ClinicalEvidence



# Primary prevention of CVD: diet

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## ABSTRACT

INTRODUCTION: Diet is important in the cause of many chronic diseases. Individual change in dietary behaviour has the potential to decrease the burden of chronic disease, particularly cardiovascular disease (CVD). METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical question: What are the effects of dietary advice in generally healthy adults without existing CVD or increased CVD risk factors to improve cardiovascular outcomes (mortality, cardiovascular events, and cardiovascular risk factors)? We searched: Medline, Embase, The Cochrane Library, and other important databases up to March 2014 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA). RESULTS: We found 14 studies that met our inclusion criteria. We performed a GRADE evaluation of the quality of evidence for interventions. CONCLUSIONS: In this systematic review, we present information relating to the effectiveness and safety of the following interventions: advice to increase fibre intake alone, advice to increase fruit and vegetable intake alone, advice to reduce and/or modify fat intake alone, and advice to reduce sodium intake alone.


## QUESTIONS



## INTERVENTIONS



## Key points

- Diet is an important cause of many chronic diseases.

  Individual change in behaviour has the potential to decrease the burden of chronic disease, particularly cardiovascular disease (CVD).
- This review examines evidence solely from RCTs and systematic reviews of RCTs.
- To reduce confounding, this review has examined the effects of separate elements of dietary advice alone in improving cardiovascular outcomes in healthy people without existing CVD or elevated risk factors.

  We have excluded non-clinical outcomes such as behavioural change (e.g., change in the proportion of saturated fats in the diet, or change in the number of servings of vegetables per week).
- Intensive advice to reduce sodium intake alone may reduce blood pressure compared with no advice in healthy people without hypertension.

  Intensive advice seems to reduce sodium intake as measured by sodium excretion.

  However, it is unclear whether advice to reduce sodium intake reduces mortality or cardiovascular events as we found insufficient evidence.

  The intensive advice interventions used in some studies may not be practicable in routine clinical practice.
- We found insufficient evidence from RCTs on the effects of advice to reduce and/or modify fat intake alone on cardiovascular outcomes.
- Some RCTs have found that advice to increase fruit and vegetable intake alone may improve systolic blood pressure at 6 to 12 months compared with no advice; we found insufficient evidence from RCTs on the effects of advice to increase fruit and vegetable intake alone on CVD events or death. However, we also found no harm from advice to increase fruit and vegetables.
- We found insufficient evidence from RCTs on the effects of advice to increase fibre intake alone on risk factors for CVD, CVD events, or death.

- RCTs may only provide limited evidence on longer-term outcomes such as mortality or cardiovascular events due to the restricted numbers included in most trials and the length of follow-up needed to identify any differences between groups.
- Large observational studies may provide important evidence on these longer term outcomes.

**DEFINITION**

Diet is important in the cause of many chronic diseases. Individual change in dietary behaviour has the potential to decrease the burden of chronic disease, particularly cardiovascular disease (CVD). This review focuses on the evidence that specific interventions to modify and improve diet may reduce CVD risk. Clinically overt ischaemic vascular disease includes acute myocardial infarction (MI), angina, stroke, and peripheral vascular disease. Many adults have no symptoms or obvious signs of vascular disease, even though they have atheroma and are at increased risk of ischaemic vascular events because of one or more risk factors. In this review, we have taken primary prevention to apply to people who have not had clinically overt CVD. **Population:** In this review, we have included studies in free living healthy adults (aged 18 years or older) with no evidence of clinically overt CVD, and with less than 10% of the population with existing cardiovascular risk factors (hypertension, dyslipidaemia, or diabetes), but have included studies in people with impaired glucose tolerance. We have included dietary advice given by healthcare professionals such as nurses, doctors, and dietitians, which may have been supplemented by paper-based self-help resources. We have excluded Web-based or electronic advice and public-health measures. Primary prevention of CVD in people with hypertension or dyslipidaemia is covered in separate *Clinical Evidence* reviews, as is secondary prevention of CVD in people with existing CVD (see reviews on Secondary prevention of ischaemic cardiac events and Angina [chronic stable]).

**INCIDENCE/ PREVALENCE**

CVD was responsible for 32% of UK deaths in men, and 21% of UK deaths in women in 2010. Half of these were from coronary heart disease (CHD), and one quarter were from stroke. CVD is also a major cause of death before 75 years of age, causing 28% of early deaths in men and 19% of deaths before 75 years of age in women. CHD deaths rose dramatically in the UK during the 20th century, peaked in the 1970s, and have fallen since then. Numbers of people living with CVD are not falling, and the British Heart Foundation estimates that there are about 1.5 million men and 1.2 million women who have or have had an MI or angina. [1] Worldwide, it is estimated that 17 million people die of CVDs every year. More than 60% of the global burden of CHD is found in resource-poor countries. [2] The US has a similar burden of heart disease to the UK; in 2002, 18% of deaths in the US were from heart disease, compared with 20% in the UK. The US lost 8 disability-adjusted life years (DALYs) per 1000 population to heart disease and a further 4 DALYs per 1000 population to stroke, and the UK lost 7 DALYs per 1000 population to heart disease and 4 DALYs per 1000 population to stroke. Afghanistan has the highest rate of DALYs lost to heart disease (36 DALYs per 1000 population), and France, Andorra, Monaco, Japan, Korea, Dominica, and Kiribati have the lowest (1–3 DALYs per 1000 population). Mongolia has the highest rate for stroke (25 DALYs per 1000 population lost) and Switzerland the lowest (2 DALYs per 1000 population lost).

**AETIOLOGY/ RISK FACTORS**

Deaths from CHD are not evenly distributed across the population. They are more common in men than in women; 67% more common in men from Scotland and the north of England than in the south of England; 58% more common in male manual workers; twice as common in female manual workers than in female non-manual workers; and about 50% higher in South Asian people living in the UK than in the average UK population. In the UK, there are 18% more CHD deaths in men, and 21% in women over the winter months compared with the rest of the year. [1] CVD in the UK generally results from the slow build-up of atherosclerosis over many decades, with or without thrombosis. The long development time of atherosclerosis means that small changes in lifestyle may have profound effects on risk of CVD over decades. However, while there is strong evidence from epidemiological studies for the importance of lifestyle factors (such as smoking, physical activity, and diet) in the process of development of CVD, [2] adjusting for confounding can be difficult, and the long timescales involved make proving the effectiveness of preventive interventions in trials difficult. In practice, risk factors — rather than disease outcomes — are often the only practical outcomes for intervention studies in low-risk people. Such risk factors include blood pressure, body mass index (BMI), serum lipids, and development of diabetes.

**PROGNOSIS**

Improvements in diet may lower the risk of cardiovascular disease by exerting favourable changes on CVD risk factors (obesity, high blood pressure, elevated serum lipids, diabetes).

**AIMS OF INTERVENTION**

To modify diet in order to reduce risk of CVD and death, with minimum adverse effects.

**OUTCOMES**

**Mortality**: total mortality or mortality attributable to CVD; **cardiovascular events**: such as MI, angina, stroke, and heart failure; **cardiovascular risk factors**: changes in risk factors such as serum lipids, weight, blood pressure, and glucose tolerance; and **adverse effects**. We have ex-

cluded behavioural change as an outcome. For example, the change in the number of servings or weight of vegetables consumed in a week after advice to increase vegetable consumption. Although many studies report these intermediate outcomes, we have only evaluated clinical outcomes in this review.

## METHODS

*Clinical Evidence* search and appraisal March 2014. The following databases were used to identify studies for this systematic review: Medline 1966 to March 2014, Embase 1980 to March 2014, and The Cochrane Database of Systematic Reviews 2014, issue 3 (1966 to date of issue). Additional searches were carried out in the Database of Abstracts of Reviews of Effects (DARE) and the Health Technology Assessment (HTA) database. We also searched for retractions of studies included in the review. An information specialist identified titles and abstracts in an initial search, which an evidence scanner then assessed against predefined criteria. An evidence analyst then assessed full texts for potentially relevant studies against predefined criteria. An expert contributor was consulted on studies selected for inclusion. An evidence analyst then extracted all data relevant to the review. **Quality issues relating to included studies:** study design criteria for inclusion in this review were published RCTs and systematic reviews of RCTs in the English language, and containing greater than or equal to 100 individuals of whom more than 80% were followed up, with at least a 6-month follow-up. We included open RCTs. We included RCTs undertaken in healthy free living adults without existing CVD and with less than 10% of the trial population with CVD risk factors (hypertension, dyslipidaemia, diabetes), in whom the intervention of interest was applied. We have included RCTs in which dietary advice was given by healthcare professionals such as nurses, doctors, and dieticians, which may have been supplemented by paper-based self-help resources, and have excluded web-based or electronic advice and public health measures. We have excluded RCTs in which food was also supplied or supplements given in addition to advice, where incentives (cash or other) were employed, where increased exercise was part of the intervention, or where weight loss was an aim of the trial. To avoid confounding and allow judgements on the application of different elements of advice in clinical practice, we have only included RCTs in which the advice given related to that single intervention only (e.g., advice on reducing or modifying fat intake only). Much of the advice given in RCTs included in reviews involved more than one element. We have excluded RCTs in which the intervention included a range of different advice in which the contribution of different individual elements was unclear. We have only reported RCTs that reported clinical outcomes in the benefits section of this review (changes in mortality, cardiovascular events, or cardiovascular risk factors [BP, lipid levels, weight, glucose tolerance]). Many RCTs we found reported behavioural change as an outcome (e.g., change in the number of servings of vegetables consumed in 1 week, or alteration in the proportion of saturated fats consumed in the diet); we have excluded these data and only report on the prespecified clinical outcomes. For the option on advice to reduce and/or modify fat intake, we have excluded RCTs that gave cholesterol-lowering advice only. Due to the paucity of RCTs reporting cardiovascular outcomes in our population group or interventions of interest, we have occasionally reported data in the Comments section, which may have included some participants outside our population group of interest, or in which the intervention was outside our intervention of interest, but we felt was still of relevance. In such cases, we have clearly described the populations and interventions included in the analysis, and how these differed from our populations and interventions of interest. We included RCTs and systematic reviews of RCTs where harms of an included intervention were studied applying the same study design criteria for inclusion as we did for benefits. In addition, we use a regular surveillance protocol to capture harms alerts from organisations such as the FDA and the MHRA, which are added to the reviews as required. **General reporting:** to aid readability of the numerical data in our reviews, we round many percentages to the nearest whole number. Readers should be aware of this when relating percentages to summary statistics such as relative risks (RRs) and odds ratios (ORs). We have performed a GRADE evaluation of the quality of evidence for interventions included in this review (see table, p 10 ). The categorisation of the quality of the evidence (into high, moderate, low, or very low) reflects the quality of evidence available for our chosen outcomes in our defined populations of interest. These categorisations are not necessarily a reflection of the overall methodological quality of any individual study, because the *Clinical Evidence* population and outcome of choice may represent only a small subset of the total outcomes reported, and population included, in any individual trial. For further details of how we perform the GRADE evaluation and the scoring system we use, please see our website (www.clinicalevidence.com).

## QUESTION

**What are the effects of dietary advice in generally healthy adults without existing CVD or increased CVD risk factors to improve cardiovascular outcomes (mortality, cardiovascular events, and cardiovascular risk factors)?**

## OPTION

**ADVICE TO REDUCE SODIUM INTAKE ALONE**

### Mortality

*Advice to reduce sodium intake alone compared with no advice* We don't know whether intensive advice to reduce sodium intake alone is more effective than no intensive advice at reducing mortality in generally healthy adults without existing CVD or increased CVD risk factors (low-quality evidence).

**Cardiovascular events**

*Advice to reduce sodium intake alone compared with no advice* We don't know whether intensive advice to reduce sodium intake alone is more effective than no intensive advice at reducing cardiovascular events in generally healthy adults without existing CVD or increased CVD risk factors (very low-quality evidence).

**Cardiovascular risk factors**

*Advice to reduce sodium intake alone compared with no advice* Intensive advice to reduce sodium intake alone may be more effective than no intensive advice at reducing systolic and diastolic blood pressure at 6 to 12 months, and reducing systolic blood pressure at 13 to 60 months, in generally healthy adults without existing CVD or increased CVD risk factors, but we don't know about diastolic blood pressure at 13 to 60 months (low-quality evidence).

**For GRADE evaluation of interventions for primary prevention of CVD: diet, see table, p 10 .**

**Benefits:**

We found two systematic reviews (search dates not reported [3] and 2010 [4]) and one subsequent report of two RCTs included in the reviews. [5]

The first systematic review included three RCTs in normotensive people [6] [7] [8] [9] and pooled data. [3] The review reported that all three RCTs were in healthy people (predominantly white, male, mean age 40 years) with high normal blood pressure who were not on antihypertensive drugs. [3] All three trials were conducted in the US. [3] Each RCT compared advice to reduce sodium intake versus no intervention/no dietary advice. Some RCTs included more than two arms; we have only reported on arms comparing advice to reduce sodium intake versus no advice here.

The first two included RCTs comprised the Trials of Hypertension Prevention (TOHP phase I and II) studies.The first RCT (744 healthy adults, aged 30–54 years, diastolic BP 80–89 mmHg over nine readings; TOHP I) had a target urinary sodium excretion of 80 mmol per day and participants were followed up to 18 months. [3] The intervention group received eight group and two individual counselling sessions over 3 months, and then less intensive support for the rest of the trial. The review reported that the regimen included a nutrition and behavioural counselling programme (including food tasting and samples, problem solving, shopping lists and guides, peer support and family involvement, field trips to supermarkets and restaurants, food diaries, and self assessment of sodium intake). The control group received no intervention. [3]

The second included RCT (1190 healthy adults, aged 30–54 years, diastolic BP 83–89 mmHg, systolic BP <140 mmHg, BMI 110%–165%; TOHP II) had a target urinary sodium excretion of 70 mmol per day and participants were followed up to 48 months. [3] The intervention group received 10 initial weekly sessions of group counselling lasting 90 minutes each, followed by bimonthly or monthly sessions for the duration of the trial. The review reported that the content of the intervention (led by dietitians, psychologists, and health counsellors) was similar to the first RCT. [3]

The third included RCT was the Hypertension Prevention Trial (HPT). This RCT (392 healthy adults, mean age 39 years, diastolic BP 78–89 mmHg) had a target urinary sodium excretion of 70 mmol per day and participants were followed up to 36 months. [3] The review reported that the intervention included 10 weekly group counselling sessions followed by semi-monthly and then bimonthly meetings throughout the trial. It included group discussions, record keeping, cooking demonstrations, self assessment, goal setting, a cookbook, newsletters, and tasting of new foods. [3]

The review reported that mortality and cardiovascular events were inconsistently reported. [3] The review did not separately pool results for normotensive people alone. The three RCTs found no significant difference between groups in mortality (first RCT: 0/327 [0%] with advice to reduce sodium intake *v* 1/417 [0.2%] with control; RR 0.42, 95% CI 0.02 to 10.39; second RCT: 3/594 [0.5%] with advice to reduce sodium intake *v* 2/596 [0.3%] with control; RR 1.51, 95% CI 0.25 to 8.97; third RCT: 1/196 [0.5%] with advice to reduce sodium intake *v* 1/196 [0.5%] with control; RR 1.0, 95% CI 0.06 to 15.87). However, these results were based on small numbers of events. The RCTs did not report on other cardiovascular events; however, one included RCT (the HPT) found "no differences among the treatment groups in gross morbidity, as indicated by periods of hospitalisation, or in deaths". [3] The review concluded that there was not enough evidence to draw reliable conclusions on mortality or cardiovascular events. [3]

The review found that advice to reduce sodium intake significantly reduced systolic and diastolic blood pressure over 6 to 12 months compared with control (systolic BP: 3 RCTs, 2124 people, –2.31 mmHg, 95% CI –3.06 mmHg to –1.55 mmHg; P <0.00001; diastolic BP: 3 RCTs, 2124 people, –1.16 mmHg, 95% CI –1.77 mmHg to –0.56 mmHg; P = 0.00017). It found that advice

significantly reduced systolic but not diastolic blood pressure over 13 to 60 months compared with control, although the result for diastolic pressure was of borderline significance (systolic BP: 3 RCTs, 2285 people, –1.09 mmHg, 95% CI –1.92 mmHg to –0.26 mmHg; P = 0.01; diastolic BP: 3 RCTs, 2285 people, –0.52 mmHg, 95% CI –1.05 mmHg to +0.01 mmHg, P = 0.053; see Comment). [3]

The review reported that in one RCT (392 people; HPT), 69% of the intervention group reported problems at some time during the trial, including issues with adherence and convenience of the diet (further details not reported). In another RCT (744 people; TOHP I), psychological well-being scores were significantly higher in people receiving advice to reduce sodium intake compared with people receiving no intervention at 18 months (P <0.01; further details not reported). [3] The review reported that one RCT (HPT) found no significant difference in weight at 3 years; one RCT (TOHP I) found that the advice group had significantly higher weight loss at 6 months (1.2 kg) and 12 months (0.8 kg) but not at 18 months (0.4 kg); and one RCT (TOHP II) found that the advice group had a significantly greater weight loss at 6 months (1.2 kg, P <0.0001), but no significant difference at 36 months, compared with the control group (further details not reported). [3]

The second review did not separately pool data on our groups of interest. [4] It included one further RCT, which was published subsequent to the first review. [10] However, the intervention also included advice on increasing carotene, vitamin C, fibre, and vegetable intake, so we have not reported it here (see Comment).

We found one subsequent long-term follow-up report at 10 to 15 years of two RCTs included in the review that reported on CVD (a composite outcome of MI, CVA, coronary artery bypass graft, percutaneous transluminal coronary angioplasty, and cardiovascular death) and total mortality. [5] The follow-up report on the first RCT (744 people; TOHP I; trial duration 18 months) found no significant difference between groups in CVD or total mortality when analysing crude rates (CVD, P = 0.24; total mortality, P = 0.82). However, after adjustment for baseline characteristics, particularly age, it found that CVD was significantly lower in people receiving advice to reduce sodium intake but found no significant difference in total mortality (CVD [analysis including 73% of those initially randomised]: 17/231 [7%] with intervention *v* 32/311 [10%] with control; HR 0.48, 95% CI 0.25 to 0.92; total mortality [analysis including 99% of those initially randomised]: 10/327 [3%] with intervention *v* 14/417 [3%] with control; HR 0.76, 95% CI 0.33 to 1.74; analysis additionally adjusted for baseline weight and sodium excretion). [5] The analysis of the second RCT (TOHP II) did not compare advice only versus control but included data on a combined advice plus weight loss intervention and weight loss intervention alone, so we have not reported these data further. The report did not specify rates of adherence to the dietary intervention after the trials had ended.

**Harms:** The reviews and RCTs did not report on adverse events. [3] [4] [5] [10]

**Comment:** The first review found that advice to reduce sodium significantly reduced urinary sodium excretion compared with no advice at 6 to 12 months and 13 to 60 months in all three RCTs. [3] The review concluded that although a low salt diet was associated with improvement in blood pressure, it is difficult to maintain a low salt diet even with an intensive intervention on an individual basis. [3] It observed that changes in food production and catering practices may represent an alternative intervention.

The second review [4] included one RCT in which decrease in sodium intake was a main aim, but in which advice on fibre and vegetable consumption, and targets for carotene and vitamin C were also given. [10] The RCT (550 adults, aged 40–69 years, 49 people on antihypertensive medication, in Japan) compared two individual 15-minute dietary counselling sessions (at an annual health check-up and at 5 months later), a group lecture, and two newsletters versus no intervention. [10] The intervention was to reduce salt intake (goal was <8 g/day in women and 10 g/day in men) by decreasing intake of salted foods (such as miso, salted vegetable pickles, salted fish) and to increase carotene and vitamin C intake by increasing fruit and vegetable intake. [10] It did not report on mortality or cardiovascular events. The RCT found that the advice intervention significantly reduced systolic blood pressure compared with no advice at 1 year, but found no significant difference between groups in diastolic blood pressure (systolic BP: difference –3.1 mmHg, 95% CI –5.4 mmHg to –0.9 mmHg, P = 0.007; diastolic BP: difference –0.9 mmHg, 95% CI –2.6 mmHg to +0.8 mmHg, P = 0.307; results adjusted for baseline values, alcohol intake, and body weight). The RCT found no significant difference between groups in body weight at 1 year (difference 0 kg, 95% CI –0.3 kg to +0.3 kg, P = 0.91). The RCT performed a subgroup analysis in normotensive people alone, which found no significant difference between groups in systolic or diastolic blood pressure, but it was not clear what cut-off point for hypertension had been taken, so we have not reported these results further. Results were based on 448/550 (81%) people randomised, and although the randomisation was by individual, the RCT reported that people within any one family were assigned

to the same group. [10] Because this was a mixed intervention (advice on both salt and fruit and vegetables), it is difficult to elucidate which element was responsible for any observed effects.

Guidance on dietary salt was published in Canada in 1999. [11] A panel was convened which drew up consensus guidelines based on the best available evidence at that time. They concluded that for normotensive individuals a reduction in dietary salt of 100 mmol daily was required to achieve a 1 mmHg reduction in systolic blood pressure and as such a low salt diet should not be recommended for this group at that time, because of insufficient evidence demonstrating that this would lead to reduced hypertension. However, it did underline the importance of avoiding excessive intake of salt through counselling to choose foods low in salt, to avoid foods high in salt, to minimise the use of salt used in cooking, and to increase awareness of the salt content of foods. [11]

**Clinical guide:**
Intensive advice to reduce sodium intake is more effective than no advice at reducing sodium intake (measured by reduced urinary sodium excretion) in people with blood pressure just below the definition of hypertension, but it is not clear whether the intensive intervention used in some studies is practical in routine clinical practice.

## OPTION ADVICE TO REDUCE AND/OR MODIFY FAT INTAKE ALONE

**We found no direct information from RCTs on the effects of advice to reduce and/or modify fat intake alone in generally healthy adults without existing CVD or increased CVD risk factors.**

**For GRADE evaluation of interventions for primary prevention of CVD: diet, see table, p 10 .**

**Benefits:** We found two systematic reviews (search dates 2010 [12] [4] ), which had different inclusion and exclusion criteria and performed different analyses. The first review included people at any level of cardiovascular risk and included any intervention to reduce or modify fats (including advice, supplements, and providing food). [12] The second review included any dietary advice (for example, advice on sodium, fats, cholesterol, fibre, general advice). [4] Neither review pooled data in our population group of interest in our intervention of interest alone. None of the individual RCTs included in either review met the quality criteria for this *Clinical Evidence* review (see Comment).

**Harms:** We found no RCTs on adverse effects.

**Comment:** We found one large additional RCT (the Women's Health Initiative [WHI] RCT). [13] This RCT [13] was excluded from the second review [4] because of extensive use of medications (oestrogens, statins, diabetic medications, aspirin) during the trial. However, it examined the effects of a dietary intervention and reported long-term cardiovascular outcomes. The RCT (48,835 post-menopausal women, aged 50–79 years, baseline fat intake of at least 32% of daily total calories, 43% hypertension [hypertension treated or BP 140/90 mmHg or greater]) examined the impact of a low fat diet on the incidence of breast and colorectal cancer, but also reported on changes in body weight [14] and CVD events, [13] and followed participants for an average of 7.5 years. Use of hormone replacement therapy (HRT) was high at study entry (44% in both intervention and control groups). In addition, many women also participated concurrently in one or more other WHI trials (oestrogen alone or with progesterone; calcium and vitamin D supplementation).

The advice intervention was designed to reduce total fat intake to 20% of calories and increase intake of vegetables/fruits to five servings per day and grains to at least six servings per day. There were no weight loss or calorie goals. It included 18 group sessions in the first year led by nutritionists with quarterly sessions thereafter, and individual sessions that used reflective listening, targeted message, and personalised feedback. Participants self-monitored total fat-gram intake, servings of vegetables, fruits, and grains. The control group received education materials only.

At 1 year, the RCT found a 1.9-kg difference in body weight between the two groups (P <0.001) and a 0.4-kg difference at 7.5 years (P = 0.01) in favour of diet. [14] Weight loss was greatest in women in either group who decreased their percentage of energy from fat. [14]

At a mean of 8.1 years, the RCT found no significant difference between groups in major CHD (non-fatal MI or CHD death: HR 0.98, 95% CI 0.88 to 1.09), composite CHD (non-fatal MI, CHD death, or coronary artery bypass graft/percutaneous coronary intervention: HR 0.97, 95% CI 0.90 to 1.06) or stroke (fatal or non-fatal: HR 1.02, 95% CI 0.90 to 1.15). [13] The results were still not significant when women with a history of CVD at baseline (1656/48,835 [3%] participants) were omitted. At 3 years, the RCT found a significant difference between groups in LDL cholesterol (mean difference –3.55 mg/dL, 95% CI –6.58 mg/dL to –0.52 mg/dL) and diastolic blood pressure (–0.31 mmHg, 95% CI –0.50 mmHg to –0.13 mmHg) in favour of diet, but no significant differences between groups in HDL cholesterol, systolic blood pressure, triglycerides, glucose, or insulin. [13]

## OPTION ADVICE TO INCREASE FRUIT AND VEGETABLE INTAKE ALONE

**Cardiovascular risk factors**

*Advice to increase fruit and vegetable intake alone compared with no advice* Advice to increase fruit and vegetable intake alone may be more effective than no advice at moderately reducing systolic blood pressure at 6 to 12 months, but we don't know about diastolic blood pressure. We don't know whether advice to increase fruit and vegetable intake is more effective than no advice at improving total cholesterol, LDL cholesterol, HDL cholesterol, or triglyceride levels at 6 to 12 months (low-quality evidence).

**Note:**

We found no evidence from RCTs on mortality or cardiovascular events. Despite this, increasing fruit and vegetables may have an impact on other diseases. We found no evidence from RCTs of long-term serious adverse effects.

**For GRADE evaluation of interventions for primary prevention of CVD: diet, see table, p 10 .**

**Benefits:**

We found one systematic review (search date 2012) that examined the effects of advice to increase fruit and vegetable consumption in primary prevention. [15] It found four RCTs. The review included adults aged 18 years and older, and trials which gave specific dietary advice to increase fruit and vegetable consumption versus no intervention (usual diet) or minimal intervention (e.g., leaflets, with no personal interaction or reinforcement). It excluded RCTs in which more than 25% of participants had cardiovascular disease at baseline (including: MI; stroke; re-vascularisation [CABG; PTCA]; angina; CHD/PAD/cerebrovascular disease defined by angiography), in which more than 25% of participants had diabetes, interventions which included fruit or vegetable extracts, mutlifactoral interventions, trials focusing on weight loss, or of less than 3 months duration.

The intervention in the largest RCT (729 people, aged 25–64 years, without serious chronic illness) was based on the brief negotiation method and participants were encouraged to discuss barriers to eating more fruit and vegetables. The recommendation was five or more portions per day, but a lower target was negotiated if this was thought to be unrealistic. Leaflets, an action plan, a portion guide, a record book, and a refrigerator magnet with a five-a-day logo were also used, and the intervention lasted for about 25 minutes. There was a reinforcing telephone call 2 weeks later, and a booklet was sent at 3 months with advice on increasing fruit and vegetables in the diet.

The second RCT (50 post-menopausal women, aged 21–50 years old, with at least one first degree relative with breast cancer) provided personal counselling every 2 weeks initially by a dietitian, then monthly, and monthly group meeting for a year, with advice to increase consumption to nine servings per day, and further additional education at the monthly meetings.

The third RCT (29 healthy women, at least 35 years old, free from chronic conditions) used individualised dietary counselling to increase consumption to nine servings per day. A dietitian provided advice on purchasing produce, recipes, and easy to prepare dishes, as well as group meetings with cooking instructions and demonstrations every month.

The fourth RCT (201 people, diagnosis of colorectal adenomatous polyp in the last 5 years, recruited from a large gastroenterology practice) involved a meeting with a nutritionist to initially increase consumption to two servings per day, up to at least eight servings per day before 3-month clinical visit. It also included behaviour modification strategies, educational materials such as tip sheets and cook books, visit reminder cards, telephone calls, refrigerator magnets, and newsletters, as well as positive reinforcement and feedback. Participants saw the nutritionist five times in total (see Comment).

None of the included RCTs presented data on mortality or clinical events. However, they reported data on cardiovascular risk factors (blood pressure, lipid levels).

The review found that advice to increase fruit and vegetable consumption significantly reduced systolic blood pressure compared with no advice at 6 to 12 months (2 RCTs, 891 people, mean difference –3.00 mmHg, 95% CI –1.09 mmHg to –4.92 mmHg, P = 0.0021), but found no significant difference between groups in diastolic blood pressure (2 RCTs, 891 people, mean difference –0.90 mmHg, 95% CI –2.03 mmHg to +0.24 mmHg, P = 0.12). [15] It found no significant difference between advice and no advice in total cholesterol at 6 to 12 months (4 RCTs, 970 people, mean difference –0.01 mmol/L, 95% CI –0.11 mmol/L to +0.09 mmol/L, P = 0.81), LDL cholesterol at 12 months (2 RCTs, 251 people, mean difference –0.17 mmol/L, 95% CI –0.38 mmol/L to +0.03 mmol/L, P = 0.10), HDL cholesterol at 12 months (2 RCTs, 251 people, mean difference –0.01 mmol/L, 95% CI –0.10 mmol/L to +0.08 mmol/L, P = 0.79), or triglycerides at 12 months (3 RCTs, 280 people, mean difference +0.10 mmol/L, 95% CI –0.06 mmol/L to +0.27 mmol/L, P = 0.20). The review noted that there was considerable variability in the interventions used, the participants recruited, and the outcomes measured. It noted that there may have been differences in serving size

recommended within interventions, but the definition of portion size was not described in trials. The review also noted that the RCTs were relatively short term, and in relatively healthy people.

**Harms:** The review reported that one RCT (201 people) found that advice significantly increased bowel movements from 9.2 to 10 per week (absolute numbers and further details not reported) and significantly increased flatulence (P = 0.01; absolute numbers and further details not reported), but this did not persist after 3 months. [15]

**Comment:** The interventions in some of the RCTs were quite intensive, and delivered over a prolonged period of time. How generalisable or reproducible these interventions are in routine primary care is a matter of debate.

The nutritional intervention used in the Women's Health Initiative study also encouraged an increase in fruit and vegetable intake and found a trend towards weight loss in women who increased their intake of fruit and vegetables (see Comment of Advice to reduce and/or modify fat intake alone, p 6 ).

**Clinical guide:**
Taken together, there seems to be insufficient evidence from RCTs on the effects of advice for increasing fruit and vegetable intake alone on risk factors for CVD, CVD events, or mortality from these conditions in the general population.

## OPTION ADVICE TO INCREASE FIBRE INTAKE ALONE

**We found no direct information from RCTs on the effects of advice to increase dietary fibre alone in generally healthy adults without existing CVD or increased CVD risk factors.**

**For GRADE evaluation of interventions for primary prevention of CVD: diet, see table, p 10 .**

**Benefits:** We found one systematic review (search date 2010), which found no RCTs of sufficient quality. [4] We found no subsequent RCTs.

**Harms:** We found no RCTs.

**Comment:** We found one large RCT that included advice to increase fibre intake (see Comment of Advice to reduce and/or modify fat intake alone, p 6 ).

## GLOSSARY

**Body mass index (BMI)** Calculated by weight (in kilograms) divided by height (in metres) squared.

**Low-quality evidence** Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

**Very low-quality evidence** Any estimate of effect is very uncertain.

## SUBSTANTIVE CHANGES

**Advice to increase fibre intake alone** One systematic review updated. [4] Categorisation unchanged (unknown effectiveness).

**Advice to increase fruit and vegetable intake alone** New evidence added. [15] Categorisation unchanged (unknown effectiveness).

**Advice to reduce and/or modify fat intake alone** Two systematic reviews updated. [4] [12] Categorisation unchanged (unknown effectiveness).

**Advice to reduce sodium intake alone** One systematic review updated. [4] Categorisation unchanged (likely to be beneficial).

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## Disclaimer

**TABLE** **GRADE evaluation of interventions for primary prevention of CVD: diet**

| **Important outcomes** | **Mortality, cardiovascular events, cardiovascular risk factors, adverse effects** | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Number of studies (participants)** | **Outcome** | **Comparison** | **Type of evidence** | **Quality** | **Consistency** | **Directness** | **Effect size** | **GRADE** | **Comment** |
| What are the effects of dietary advice in generally healthy adults without existing CVD or increased CVD risk factors to improve cardiovascular outcomes (mortality, cardiovascular events, cardiovascular risk factors)? | | | | | | | | | |
| 3 (2326) [3] [5] | Mortality | Advice to reduce sodium intake alone *v* no advice | 4 | 0 | 0 | –2 | 0 | Low | Directness points deducted for unclear generalisability of intensive regimen and small number of events (31 in total) |
| 3 (2326) [3] [5] | Cardiovascular events | Advice to reduce sodium intake alone *v* no advice | 4 | –1 | 0 | –2 | 0 | Very low | Quality point deducted for incomplete reporting of results; directness points deducted for unclear generalisability of intensive regimen and use of composite outcome including mortality and morbidity in 1 RCT |
| 3 (at least 2285) [3] | Cardiovascular risk factors | Advice to reduce sodium intake alone *v* no advice | 4 | 0 | 0 | –2 | 0 | Low | Directness points deducted for unclear generalisability of intensive regimen and unclear importance longer term (13–60 months) |
| 4 (970) [15] | Cardiovascular risk factors | Advice to increase fruit and vegetable intake alone *v* no advice | 4 | 0 | 0 | –2 | 0 | Low | Directness points deducted for heterogeneity of interventions between trials and unclear generalisability of intensive regimen |

Type of evidence: 4 = RCT. Consistency: similarity of results across studies.
Directness: generalisability of population or outcomes.
Effect size: based on relative risk or odds ratio.