Conference on ‘Dietary strategies for the management of cardiovascular risk’

Fruit and vegetable intake and risk of cardiovascular disease

Jayne V. Woodside*, Ian S. Young and Michelle C. McKinley
Centre for Public Health, Queen’s University Belfast, Grosvenor Road, Belfast BT12 6BJ, UK

A high intake of fruit and vegetables (FV) has been shown to be associated with reduced risk of a number of chronic diseases, including CVD. This review aims to provide an overview of the evidence that increased FV intake reduces risk of CVD, focusing on studies examining total FV intake. This evidence so far available is largely based on prospective cohort studies, with meta-analyses demonstrating an association between increased FV intake and reduced risk of both CHD and stroke. Controlled intervention trials examining either clinical or cardiovascular risk factor endpoints are scarce. However, such trials have shown that an increase in FV consumption can lower blood pressure and also improve microvascular function, both of which are commensurate with a reduced risk of CVD. The effects of increased FV consumption on plasma lipid levels, risk of diabetes and body weight have yet to be firmly established. In conclusion, evidence that FV consumption reduces the risk of CVD is so far largely confined to observational epidemiology, with further intervention studies required.

CHD: CVD: Diabetes: Diet: Fruit and vegetables

Diets rich in fruit and vegetables (FV) are associated with a reduced risk of chronic disease(1). General healthy eating guidelines(2,3) and also specific national heart disease prevention guidelines include the recommendation to eat plenty of FV(4), although the exact number of portions recommended and portion size descriptions varies between countries(5). This review will provide an overview of the evidence that increased FV intake reduces risk of CVD. The review will focus on studies examining the total FV intake, not specific compounds found in FV or specific classes of FV or individual fruits or vegetables.

CVD, which includes CHD, cerebrovascular disease and peripheral vascular disease, is still the leading cause of death in the UK, being responsible for 35% of all deaths(6). Therefore, both the management and prevention of CVD are major public health issues in the UK. Although mortality from CHD in the UK has been falling in the last four decades(6), it remains the major cause of premature death (before 75 years) in most affluent societies(7). Risk factors for CHD can be non-modifiable or modifiable. The non-modifiable risk factors include family history, gender and age(8,9). However, the majority of risk factors that contribute to CHD risk, including dyslipidaemia, hypertension, smoking and diabetes, are modifiable(10). Diet is also thought to be a major factor in the development of CHD(11). A variety of dietary factors have been studied in relation to CHD risk including the Mediterranean diet, fat intake, fish intake and folate(12), as well as FV intake, which is the focus of this review.

Current intake of fruit and vegetables in the UK

The National Diet and Nutrition Survey is a nationally representative survey, designed to assess the diet, nutrient intake and nutritional status of the general population aged 18 months upwards living in private households in the UK. The National Diet and Nutrition Survey was previously conducted on a large scale approximately every 10–15 years and data from the last survey, conducted in 2000–2001, indicated that the mean daily FV intake was 2.7 portions/d for men and 2.9 portions/d for women(13). Since the 2000–2001 National Diet and Nutrition Survey, the methodology has changed and a ‘rolling programme’ has been established, which surveys 1000 people per year,

---

**Abbreviations:** BP, blood pressure; CRP, C-reactive protein; FV, fruit and vegetables; HR, hazard ratio; RR, relative risk.

*Corresponding author: Professor Jayne V. Woodside, fax +0044 2890 235900, email j.woodside@qub.ac.uk
aged from 1·5 years upwards. The rolling programme has the advantage that it will generate data more rapidly, and will allow changes over time to be tracked more contemporaneously. The latest data available from this rolling programme are for years 1–3 combined, with the data collected during 2008–2009 to 2010–2011. Data from that period suggest that adults (19–64 years) consumed on average 4·1 portions/d and older adults (>65 years) consumed 4·4 portions/d, with 31% of adults meeting the ‘5-a-day’ recommendation. Estimates of FV intake from the 2000–2001 National Diet and Nutrition Survey and the new rolling programme therefore suggest that FV intake has increased over the last decade. However, the dietary assessment methodologies differed between these two surveys (moving from a 7 d weighed food diary in 2001 to a 4 d estimated diary in the rolling programme and, importantly, including the disaggregation of FV in composite foods within the latter survey), and, therefore, direct comparisons between the surveys and conclusions around trends in consumption over time are not appropriate. One conclusion that can be drawn, however, is that the majority of the adult population is still not meeting the 5-a-day recommendation.

Current intake of fruit and vegetables worldwide

Hall et al. (15) have confirmed a low intake of FV worldwide. The authors found that of 196 373 respondents who resided in fifty-two countries of mostly low and middle income, approximately 78% of both males and females consumed less than five portions of FV daily. FV intakes were assessed within this World Health Survey using specific questions about FV (‘How many servings of fruit do you eat on a typical day?’ and ‘How many servings of vegetables do you eat on a typical day?’), rather than measuring whole diet and attempts were made to standardize serving size and number of servings reported.

Fruit and vegetables and CVD risk

The following sections will review the various types of evidence that exists to demonstrate a link between an increased intake of FV and reduced risk of CVD.

Ecological/modelling studies

Macrosimulation modelling of data from the Expenditure and Food Survey has examined the potential health benefits of adhering to UK dietary recommendations. It was estimated that approximately 33 000 deaths per year (20 800 of these from CHD and 5876 from stroke) could be avoided if UK dietary recommendations were met. Examining which specific dietary recommendation was contributing to the estimated reduction in deaths showed that more than 15 000 of these avoided deaths (45%) would be due to increased FV intake.

An earlier study, but including global data, examined associations between FV consumption in the population and six health outcomes (IHD, stroke and cancers of the stomach, oesophagus, colon, rectum and lung) (17). Data were obtained from either national representative dietary surveys or the FAO, with analyses being stratified by fourteen geographical regions, and also sex and age. The analysis suggested that 2·6 million deaths worldwide and 31% of CHD and 19% of ischaemic stroke may be due to inadequate consumption of FV. An estimated 1·8% of the total burden of disease worldwide was calculated to be attributable to inadequate FV consumption (with an ideal FV intake estimated at 600 g/d), compared with 1·3% for physical activity, 2·3% for overweight and obesity, 2·8% for high cholesterol and 4·1% for tobacco (17). The authors concluded that promotion of FV intake was a crucial component of any global diet strategy.

Observational studies

FV and CVD risk. A series of meta-analyses conducted in the mid-2000s of observational studies showed an association between increased FV intake and reduced CHD (18,19) and stroke risk (20,21), with some evidence of a dose–response effect. A group from the University of London (18,20) examined the effect of consuming three to five servings or more than five servings/d compared with less than three servings/d on CHD (18) and stroke (20) endpoints. For CHD (18), twelve studies, including thirteen independent cohorts (278 549 individuals; 9143 CHD events; median follow-up 11 years) were included. Compared with those who consumed less than three servings FV/d, the pooled relative risk (RR) of CHD was 0·93 (95% CI 0·86, 1·00; P = 0·06) for those consuming three to five servings/d and 0·83 (0·77, 0·89, P < 0·0001) for those consuming more than five servings/d. For stroke (20), eight studies, including nine independent cohorts (257 551 individuals; 4917 stroke events; median follow-up 13 years) were included. Compared with those who consumed less than three servings FV/d, the pooled RR of stroke was 0·89 (95% CI 0·83, 0·97) for those who consumed three to five servings/d, and 0·74 (0·69, 0·79) for those who consumed more than five servings/d. FV intake was significantly associated with both ischaemic and haemorrhagic stroke (20). Dauchet et al. (19,21) carried out their analyses differently from He et al. (18,20), calculating the RR per portion increase in FV intake. For CHD, nine studies were included (221 080 individuals; 5007 CHD events; range of follow-up 5–19 years). The pooled RR per portion increase in FV was 0·96 (95% CI 0·93, 0·99), P = 0·003, in a random effects model (19). Similarly for stroke, seven studies were included (232 049 individuals; 2955 CHD events). The pooled RR per portion increase in FV was 0·95 (95% CI 0·92, 0·97) (21).

Individual prospective cohort studies published since the meta-analyses (18–21) have tended to confirm the association (22–28), although these studies do vary in terms of the dietary assessment and statistical analysis methodology used. Within these later studies there has also been some inconsistency in terms of whether it is total FV intake that is associated with reduced CHD risk, or fruit or vegetables alone (22–24) or specific classes of FV (26). It is also unclear whether the association is equally strong in both genders (22), or is stronger in a particular subset of the population studied, for example, smokers (23).
The largest single study to examine FV intake and CVD risk was published in 2011 by European Prospective Investigation into Cancer and Nutrition (EPIC)-Heart study investigators. A total of 313,074 men and women without previous history of myocardial infarction or stroke from eight European countries were followed for an average of 8-4 years. There were 1636 IHD events during the follow-up period. Participants consuming at least eight portions of FV/d had a 22% lower risk of fatal IHD than those consuming less than three portions/d (RR = 0.78, 95% CI 0.56, 0.95). The authors calibrated the FV intake estimates to account for the different dietary assessment techniques used in each centre, and, after this adjustment, also found that there is a one portion increment in FV was associated with a 4% lower risk of fatal IHD (95% CI 0·92, 1·00; P for trend = 0·033). Such an observation is in agreement with Dauchet’s previous meta-analysis, which demonstrated a similar estimate of difference in risk per portion increase in daily FV intake. The EPIC study found significant heterogeneity in the association of combined FV intake with risk of IHD death by gender (P = 0·007), with the RR reduction per one portion FV increase being 15% for women (RR = 0·85, 95% CI 0·77, 0·94), but this was only 2% for men and was not statistically significant (RR 0·98, 95% CI 0·94, 1·02). Excluding participants who died within the first 2 years of follow up from IHD did not alter the association observed.

**FV and CVD risk – quantity, variety, colour and degree of processing.** Most individual observational studies and meta-analyses to date have focused on the quantity of FV consumed. However, dietary guidelines also emphasise consuming a variety of FV, although relatively little is known about whether variety is more closely associated with CVD risk than quantity. A number of studies have examined the association between FV variety and CVD risk, and these have been discussed more fully elsewhere, but as yet, the studies are limited in number and do not allow firm conclusions.

Similarly, instead of examining total FV intake, more recent studies have attempted to classify FV, either by colour, or by whether FV was consumed in the raw or processed state. Again studies to date are limited in number, but suggest that there is some evidence of a differential association of FV with CVD risk, both by method of classification of FV (colour; degree of processing), and depending on CVD sub-type, with results differing for CHD and stroke endpoints.

In conclusion, meta-analyses of observational studies conducted in the mid-2000s suggest an association between increased FV intake and reduced risk of both CHD and stroke, and this association has largely been confirmed by more recent cohort studies. There is some heterogeneity within study results, for example by gender or smoking status, and there is also heterogeneity between results of difference studies, which will be at least partly due to differences in study design, endpoints chosen or dietary assessment methods. For example, the association between vegetable intake and CHD was stronger in studies using mortality as an endpoint rather than incidence. Finally, the effect of the specific classes of FV, fruit or vegetables alone, the effect of quantity v. variety of FV consumed and the degree of processing on demonstrated associations remains uncertain. Some of these uncertainties could be answered in future pooling projects.

**FV and diabetes.** A first meta-analysis of the association between FV intake and risk of type 2 diabetes was carried out by Carter et al. Six studies were included, with 223,512 individuals and 9581 cases of diabetes were reported over a median follow-up of 13-4 years. No significant associations where found between fruit only (hazard ratio (HR) = 0·93, 95% CI 0·83, 1·01), vegetables only (HR = 0·91, 95% CI 0·76, 1·09), or FV combined (HR = 1·00, 95% CI 0·92, 1·09) and incidence of diabetes, although an association between increased leafy green vegetable intake and reduced risk of diabetes was reported (HR = 0·86, 95% CI 0·77, 0·97; P = 0·01).

Cooper et al. have since published a similar meta-analysis to Carter et al. but included their own data from a large case–cohort study, the EPIC-InterAct study. In their meta-analysis, the authors found similar associations in relation to green leafy vegetables (RR = 0·84, 95% CI 0·74, 0·94) and also observed a weak association between total FV intake and diabetes risk when comparing the lowest and highest quartiles of FV intake (RR = 0·93, 95% CI 0·87, 1·00). Furthermore, the EPIC-InterAct data suggested an inverse association between root vegetables and diabetes risk (HR = 0·87, 95% CI 0·77, 0·99); however, this was not evident in two other studies that examined this vegetable sub-group.

Therefore, the results of both meta-analyses suggest that an increased consumption of green leafy vegetables may reduce the incidence of diabetes, with no association or weak associations demonstrated for total FV intake. The proposed link between green leafy vegetables and diabetes risk is based on a limited number of studies at present, with other classes of FV, such as root vegetables, also potentially playing a role.

**Observational v. intervention studies.** Studies examining FV and CVD risk have mostly been observational, thus only allowing associations, rather than cause and effect, to be tested. Lifestyle behaviours tend to cluster, meaning that a higher intake of FV is also associated with a better overall diet, increased levels of physical activity, not smoking and being of a higher socioeconomic status. Statistical analysis can attempt to control for other lifestyle behaviours, yet it is likely that this is not always completely successful, and therefore that residual confounding will account for at least part of the demonstrated associations in prospective cohort studies.

Therefore to firmly demonstrate an effect of increased FV intake on CVD risk requires the addition of intervention studies to the evidence base. Dietary intervention studies are time- and resource-heavy, particularly when clinical endpoints are required.

**Intervention studies with clinical endpoints.** A limited number of FV intervention studies with clinical endpoints exist, and in these an increase in FV...
intake has been combined with another dietary or lifestyle change (48–53). For example, the Women’s Health Initiative randomised controlled dietary modification trial tested the effect of a low-fat dietary pattern, rich in FV and high in wholegrains, on the risk of CVD in nearly 50,000 postmenopausal women (53). After 6 years, there was no effect of the intervention diet on major CVD events: CHD (HR 0.97, 95% CI 0.90, 1.06), stroke (HR 1.02, 95% CI 0.90, 1.15) or CVD (HR 0.98, 95% CI 0.92, 1.05). When women with CVD at baseline were excluded, the HR for CHD was reduced but remained non-significant (HR 0.94, 95% CI 0.86, 1.02). Similarly, when post hoc analyses examined those who had most closely adhered to the diet, those who had achieved ≥6.5 servings/d had an 11% reduction in risk of CHD compared with the control group (HR 0.89, 95% CI 0.74, 1.06; P = 0.11), but this was NS (53). In the whole population, at 1 and 6 years, respectively, the intake of FV was only 1.2 and 1.1 servings/d higher in the intervention group than in the control group, so it is possible that such an increase was not large enough to produce an effect on the endpoints.

In the Diet and Reinforcement Trial II, an intervention to increase consumption of FV, fibre and orange juice had no effect on cardiac death in patients with angina pectoris (48). However, as with the Women’s Health Initiative trial, intervention participants achieved only a small increase in FV intake compared with control participants (about 20 g extra, therefore less than half a portion), and this may well have explained the lack of effect on the primary endpoint.

In contrast, the PREDIMED study and the Lyon Diet Heart Study have demonstrated significant benefits of the Mediterranean Diet on primary and secondary prevention of CVD, respectively (50,54). The Mediterranean Diet is an FV-rich diet, but also focuses on altering fat type, with the inclusion of olive oil, fish and nuts. In particular, in a sub-analysis of the PREDIMED study at 3 months, significant dietary changes were only seen in olive oil, nuts and red meat within the intervention groups and, therefore, any clinical benefit cannot be directly attributed to a change in FV intake (55).

**Intervention studies with intermediate endpoints**

A somewhat larger number of intervention studies with intermediate endpoints, such as cardiovascular risk markers, have also been conducted.

**FV and blood pressure.** A number of intervention studies have demonstrated an effect of increased FV intake on blood pressure (BP), although the study designs, participant characteristics (in terms of degree of hypertension at baseline) and methods used to achieve an increase in FV intake have been quite different. The ‘fruit and vegetables’ arm of the Dietary Approaches to Stop Hypertension study demonstrated an effect of increased FV intake on BP over 8 weeks, with systolic BP and diastolic BP decreasing by ≥8 mm Hg and ≥1 mm Hg, respectively (56) compared with the control diet which was consistent with a typical American diet. Participants with hypertension at baseline had greater reductions in BP than those without hypertension. All food to be consumed was provided, and participants consumed one meal every weekday under supervision. Those in the FV arm consumed 5-2 servings of FV/d compared with 1-6 servings/d in the control arm.

A similar BP lowering effect was demonstrated by John et al. (57), in a study of brief negotiation to increase FV to at least five portions/d within the primary care setting. At 6 months, systolic BP fell more in intervention group than in controls (adjusted difference 4.0 mm Hg; 95% CI 2.0-6.0; P < 0.0001), as did diastolic BP (adjusted difference 1.5 mm Hg; 95% CI 0.2-2.7; P = 0.02). At this timepoint, there was a difference in self-reported intake of FV of 1.4 portions/d between intervention and control groups, and this was confirmed by changes in blood biomarkers of FV intake.

Three further studies have shown no effect of increasing FV on BP (58–60). The first was a study of increased FV intake on vascular function in people with hypertension (58). The study was not powered to detect changes in BP but results indicated a trend towards a reduction in systolic BP. In the second study, Berry et al. (59) showed no effect of increased potassium-rich FV over 6 weeks on BP in free-living participants with early stages of hypertension (diastolic BP > 80 and < 100 mm Hg), whilst Broekmans et al. (60) showed no effect of a high FV diet on BP in healthy volunteers in a well-controlled study where all food was provided. Therefore, some debate exists regarding these heterogeneous studies and the true effect of increased FV intake on BP in the long-term and in different population groups.

**FV and lipids.** Evidence for the effects of increased FV intake on hypercholesterolaemia is limited to date, with many studies either not being specifically designed to test the effects on hypercholesterolaemia, or where increased FV was combined with some other dietary intervention, such as reduced fat intake (61). The 6-month primary care-based study discussed earlier, which demonstrated a positive effect of increased FV intake on BP, showed no effect on total cholesterol (57). Similarly there was no effect of increased FV (eight servings/d) over 8 weeks on lipids (total cholesterol, TAG, HDL cholesterol) in ninety volunteers with no history of chronic disease and normal lipid levels (62), or over 4 weeks in a further study of healthy volunteers (60). Therefore, further appropriately designed studies are required to confirm or refute the few studies that have been performed, perhaps particularly focusing on a sub-population with initially raised cholesterol concentrations.

**FV and vascular function.** A beneficial dose–response effect of increased FV consumption on microvascular function (forearm blood flow) has recently been demonstrated in an 8-week study of hypertensive patients. Participants were randomised to one, three or six portions of FV/d and had weekly delivery of FV plus contact with the study team to encourage compliance (58). Further studies of vascular function have either shown no effect of increased potassium-rich FV over 6 weeks on carotid femoral pulse wave velocity, pulse wave analysis or flow mediated dilation in free-living participants with early stages of hypertension (diastolic BP > 80 and < 100 mm Hg) (58), or have shown a trend towards an effect of FV puree-based drinks (200 ml/d for 6 weeks) on endothelium dependent vasodilation using laser Doppler imaging with ionicophoresis in
FV intake and risk of CVD

Fruit and vegetables and CVD: challenges and future directions

As FV are a complex food group, judging the biological plausibility of the association demonstrated in observational studies is challenging, as is defining the protective mechanism. Increasing FV intake will also displace other foods richer in fat or energy rather than supplemented to usual diet. Therefore, it remains possible that combining increased FV intake with other dietary recommendations may promote satiety and weight loss, and suggestions for improvements to strengthen future studies have been put forward.

Much attention has been paid to specific bioactive compounds found in FV, such as vitamin C, carotenoids, and polyphenols, yet these foods are also rich in fibre and nitrate and, therefore, a diet rich in FV will be rich in a complex mixture of micronutrients, phytochemicals and fibre, with the exact combination dependent on the range of FV consumed. Many components of FV have potential health benefits and while this is scientifically interesting, and ultimately may be important both clinically and to public health, evidence is, as yet, too limited to merit a change public health guidelines to focus on a particular class of FV. Caution must be taken in extrapolating the potential health benefits of one class of compounds found in FV without detailed scientific investigation, including randomised controlled trials with clinical endpoints. For example, despite detailed biological evidence for a role for both folate and the antioxidant vitamins in chronic disease prevention and observational epidemiological data also supporting a role, meta-analyses of trials with folate, vitamin C and carotenoids failed to demonstrate a role in either CVD prevention or mortality. Although there are possible design issues with these trials, including dose, duration, vitamin combination or formulation, and participant characteristics, such outcomes indicate that careful consideration of the design of future trials of compounds found in FV thought to protect against CVD is vital.

The lack of FV intervention studies with clinical endpoints has already been highlighted, as has the relative lack of intervention studies with intermediate endpoints, and their heterogeneity in design and in populations studied. In addition, very few intervention studies have examined dose response within their design, and it will be important to address this in on-going and future studies to provide clarification regarding the optimum protective level of intake, and therefore be as directly relevant to dietary recommendations and policy as possible. It has recently been shown that there may be genetic variation in the metabolic response to intake of compounds found in FV such as vitamin C and carotenoids, and future studies are also required to determine if the association between FV intake and CVD risk varies by genetic background.

The debate over the effect of FV on CVD risk is exemplified by a number of recent reviews which have disagreed over the strength of evidence currently available. In a systematic review of evidence supporting a causal link between dietary factors and CHD, Bradford Hill guidelines were used to derive a causation score for each dietary exposure from cohort studies and then examined for consistency with the findings of randomised interventions. The evidence for FV was ranked as strong for vegetables and moderate for fruit. In a report which examined other comprehensive reviews that had been performed, largely for policy-making, a consideration of randomised controlled trials of FV-rich diets with physiological endpoints (which included a range of other dietary changes) and the evidence from prospective cohort studies led to the conclusion that there was strong concordant evidence that FV consumption lowers CVD risk. Similarly a recent, comprehensive critical review of the role of FV in the prevention of chronic disease, judged the evidence for hypertension, CHD and stroke as convincing, the evidence for body weight gain was judged to be possible and concluded that it is probable, apart from the indirect effect of increased FV on diabetes risk via prevention of overweight, that there is no influence of increased FV consumption on type 2 diabetes. In contrast to these reviews, which have rated the current evidence as moderate–strong, a 2009 review considered the evidence to be scarce. The reason for this somewhat contrasting conclusion...
appears to be in the weighting given to the observational prospective cohort studies so far conducted, the likely residual confounding that will remain as a result of FV intake being associated with other social, cultural and lifestyle characteristics, and the inability to derive causality from such studies\(^{(6)}\).

### Conclusion

The majority of UK population still do not meet current target of consuming five portions of FV per day. While observational epidemiological evidence for the association between increased FV intake and reduced risk of CHD and stroke is relatively strong and consistent, the evidence is currently weaker for diabetes endpoints. Currently, there are no intervention studies of FV alone with clinical endpoints; other studies have included an increase in FV alongside alterations in fat or fibre intake, or to follow a Mediterranean diet, and therefore conclusions regarding the effects of increasing FV alone are not possible. The evidence base from randomised controlled trials of increasing FV intake with intermediate risk markers is developing, particularly for an effect on BP and microvascular function, but further studies are required. However, based on the current evidence for prevention of CVD and other chronic diseases, a FV-rich diet should be consumed and national dietary and CVD-specific guidelines should continue to promote increased consumption of a variety of FV.

### Acknowledgements

None.

### Financial Support

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

### Conflicts of Interest

The authors declare no conflicts of interest.

### Authorship

J. V. W. drafted the manuscript and produced the final version after critical review by I. S. Y and M. C. M.

### References


