Does vitamin C reduce blood pressure? Results of a large study of people aged 65 or older

Christopher J. Bates[a], Catherine M. Walmsley[a], Ann Prentice[a] and Steven Finch[b]

Objective **To characterize relationships among blood pressure, pulse rate, vitamin C status and other protective and risk factors for older British people, from a national survey.**

Design **A cross-sectional analysis of survey data.**

Setting **A population study, representative of mainland Britain.**

Subjects **Among 914 people of both sexes living in the community, 373 were taking blood-pressure-lowering drugs and were therefore excluded from the analyses.**

Interventions **Completion of an interview on health, lifestyle and dietary habits, recording of a 4-day dietary record, anthropometry and taking of a blood sample to determine haematological and biochemical status.**

Main outcome measures **Systolic and diastolic blood pressures, pulse rate, indices of micronutrient status including plasma ascorbate concentration, nutrient intake and haematology.**

Results **Plasma ascorbate concentration was inversely correlated to systolic and diastolic blood pressures and pulse rate. Other covariates of blood pressure included age, sex, domicile, plasma retinol, fibrinogen and γ-tocopherol concentrations, erythrocyte count, prothrombin time and urine sodium : creatinine ratio. Covariates of pulse rate included sex, domicile, plasma fibrinogen and platelet count. Blood pressure was also correlated to intake of vitamin C.**

Conclusions **Plasma ascorbate concentration and intake of vitamin C are covariates of blood pressure in older people living in Britain. New intervention studies are now needed, to test for possible causalities.** ***J Hypertens*** **16:925–932 © 1998 Lippincott-Raven Publishers.**

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[a]Medical Research Council Dunn Nutrition Unit, Milton Road, Cambridge and [b]Social and Community Planning Research, London, UK

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Correspondence and requests for reprints to Dr C.J. Bates, MRC Dunn Nutrition Unit, Milton Road, Cambridge CB4 1XJ, UK.

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Introduction

The established risk factors for cardiovascular disease include smoking, high plasma lipid concentrations (particularly cholesterol), high blood pressure, obesity, factors associated with fetal and infant growth, diabetes, risk of thrombogenesis, lack of physical activity and some dietary factors [1–5]. Dietary factors and the biochemical status indices which they control are, of course, extremely complex, but one potentially important aspect is the postulated role of the so-called 'anti-oxidant' nutrients, including vitamin C, which may modulate other established risk factors and processes, thereby reducing the risk of overt disease [1–4,6–9]. High blood pressure is an important risk factor [1–5], which has been found to be significantly inversely associated with intake of vitamin C and its status indices in a variety of studies with several populations [9–19]. Results of some intervention trials have been reported [20–26].

A new cross-sectional national diet and nutrition survey of older people was carried out in mainland Britain during 1994–1995 [27] and included measurements of blood pressure, of food and nutrient intakes and of a wide range of nutrient status indices, in addition to haematology, anthropometry and determinations of other potential risk factors and protective factors. There was thus an opportunity to consider the cross-sectional relationships among blood pressure, intake and status of vitamin C, and other relevant indices, for this large UK population sample.

Methods

The design and execution of the National Diet and Nutrition Survey of People Aged 65 Years or Over in mainland Britain has been described elsewhere [27]; therefore only the main features are summarized here. This series of surveys was commissioned by the British

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government (Department of Health and Ministry of Agriculture, Fisheries and Food). Ethical approval for this survey was given by the National Health Service Local Research Ethics Committees corresponding to each of the postal code sectors involved and by the Medical Research Council's Dunn Nutrition Unit's ethics committee. Potential participants were randomly selected from 80 randomly chosen postcode sectors, by Social and Community Planning Research. Within each sector, private households (the 'non-institution' sample) and long-stay institutions such as nursing homes (the 'institution' sample) were both represented, but the present study was confined to data for the non-institution sample. Predetermined numbers, for statistical adequacy, were recruited from each sex group and from the three age groups 65–74, 75–84 and 85+ years. This required deliberate over-sampling of male subjects and the older groups [27]. Although fewer than half of the non-institution sample subjects provided a blood sample and about 59% of the non-institution sample subjects provided a 4-day dietary record, there was little evidence of self-selection bias in the characteristics of the responding sample.

A structured interview, by a trained fieldworker, provided information on health and lifestyle factors. Then each subject was asked to provide a 4-day weighed dietary record. A trained nurse performed anthropometric measurements and obtained a single early morning urine sample and an early morning blood sample, usually from fasting subjects. Detailed information about use of drugs was obtained by the nurse, who recorded information about brand name, strength, amount and frequency of use and product licence number, for each drug used (by reference to the information on the bottle, packet, etc). Ambulatory blood pressures [diastolic blood pressure (DBP), systolic blood pressure (SBP) and mean arterial pressure] and pulse rates were measured by the nurse with a Dinamap 8100 blood pressure monitor (Johnson and Johnson Medical, Bracknell, Berkshire, UK).

The subjects, who had been asked not to eat, drink alcohol and smoke during the 30 min beforehand, were seated and the blood pressure measurement was recorded three times in rapid succession. The first measurement was discarded, to minimize any effect of initial anxiety and the mean of the second and third measurements was used. The Dinamap 8100 device has been validated [28] and is believed to yield consistent results, adequate for surveys [27].

The blood samples (30 ml maximum) were collected into four Sarstedt monovettes (Sarstedt Ltd, Leicester, UK) for routine haematology and for determinations of haematinic indices (folate, vitamin B_{12} and ferritin levels), clotting factors (prothrombin time, activated partial thromboplastin time and fibrinogen level) and biochemical indices, including routine clinical chemistry and a wide range of special tests for micronutrient status. A list of all measurements performed, together with details of the methodology, can be found in the survey report [27]. Immediately after collection, the heparinized sub-sample for determination of biochemical indices was rapidly chilled in a cool box containing a freezer pack to maintain it at 4–8°C during transportation to a local hospital laboratory (1–4 h journey time) and was immediately separated into plasma and erythrocytes, which were washed with saline before storage. One portion of plasma was stabilized with metaphosphoric acid (5% wt : vol final concentration) for the plasma ascorbate analyses [29]. This and all other analyses for biochemical indices, apart from the determinations of erythrocyte haemoglobin A1c, were carried out at the Medical Research Council's Dunn Nutrition Unit, Cambridge, UK, to which they were transported on solid CO_2 and thereafter stored at –85°C. The haemoglobin A1c (glycosylated haemoglobin) assays were carried out by Dr G.A. Maguire at the Department of Clinical Biochemistry, Addenbrookes Hospital, Cambridge, UK, using an automated high-performance liquid chromatography procedure (Diamat; BioRad, Hemel Hempstead, Hertfordshire, UK) [30].

Diet records were coded at Social and Community Planning Research, University College, London and Ministry of Agriculture, Fisheries and Food. They were used to calculate individual daily nutrient intakes from tables. Estimates of supplementary vitamin intakes (tablets, syrups etc.) were included.

The analyses in this paper are confined to data for people not living in institutions (such as nursing homes) because people in institutions often have lower blood pressures and poorer nutritional indices. Reduction of data was performed with Microsoft 'Excel' (Microsoft Corp., Redmond, Washington, USA) and Data Description Inc. 'DataDesk' (Data Description Inc., Ithaca, New York, USA) computer programmes, using univariate and multiple linear regression models, with or without logarithmic transformation. Two-tailed hypothesis tests were used throughout. $P < 0.05$ was deemed statistically significant.

Results

In Table 1 we enumerate the non-institution survey participants by categories of age group, sex and whether they were taking blood-pressure-lowering drugs. The categories of blood-pressure-lowering drugs used by survey participants are listed in the footnote to Table 1. Many of the subjects who were taking blood-pressure-lowering drugs were taking several drugs simultaneously.

In Table 2 we list characteristics of subjects who were taking blood-pressure-lowering drugs (subdivided into two groups according to the type of drugs used) and of those who were not. Blood pressures and pulse rates

Table 1 **Number of participants by age, sex and use of blood pressure-lowering drugs**

	Number of participants providing the data set			
	Subjects not taking blood-pressure-lowering drugs		Subjects taking blood-pressure-lowering drugs	
Entire survey	Males	Females	Males	Females
65–74 years	142 (16)	104 (11)	68 (7)	78 (8)
75–84 years	122 (13)	82 (9)	71 (8)	72 (8)
85+ years	36 (4)	55 (6)	33 (4)	51 (6)

Values are expressed as numbers (percentages). Of the 2172 approached, 1275 provided 4-day diet records and 914 provided blood for plasma ascorbate assays among whom blood pressure data were available for 878 and pulse data for 887. Of the 914 who provided blood for plasma ascorbate, 541 were not taking blood-pressure-lowering drugs; 373 were taking drugs of this kind. For the purposes of this study we classified as blood-pressure-lowering drugs diuretics, β-blockers, combinations of diuretics and β-blockers; angiotensin converting enzyme inhibitors, vasodilators and centrally acting drugs, sympatholytics and calcium antagonists. Other cardiovascular drugs that were recorded, but were excluded from this list because they are not prescribed for hypertension, were anticoagulants, lipid-level-lowering drugs, antiplatelet drugs including aspirin, anti-arrhythmic drugs, positive inotropics, peripheral vasodilators and nitrates. After this initial subdivision into groups of people taking and not taking blood-pressure-lowering drugs, subjects were then further subdivided by age and sex, yielding the numbers and percentages in the table. For the purposes of the main survey, the selected sample had a greater proportion of older subjects, especially men, than existed in the population of the country, in order to achieve adequate numbers in each age–sex category for the statistical comparisons of the survey report [27].

Table 2 **Comparisons between subjects taking blood-pressure-lowering drugs and those not taking blood-pressure-lowering drugs, within the survey sample**

Index	Subjects not taking blood-pressure-lowering drugs (n = 541)	Subjects taking diuretic drugs for lowering of blood pressure (n = 246)	Subjects taking other drugs to lower blood pressure (n = 127)	Significance for inter-group difference (*P*)
Age (years)	76.0 ± 7.2 (541)	78.1 ± 7.6 (246)	74.9 ± 6.9 (127)	< 0.0001
Systolic blood pressure (mmHg)	152.1 ± 23.2 (525)	150.6 ± 22.5 (234)	155.0 ± 25.1 (119)	0.25
Diastolic blood pressure (mmHg)	78.2 ± 13.1 (525)	77.2 ± 14.4 (234)	79.9 ± 13.5 (119)	0.21
Pulse rate (beats/min)	69.3 ± 13.0 (528)	70.0 ± 15.0 (240)	66.3 ± 12.7 (119)	0.45
Height (cm)	163.1 ± 9.7 (529)	160.5 ± 9.7 (244)	163.0 ± 9.1 (126)	0.002
Body mass index (kg/m^2)	26.0 ± 4.0 (528)	27.0 ± 4.4 (244)	26.6 ± 4.1 (126)	0.004
Grip strength (kg)	27.7 ± 11.6 (520)	23.5 ± 10.6 (239)	26.6 ± 11.8 (122)	< 0.0001
Diet				
Energy (MJ/day)	7.24 ± 2.02 (518)	6.56 ± 1.80 (238)	6.90 ± 1.94 (124)	< 0.0001
Fat (g/day)	69.0 ± 23.2 (518)	62.9 ± 20.7 (238)	63.0 ± 21.0 (124)	0.0004
Vitamin C (mg/day)	68.0 ± 58.9 (518)	74.3 ± 89.2 (238)	68.5 ± 49.5 (124)	0.48
Sodium (g/day)	2.41 ± 0.85 (518)	2.36 ± 0.91 (238)	2.33 ± 0.78 (124)	0.56
Blood				
Haemoglobin (g/l)	140 ± 14.0 (533)	138 ± 14.0 (244)	138 ± 14.0 (124)	0.044
Haemoglobin A1c (%)	5.13 ± 1.01 (538)	5.38 ± 1.16 (240)	5.18 ± 1.19 (125)	0.014
Plasma urea (mmol/l)	5.78 ± 1.74 (519)	7.08 ± 2.73 (234)	5.83 ± 2.03 (120)	< 0.0001
Plasma α_1-antichymotrypsin (g/l)	0.39 ± 0.10 (526)	0.41 ± 0.09 (234)	0.37 ± 0.07 (119)	0.001
Plasma ascorbate (μmol/l)	40.9 ± 25.0 (541)	43.6 ± 25.3 (245)	41.4 ± 22.3 (126)	0.43
Erythrocyte folate (nmol/l)	471 ± 267 (538)	560 ± 342 (242)	498 ± 246 (124)	0.0003
Plasma retinol (μmol/l)	2.13 ± 0.58 (499)	2.32 ± 0.73 (224)	2.18 ± 0.51 (114)	< 0.0009
Urine				
Sodium : potassium ratio	3.35 ± 1.57 (537)	3.50 ± 2.49 (240)	3.63 ± 1.90 (123)	0.27
Potassium : creatinine ratio	5.06 ± 2.06 (537)	4.54 ± 2.04 (240)	5.11 ± 2.48 (123)	0.004

Values are expressed as means ± SD (number of subjects). Significances of inter-group differences were calculated by analysis of variance. Participants who were taking blood-pressure-lowering drugs also had a lower average annual income ($P = 0.005$) and were more likely to be receiving social security benefits ($P = 0.002$) than were people not taking these drugs [27]. Subjects in the middle column were taking diuretics or a combination of diuretics and other drugs prescribed for hypertension. The other categories of antihypertensive drugs, all included in the right-hand column, were angiotensin converting enzyme inhibitors, vasodilators, centrally acting drugs, sympatholytics and calcium antagonists. All subjects who were taking diuretic drugs were included in the middle column, even if they were taking other drugs too.

of users and non-users of blood-pressure-lowering drugs were not significantly different. People taking diuretic drugs were slightly older and slightly shorter, with a greater body mass index. Their muscle strength, indicated by their grip strength, was also substantially less. The values observed for people taking other types of blood-pressure-lowering drugs were more similar to those of people not taking any of these drugs. With respect to nutrient intakes, people taking blood-pressure-lowering drugs had lower intakes of energy and especially of fat; however, their intakes of vitamin C were not significantly different. Mean plasma urea concentration of people taking diuretic drugs was higher, which might imply that their renal efficiency was impaired. Mean plasma

Table 3 Significant associations for subjects not using blood-pressure-lowering drugs, with blood pressure and pulse as dependent variables, by multiple linear regression with age and sex included

	Dependent variables						
	Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)		Pulse (beat/min)		
Independent variables (units)	Regression coefficient	Significance (*P*)	Regression coefficient	Significance (*P*)	Regression coefficient	Significance (*P*)	Degrees of freedom[b]
Income[a]	Negative	< 0.0001	Negative	0.021	Negative	0.86	532
Body mass index (kg/m^2)	+0.62 ± 0.22	0.0006	+0.34 ± 0.13	0.008	−0.04 ± 0.14	0.77	648
MUAC (mm)	+0.88 ± 0.27	0.001	+0.35 ± 0.16	0.025	−0.09 ± 0.16	0.58	665
Diet							
Fibre[c] (g/day)	−13.6 ± 5.0	0.007	−6.5 ± 2.9	0.026	−8.4 ± 3.1	0.007	632
Vitamin C[c] (mg/day)	−10.7 ± 2.9	0.0003	−4.3 ± 1.7	0.012	−3.3 ± 1.8	0.07	632
β-Carotene[c] (μg/day)	−8.4 ± 2.5	0.0006	−3.4 ± 1.4	0.02	−3.6 ± 1.5	0.02	632
Glucose[c] (g/day)	−13.0 ± 3.4	0.0002	−3.6 ± 2.0	0.07	−4.3 ± 2.1	0.04	632
Blood							
Haemoglobin (g/l)	+0.124 ± 0.080	0.12	+0.154 ± 0.045	< 0.0007	+0.019 ± 0.044	0.66	553
Erythrocyte count (10^{12}/l)	+5.77 ± 2.41	< 0.017	+5.88 ± 1.35	< 0.0001	+5.88 ± 1.35	< 0.007	552
Platelet count (10^9/l)	+0.037 ± 0.015	0.01	+0.016 ± 0.008	0.06	+0.043 ± 0.008	< 0.0001	541
White-cell count (10^9/l)	+1.58 ± 0.54	0.04	+0.48 ± 0.30	0.12	+1.08 ± 0.29	0.0002	544
Haemoglobin A1c (%)	+2.83 ± 1.01	0.05	+0.57 ± 0.57	0.31	+0.96 ± 0.56	0.08	528
Plasma cholesterol (mmol/l)	+2.23 ± 0.75	0.003	+0.94 ± 0.42	0.03	+0.25 ± 0.42	0.56	510
Triglycerides[c] (mmol/l)	+21.4 ± 5.1	< 0.0001	+5.7 ± 2.9	0.046	+5.8 ± 2.9	0.042	510
Retinol (μmol/l)	+6.03 ± 1.76	< 0.0007	+0.73 ± 1.01	0.47	−0.87 ± 1.01	0.39	488
α-Tocopherol (μmol/l)	+0.39 ± 0.09	< 0.0001	+0.12 ± 0.05	0.03	−0.02 ± 0.05	0.72	488
γ-Tocopherol[c] (μmol/l)	+19.1 ± 5.2	0.0002	+5.4 ± 3.0	0.07	+41.4 ± 3.0	0.64	486
Ascorbate (μmol/l)	−017 ± 0.04	< 0.0001	−0.06 ± 0.02	0.01	−0.06 ± 0.02	0.005	523
Zinc (μmol/l)	+1.07 ± 0.49	0.03	+0.44 ± 0.28	0.11	+0.47 ± 0.28	0.09	452
Copper (μmol/l)	+0.68 ± 0.32	0.03	+0.26 ± 0.18	0.15	+0.64 ± 0.18	0.0003	449
Fibrinogen[c] (g/l)	+2.14 ± 0.64	0.0008	+0.71 ± 0.37	0.05	+1.27 ± 0.36	0.0005	485
α_1-Antichymotrypsin (g/l)	+18.3 ± 10.8	0.09	+1.62 ± 6.00	0.79	+17.3 ± 5.9	0.004	515
Prothrombin time (s)	−0.97 ± 0.42	0.02	−0.48 ± 0.24	0.047	−0.06 ± 0.24	0.080	497

Values are expressed as means ± SEM. Each index variable was entered singly after age and sex, in the multiple regression model. [a]Income was registered by category (three categories: less than £4000 *per annum*; £4000–£7999 *per annum* and more than £8000 *per annum*). All the other variables, except sex, were continuous. MUAC, mid-upper-arm circumference. [b]Degrees of freedom: as stated for systolic and diastolic blood pressures; subtract 7 from these values for pulse rate. [c]Regression of logarithmically transformed indices, for those for which the untransformed distribution was not Gaussian. The univariate regression significance (*P*) values for age, sex and domicile (non-institution or institution) versus blood pressure and pulse rates were as follows (668 degrees of freedom):

	Systolic blood pressure	Diastolic blood pressure	Pulse
Age	0.002 (+)	0.023 (–)	0.28 (+)
Sex	0.002 (+)	0.016 (–)	< 0.0001 (+)

The + and – signs after the *P* values indicate whether the relationship is direct or inverse. A direct relation with sex indicates higher values for men; an inverse relation with sex indicates higher values for women.

α_1-antichymotrypsin, an acute phase marker, was greater than normal, and the concentration of a marker of diabetic risk (haemoglobin A1c) was also greater than normal for this group. Plasma total cholesterol (data not shown) did not differ among the groups. Mean urine concentrations of potassium, relative to those of creatinine, were lower for those taking diuretic drugs, but the sodium : potassium ratio did not significantly differ from normal. Two of the micronutrient status indices (erythrocyte folate concentration and plasma retinol) revealed unexpected differences, which will be discussed elsewhere.

In Table 3 we focus on those subjects who were not taking blood-pressure-lowering drugs (i.e. any of the categories of drugs listed in the footnote to Table 1). It concerns risk indices, nutrient intakes including vitamin C and indices of blood status, including plasma ascorbate level, in relation to SBP, DBP and pulse rate. Because age and sex sometimes were important covariates, they are included in all the models in Tables 3–5. Relatively high income (a proxy for social class) was associated with lower SBP and DBP. The indices of adiposity (body mass index and mid-upper-arm circumference) were directly related both to SBP and to DBP. Of the dietary nutrient intakes tested, four exhibited significant relationships. Fibre, β-carotene, vitamin C and glucose intakes were inversely related to blood pressure and pulse rate. Dietary sodium and potassium intakes could not be assessed accurately from diet records; therefore these nutrient intakes were assessed by measuring urinary excretion of these elements (Table 4). Intakes of dietary energy, protein, fat, cholesterol, carbohydrate, starch, sucrose, magnesium, iron, copper, zinc, thiamin, riboflavin, niacin equivalents, vitamin B_6, folate, vitamin B_{12} and vitamins A, D and E (data not shown) were not related to blood pressure and pulse (judged by linear regression).

Of the blood indices, many were directly related to SBP and some were related to DBP and to pulse rate (Table 3). The direct correlations between blood pressure and either α-tocopherol or γ-tocopherol concentration ceased to be significant if these two indices were expressed as ratios to cholesterol concentration (data not shown). Only two blood indices were inversely related to blood pressure and pulse rate, namely plasma ascorbate (vitamin C) and prothrombin time. If plasma ascorbate and vitamin C intake were both introduced into the model together, for vitamin C intake there was no longer a significant correlation whereas plasma ascorbate concentration retained its significance. The blood indices plasma high-density lipoprotein cholesterol concentration, alkaline phosphatase activity, calcium, phosphate, iron and transferrin saturation, γ-glutamyl transferase, urea, creatinine, 25-hydroxyvitamin D, serum and erythrocyte folate concentration, serum vitamin B_{12} and ferritin concentrations, concentrations of five plasma carotenoids and the erythrocyte indices of thiamin, riboflavin and selenium status (data not shown) were not related to blood pressure and pulse (judged by linear regression).

Table 4 concerns the assessment of which of the diet and blood (or urine) indices are sufficiently robust covariates with the outcome indices to survive as significant contributors in an extended multiple linear regression model. The dietary nutrient intake estimates were assessed in a separate model from the blood (or urine) indices. Of the dietary intakes, only vitamin C and β-carotene intakes (inverse) survived into the model for SBP. The contributions by vitamin C and by β-carotene intakes remained essentially unchanged when they were expressed as ratios to energy intake (data not shown). In the nutritional status index model for SBP, seven blood indices were sufficiently robust to survive. As in Table 3, plasma ascorbate concentration and prothrombin time were the only inversely related indices to contribute significantly, plasma ascorbate concentration being a major contributor for SBP, DBP and pulse rate. Among the directly related contributors, two other well-established cardiovascular risk indices, erythrocyte count (a proxy for viscosity), and tendency for clotting (plasma fibrinogen and platelet counts), were significant contributors. For pulse rate, platelet count was a highly significant covariate. Urine sodium : creatinine ratio, which failed to contribute significantly in the simpler models depicted in Table 3, was a significant contributor to the variance of SBP in Table 4 (the creatinine denominator was used as a means of correcting for dilution, because timed urine samples could not be collected).

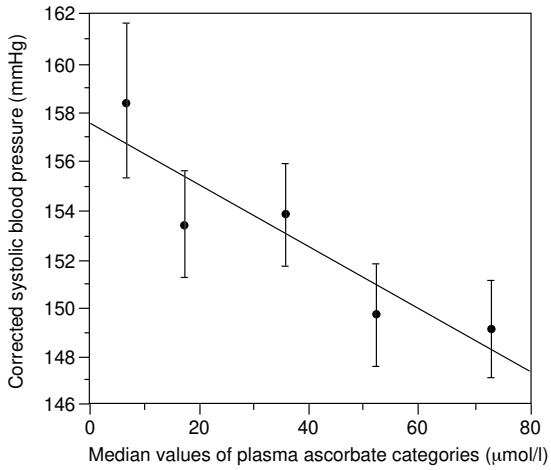
The analyses in Table 4 were repeated for the subjects who were taking blood-pressure-lowering drugs (Tables 1, 2). Whereas the relationships for age, sex, domicile and erythrocyte count as significant contributors to the variances of the outcome variables SBP, DBP and pulse were similar to those for the participants not taking blood-pressure-lowering drugs, those for all the other diet and blood indices, including vitamin C (intake and plasma concentration) failed to attain statistical significance (data not shown). Exclusion of data for a subgroup of 46 subjects who were taking antidiabetic drugs or had haemoglobin A1c concentrations above 6.3%, or both, had no discernible effect on the relationships between the outcome parameters and the blood indices shown in Table 4.

Table 4 Analysis by simultaneous multiple linear regression of all significant covariates of blood pressure and pulse rate for all subjects not using blood pressure-lowering drugs

	Dependent variables					
	Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)		Pulse rate (beats/min)	
Independent variables (units)	Regression coefficient	Significance (*P*)	Regression coefficient	Significance (*P*)	Regression coefficient	Significance (*P*)
Diet model						
Sex	Positive	0.10	Negative	0.005	Positive	0.0005
Age (years)	+0.22 ± 0.13	0.08	−0.16 ± 0.07	0.03	+0.012 ± 0.078	0.87
Vitamin C intake[a] (mg/day)	−7.7 ± 3.3	0.02	−3.13 ± 1.91	0.10	−1.73 ± 2.03	0.40
β-Carotene intake[a] (μg/day)	−7.7 ± 3.3	0.04	−2.20 ± 1.60	0.17	−2.94 ± 1.70	0.08
Degrees of freedom	631		631		638	
Variance explained (%)	4.5		2.9		3.4	
Blood model						
Sex	Positive	0.025	Negative	0.35	Positive	0.0006
Age (years)	+0.65 ± 0.16	< 0.0001	−0.077 ± 0.093	0.40	+0.113 ± 0.092	0.22
Plasma ascorbate[a] (μmol/l)	−7.2 ± 2.4	0.003	−3.7 ± 1.4	0.01	−4.5 ± 1.4	0.002
Erythrocyte count (10^{12}/l)	+7.37 ± 2.7	0.007	+5.5 ± 1.6	0.0006	+2.7 ± 1.6	0.09
Plasma fibrinogen[a] (g/l)	+20.6 ± 9.5	0.03	+3.9 ± 5.7	0.49	+13.0 ± 5.6	0.02
Plasma retinol (μmol/l)	+4.8 ± 1.8	0.01	+0.12 ± 1.09	0.91	−0.24 ± 1.09	0.82
Prothrombin time (s)	−2.2 ± 0.9	0.02	−0.32 ± 0.55	0.57	+0.19 ± 0.55	0.72
γ-Tocopherol (μmol/l)	+2.9 ± 1.0	0.02	+0.45 ± 0.57	0.43	+0.29 ± 0.56	0.61
Urine Na : creatinine (molar ratio)	+0.39 ± 0.14	0.04	+0.13 ± 0.08	0.11	−0.075 ± 0.080	0.24
Platelet count (10^9/l)	+0.022 ± 0.017	0.18	+0.021 ± 0.010	0.03	+0.044 ± 0.010	< 0.0001
Degrees of freedom	397		397		400	
Variance explained	19.8		8.9		14.4	

Values are expressed as means ± SEM. In each of the two models (diet and biochemical), all of the relevant indices were entered simultaneously, together with age and sex. [a]Logarithmically transformed data when the untransformed data were not Gaussian.

Fig. 1



Corrected systolic blood pressure by category of increasing plasma ascorbate concentration. The analysis included all subjects not taking blood-pressure-lowering drugs. The median plasma ascorbate concentrations (μmol/l) for people in the five ascending categories were 6.6, 17.0, 35.6, 52.1 and 72.8. There were 57–99 results in each category and the mean systolic blood pressure in each category was corrected for the effects of the covariates age, sex, plasma retinol concentration, γ-tocopherol concentration, erythrocyte and platelet counts, log [plasma fibrinogen], prothrombin time and urine sodium : creatinine ratio (Table 4). The results are given as means ± SEM for each plasma ascorbate concentration category, with a best-fit linear regression line. An increase of 50 μmol/l in plasma ascorbate concentration was associated with a fall of 7 mmHg (95% confidence interval 3–12).

Figure 1 depicts the corrected SBP by category of increasing plasma ascorbate concentration. The data sets were subdivided into five categories by increasing plasma ascorbate concentration and used to construct a multiple linear regression model, with SBP as the dependent variable and the other significant contributors (Table 4) as the independent covariates.

Table 5 lists the significant correlations between the three outcome parameters and the amounts of different groups of food items eaten by the survey participants, which were observed in a multiple regression model that contained age and sex in addition to each food group, entered singly.

Discussion

Because the use of blood-pressure-lowering drugs is likely to confuse any genuine relationships among diet, biochemical indices and blood pressure, the principal analyses were confined to data for the subset of participants who were not taking blood-pressure-lowering drugs.

The indices which were significantly correlated to blood pressure and pulse rate in the present survey are similar to those of previous studies and surveys [1,2]. Some of these indices reflected known risk factors, such as blood viscosity (cell counts), tendency for clotting (platelet count and fibrinogen) and diabetes (haemoglobin A1c). Prothrombin time is likely to reflect tendency for clotting and concentrations of fibrinogen. The direct correlation to plasma vitamin E concentration (Table 3) might reflect its interdependence with plasma cholesterol concentration, because the vitamin E : cholesterol concentration ratio was not significantly related to blood pressure. For people who were taking blood-pressure-lowering drugs, the relationships of diet and blood status indices to SBP, DBP and pulse were attenuated, possibly because the powerful effects of drugs overwhelmed the weaker contributions of diet and biochemical status indices. DBP was somewhat less strongly related to the nutrition indices than was SBP, and is also considered to be the less powerful predictor of vascular disease among older people [31].

The covariates of pulse rate were somewhat different from those of SBP and DBP. Platelet counts were strongly

Table 5 Correlation of food choices with blood pressure and pulse rate in subjects not using blood-pressure-lowering drugs

	Dependent variables					
	Systolic blood pressure (mmHg)		Diastolic blood pressure (mmHg)		Pulse rate (beats/min)	
Food category (g/d)	Regression coefficient	Significance (*P*)	Regression coefficient	Significance (*P*)	Regression coefficient	Significance (*P*)
Fromage frais	−0.097 ± 0.039	0.013	−0.049 ± 0.023	0.034	−0.009 ± 0.024	0.72
Egg dishes	−0.025 ± 0.012	0.041	−0.014 ± 0.007	0.044	−0.004 ± 0.008	0.60
Non-polyunsaturated soft margarine	+0.069 ± 0.039	0.019	+0.011 ± 0.0017	0.51	+0.012 ± 0.018	0.23
Raw carrot	+0.007 ± 0.34	0.83	0.019 ± 0.020	0.92	−0.051 ± 0.020	0.012
Boiled/baked potatoes	−0.0002 ± 0.002	0.93	−0.0014 ± 0.001	0.29	−0.0020 ± 0.001	0.03
Soft fruit	−0.010 ± 0.003	0.003	−0.0027 ± 0.002	0.16	−0.0045 ± 0.0002	0.82
Preserves	−0.023 ± 0.010	0.03	−0.0062 ± ⁻0.006	0.30	+0.006 ± 0.006	0.34
Beer/lager	+0.001 ± 0.0004	0.011	+0.0005 ± 0.002	0.042	+0.0003 ± 0.0003	0.20
Total alcoholic drinks	+0.001 ± 0.014	0.014	+0.0006 ± 0.0002	0.22	+0.0003 ± 0.0003	0.21
Sauces and pickles	−0.0037 ± 0.006	0.56	−0.0074 ± 0.004	0.05	+0.0011 ± 0.004	0.78

The amounts eaten in each food category (g/7 days) were entered one at a time into the multiple regression model, as independent variables after we had added age and sex. Of 107 food categories available for this analysis, only 10 yielded at least one significant correlation ($P < 0.05$, 627–636 degrees of freedom).

predictive of pulse rate, but not of SBP and DBP. Because less is known about pulse rate as a predictor of risk of disease than is known about blood pressure, such differences are not easy to interpret, but they seem intriguing and deserve further investigation.

The only nutrient found to be consistently inversely related both to blood pressure and to pulse rate was vitamin C. This was true both for dietary intake of this vitamin and for its plasma concentration. The relationships with vitamin C intake were less robust than were those with its plasma concentrations. Therefore the predictive power of plasma vitamin C might include both a diet-related component (e.g. high intake of fruit and vegetables) and a health-related component [because the rate of turnover of vitamin C *in vivo* is considered to be an important marker of (and covariate with) certain types of metabolic stress]. An inverse correlation between vitamin C intake or status and blood pressure has now been recorded for a wide range of populations [9–18], but the significance of this observation for public health has not yet been recognized widely. In a recent study of a typical British population of adults, whose mean age was lower than that of the present population sample [17], it was estimated that the decreases in SBP and DBP for a 50 μmol/l increase in plasma vitamin C were 3.6 and 2.6 mmHg, respectively. In the present study, the mean change in SBP that was associated with a 50 μmol/l increase in plasma vitamin C was a decrease of 7 mmHg (95% confidence interval 3–12) or a 5% decrease, whereas the change in pulse rate that was associated with a 50 μmol/l increase in plasma vitamin C was a 4% decrease. The mean SBP observed in the present study was 17 mmHg higher than that found in the previous UK study [17] but the DBP was 4 mmHg lower. These differences may be age-related, because the present survey was of a much older sample.

Whereas the observed relationship between vitamin C status (plasma concentration) and blood pressure might be confounded by factors such as stress, the acute phase reaction and so on, the relationship with vitamin C intake cannot easily be explained in this way. It is, of course, possible that health-conscious people who are fitter, leaner and have a lower blood pressure than the average also have a more 'healthy' eating pattern by choice, including a high intake of fruit and vegetables and correspondingly high intakes and blood concentrations of vitamin C. If the relationship between vitamin C intake and blood pressure is causal, however, it clearly has major implications for the reduction of cardiovascular disease risk and thus for possible dietary interventions [1–9].

Unfortunately, previous dietary intervention trials of vitamin C supplements for human subjects have produced inconsistent results [20–26]. Koh [20] and Feldman *et al.* [22] did not include control groups in their trials, so their results are difficult to interpret; likewise, results of a study by Mostafa *et al.* [25] are ambiguous because they reported only the results from their ascorbic acid-treated subjects (they did not report those from their control group). Osileso *et al.* [21] obtained evidence for a significant reduction in SBP (but not DBP) in 20 Nigerian subjects administered 1 g ascorbic acid daily for 6 weeks in a randomized study with a cross-over design. Lovat *et al.* [24] encountered differences between the cross-over arms of their study of British hypertensive elderly subjects, which made it difficult to interpret their results. Ghosh *et al.* [26] obtained a result for Welsh hypertensive subjects, which, although it was compatible with an effect of a twice daily 250 mg vitamin C supplement, did not attain conventional significance. Salonen *et al.* [23] observed a significant reduction in SBP in a controlled trial of mixed anti-oxidants (ascorbic acid, organic selenium, vitamin E and β-carotene) with Finnish smokers. Results of a recently reported study in People's Republic of China [32] were consistent with, but did not yield unequivocal proof of, there being a beneficial effect of vitamin C supplements on hypertension. Thus the trials performed to date on human subjects have yielded results that, although they are not inconsistent with there being a beneficial effect of vitamin C on blood pressure, do not unequivocally support this hypothesis, mainly because of their methodological inadequacies [17]. Two well-controlled studies of vitamin C supplementation and blood pressure in rats have, however, demonstrated that the vitamin exerts a significant blood-pressure-lowering effect [33,34]. Possible mechanisms by which vitamin C might exert a blood pressure-lowering effect have recently been discussed [17].

Interest in anti-oxidant nutrients, such as vitamins C and E, selenium compounds, carotenoids and bioflavonoids, as dietary factors that may be able to modulate some degenerative diseases in humans, has gained considerable ground in recent years, particularly because the micronutrient content of the diet can be modulated safely, cheaply and easily. The relatively specific relationships of vitamin C with blood pressure and with pulse rate are now amenable to further investigation, both using animal models and by new and better-controlled intervention studies of human populations. Clearly this research has important public health implications and should be given priority funding.

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