22). This will have increased the chance of detecting associations between dietary antioxidants and asthma, as intakes of fruit and vegetables, antioxidant vitamins, and selenium-rich foods, such as fish and wholemeal bread, vary with income (23, 24). This contrasts with a previous study of women from one professional group (6).

### Direction of Association, Response Rates, and Confounding

Some individuals with asthma may be sensitive to wine, apples, or selenium-rich foods, such as dairy products, fish, and

**TABLE 2. ASSOCIATION BETWEEN ASTHMA AND FREQUENCY OF CONSUMPTION OF FLAVONOID-RICH FOODS AND DRINKS**

Food/Drink	Group	n (Cases)	n (Controls)	Crude OR (95% CI)	p (Trend)	OR* (95% CI)	p (Trend)
Apples	< Once/mo	150	133	1.0		1.0	
	1–3 per mo	169	146	0.97 (0.71, 1.34)		0.96 (0.69, 1.34)	
	Once/wk	132	103	0.88 (0.62, 1.25)		0.90 (0.63, 1.30)	
	2–4/wk	228	123	0.61 (0.44, 0.84)		0.68 (0.48, 0.95)	
	≥ 5/wk	185	102	0.62 (0.44, 0.87)	0.0001	0.68 (0.47, 0.98)	0.0057
Onions	< Once/mo	104	89	1.0		1.0	
	1–3/mo	102	83	0.95 (0.63, 1.43)		1.13 (0.74, 1.72)	
	Once/wk	171	125	0.85 (0.59, 1.23)		1.02 (0.70, 1.49)	
	2–4/wk	309	196	0.74 (0.53, 1.04)		0.92 (0.65, 1.31)	
	≥ 5/wk	178	114	0.75 (0.52, 1.08)	0.037	0.92 (0.62, 1.36)	0.37
Tea	Never	91	73	1.0		1.0	
	< Once/d	138	111	1.00 (0.67, 1.49)		1.10 (0.73, 1.66)	
	Once/d	84	60	0.89 (0.57, 1.40)		1.04 (0.65, 1.67)	
	2–3/d	269	155	0.72 (0.50, 1.04)		0.83 (0.57, 1.22)	
	4–5/d	166	108	0.81 (0.55, 1.20)		0.95 (0.63, 1.44)	
	6+/d	116	100	1.07 (0.71, 1.62)	0.58	1.21 (0.79, 1.86)	0.94
Red wine	< 1 glass/wk	413	343	1.0		1.0	
	1–2 glasses/wk	112	87	0.94 (0.68, 1.28)		1.10 (0.79, 1.53)	
	3–5 glasses/wk	89	52	0.70 (0.49, 1.02)		0.86 (0.58, 1.27)	
	1–2 glasses/d	84	45	0.65 (0.44, 0.95)		0.82 (0.54, 1.24)	
	3–4 glasses/d	80	38	0.57 (0.38, 0.86)		0.85 (0.55, 1.33)	
	≥5 glasses/d	86	42	0.59 (0.40, 0.87)	0.0001	0.95 (0.61, 1.48)	0.38

\* Controlling for age, sex, body mass index, social class, housing tenure, employment status, whether a single parent, smoking, passive smoke exposure at home, and total energy intake.

nuts, leading to avoidance and a lower intake. This is unlikely to explain the associations between asthma and intake of selenium and apples, which did not change when we excluded individuals who said that they avoided certain foods because of asthma or allergies from the analyses. In contrast, similar analyses for red wine suggested that avoidance may explain part of the association with asthma severity, although it is unlikely to offer a full explanation, as intake of white wine, which is almost as common a trigger for asthma as red wine (25), was unrelated to asthma severity.

The response rates, which were not high, are of potential concern. The most likely reason for nonresponse is reluctance to spend the substantial amount of time needed to complete the FFQ. This problem is inevitable when detailed dietary in-

formation is requested, and comparable rates have been seen in other population-based studies of diet and respiratory health that have used long FFQs (4, 26). Response rates were similar in cases and controls, and intake of selenium and apples would have to be strongly positively associated with asthma in nonparticipants (which seems unlikely) to explain our results.

The effects of apple consumption and selenium intake were not explained by socioeconomic status (which we measured in some detail), by other adult risk factors, or by other dietary factors. A limitation of previous studies is that they have tended to focus on particular nutrients or foods in isolation. We found that after controlling for intake of selenium and apples, weak associations between asthma and intakes of zinc, magnesium,

**TABLE 3. ASSOCIATION BETWEEN ASTHMA AND DIETARY INTAKE OF ANTIOXIDANT TRACE ELEMENTS**

Nutrient	Quintile	Median Intake (Interquartile Range)	Crude Odds Ratio (95% CI)	p (Trend)	Odds Ratio* (95% CI)	p (Trend)
Selenium, µg/day	1	27.1 (23.6, 29.8)	1.0		1.0	
	2	37.1 (34.6, 39.5)	0.86 (0.62, 1.20)		0.95 (0.66, 1.36)	
	3	46.2 (44.1, 48.4)	0.70 (0.50, 0.97)		0.69 (0.46, 1.03)	
	4	57.0 (53.8, 60.4)	0.56 (0.40, 0.78)		0.53 (0.34, 0.81)	
	5	80.1 (70.9, 97.5)	0.63 (0.45, 0.87)	0.0003	0.56 (0.35, 0.89)	0.0015
Manganese, mg/day	1	2.1 (1.7, 2.4)	1.0		1.0	
	2	3.0 (2.9, 3.2)	0.66 (0.48, 0.93)		0.70 (0.49, 1.00)	
	3	3.8 (3.6, 4.0)	0.66 (0.48, 0.92)		0.71 (0.49, 1.03)	
	4	4.7 (4.4, 5.0)	0.59 (0.42, 0.82)		0.66 (0.44, 0.99)	
	5	6.3 (5.7, 7.6)	0.64 (0.46, 0.89)	0.0077	0.72 (0.47, 1.11)	0.17
Copper, mg/day	1	0.9 (0.7, 1.0)	1.0		1.0	
	2	1.2 (1.2, 1.3)	0.86 (0.62, 1.19)		1.01 (0.69, 1.47)	
	3	1.5 (1.4, 1.6)	0.80 (0.58, 1.12)		0.93 (0.61, 1.42)	
	4	1.9 (1.8, 2.0)	0.74 (0.53, 1.03)		0.82 (0.52, 1.31)	
	5	2.6 (2.3, 3.0)	0.77 (0.55, 1.07)	0.076	0.78 (0.46, 1.32)	0.26
Zinc, mg/day	1	6.7 (5.7, 7.5)	1.0		1.0	
	2	9.0 (8.5, 9.4)	0.84 (0.60, 1.16)		0.89 (0.60, 1.30)	
	3	10.9 (10.4, 11.4)	0.76 (0.55, 1.06)		0.72 (0.47, 1.10)	
	4	13.0 (12.4, 13.7)	0.74 (0.53, 1.03)		0.65 (0.40, 1.03)	
	5	17.3 (15.8, 21.2)	0.76 (0.55, 1.06)	0.077	0.60 (0.36, 1.02)	0.037

\* Controlling for age, sex, body mass index, social class, housing tenure, employment status, whether a single parent, smoking, passive smoke exposure at home, and total energy intake.

TABLE 4. ASSOCIATION BETWEEN ASTHMA AND DIETARY INTAKE OF ANTIOXIDANT VITAMINS

Nutrient	Quintile	Median Intake (Interquartile Range)	Crude Odds Ratio (95% CI)	p (Trend)	Odds Ratio* (95% CI)	p (Trend)
Vitamin C, mg/day <sup>†</sup>	1	34.8 (28.1, 39.6)	1.0		1.0	
	2	52.4 (48.1, 57.5)	0.80 (0.57, 1.11)		0.89 (0.63, 1.26)	
	3	72.8 (67.2, 78.1)	0.97 (0.70, 1.35)		1.15 (0.81, 1.64)	
	4	102.9 (94.4, 110.9)	0.74 (0.53, 1.03)		0.86 (0.59, 1.23)	
	5	158.0 (133.1, 224.5)	0.83 (0.60, 1.15)	0.23	0.92 (0.64, 1.34)	0.64
Vitamin E, mg/day	1	4.3 (3.6, 4.9)	1.0		1.0	
	2	6.4 (6.0, 6.8)	0.82 (0.59, 1.14)		0.89 (0.62, 1.29)	
	3	8.3 (7.9, 8.7)	0.64 (0.46, 0.89)		0.68 (0.46, 1.01)	
	4	10.8 (10.1, 11.7)	0.78 (0.56, 1.08)		0.79 (0.52, 1.20)	
	5	15.7 (13.9, 18.7)	0.80 (0.58, 1.11)	0.19	0.76 (0.48, 1.20)	0.23
Carotene, $\mu$ g/day <sup>†</sup>	1	527 (409, 608)	1.0		1.0	
	2	845 (775, 916)	0.93 (0.67, 1.30)		1.12 (0.79, 1.59)	
	3	1,154 (1,081, 1,257)	1.18 (0.85, 1.64)		1.57 (1.10, 2.25)	
	4	1,552 (1,439, 1,688)	0.85 (0.61, 1.18)		1.17 (0.81, 1.70)	
	5	2,391 (2,108, 2,994)	1.05 (0.76, 1.46)	1.0	1.43 (0.98, 2.09)	0.090

\* Controlling for age, sex, body mass index, social class, housing tenure, employment status, whether a single parent, smoking, passive smoke exposure at home, and total energy intake.

<sup>†</sup> Corrected for overreporting of fruit and vegetable intake.

fish, and n3 fatty acids, which have previously been reported (7, 27–29), were no longer apparent. Furthermore, the effects of current apple and selenium intake did not seem to be confounded by prenatal or postnatal risk factors, although we acknowledge that for some of these “early life” variables information was incomplete and recall may have been unreliable.

#### Dietary Assessment: Biased Reporting and Misclassification of Intake

We do not think that the main findings can be explained by biased reporting of food intake. Unlike previous studies, we corrected our estimates of vitamin C and carotene intake for overreporting of fruit and vegetable intake, a common problem with long FFQs (30), and the findings for apple and selenium intake were not altered by excluding low energy reporters from the analyses. Participants were unaware of the antioxidant hypothesis being tested, and the specificity of the associations with selenium and apples would argue against a general bias toward underreporting of food intake by individuals with asthma. Individuals may estimate intake of apples better than intake of other foods such as onions. This is supported by the calibration and repeatability data, which show that estimates of tea intake are better still (*see* online data supplement). Nevertheless, for the association between apple intake and asthma to have arisen spuriously, one would have to argue that cases were more likely than controls to underreport apple intake, which seems unlikely.

Food composition data for selenium are considered unreliable because there is wide variation in the content of major food sources, such as cereals, depending on soil levels and geographic origin of the foods (31). Hence, misclassification of intake estimated by FFQ, which is likely to be random with respect to asthma, would tend to bias risk estimates toward the null (20). Despite these limitations, we observed a strong association between dietary selenium and asthma, and the magnitude of the relation, which increased on correcting for measurement error, would suggest that the true effect may be considerable. The correlations between FFQ and weighed record estimates of vitamin C and carotene intakes were satisfactory, insofar as they were almost identical to those seen in a previous study that compared similar instruments (30). However, FFQ estimates of vitamin E and copper intakes correlated poorly with weighed record estimates, and this is likely to have limited our ability to detect associations between these nutrients and asthma.

#### Previous Epidemiological Studies

Protective effects of a higher intake of apples on asthma and of a higher consumption of red wine on asthma severity, have not been reported before. However, there is evidence that eating more apples and hard fruit may protect against impaired lung function (32) and chronic obstructive pulmonary disease (COPD) (33, 34), and studies of lung cancer suggest that a higher intake of apples and red wine may benefit lung health more generally (35, 36). Reduced blood selenium levels have consistently been observed in adults with asthma (37) and are also associated with lower lung function (38), although these observations could simply reflect selenium depletion by oxidative stress in obstructive lung disease. Few studies of obstructive lung disease have estimated dietary selenium intake and our findings contrast with a small study that found no relation between dietary selenium and BHR (7), and another that found no association with incidence of COPD (33). There is some evidence that intake of fish and cereals or whole grains may protect against asthma in children (28, 39) and impaired lung function and COPD in adults (40, 41). Although these foods are rich sources of n3 fatty acids and vitamin E, respectively, it is possible that protective effects may be attributable in part to their high selenium content. One study, which did not control for socioeconomic status, reported strong associations between BHR and intake of manganese and vitamin C (7), but we did not find convincing evidence for a relation between asthma and manganese intake, after controlling for confounders. Nor did we observe an association with vitamin C intake, which is in keeping with three large studies of asthma symptoms (4, 5) and incident asthma (6) in adults. Vitamin C intake appears to have a more important influence on lung function (40). After correcting carotene intake for overreporting of fruit and vegetables, we found weak evidence to suggest that a higher carotene intake may be associated with an increased risk of asthma, which is consistent with a large Dutch study (4), though not with others (6–8).

#### Mechanisms

The trend in the associations between asthma and intake of apples and selenium would support a causal interpretation. Similarly, the findings for red wine suggest that a higher intake may reduce severity of asthma in some individuals. Apples contain different subclasses of flavonoid, including flavonols (such as quercetin) and flavans (such as the catechins), but these are unlikely to explain the association between asthma as

they are also found in onions and tea (42), which were unrelated to asthma prevalence. This interpretation is in keeping with a recent study that found that intakes of tea, flavonols, and flavones were unrelated to COPD, but suggested that catechins not derived from tea might be protective (34). We speculate that other types of flavonoid might underlie our observations, for example, anthocyanins, which are found in apples and red wine (42), or phloridzin and its derivatives, which are relatively specific to apples (43). Alternatively, the beneficial effect of apples may reflect antioxidant activity of nonflavonoid phenolic compounds (44). Flavonoids could plausibly reduce asthma inflammation through antioxidant, antiallergic, and antiinflammatory properties. They are avid scavengers of nitric oxide (45), can inhibit histamine release, arachidonic acid metabolism, and cytokine production (46), and *trans*-resveratrol, a flavonoid found in red wine, can down-regulate the transcription factor NF- $\kappa$ B (47). Furthermore, one particular flavonoid, khellin, known for its bronchodilator properties, was used historically to treat asthma (48).

A higher intake of selenium may suppress asthma inflammation by saturating glutathione peroxidase. This enzyme catalyzes reduction of peroxides by the antioxidant glutathione, which is thought to play a role in defense against oxidative stress in asthmatic airways (49), and thus down-regulates the transcription factor NF- $\kappa$ B (50). We were surprised that apple consumption and selenium intake were associated with asthma prevalence but not severity. Since current dietary patterns are formed to a large extent in childhood (51, 52), a speculative explanation for the associations with current intake of apples and selenium is that they reflect a protective effect of a higher intake on the inception of asthma in childhood, when a high proportion of adult asthma begins. In keeping with this, a study from New Zealand found that children with a low selenium status were more likely to develop asthma subsequently (53). If this hypothesis were true, one would expect current diet to be more strongly associated with asthma of early rather than late onset. Although our ability to test this hypothesis was limited because information on age of onset of asthma was incomplete and some older adults will have forgotten about symptoms in childhood (54), there was a suggestion in our data that apple intake (but not selenium intake) was more strongly protective for early-onset asthma. An alternative explanation for this observation is that early- and late-onset asthma represent different phenotypes and that current apple intake has a stronger effect on the former phenotype than on the latter.

## Conclusions

We have found evidence to suggest that a higher consumption of apples and a higher intake of selenium may protect against asthma in adults, and that a higher consumption of red wine might reduce asthma severity in some individuals. The association with apples suggests that we need a better understanding of how flavonoids, or other constituents of apples, influence respiratory health. The findings for selenium may have important implications for food policy in Britain in view of the nation's declining selenium status in recent years (55).

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