Diet, lung function, and lung function decline in a cohort of 2512 middle aged men

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Abstract

Background—A prospective cohort study of 2512 Welshmen aged 45–59 living in Caerphilly in 1979–1983 was used to investigate associations between diet and lung function.

Methods—At baseline (phase I) and at five year follow up (phase II), forced expiratory volume in one second (FEV₁) was measured using a McDermott spirometer and dietary data were obtained using a semi-quantitative food frequency questionnaire.

Results—Good lung function, indicated by high maximum FEV₁, given age and height, was associated with high intakes of vitamin C, vitamin E, β-carotene, citrus fruit, apples, and the frequent consumption of fruit juices/squashes. Lung function was inversely associated with magnesium intake but there was no evidence of an association with fatty fish. Following adjustment for confounders including body mass index, smoking history, social class, exercise, and total energy intake, only the associations with vitamin E and apples persisted, with lung function estimated to be 39 ml (95% confidence interval (CI) 9 to 69) higher for vitamin E intakes one standard deviation (SD) apart and 138 ml higher (95% CI 58 to 218) for those eating five or more apples per week compared with non-consumers. Decline in lung function between phases was not significantly associated with the changing intakes of apples or vitamin E. An association between high average apple consumption and slow decline in lung function lost significance after adjustment for confounders.

Conclusions—A strong positive association is seen between lung function and the number of apples eaten per week cross sectionally, consistent with a protective effect of hard fruit rather than soft/citrus fruit. The recent suggestion that such effects are reversible was not supported by our longitudinal analysis.

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Keywords: diet; lung function; apples
occupations. Height in bare feet was measured in mm using the Holtain stadiometer and weight in light clothes was measured in kg using scales. Lung function tests were performed using a McDermott spirometer. After a demonstration, each man was asked to perform the test until three technically satisfactory readings were obtained. Dietary data were collected using a self-administered semi-quantitative food frequency questionnaire which, after some initial instruction, the men took home and completed with the help of their spouse.

PHASE II

After a period of five years the cohort was contacted again and asked to attend a second evening clinic. Dietary data were collected using a slightly different version of the self-administered semi-quantitative food frequency questionnaire and completed questionnaires were checked through with the subject, usually by a dietitian/nutritionist. Men were asked again about their smoking history. Respiratory function tests were performed as in phase I but administered by a doctor rather than an interviewer and weight in light clothes was measured in kg using a beam balance.

DIETARY DATA

Food and nutrient intakes were assessed by the semi-quantitative food frequency questionnaires. These contained questions about the frequency of consumption (number of times per week at phase I and number of days per week at phase II) of a large number of foods normally eaten as part of the UK diet. For some foods questions were asked about the quantity consumed—for example, the number and size of slices of bread, the amount of milk consumed per day, the number of eggs eaten per week, the amount of butter/margarine consumed per week. For other foods such as meat and fish, quantities were assessed by combining frequency information with average portion size.

The average portion sizes used in this study were calculated from seven day weighed dietary records completed by a one third systematic sample of the Caerphilly cohort at phase I. A comparison of nutrient intakes for the first 119 of these men, as calculated from their weighed dietary records versus their phase I food frequency questionnaires, has been published elsewhere.

The semi-quantitative food frequency questionnaires from phase I and phase II were used to assess intakes of vitamin C, vitamin E, beta-carotene, and magnesium. The questionnaires differed slightly between phases, particularly in the way they recorded fats, cakes, and tinned fruit, but both asked about the number of apples eaten per week, the number of oranges or grapefruit eaten per week, the frequency of drinking fruit juices and squashes, and the frequency of eating fatty fish (including kippers, herring, pilchards, tuna, sardines and salmon).

STATISTICAL METHODS

Multiple regression models were fitted using Stata to investigate associations of dietary factors (explanatory variables) with maximum FEV1 (dependent variable). The dietary factors considered were vitamin C, vitamin E, beta-carotene, magnesium, apples, citrus fruit (oranges or grapefruit), and intake frequencies for fatty fish and fruit juices/squashes. By including additional variables in the regression models, all associations were initially adjusted for age, height, age², and height³ and subsequently for the confounding effects of body mass index, smoking, social class, work exercise, leisure exercise, and total energy intake. Smoking was entered into models as one eight-level factor (never smoked, ex-smoker for <1 year, ex-smoker for 1–4 years, ex-smoker for 5–9 years, ex-smoker for ≥10 years, cigar/pipe smoker, cigarette smoker, mixed smoker) and three continuous variables (number of cigarettes currently smoked per day, number of cigars currently smoked per day, and number of ounces of tobacco currently smoked per week). Separate analyses within smoking subgroups (never smoked, ex-smoker, cigar/pipe smoker, cigarette smoker) were also conducted due to the prior hypothesis that the protective effects of antioxidant vitamins and antioxidant rich foods would be stronger among smokers.

For each dietary factor that appeared to be related to lung function cross sectionally, change in that factor between phases was investigated as a predictor of change in maximum FEV1 over the same period. Associations were modelled using multiple regression in Stata adjusting initially for average age, average age squared, height, and height squared and subsequently for average body mass index, change in body mass index, “average” smoking, change in smoking, social class at phase I, work exercise at phase I, leisure exercise at phase I, average energy intake, and change in energy intake. “Average” smoking was entered into the model as one seven-level factor and three continuous variables while change in smoking was entered as a nine-level factor and three continuous variables. Different lengths of follow up were adjusted for by modelling change in FEV1 per year, then multiplying predicted values by 5.

Results

The cohort consisted of 2512 middle aged men of mean (SD) age 52.1 (4.6) years of whom 55% were current smokers and 29% were ex-smokers, with 66% employed in manual occupations. The estimated mean (SD) daily intakes of vitamin C, vitamin E, beta-carotene, and magnesium were 51.4 (20.7) mg/day (n = 2414), 5.1 (2.0) mg/day (n = 2389), 2625 (1682) µg/day (n = 2293), and 264.7 (87.6) µg/day (n = 2334), respectively. At least one FEV1 reading was provided by 2406 men at phase I (2162 provided three readings) and 1890 men at phase II (1870 provided three readings), with information at both phases provided by 1827 men. Using all available readings the mean (SD) maximum FEV1, at phase I was 2752 (762) ml with change in
maximum FEV1, between phases averaging –19 (368) ml. Changes in vitamin C and vitamin E intakes between phases averaged –2.0 (22.6) mg/day (n = 1894) and –0.1 (2.1) mg/day (n = 1878), respectively.

**CROSS SECTIONAL ANALYSIS**

Lung function measured as maximum FEV1 was positively associated with vitamin C, vitamin E, and β-carotene (p<0.001, p = 0.009, p = 0.031, respectively; table 1). However, regression coefficients, though essentially unconfounded by body mass index, were substantially reduced in magnitude and lost significance following adjustment for smoking and social class (p = 0.137, p = 0.160, p = 0.431, respectively; table 1). The size and significance of the association between lung function and vitamin E was restored following additional adjustment for total energy intake (p<0.01) with lung function estimated to be 39.1 ml (95% confidence interval (CI) 9.4 to 68.8) higher for vitamin E intakes one standard deviation above the mean (2 mg/day) (table 1). This reduced slightly to 31.7 ml (95% CI 0.9 to 62.5) following additional adjustment for vitamin C and the frequency of apple intake.

There was a significant negative association between magnesium and lung function (p = 0.028) which appeared unconfounded by body mass index, smoking, social class, or exercise but completely disappeared following additional adjustment for total energy intake (p = 0.888; table 1).

Lung function was positively associated with frequent consumption of citrus fruit, fruit juices/squashes, and apples (p = 0.004, p = 0.012, p<0.001, respectively). The associations with citrus fruit and fruit juices/squashes lost significance following adjustment for smoking but the association with apples persisted even following additional adjustment for body mass index, social class, exercise, and total energy intake (table 2). Regression coefficients suggested that lung function was 138.1 ml (95% CI 58.1 to 218.1) higher for those eating five or more apples per week compared with non-consumers (table 2). This reduced slightly to 115.3 ml (95% CI 30.6 to 200.0) following adjustment for vitamins C and E.

There was a significant negative association between total energy intake and lung function which persisted after adjustment for confounding (p<0.001). Regression coefficients suggested lung function was 48.8 ml (95% CI 14.0 – 57.4) lower for every 100 kcal increase in daily energy intake.

**Table 1** Cross sectional analysis: differences in forced expiratory volume in one second (FEV1) in ml associated with a one standard deviation increase in nutrient intake at phase I.

<table>
<thead>
<tr>
<th>Adjusted for</th>
<th>Vitamin C (n = 2136)</th>
<th>Vitamin E (n = 2136)</th>
<th>Magnesium (n = 2136)</th>
<th>β-carotene (n = 2035)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Difference 95% CI</td>
<td>Difference 95% CI</td>
<td>Difference 95% CI</td>
<td>Difference 95% CI</td>
</tr>
<tr>
<td>(1) Age, height, age², height³</td>
<td>67.8*** 39.6 to 96.1</td>
<td>37.9** 9.3 to 66.6</td>
<td>–31.8* –60.0 to –3.5</td>
<td>31.9* 2.9 to 60.8</td>
</tr>
<tr>
<td>(2) Model 1 + body mass index</td>
<td>65.0*** 36.8 to 93.1</td>
<td>37.0* 8.4 to 65.5</td>
<td>–32.1* –60.5 to –4.3</td>
<td>29.7* 0.6 to 57.8</td>
</tr>
<tr>
<td>(3) Model 2 + smoking history</td>
<td>37.3* 9.5 to 65.1</td>
<td>23.2 –4.5 to 50.9</td>
<td>–31.5* –58.8 to –4.3</td>
<td>14.3 –13.9 to 42.4</td>
</tr>
<tr>
<td>(4) Model 3 + social class</td>
<td>21.1 –6.8 to 49.0</td>
<td>19.7 –7.8 to 47.2</td>
<td>–31.3* –58.0 to –4.1</td>
<td>11.2 –16.7 to 43.1</td>
</tr>
<tr>
<td>(5) Model 4 + work exercise and leisure exercise</td>
<td>16.2 –11.6 to 44.0</td>
<td>14.0 –13.4 to 41.4</td>
<td>–35.4* –62.4 to –8.5</td>
<td>7.5 –20.4 to 35.3</td>
</tr>
<tr>
<td>(6) Model 5 + total energy intake</td>
<td>26.2 –2.0 to 54.4</td>
<td>39.1** 9.4 to 68.8</td>
<td>–2.7 –41.1 to 35.6</td>
<td>14.1 –13.9 to 42.1</td>
</tr>
</tbody>
</table>

*Test for trend based on ungrouped variable. †Test for trend based on ungrouped variable (0, 1, 2, 3, 4, 5, 6, 7).
21.4 to 76.3) lower for total energy intakes one standard deviation (597 kcal/day) apart. There was no significant association between lung function and the frequency of fatty fish consumption either before (p = 0.572) or after adjustment for confounders (p = 0.851; table 2).

There was no evidence to suggest that the strong positive association observed between lung function and apple differed between smoking groups (never smoked, ex-smoker, cigar/pipe smoker and current smoker; table 3). However, there was some suggestion that the association with vitamin E might be stronger among the never smoked and that the association with total energy intake might be restricted to those not currently smoking cigarettes, although in both cases the test for a statistical interaction with smoking group failed to reach significance (p = 0.466, p = 0.111, respectively).

When we excluded from the full Caerphilly cohort (n = 2512) the 244 men with only one or two FEV1 readings at phase I, those on asthma medication (n = 74), and those taking vitamin supplements that might contain vitamins A, C or E (n = 48), the associations between lung function and apples, vitamin E, and vitamin C were little changed (p<0.001, p = 0.024, p = 0.076, respectively). The inverse association between lung function and total energy persisted (p = 0.013) although the magnitude of the estimated fall in maximum FEV1 across an increase in energy intake of one standard deviation was reduced from 48.8 ml to 35.5 ml.

**LONGITUDINAL ANALYSIS**

The number of apples per week and intakes of vitamin E and vitamin C were investigated further in a longitudinal analysis. Change in lung function between phase I and phase II was not significantly associated with change in any of these three dietary factors, either before or after adjustment for confounders. The coefficients for apple consumption did tend to go in the hypothesised direction, suggesting that eating more than two extra apples per week compared with no change was associated with a 16.7 ml (95% CI –36.1 to 69.5) reduction in decline in lung function (table 4), but the trend was weak as well as non-significant (p = 0.174) and became slightly weaker (p = 0.184) after additional adjustment for average apple consumption. The coefficients for vitamin E and vitamin C went in the opposite direction to that hypothesised.

Average apple consumption was significantly (p = 0.004) associated with change in lung function between phases suggesting that eating five or more apples per week compared with none was associated with a decrease in lung function decline of 74.1 ml (95% CI 17.7 to 130.6) over five years (table 4). However, after adjustment for confounders the magnitude of the association decreased markedly, suggesting only a 47.7 ml (95% CI 10.7 to 106.2) reduction and lost statistical significance (p = 0.098;
Additional adjustment for change in apple consumption had little effect. Associations with average vitamin C and vitamin E intake were also positive but failed to reach statistical significance either before or after adjustment for confounders.

**Discussion**

**APPLES**

In a large prospective study of middle aged Welshman we found a strong cross sectional positive association between the number of apples eaten per week and lung function as measured by maximum FEV₁. After adjusting for confounders including body mass index, smoking history, social class, work exercise, leisure exercise, and total energy intake, in addition to age and height, model coefficients suggested that lung function was 138 ml (95% CI 58 to 218) higher for those eating five or more apples per week compared with non-consumers. This finding is consistent with results from other large epidemiological studies which have reported positive associations between lung function and the consumption of fresh fruit.

It has been hypothesised that the observed association between lung function and fresh fruit intake is due to the antioxidant vitamin C—namely, fruit juices/squashes and citrus fruit—lost statistical significance (p = 0.918 and p = 0.393, respectively). Furthermore, the association between lung function and apples appeared to be independent of both vitamin C and vitamin E intake. It is possible that apples may be acting as a marker for a more healthy diet, although additional adjustment for the frequency of green vegetable/salad consumption had little if any effect on the results presented for apples in table 2 (data not shown). When reporting an inverse association between hard fruit and chronic non-specific lung disease in elderly men in the Zutphen study, the antioxidant effects of flavonoids such as quercetin were suggested as a possible mechanism. Quercetin is found in high concentrations in apples, onions, tea, and red wine and may therefore help to explain our findings in Caerphilly.

**VITAMIN E**

In our preliminary analysis we found a significant positive association between lung function and vitamin E intake but this appeared to be explained by smoking and social class, both of which were positive confounders. However, when additional adjustment was made for total energy intake, the coefficient for vitamin E almost tripled and regained statistical significance (p<0.01) with lung function estimated to be 39 ml (95% CI 9 to 69) higher for vitamin E intake one standard deviation (2 mg/day) apart. A significant (p<0.001) positive association was also observed between lung function and the ratio of vitamin E to total fat intake, even after adjustment for age, height, body mass index, smoking, social class, and exercise (data not shown). Any effect of vitamin E may therefore depend on the relative rather than the absolute amount in the diet, a possible reflection of the positive association that is known to exist between vitamin E requirement and the dietary intake of polyunsaturated fatty acid.

Positive associations between lung function and dietary vitamin E have been reported previously by Dow et al in a small survey of elderly men and women and by Britton et al in a large random sample of the Nottingham adult population. A negative association between vitamin E and diagnosed asthma reported by the Nurses Health Study may have been inflated by the avoidance of peanuts among asthmatics. A similar explanation cannot be levelled here as the dietary questionnaire on which vitamin E intake was assessed did not collect any information on peanuts or nuts which were rarely eaten in this population.

The association also appeared to be independent of vitamin C intake. Another possible explanation is that this is one spurious result out of nine significance tests. Bonferroni's correction suggests that, with nine significance tests, we should use p<0.0055 as the cut off for statistical significance rather than p<0.05, although this is a highly conservative approach.

**TOTAL ENERGY INTAKE**

The strong inverse association observed between lung function and energy intake, though unexpected, appeared to be independent of body mass index. This suggested that it could not be explained in terms of reduced lung function with increasing obesity, although there is still the possibility that lung function depends on aspects of body fatness not well measured by body mass index and that energy intake is simply acting as a marker for these. Whether it is then appropriate to adjust all our analyses for energy intake is debatable. It is clear that, without adjustment, observed associations may simply reflect the effects of other nutrients. However, to adjust may be an over-adjustment helping to mask a real association that depends on the absolute amount in the diet rather than the relative amount. This makes it difficult to interpret not only our results for vitamin E but also those for magnesium. However, the strong negative association observed between lung function and magnesium prior to adjustment for energy intake was in the opposite direction to that hypothesised, making confounding by energy intake a plausible explanation.

**FATTY FISH**

Our failure to demonstrate a positive association between the frequency of eating fatty fish and lung function is in contrast to results from the Second National Health and Nutrition Examination Survey (NHANES II) which reported an inverse association between wheeze and dietary fish, and to results from studies of Australian children, one of which reported an odds ratio for current asthma by
diet, with or without oily fish, of 0.26 (95% CI 0.09 to 0.72).
However, there was no evidence of an inverse association between
diagnosed asthma and omega-3 fatty acids in
the American Nurses Health Study and studies
of asthmatics treated with fish oil have pro-
vided little evidence of any beneficial effect. 31–33

PREDICTING DECLINE IN LUNG FUNCTION
Several studies have reported cross sectional
associations between fresh fruit or antioxidant
vitamins and lung function in both children and
adults, but only one other study has so far
looked at the longitudinal effects of change
in diet on decline in lung function. Carey et al. reporting on data from successive health and
lifestyle surveys, found a strong association
between increasing fresh fruit consumption
over time and reduced lung function decline.
The lack of an independent association with
average fresh fruit consumption over the same
period led them to hypothesise that the protec-
tive effect of fresh fruit was totally reversible
rather than progressive. In our longitudinal
analysis we found no support for this hypo-
thesis. Average apple consumption and change
in apple consumption appeared to increase with
increasing lung function, although neither
association was statistically significant after
adjustment for confounders. There was no evi-
dence of an association between change in
vitamin E or vitamin C intake over five years
and decline in lung function over the same
period.

DIETARY DATA
Our failure to demonstrate significant positive
associations for vitamin C and β-carotene with
lung function may be due to the way in which
these nutrients were estimated, since misclassi-
fication of nutrient intakes tends to bias
associations towards the null. Significant
associations reported between vitamin C and
lung function by studies using food frequency
questionnaires tend to be small and not
inconsistent with our own estimate of 26 ml
(95% CI –5 to 54) per standard deviation vita-
min C (table 1). One possible reason for nutrient
misclassification in phase I is that the dietary
questionnaire did not ask about the fre-
quency of eating tinned fruit, although this was
rectified in phase II. Changes in the food
frequency questionnaire between phases may
also help to explain the lack of an association
longitudinally between decline in lung function
and changes in vitamin intake.

These problems were not shared to the same
extent by our food frequency variables which
were simply responses to single questions on
the dietary questionnaire. For apples the ques-
tion was essentially the same at both phases—that
is, “number of apples eaten per week (please specify)” at phase I and “how many apples do you eat per week?” at phase II—providing suitably comparable data for a
longitudinal analysis. The ability of Hertog et al. to
demonstrate a significant association between
digestive cancer and fruit and vegetable
consumption at phase I provides further
evidence for the validity of our information on
apples and citrus fruit.

CONCLUSION
We have demonstrated a positive cross sec-
tional association between lung function and
the number of apples eaten per week in a
cohort of middle aged Welshmen. This associ-
ation appeared to be independent of vitamin E
and vitamin C intakes and may therefore be
explained by other antioxidant constituents of
apples such as flavonoids (e.g. quercetin). The
recent suggestion that such effects are revers-
ible was not supported by our longitudinal
analysis.

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