Effects of fruit and vegetable consumption on plasma antioxidant concentrations and blood pressure: a randomised controlled trial

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Summary

Background High dietary intakes of fruit and vegetables are associated with reduced risks of cancer and cardiovascular disease. Short-term intensive dietary interventions in selected populations increase fruit and vegetable intake, raise plasma antioxidant concentrations, and lower blood pressure, but long-term effects of interventions in the general population are not certain. We assessed the effect of an intervention to increase fruit and vegetable consumption on plasma concentrations of antioxidant vitamins, daily fruit and vegetable intake, and blood pressure.

Methods We undertook a 6-month, randomised, controlled trial of a brief negotiation method to encourage an increase in consumption of fruit and vegetables to at least five daily portions. We included 690 healthy participants aged 25–64 years recruited from a primary-care health centre.

Findings Plasma concentrations of α-carotene, β-carotene, lutein, β-cryptoxanthin, and ascorbic acid increased by more in the intervention group than in controls (significance of between-group differences ranged from p=0·032 to 0·0002). Groups did not differ for changes in lycopene, retinol, α-tocopherol, γ-tocopherol, or total cholesterol concentrations. Self-reported fruit and vegetable intake increased by a mean 1·4 (SD 1·7) portions in the intervention group and by 0·1 (1·3) portion in the control group (between-group difference=1·4, 95% CI 1·2–1·6; p<0·0001). Systolic blood pressure fell more in the intervention group than in controls (difference=4·0 mm Hg, 2·0–6·0; p<0·0001), as did diastolic blood pressure (1·5 mm Hg, 0·2–2·7; p=0·02).

Interpretation The effects of the intervention on fruit and vegetable consumption, plasma antioxidants, and blood pressure would be expected to reduce cardiovascular disease in the general population.

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Introduction

Ecological and epidemiological evidence suggest that high consumption of fruit and vegetables is associated with a reduced risk of cancer[1] and cardiovascular disease.[2] Several mechanisms have been proposed for this process, including an increased nutrient intake of antioxidant compounds. However, intervention trials of vitamin supplements to increase circulating plasma concentrations of antioxidant vitamins have produced little evidence to support this hypothesis.[3–6] The health benefits of eating fruit and vegetables may be due, in part, to mechanisms other than their antioxidant vitamin content such as blood pressure lowering.[7] Current evidence, including unpublished trial data (http://www.hpsinfo.org), therefore points to the beneficial effects of eating more fruit and vegetables rather than vitamin supplementation.

An average daily intake of at least five portions of fruit and vegetables is recommended in the UK,[8] which would represent an increase in consumption of 50%[9] with only about 40% of men and women currently achieving this target.[10] Although short-term intensive dietary interventions in highly selected populations increase fruit and vegetable intake substantially,[11,12] raise plasma antioxidant concentrations,[12] and lower blood pressure,[7] whether such interventions are feasible in the general population is uncertain. We did a randomised, controlled trial to investigate the effect of a 6-month primary-care intervention to increase fruit and vegetable consumption in a healthy general population with a wide range of eating habits.

Methods

Participants

We identified all patients aged 25–64 years without serious chronic illness from the lists of two general practices based in a health centre in Thame, Oxfordshire, UK. The general practices had few patients from ethnic minorities. We excluded patients with cardiovascular diseases (other than hypertension), gastrointestinal disease, cancer, serious psychiatric disorders, or hypercholesterolaemia; patients who had undergone a recent traumatic event, such as bereavement; and those unable to give informed consent. We mailed letters to patients sequentially until the target number of patients had been recruited. The letters invited patients to participate in a project giving advice about increasing "natural protective factors" against cancer and heart disease. To ensure that we recruited only one participant from each household we ordered the list by street name and house number, day of month on which born, and forename; we invited only the first-named patient at any address to participate. Our intention was to recruit patients at regular intervals during 1 year to nullify the effects of seasonal changes in food consumption, but recruitment actually continued for 14 months (from Aug 1, 1997, to Sept 30, 1998). We excluded respondents

who reported using dietary supplements, or who were pregnant or attempting to conceive. Ethical approval for the trial was obtained from the Central Oxford Research Ethics Committee. All participants gave written informed consent.

Procedures

We allocated eligible participants sequentially to the intervention or control group with a computer-generated randomisation list. Randomisation was in blocks of four, and was stratified by reported smoking status. We invited participants to attend two appointments at an interval of 6 months with a trained research nurse at the health centre. Before each of the two appointments, we mailed participants a self-completion questionnaire. Both questionnaires contained the DINE food frequency questionnaire[13] modified to assess intake of fruit and vegetables and to include "stage of change" questions for exercise and intake of fat, fruit, and vegetables.[14] Questions about fruit and vegetables were embedded within other questions to avoid alerting controls to the nature of the intervention. At the baseline visit, participants were asked about their exercise habits, family history of premature coronary heart disease and cancer, and at both visits about smoking.

Health checks were done at both visits by study research nurses, and included measurement of blood pressure (mean of two readings taken 10 min apart with a Copal UA731 electronic automatic sphygmomanometer [A&D Instruments; Abingdon, UK]), height, and weight using a stadiometer and scales. A 10-mL non-fasting venous blood sample was taken for measurement of antioxidant vitamins and total cholesterol concentrations. The occupation of patients was recorded and social class was established with the UK Registrar General's standard occupational classification.[15]

Immediately after the health check, the research nurse introduced the benefits of eating more fruit and vegetables and presented a pictorial portion guide. A portion was defined as an 80 g serving. An eating pattern assessment questionnaire (EPAQ) was used to elicit meal and snack patterns on weekdays and weekends. This assessment was used not only to identify the number of fruit and vegetable portions the participant was eating, but also acted as a visual representation to show where increases in consumption might be made. The brief negotiation method[16] was used to encourage participants to identify specific and practical ways that were consistent with their habits and preferences of eating more fruit and vegetables. The study nurses did a 2-day training course on the use of the brief negotiation method, which included discussion of behavioural change theory and role-play activities.

Participants were encouraged to discuss possible barriers to eating more fruit and vegetables such as cost, eating out, and catering for children. We had prepared leaflets and other materials designed to address these difficulties, which we gave to every participant according to need. The recommendation of five or more portions a day was advocated if achievable, but a lower target was negotiated for about a quarter of participants who thought this amount was an unrealistic goal. Participants who were already eating five or more portions a day (about 20%) were congratulated and given a leaflet describing the importance of variety. Participants were given a copy of their action plan, a refrigerator magnet with the five-a-day logo, a portion guide, and a 2-week self-monitoring record book. The dietary intervention took about 25 min. All intervention interviews were audiotaped and, throughout the study, 30 randomly selected interviews were reviewed to ensure that the content and delivery remained consistent.

2 weeks after the initial intervention, a research nurse telephoned participants to reinforce the message and discuss any problems. At 3 months, a letter was sent reinforcing the five-a-day message, together with a booklet of seasonal recipes, and a strategy check list suggesting various ways of incorporating additional portions of fruit and vegetables into the diet.[11]

Controls were randomly assigned to receive the intervention after 6 months. They received the same health check, self-completed questionnaire, and blood sampling as the intervention group. The nurse explained that they would receive specific advice at their 6-month follow-up appointment. Controls were asked to carry on as usual until then and were not told that the trial was of a dietary intervention. At 6-months' follow-up, they were given information about the benefits of eating fruit and vegetables, and offered the same materials as the intervention group.

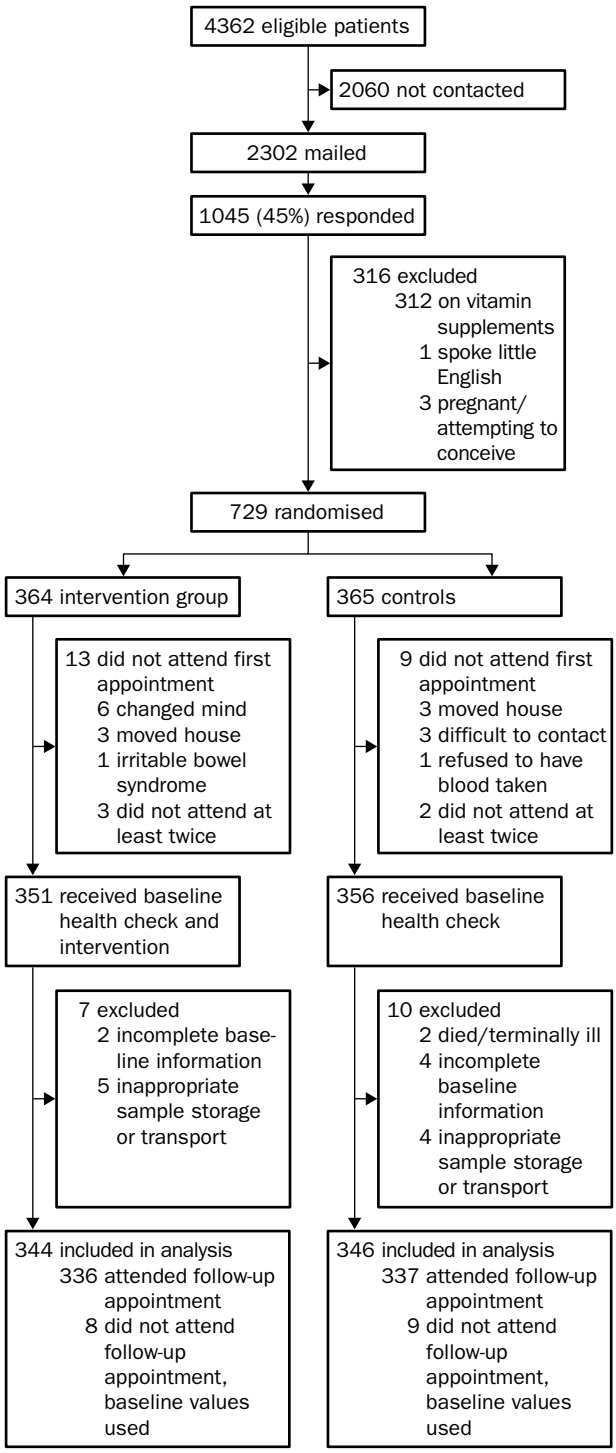
Primary outcome measures were the between-group differences in mean individual changes, from baseline to 6 months, in plasma concentrations of α-carotene, β-carotene, lycopene, β-cryptoxanthin, lutein, retinol, α-tocopherol, γ-tocopherol, and ascorbic acid. Secondary outcome measures were changes in self-reported fruit and vegetable intake assessed by a dietary questionnaire, weight, and blood pressure.

We stored plasma samples at −80°C. Lipid-soluble vitamin standards and plasma samples were analysed by the Clinical Trial Services Unit, University of Oxford, Oxford, UK, by high-performance liquid chromatography (HPLC) using a Waters system (Waters Corporation; MA, USA) fitted with a photodiode array detector. Total cholesterol was measured on a Beckman Synchron CX4 clinical chemistry analyser with Beckman reagents (Beckman; Brea, CA, USA). Plasma ascorbic acid was assayed using HPLC[17] by the Department of Clinical Biochemistry, Glasgow Royal Infirmary, Glasgow, UK. The inter-assay coefficient of variation (CV) for total cholesterol was 2·0%, for ascorbic acid 3·9%, and ranged from 6·7% to 11·8% for lipid-soluble vitamins. The corresponding intra-assay CVs were 1·0%, 1·0%, and 4·6–6·7%. Laboratories were masked to the assignment of patients.

We aimed to detect changes of 7–10% in the intervention group with a 90% power at a two-tailed level of significance of 5%, assuming no change in controls. The power calculation was based on antioxidant data that we had obtained previously.[18] Baseline means (SDs) of changes in plasma concentrations of antioxidants used in the calculations were (in μmol/L) α-carotene 0·090 (0·035), β-carotene 0·39 (0·11), α-tocopherol 35 (5·6), lutein 0·340 (0·095), lycopene 0·50 (0·19), and β-cryptoxanthin 0·23 (0·16). We calculated that a study size of 320 participants per group would enable us to detect a change of 10% in concentrations of α-carotene, 7% in β-carotene, 4% in α-tocopherol, 7% in lutein, 10% in lycopene, and 18% in β-cryptoxanthin.

Statistical methods

We undertook a modified intention-to-treat analysis in which we excluded patients who were assigned to a group but who did not attend the initial appointment. For participants who attended the first appointment but were lost to follow-up, we carried forward values from the first appointment. We excluded a few participants from each group (up to a maximum of 12) with plasma concentrations more than three SDs higher than the mean



Trial profile

(after log transformation of the distribution to normal, if necessary) from the analysis for each particular antioxidant, since such outlying values were more likely to result from dietary supplements than from fruit and vegetable consumption. We did not remove outliers for lycopene (since we knew of no lycopene supplements) or cholesterol, but some samples for measurement of cholesterol and for antioxidants were missing or spoiled. Results for tocopherols were also expressed as the ratio of tocopherol to total cholesterol.

Comparisons between proportions were made with χ^2 and between means with *t* test. Adjustment for covariates was done by multiple regression analysis. Results were adjusted for baseline antioxidant concentrations and sex (which was unbalanced in the trial groups), but not for other characteristics (smoking, age, social class, body-mass index) since these made no material difference to the results. Differences in outcome between the intervention group and controls are shown with 95% CIs. We used SPSS (version 9.0) and CIA (Confidence Interval Analysis, version 1.1) in analyses.

We did prespecified subgroup analyses on the basis of sex, smoking, social class, family history of cancer or heart disease, and low self-reported baseline intake of fruit and vegetables (three or fewer portions per day). We tested interaction between the intervention and subgroup in a multiple regression model, which included the main effects of the intervention, baseline antioxidant concentration, sex, and the factor under scrutiny.

Role of the funding source

The sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Participants

1045 (45%) of 2302 eligible mailed patients responded to the initial invitation (figure). Respondents were older than non-respondents (mean [SD] age 46·1 [10·1] years *vs* 40·1 [10·3] years; difference 6·0 years, 95% CI 5·2–6·9) and a higher proportion were women (55% *vs* 48%; difference 7%, 2·9–11·1). Respondents were less materially deprived than non-respondents (mean Townsend material deprivation score[19] –0·98 (1·35) *vs* –0·75 (1·38); difference –0·23, –0·34 to –0·12). 316 respondents (207 women [66%]) were excluded before randomisation (figure). Of 729 participants assigned to groups, 690 were included in the final analysis. By chance, there were substantially more men in the intervention group than controls (53 *vs* 45%) but groups were similar in age, social class, and body-mass index (table 1). Smoking prevalence at baseline was 16% in the intervention group and 17% in controls, and the corresponding figures after 6 months in the 655 patients who returned questionnaires were 18% and 16%, respectively.

Table 2 shows the results of an intention-to-treat analysis. Plasma antioxidant concentrations in the two groups were similar at baseline. At 6 months, after adjustment for baseline antioxidant concentrations and sex, the intervention group showed greater increases than the controls in α-carotene (adjusted difference 7% of

	Intervention group (n=344)	Controls (n=346)
Sex		
Male	183 (53%)	155 (45%)
Female	161 (47%)	191 (55%)
Age (years, mean [SD])	45·7 (10·1)	46·0 (10·1)
Current smoker	55 (16%)	59 (17%)
Social class		
I and II	174 (51%)	163 (47%)
III non-manual	57 (17%)	57 (17%)
III manual	56 (16%)	43 (12%)
IV and V	29 (8%)	41 (12%)
Housewife	23 (7%)	29 (8%)
Armed Forces and not known	5 (2%)	13 (4%)
Body-mass index (kg/m^2, mean [SD])		
Men	26·1 (3·2)	26·7 (3.6)
Women	25·4 (4·6)	25·3 (4·6)

Values are number (percentage) except where stated otherwise.

Table 1: **Baseline characteristics**

	n	Baseline, mean (SD)	Change at 6-months' follow-up, mean (SD)	Between-group difference in change (95% CI)	Adjusted difference in change* (95% CI)	p for adjusted difference
Antioxidant (μmol/L)						
α-carotene						
I	325	0·122 (0·09)	0·002 (0·06)	0·007 (–0·002 to 0·017)	0·009 (0·001 to 0·017)	0·027
C	329	0·121 (0·09)	–0·005 (0·06)			
β-carotene						
I	331	0·434 (0·27)	0·001 (0·17)	0·027 (0·003 to 0·051)	0·031 (0·010 to 0·053)	0·005
C	333	0·431 (0·28)	–0·026 (0·15)			
Lutein						
I	339	0·405 (0·17)	0·011 (0·13)	0·018 (0·0003 to 0·051)	0·018 (0·002 to 0·035)	0·032
C	334	0·407 (0·18)	–0·007 (0·10)			
Lycopene						
I	339	0·522 (0·23)	–0·020 (0·17)	–0·010 (–0·037 to 0·016)	–0·013 (–0·038 to 0·011)	0·29
C	343	0·533 (0·25)	–0·010 (0·18)			
β-cryptoxanthin						
I	324	0·200 (0·17)	0·067 (0·19)	0·047 (0·020 to 0·073)	0·050 (0·023 to 0·076)	0·0002
C	323	0·191 (0·15)	0·021 (0·16)			
Retinol						
I	335	1·770 (0·42)	–0·030 (0·31)	0·001 (–0·048 to 0·049)	–0·008 (–0·053 to 0·037)	0·73
C	340	1·800 (0·48)	–0·030 (0·33)			
Ascorbic acid						
I	334	34·25 (15·58)	0·92 (15·57)	1·91 (–0·37 to 4·20)	2·38 (0·33 to 4·43)	0·023
C	344	34·38 (15·00)	–0·99 (14·48)			
α-tocopherol						
I	337	25·776 (6·35)	0·431 (4·04)	0·117 (–0·493 to 0·726)	0·093 (–0·502 to 0·688)	0·76
C	341	26·041 (6·48)	0·314 (4·04)			
α-tocopherol (adjusted for cholesterol)						
I	333	5·167 (0·99)	0·134 (0·73)	0·034 (–0·071 to 0·138)	0·036 (–0·065 to 0·137)	0·49
C	339	5·127 (0·98)	0·101 (0·65)			
γ-tocopherol						
I	336	1·764 (0·80)	–0·048 (0·67)	–0·038 (–0·141 to 0·065)	–0·023 (–0·117 to 0·071)	0·63
C	342	1·699 (0·77)	–0·009 (0·69)			
γ-tocopherol (adjusted for cholesterol)						
I	332	0·353 (0·15)	–0·004 (0·15)	–0·005 (–0·027 to 0·016)	0·001 (–0·018 to 0·020)	0·91
C	340	0·333 (0·14)	0·001 (0·14)			
Total cholesterol (mmol/L)						
I	340	5·037 (0·96)	–0·018 (0·87)	0·018 (–0·092 to 0·128)	0·010 (–0·097 to 0·116)	0·86
C	344	5·123 (1·02)	–0·036 (0·56)			

I=intervention group. C=controls. *Adjusted for baseline value and sex.

Table 2: **Plasma concentrations of antioxidants and total cholesterol**

baseline in the intervention group), β-carotene (7%), lutein (4%), β-cryptoxanthin (25%), and ascorbic acid (7%); the significance of the differences ranged from p=0·032 to 0·0002. Groups did not differ with respect to retinol, lycopene, α-tocopherol, γ-tocopherol, or for cholesterol. The effect of the intervention did not vary between subgroups.

Table 3 shows that, based on a 95% response rate to the final questionnaire (655 responses from 690 participants), at 6-months' follow-up the intervention group reported a greater increase in fruit and vegetable intake (mean change from 3·4 [1·7] to 4·9 [1·6] daily portions) than the control group (3·4 [1·5] to 3·5 [1·6] daily portions). After adjustment for baseline characteristics the difference in change between the groups was 1·4 daily portions (1·2–1·6). There was a similar small increase in weight in both groups. The intervention effect was greater in men than women (p=0·02), in smokers than non-smokers (p=0·03), and in those with baseline intake of three or fewer portions per day (p=0·03).

Diastolic and systolic blood pressures fell in the intervention group and a small reduction in diastolic but not systolic blood pressure occurred in controls

	n	Baseline, mean (SD)	Change at 6-months' follow-up, mean (SD)	Between-group difference in change (95% CI)	Adjusted difference in change* (95% CI)	p for adjusted difference
Self-reported daily intake of fruit and vegetables (portions)						
I	329	3·4 (1·7)	1·4 (1·7)	1·3 (1·1 to 1·6)	1·4 (1·2 to 1·6)	<0·0001
C	326	3·4 (1·5)	0·1 (1·3)			
Systolic blood pressure (mm Hg)						
I	344	130·2 (19·7)	–2·0 (13·5)	3·4 (1·3 to 5·5)	4·0 (2·0 to 6·0)	<0·0001
C	346	129·3 (19·6)	1·4 (14·6)			
Diastolic blood pressure (mm Hg)						
I	344	79·2 (11·4)	–1·6 (8·7)	1·4 (0·1 to 2·7)	1·5 (0·2 to 2·7)	0·02
C	346	79·9 (11·9)	–0·3 (8·7)			
Weight (kg)						
I	344	76·1 (13·8)	0·6 (2·6)	0·0 (–0·3 to 0·5)	0·1 (–0·4 to 0·6)	0·68
C	346	75·6 (14·9)	0·6 (2·6)			

I=intervention group. C=controls.*Adjusted for baseline value and sex.

Table 3: **Self-reported intake of fruit and vegetables, blood pressure, and bodyweight**

(difference in changes between groups for systolic pressure 4·0 mm Hg [2·0–6·0, p<0·0001] and for diastolic pressure 1·5 mm Hg [0·2–2·7, p=0·02]).

Discussion

Our results show that a primary-care intervention can increase self-reported fruit and vegetable intake; raise plasma concentrations of α-carotene, β-carotene, lycopene, β-cryptoxanthin, and ascorbic acid; and result in significant decreases in systolic and diastolic blood pressure.

Our analysis included all possible randomised patients irrespective of complete data or compliance. The study population was demographically heterogeneous with men and women aged 25–64 years being eligible for inclusion whatever their baseline fruit and vegetable intake, and recruitment was not restricted to individuals contemplating dietary change.[14] The high response rate from a primary-care population increases the general applicability of the findings and, furthermore, the intervention is appropriate for a wide range of people. The findings, however, cannot be extrapolated to ethnic minorities, and the socioeconomic class of participants was higher than the national UK average. Participants might also have been more health conscious, although this bias is likely to have been attenuated by the exclusion of people who reported taking vitamin supplements. We planned to assign participants to groups throughout 1 year to offset effects of seasonal changes in food intake, but recruitment took 14 months. The 2 extra months fell in winter, which could explain the small reduction in most plasma antioxidants between baseline and the end of the trial in controls.

Our results accord with those of the DASH (Dietary Approaches to Stop Hypertension) trial,[7] in which an increase in dietary fruit and vegetables for 8 weeks reduced systolic blood pressure by 2·8 mm Hg and diastolic pressure by 1·1 mm Hg more than a control diet. DASH differed fundamentally from our study in design, however, being a controlled feeding trial with meals prepared to a common protocol in research kitchens. DASH investigators also reported a larger lowering of blood pressure in participants assigned a combination diet (low in dairy products with reduced saturated and total fat content in addition to being enriched with fruit and vegetables).

We did not advise participants to reduce fat intake, and noted no change in total cholesterol concentration and a small increase in bodyweight. Therefore, the fall in blood pressure achieved in our study is unlikely to be attributable to reduced fat intake or changes in physical activity. The reduction in blood pressure probably resulted from increased potassium intake,[20] and possibly from some reduction in sodium, although participants were not advised specifically to reduce salt intake. The rise in plasma ascorbic acid concentration was too small to have affected blood pressure.[21] Our results extend the findings of the DASH trial by showing that people making their own food choices can adhere to advice to increase dietary fruit and vegetables.

In an 8-week, UK trial,[11] an increase of 4·5 daily portions was reported. The intervention programme was more intensive than ours, and included a lecture, food-tasting sessions, and distribution of recipes and lunch boxes. Furthermore, participants consuming more than five portions daily were excluded and plasma antioxidants were not measured. In a New Zealand trial,[12] after an intensive 8-week intervention programme, increases of 71% in plasma concentration for α-carotene, 50% for β-carotene, and 78% for ascorbic acid were reported, with an increase of 4·7 daily portions after 4 weeks. These changes are much larger than ours, probably because of differences in study design. In the New Zealand trial, 90 volunteers eating three or fewer servings of fruit and vegetables daily were recruited by advertisement, and a much higher proportion of participants (71%) were women than in our study. The intervention was more intensive than ours, with participants receiving detailed, individual, dietary counselling every fortnight. Our intervention was less intensive, more generally applicable, and increased consumption of fruit and vegetables over a longer period. However, we do not know whether the results could be sustained for more than 6 months.

The clinical significance of the small rise in antioxidant concentrations is unclear. In prospective studies, participants with high concentrations of plasma antioxidants had low risks of epithelial cancers,[22] coronary heart disease,[23] stroke,[24] and progression of intima-media thickness of the common carotid arteries,[25] but the concentrations were substantially higher than those achieved in our trial.

The falls in blood pressure in our study (4·0 mm Hg systolic and 1·5 mm Hg diastolic) would be expected to produce small clinical effects, but would substantially reduce cardiovascular disease at the population level. A reduction of 2 mm Hg in diastolic blood pressure results in a decrease of about 17% in the incidence of hypertension, 6% in the risk of coronary heart disease, and 15% in the risk of stroke and transient ischaemic attack.[26]

Contributors

H A W Neil, L S Roe, and S Ziebland conceived the study. The final protocol was designed in collaboration with J H John and P Yudkin. The authors developed the intervention with J Jay and J Robertson who were the trial research nurses. J H John coordinated the trial and undertook the analyses, supervised by P Yudkin. J H John and H A W Neil wrote the paper and all authors were involved in interpreting the results and critical revision of the paper.

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Conflict of interest statement

None declared.

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