

1.1.1 *Fruit and vegetables*

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1.1.1.1 Introduction

This paper is a summary of the published evidence on the relationship between fruit and vegetables and cardiovascular disease since 2002.

1.1.1.2 Methods

1.1.1.2.1 Literature Search

A search was conducted to identify systematic reviews and meta-analyses published on the relationship between fruit and vegetables and cardiovascular disease (CVD) since 2002. We searched Medline, Embase and Cochrane electronic databases for papers published from 2001 to the present (December 2009).

Both free text and MeSH terms were used with limits set as; humans, 2001 and being published in the English language. MeSH terms used were cardiovascular disease AND (fruit OR vegetables). A free text search was performed using “fruit* OR vegetable* OR legume* AND (cardiovascular disease* OR stroke OR CVA OR heart disease OR coronary disease OR peripheral vascular disease OR coronary artery disease OR myocardial infarction OR MI OR heart attack)”. They were then refined by either selecting only meta-analysis or by adding “systematic review” into the search criteria.

An additional search of literature reviews on “Mediterranean diets” was conducted for completeness. This was carried out in a similar way to the original search using the same search terms for CVD endpoints as before. Papers would be included if the study focus was on fruit and vegetable intake and a CVD outcome.

To ensure that no important recent papers were missed, a final search was included to look specifically for interventions impacting on CVD outcomes. The same search terms were used as in the original search except “meta-analysis” OR “systematic review” was replaced with “intervention” OR “trial”. Limits were set as humans, English, publication date from 2002/01/01 to 2010/02/15 with the search field set as Title/Abstract. This search produced 69 papers. None of the studies found looked at CVD (heart disease or stroke) as an endpoint. They all looked only at intermediate risk factors for cardiovascular disease e.g. BP, obesity or specific plasma serum levels.

1.1.1.2.2 Inclusion criteria

Papers were included if they were reviews of either fruit and/or vegetable consumption and had an aspect of CVD as an endpoint. Studies of the Mediterranean diet were only considered if the focus was on fruit and vegetable intake and the analysis permitted the impact of fruit and vegetable intake on cardiovascular disease to be examined

separately taking into account the obvious confounding factors of other dietary influences.

Fruit and vegetables had to be eaten as part of the diet, in vitro studies were not included. We excluded those papers that looked only at dietary supplements or selected plant components, e.g. Vitamin C supplements or garlic supplements. Papers also had to include some measure of cardiovascular disease as an end point, or an intermediate outcome which is a well recognised as a risk factor for CVD, such as blood pressure or serum cholesterol.

The search strategy in Medline, Embase and Cochrane identified 26 potentially relevant unduplicated studies, of which only seven met the inclusion criteria.

1.1.1.2.3 Definition of fruit and vegetables used in this review

As mentioned in the inclusion criteria we used a broad definition of fruit and vegetables in our search terms. MeSH terms were used in our original search as well as free text. We did not include meta-analysis on specific fruits or vegetables (e.g. garlic alone) or studies that looked at supplements based on fruit or vegetable components (e.g. vitamin C).

The seven papers that have been included in this paper used similarly broad definitions of fruit and vegetables. Table 1 illustrates the definitions used by the authors for the different systematic reviews, if this was stated.

A number of the papers included in this study have used cohorts that incorporated potatoes in their definition of vegetables. Although potatoes are not included in the UK's '5-a-day' campaign¹ we did not exclude these papers. This is because without them there would not be enough evidence to draw on. Also, if potatoes have been included in the studies then it is likely that the effect of fruit and vegetables on CVD will be underestimated, not overestimated.

Table 1 Definitions of fruit and vegetables used in the papers

Dauchet et al	He et al	Mente et al	Huxley et al	Pereira et al	Dauchet et al	He et al
Fruit and vegetable consumption and risk of coronary heart disease: a meta-analysis of cohort studies ²	Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies ³	A Systematic Review of the Evidence Supporting a Causal Link Between Dietary Factors and Coronary Heart Disease ⁴	The relation between dietary flavonol intake and coronary heart disease mortality: a meta-analysis of prospective cohort studies ⁵	Dietary fibre and risk of coronary heart disease: a pooled analysis of cohort studies ⁶	Fruit and vegetable consumption and risk of stroke: a meta-analysis of cohort studies ⁷	Fruit and vegetable consumption and stroke: meta-analysis of cohort studies ⁸
'...included in the analysis only...'vegetables,' 'all vegetables,' 'vegetables rich in carotenoids,' 'fruit,' or 'all fruit.' Individual fruit or vegetables...were excluded... fruit	No specific definition stated. Literature search used MeSH and text words for fruits and vegetables. Authors excluded	No mention of definitions used for fruit and vegetables.	Looked at flavonol intake (search terms included 'flavonols' and 'flavonoids'). Mentions the main source of flavonol intake for each of the studies; tea	Looked at the fibre content of the fruit and vegetables. Mentions that potatoes were included in the vegetable group for two of the cohorts.	'...the exposure variable was always fruits and vegetables, the definition of this variable could vary between studies. For	No specific definition stated (only mentions 'fruit' and 'vegetable'). Authors excluded studies that only looked at 'surrogate

juices were included with fruit in some studies and potatoes with vegetables in others'	studies that only looked at 'surrogate nutrients of fruits or vegetables'.	(+/- milk), onions, apples, broccoli, vegetables	instance, fruit juices were included with fruit in some studies and potatoes with vegetables in others'.	nutrients of fruits or vegetables'.
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1.1.1.3 Results

There were seven reviews relevant to this paper. Five were about fruit and vegetable intake, one focused on dietary fibre and one looked at dietary flavonol intake. All the reviews included both men and women, although not all were analysed or presented in subgroup analyses. All the papers used a mixture of single and mixed sex cohorts so the overall results are felt to reflect both male and females. The reviews included a combination of studies from Europe and USA, with one cohort from Japan, although the majority of reviews were more heavily weighted by USA cohorts.

Six out of the seven papers state in the title that they are an analysis of cohort studies. The only paper that looked at both cohort studies and intervention studies was by Mente and colleagues.⁴ However, this paper did not actually include any evidence from RCTs in the section on fruit and vegetables and used cohort data only like the other six papers. Of interest this paper looked at many different dietary components including the 'Mediterranean diet'. This was one of the few dietary factors that had findings that were also supported by RCT evidence.

Of the reviews that met the inclusion criteria, the majority studied coronary heart disease (CHD) as the cardiovascular outcome. However there were two reviews that focused on stroke as an outcome. There were insufficient published studies to look at the effects of fruit and vegetables on any other disease end points.

The key parts of the papers looking at coronary heart disease as the outcome are summarised in Table 2. Those that used stroke as the endpoint are presented in Table 3.

Table 2 Summary of papers included in this review with CHD as outcome of interest

Name and year of study	Author	Type of study and inclusion criteria	Data Sets used	Key Results
Fruit and vegetable consumption and risk of coronary heart disease: a meta-analysis of cohort studies 2006 ²	Dauchet, L. Amouyel, P. Herberg, S. Dallongeville, J.	Meta-analysis of published prospective cohort studies. Studies were included if they reported RR and 95% CI for CHD or mortality and if they presented a quantitative assessment of fruit and vegetable intake. Studies had to look at fruit and vegetable intake <i>per se</i> and not just the nutrient content.	Nine cohorts- 91,279 men, 129,701 women and 5007 CHD events. Seven cohorts from USA, two from Finland. Range of follow up was 5–19 years. Subjects ranged in age from 25–84.	CHD risk decreased by 4% [RR (95%CI): 0.96 (0.93-0.99), P 0.0027] for each additional portion per day of fruit and vegetables intake and by 7% [0.93 (0.89 – 0.96), p< 0.0001] for fruit intake. The association between vegetable intake and CHD risk was heterogeneous.
Increased consumption of fruit and vegetables is related to a reduced risk of coronary heart disease: meta-analysis of cohort studies 2007 ³	He, F. J. Nowson, C. A. Lucas, M. MacGregor, G. A.	Meta-analysis of published prospective cohort studies. Studies were included if they reported RR and 95%CI of CHD with respect to frequency of fruit and vegetable intake.	Twelve studies of 13 cohorts. 278,459 individuals with 9,143 CHD events. Nine cohorts from USA and four from Europe. Range of follow-up was 5-26 years. Subject age ranged 25-84.	Compared with individuals who had <3 servings/day of fruit and vegetables, the pooled RR of CHD was 0.93 (95% CI: 0.86-1.00, P=0.06) for those with 3-5 servings/day and 0.83 (0.77-0.89, P<0.0001) for those with 5+ servings/day.
A Systematic Review of the Evidence Supporting a Causal Link Between Dietary Factors and Coronary Heart Disease 2009 ⁴	Mente, A. de Koning, L. Shannon, H. S. Anand, S. S.	Systematic review. Search of MEDLINE for prospective cohort studies or RCTs investigating dietary exposures in relation to CHD. The Bradford Hill guidelines were used to evaluate systematically whether a causal link between the exposure of interest and CHD exists.	Vegetables – 220,564 subjects, nine cohorts. Men, women, Europe, USA, primary prevention. Fruits – 222,706 subjects, 10 cohorts. Men, women, Europe, USA, primary prevention. Fruit and vegetables – 199,514 subjects, seven cohorts. Men, women, Europe, USA, primary prevention	Vegetables – 0.77 RR (0.68-0.87) 95%CI 4/4 Bradford criteria met. Fruits – 0.81 RR (0.68-0.94) 95%CI 3/4 Bradford criteria met. Fruit and vegetables – 0.79 RR (0.72-0.87) 95%CI 3/4 Bradford criteria met.
The relation between dietary flavonol intake and coronary heart disease mortality: a meta-analysis of prospective cohort studies 2003. ⁵	Huxley, R. R. Neil, H. A.	Meta-analysis of prospective cohort studies published before September 2001. Studies were included if they reported data on flavonol intake and CHD mortality.	Seven prospective cohorts of men and women were identified, approximately 105,000 people with a total of 2087 fatal CHD events. Five European and two USA cohorts. Follow up 6-25 years. Age range 30-84.	Comparison of individuals in the top third with those in the bottom third of dietary flavonol intake yielded a combined risk ratio of 0.80 (95% CI 0.69-0.93) after adjustment for known CHD risk factors and other dietary components
Dietary fiber and risk of coronary heart disease: a pooled analysis of cohort studies 2004 ⁶	Pereira, M. A. O'Reilly, E. Augustsson, K. Fraser, G. E. Goldbourt, U. Heitmann, B. L. Et al	Pooled analysis of published prospective cohort studies. Studies had to have at least 150 incident coronary cases, include assessment of usual dietary intake, and used a validation study of the diet assessment method or a closely related tool.	Eleven cohorts totalling 336,244 individuals and 5249 CHD events. Men and women included. Cohorts from USA and Europe. Follow up range 6–10 years. Age range 35-99.	RR of CHD was 0.84 (95%CI: 0.70-0.99, p=0.04) for fruit fibre. RR was 0.9 (95%CI: 0.77–1.07, p=0.23) for cereal fibre. RR for vegetable fibre was 1.00 (95%CI: 0.88–1.13, p=0.97). A regression model suggested that the effects of fruit and cereal fibre were independent of one another.

Table 3 Summary of papers included in this review with stroke as outcome of interest

Name and year of study	Author	Type of study and inclusion criteria	Data Sets used	Key Results
Fruit and vegetable consumption and risk of stroke: a meta-analysis of cohort studies ⁷ 2005	Dauchet, L. Amouyel, P. Dallongeville, J.	Meta-analysis of published prospective studies. Studies were selected if they had RR and 95% CI for any type of stroke and used a validated questionnaire for food intake assessment.	Seven studies were eligible for the meta-analysis, including 90,513 men, 141,536 women, and 2,955 stroke events. Five cohorts from USA, one from Europe and one from Japan. Follow up ranged from 3-20 years. Age range was 25-103.	The risk of stroke was decreased by 11% (RR 95% CI: 0.89 [0.85 to 0.93]) for each additional portion per day of fruit, by 5% (RR: 0.95 [0.92 to 0.97]) for fruit and vegetables, and by 3% (RR: 0.97 [0.92 to 1.02]; NS) for vegetables
Fruit and vegetable consumption and stroke: meta-analysis of cohort studies ⁸ 2006	He, F. J. Nowson, C. A. MacGregor, G. A.	Meta-analysis of published prospective cohort studies. Studies were included if they reported RR or hazard ratios and 95% CI and gave details on the frequency of fruit and vegetable consumption	Eight studies consisting of nine cohorts – 257551 individuals and 4917 stroke events. Five USA cohorts, three from Europe and one from Japan. Men and women included. Follow up 3-20 years. Age range 25-103.	RR of stroke was 0.89 (0.69-0.79) for those with between three and five servings a day compared with individuals who had less than three servings a day. RR was 0.74 (0.69-0.79) for those with more than five servings day.

1.1.1.4 Fruit and Vegetables and CHD

To start off with we shall look at the results published about the combined effects of fruit and vegetable consumption. Dauchet and colleagues published a meta-analysis of nine cohorts looking at the risk of coronary heart disease and its relationship to fruit and vegetable intake.² The paper extracted relative risk data from each paper for each additional portion of fruit and vegetables eaten per day and the effect of CHD. The risk of CHD decreased by 4% [RR=0.96 95%CI (0.93-0.99), p=0.0027] for each additional portion of fruit and vegetables eaten per day. The paper showed a linear trend suggesting the risk reduction improved with higher fruit and vegetable consumption. There was no evidence of heterogeneity between studies.

He and colleagues also published a meta-analysis looking at fruit and vegetable consumption and the effect on CHD.⁸ This paper looked at data from eight studies, split into nine cohorts. The paper presented the results by dividing daily intake into three categories; less than three portions of fruit and vegetables per day, three to five portions per day and more than five portions per day. The relative risk was then worked out in comparison to the risk of the group who ate less than three portions per day (i.e. RR in that category = 1). Higher fruit and vegetable intake resulted in a reduced risk in CHD. Those individuals in the three to five portions a day category had a risk reduction of 7% [RR=0.93 95% CI (0.86-1.00), P=0.06] and those who ate more than five portions per day reduced their risk by 17% [RR=0.83 95%CI (0.77-0.89), P<0.0001]. This paper again illustrated that fruit and vegetable consumption is not only protective against CHD, but the more fruit and vegetables eaten, the greater the protection afforded.

The paper by Mente and colleagues⁴ had a different premise, in so much as they wished to find a causal link between dietary factors and CHD. It looked at different dietary exposures and their influence on coronary heart disease. This paper used both prospective cohort studies and randomised controlled trials. Odds ratios or relative

risks were calculated from the cohort studies by comparing the highest intake quantile with the lowest intake quantile (usually quartiles or quintiles). Each exposure was then analysed using the Bradford Hill criteria⁹ to find if a causal link existed. This paper showed that fruit and vegetable intake resulted in a 21% reduction in the risk of coronary heart disease [RR=0.79 95%CI (0.72-0.87)]. Data from seven cohorts was used to calculate this figure. However, as the paper did not specify the exact type of dietary exposure, so the amount of fruit and vegetables consumed to produce this risk reduction is not clear. Fruit and vegetable intake was found to have moderate evidence to support the causal link with coronary heart disease according to their modified Bradford Hill criteria.

The evidence suggests that eating more portions of fruit and vegetables will significantly reduce the risk of CHD. The more consumed the greater the risk reduction.

1.1.1.5 Fruit and CHD

Four of the included studies had data on fruit alone and its influence on CHD. Increased fruit intake was shown to protect against coronary heart disease with Dauchet and colleagues² quoting a risk reduction of 7% [RR=0.93 95%CI(0.89-0.96), p<0.0001] for each additional portion of fruit eaten per day. Pereira and colleagues⁶ carried out a pooled analysis of 10 prospective cohort studies. The paper analysed the links between dietary fibre and CHD, producing data on cereal fibre, fruit fibre and vegetable fibre. The paper attributed a 16% reduction in the risk of CHD [RR=0.84 95%CI (0.70-0.99), p=0.04] to fruit fibre. Further analysis of the data showed that the beneficial effect of fruit fibre was independent to that of cereal fibre. The Mente paper⁴ showed a risk reduction of 19% [RR=0.81 95%CI(0.68-0.94)]. As mentioned previously with this paper, there was no information in the amount of fruit consumed that related to this benefit. There was moderate evidence that this was a causal link, with three out of the four modified Bradford Hill criteria being met. The meta-analysis carried out by He and colleagues³ showed that by eating three to five portions of fruit per day one could reduce the risk of CHD by 11% [RR=0.89 95%CI(0.82-0.98) and by eating more than five portions this reduction in risk grew to 28% [RR=0.72 95%CI(0.66-0.79)] compared to those individuals who ate less than three portions of fruit per day. This was a greater reduction in risk than the data for combined fruit and vegetable consumption.

The evidence suggests that eating more portions of fruit will significantly reduce the risk of CHD. Eating five portions per day has a greater effect than eating three portions.

1.1.1.6 Vegetables and CHD

Mente and colleagues⁴ found that vegetable intake decreased the risk of CHD by 23% [RR=0.77 95%CI (0.68-0.87)]. This was one of the few dietary influences that scored four out of four in the modified Bradford Hill criteria, corresponding to strong evidence of a causal link between vegetable consumption and CHD. The Pereira paper⁶ found that vegetable fibre had no influence of CHD outcomes [RR=1.00 95%CI (0.88-1.13), p=0.97]. However the Dauchet paper,² which looked at the vegetable

consumption as a whole entity, found that eating an additional portion of vegetables reduced the risk of CHD by 11% [RR=0.89 95%CI (0.83-0.95), p=0.0023]. He and colleagues³ also found a benefit to vegetable consumption and reduction in CHD, although this was less profound compared to the effects of fruit consumption. Individuals who ate three to five portions per day had a 7% reduction in risk [RR=0.93 95%CI (0.82-1.06)]. Those who ate greater than five portions per day extended this reduction in risk to 19% [RR=0.81 (95%CI (0.72-0.90))].

The evidence suggests that eating more portions of vegetables will reduce the risk of CHD. The evidence does not suggest that it is the fibre content that results in the benefit. There is strong evidence of a causal link between vegetable consumption and CHD.

1.1.1.7 Fruit and Vegetables and stroke

Dauchet and colleagues also published a study looking at the relationship between fruit and vegetables intake and stroke.⁷ This was a meta-analysis of seven cohorts from the USA, Europe and Japan. The risk of stroke was shown to decrease by 5% [RR=0.95 95%CI (0.92 to 0.97)] for each additional portion of fruit and vegetables eaten. This paper also showed a linear trend suggesting the risk reduction with regards to stroke improved with higher fruit and vegetable consumption, as it also did for CHD.

He and colleagues also published a study looking at the relationship between fruit and vegetables and stroke.⁸ This was a meta-analysis of eight studies consisting of nine cohorts. Again it included data from the USA, Europe and Japan. The paper showed the risk of stroke reduced by 11% [RR=0.89 95%CI (0.83-0.97)] for those who ate between three and five portions of fruit and vegetables per day, compared to those who ate less than three portions of fruit and vegetables per day. Those who ate more than five portions per day had a 26% reduction in stroke [RR= 0.74 95%CI (0.69- 0.79)].

The evidence suggests that eating more portions of fruit and vegetables per day significantly reduces the risk of stroke. The more consumed, the greater the risk reduction.

1.1.1.8 Fruit and stroke

Both the Dauchet and He papers analysed the data in separate groups for fruit and vegetable intake. In the paper by Dauchet and colleagues increased fruit intake was shown to decrease the risk of stroke by 11% [RR=0.89 95%CI (0.85-0.93)] for each additional portion eaten per day.⁷ In the study by He and colleagues⁸ those who ate three to five portions of fruit per day reduced their risk of stroke by 10% [RR=0.90 95%CI(0.83-0.98)] compared to those who only ate three portions or less of fruit per day. Those who ate more than five portions per day reduced their risk by 13% [RR=0.87 95%CI (0.80-0.95)]. So both these studies illustrated a beneficial effect of fruit intake on the risk of stroke, which was greater the more fruit that was consumed.

The evidence suggests that eating more portions of fruit per day significantly reduces the risk of stroke. Eating three portions per day results in a benefit, but eating more than five portions per day increases this benefit further.

1.1.1.9 Vegetables and stroke

Vegetable intake also seems to influence the incidence of stroke. Dauchet and colleagues⁷ found a 3% reduction in the risk of stroke [RR=0.97 95%CI (0.92-1.02)] with each additional portion of vegetables eaten per day. Although the 95% confidence interval suggests that this may not be statistically significant. The He paper⁸ showed a reduction in stroke risk of 8% [RR=0.92 95%CI(0.87-0.97)] for those who ate three to five portions of vegetables per day, and a reduction of 16% [RR=0.84 95%CI(0.76-0.92)] for those who ate more than five portions per day. These risks are in comparison to individuals who ate less than three portions per day.

The evidence suggests that eating more portions of vegetables per day reduces the risk of stroke. Eating three portions per day results in a benefit, but eating more than five portions per day increases this benefit further.

1.1.1.10 Dietary components

A further paper has been included in this review; Huxley and colleagues.¹⁰ This paper looked at the relationship between dietary flavonol and coronary heart disease. Flavonol is found in high quantities in tea however it is also found in fruits and vegetables such as onions, apples and broccoli. Those in the top third group of dietary flavonol intake had a 20% reduction in the risk of CHD [RR=0.80 95%CI (0.69-0.93)] compared to those in the bottom third for intake. The main source of flavonoid intake was noted for each group. For many the main source was tea, but there were two studies from Finland where 64% of flavanoid intake came from apples and onions. These two studies produced a greater risk reduction [RR=0.73 95%CI (0.41-1.32) for women and RR=0.67 95%CI (0.44-1.00) for men] than the combined data. However, as these subset groups are much smaller the confidence interval is much wider, making the results less significant.

The evidence suggests that dietary flavonol may result in a reduced risk in CHD. However, these results come from small amounts of data and are not statistically significant.

1.1.1.11 Discussion

There appears to be a growing body of evidence linking diet, specifically fruit and vegetable intake to cardiovascular outcomes. The degree of protection eating fruit and vegetables gives you varies between the studies, as illustrated in Table 4 (CHD as outcome) and Table 5 (stroke as outcome). In these tables we have extrapolated some of the data to try and make comparison between the studies easier, by trying to convert risk reductions into those gained from eating five portions of fruit or vegetables per day.

There does not seem to be a clear picture as to whether fruit or vegetables offer more protection. Of the six studies that analysed the results by fruit and vegetable groups, three studies showed greater protection from vegetables, and three showed greater protection from fruits. In the review only considering fibre, fruit fibre afforded a 16% reduction in CHD risk, compared to no risk reduction from vegetable fibre.⁶ However, studies do seem to agree that the more portions of fruit and vegetables you eat, the greater the risk reduction, i.e. there is no upper limit for fruit and vegetable consumption with regards to benefit on CVD risk.

Table 4 CHD and results split by group; fruit and vegetables, fruit alone and vegetables alone

Study	Fruit and Vegetables	Fruit alone	Vegetables alone
<i>Dauchet et al</i>	RR - 4% reduction for each additional portion (106g) eaten per day. Linear response, so for five portions 20% reduction.	RR - 7% reduction for each additional portion eaten per day. Five portions results in 35% reduction.	RR - 11% reduction for each additional portion eaten per day. Five portions results in 55% reduction.
<i>He et al</i>	RR - 17% reduction for 5+ portions eaten per day.	RR - 28% reduction for 5+ portions eaten per day.	RR - 19% reduction for 5+ portions eaten per day.
<i>Mente et al</i>	RR - 21% reduction comparing highest and lowest eating groups – highest group likely to consume 5+ portions per day.	RR - 19% reduction comparing highest and lowest eating groups – highest group likely to consume 5+ portions per day.	RR - 23% reduction comparing highest and lowest eating groups – highest group likely to consume 5+ portions per day.
Range of results for 5 portions per day	17-21% reduction in CHD risk by eating ~5 portions per day	19-35% reduction in CHD risk by eating ~5 portions per day	11-55% reduction in CHD risk by eating ~5 portions per day

Table 5 Stroke and results split by group; fruit and vegetables, fruit alone and vegetables alone

Study	Fruit and Vegetables	Fruit alone	Vegetables alone
<i>Dauchet et al</i>	RR 5% reduction for each additional portion (106g) eaten per day. Linear response, so for five portions 25% reduction.	RR 11% reduction for each additional portion eaten per day. Five portions results in 55% reduction.	RR 3% reduction for each additional portion eaten per day. Five portions results in 15% reduction.
<i>He et al</i>	RR - 26% reduction for 5+ portions eaten per day.	RR - 13% reduction for 5+ portions eaten per day.	RR - 16% reduction for 5+ portions eaten per day.
Range of results for 5 portions per day	25-26% reduction in stroke risk by eating ~5 portions per day	13-55% reduction in stroke risk by eating ~5 portions per day	15-16% reduction in stroke risk by eating ~5 portions per day

The reviews do not reveal any difference in the relationship of fruit or vegetable intake and different CVD outcomes. Two studies produced results where vegetables offered

more benefit with regards to CHD, and two showed fruit to be the category with a larger risk reduction. Of the two studies that focused on stroke as an endpoint, He and colleagues⁸ showed that vegetables offered more protection, whereas Dauchet and colleagues⁷ produced results showing fruit consumption was more protective. However, all papers agreed that fruit and vegetables, in some combination would reduce the risk of both coronary heart disease and stroke.

Due to the nature of the study designs we are unable to say from these reviews that there is definite causal link between fruit and vegetable intake and cardiovascular risk, there is only evidence of a correlation. However other studies including Mente and colleagues have¹¹ attempted to address this by looking at the Bradford Hill criteria¹² and also by trying to find intervention studies to help show causation. As demonstrated by the additional literature search, there is a lack of published trials looking at dietary interventions (specifically fruit and vegetable intake) and CVD outcomes. Intervention studies would need to be undertaken to show a causal link between dietary factors and CVD. However, despite this lack of trial data the current body of scientific literature provides a strong and consistent evidence base for a relationship between increased intake of fruits and vegetables being protective for CVD.

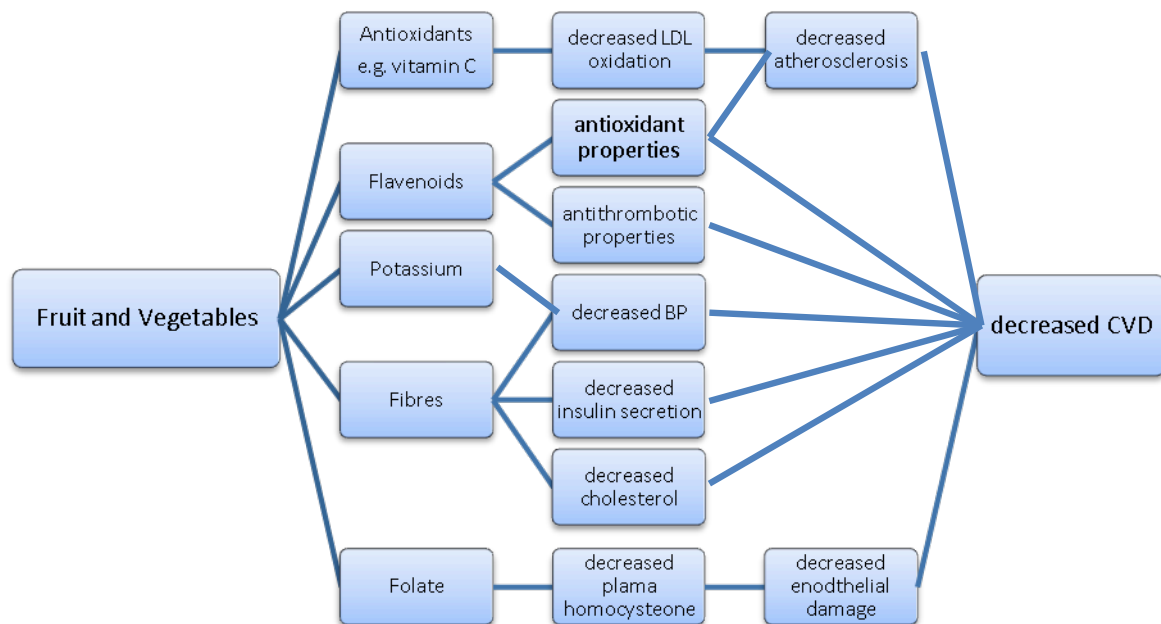
There are various potential mechanisms by which fruit and vegetable intake could influence the risk of cardiovascular disease, and a summary of these is presented in Figure 10. Knekt and colleagues¹³ wrote a paper that looked at antioxidant vitamins and coronary heart disease by carrying out a pooled analysis of nine cohorts. The paper showed that the antioxidant vitamins contained within dietary fruit and vegetables did not appear to offer much protection against the incidence of CHD. Those in the highest quintile of vitamin C intake had a relative risk of 1.23 [95%CI (1.04-1.45), p=0.17] compared to those in the lowest quintile. However supplemental vitamin C did significantly reduce the risk. Those who took >700mg of supplemental vitamin C per day reduced their risk by 25% [RR=0.75 95%CI (0.63-0.93), p<0.001]. Flavonoids, which are found in fruit and vegetables, are known to have antioxidant properties. Huxley and colleagues⁵ showed that eating foods that contained flavonoids, such as apples, onions and tea did translate into a reduction in the risk of mortality from coronary heart disease. However, it is still not clear if it is the flavonoids within these foodstuffs that give the benefit or some other aspect of the foods studied.

Pereira and colleagues⁶ suggest that it is the fibre content of fruit that is the protective factor against CHD, although no such protection was offered from vegetable fibre. It is thought that dietary fibre alters the metabolism of bile acid, which lowers cholesterol.¹⁴ There is also evidence that dietary fibre reduces blood pressure¹⁵ and decreases insulin secretion.¹⁶ It has also been hypothesised that it is the potassium in the fruit and vegetables that afford the risk reduction,¹⁷ although this as a theory was not tested by any of the studies in this review.

As the mechanisms of action regarding fruit and vegetable consumption and their protection against CHD are still not well understood it is difficult to propose what the essential protective ingredients of a diet rich in fruits and vegetables might be.

During the research for this paper there were a number of papers found that focused on the Mediterranean diet and its influence on cardiovascular disease. Mediterranean diets are considered to be those that are based on plant foods, such as fruits, vegetables, cereals, nuts, beans and seeds.¹⁸ As fruit and vegetables take up a high content of the diet we looked at some of the data available. Sofi and colleagues¹⁹ looked at how following a Mediterranean diet influenced the incidence of various diseases. When looking at cardiovascular mortality they found such a diet reduced the risk by 9% [RR=0.91 95%CI (0.87-0.95), p<0.0001]. Panagiotakos and colleagues²⁰ looked at six studies which related to following a Mediterranean diet and its influence on cardiovascular disease. All the studies showed a reduction in risk, and this varied from 8% to 45% depending on the study. Despite the obvious confounding factors of other dietary influences that make up the Mediterranean diet, such as using largely olive oil and only eating small amounts of meat, specifically rarely consuming red meats, it could be hypothesized that part of this protection against cardiovascular disease comes from the high fruit and vegetable intake. However, none of the reviews analysed the impact of high fruit and vegetable intake separately and so it is not possible to comment further on these.

Figure 1 Possible mechanisms of fruit and vegetable consumption and CVD



1.1.1.12 Limitations

With all these studies there will be many confounding factors. There are many influences on dietary habits which makes it difficult to dissect the evidence. It is likely that those who eat more fruit and vegetables live a more ‘healthy lifestyle’ and so do not smoke and also exercise more. Both these factors are known to reduce risk with regards to cardiovascular disease. In this sense there may well have been some overestimation in the effects of fruit and vegetable consumption as a variable. However some of the papers did try and adjust for these potential confounding factors.

The paper by Dauchet and colleagues on coronary heart disease mentioned that there was likely to be an overestimation of the risk reduction due to publication bias. All the papers highlighted the problem of actually getting accurate data on the classification and exact amount of fruit and vegetables eaten, which is a problem inherent in these sorts of studies.

1.1.1.13 Conclusions

Evidence from systematic reviews and meta-analyses since 2002 show that eating more fruit and vegetables will decrease the risk of cardiovascular disease, with particular reference to coronary heart disease and stroke. The benefit of fruit and vegetable consumption has been found to be linear, with no upper limit as yet found. The exact risk reduction varies between papers, and the way it is presented also varies. However there seems to be a 17-21% reduction in the risk of CHD if an individual eats five portions of fruit or vegetables per day. Similarly this quantity of fruit and vegetables is also reflected in a 25-26% reduction in the risk of stroke. When divided into categories of either fruit or vegetables the range becomes much larger, and the data less reliable due to the smaller size of data available for analysis.

At present it is not clear what the underlying mechanisms behind these findings are; whether it is the antioxidant properties, the high potassium content, the fibre contained within the fruits and vegetables, or some other process or factor entirely. Nor is it clear if fruits or vegetables, or specific fruits or vegetables, confer greater benefits. More information needs to be gathered as to the mechanisms of action, and perhaps into individual fruit or vegetable benefits. However, it is not necessary to wait to discover the underlying mechanism, before recommending a diet rich in fruit and vegetables to help reduce the burden of cardiovascular disease.

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