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Increased consumption of fruit and vegetables for the primary prevention of cardiovascular diseases

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Abstract

This is the protocol for a review and there is no abstract. The objectives are as follows:

The primary objective is to determine the effectiveness of i) advice to increase fruit and vegetable consumption ii) the provision of fruit and vegetables to increase consumption, for the primary prevention of CVD.

BACKGROUND

Description of the condition

Cardiovascular disease (CVD) is one of the leading causes of death worldwide (WHO 2011). In 2008 it accounted for 30% of total global deaths, with 6.2 million deaths the consequence of stroke and 7.2 million due to coronary heart disease (CHD) (WHO 2011). The burden of CVD also varies hugely between regions (Müller-Nordhorn 2008; Reddy 1998), for example, death from ischaemic heart disease in France is a quarter of that of the United Kingdom (UK) (Law 1999).

Dietary factors may play a vital role in the development of CVD and its risk factors and may contribute to the geographic variability in CVD morbidity and mortality (Epstein 1996). Such factors are important not only because they have been linked to CVD development but also because they can be modified. This makes them the main target for interventions aimed at primary prevention and management of CVD.

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None known.

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One dietary factor that should be considered is fruit and vegetable intake. Indeed, a low consumption of fruit and vegetables (less than 400 grammes [g] per day) is thought to be one of the top ten risk factors for global mortality and it is estimated results in 1.7 million global deaths a year (WHO 2004). Of these global deaths, 14% are from gastrointestinal cancer, 11% are due to ischaemic heart disease and 9% are from stroke. In the European Union, New Zealand and Australia 3.5%, 2.1% and 2.8% respectively of disease burden is considered to be a consequence of low fruit and vegetable intake (Begg 2007; Pomerleau 2004; Tobias 2001), with, in particular, 9.6% of the CVD disease burden in Australia due to a low intake of fruit and vegetables (Begg 2007).

Conversely, it has been shown that a high consumption of fruit and vegetables can have a protective role for some chronic diseases including CVD (Hooper 2007). A number of cohort studies have shown that the risk of CHD is decreased by a high consumption of fruit and vegetables (Bazzano 2002; Liu 2000; Liu 2001). Joshipura and colleagues, for example, showed that in 84,251 women and 42,148 men a high intake of fruit of vegetables was associated with a protective effect against developing CHD. This was particularly the case for those fruit and vegetables rich in vitamin C and leafy green vegetables (Joshipura 2001). Evidence also suggests that an increase in fruit and vegetable intake could reduce the burden of ischaemic stroke and ischaemic heart disease by as much as 19% and 31% respectively (Lock 2005). Furthermore, it is estimated that approximately 2.7 million lives a year could be saved by increasing fruit and vegetable consumption to 400g per day or over (WHO 2004).

Description of the intervention

Evidence suggests that high levels of fruit and vegetable intake reduce the risk of CVD (Joshipura 2001; Liu 2000; Liu 2001). This may be the result of confounding by physical activity (Serdula 1996), socio-economic status (Dubowitz 2008), smoking status (Serdula 1996) or other unidentified factors, but may also be due to several mechanisms such as an increase in potassium which lowers blood pressure or an increase in antioxidant vitamins. As a result, many national and international guidelines recommend at least five portions of fruit and/or vegetables a day (a portion equates to 80g) (Agudo 2004; Cardiovascular Review Group 1994; Johansson 1998; NHS 2009; U.S. Department of Agriculture 2005).

However, such guidelines are not always followed. This appears to be the case in the UK where it is estimated that only 40% of the general population reach this target (Hunt 2000). The interventions investigated in this review will include those that provide advice to increase fruit and vegetable consumption or those that provide fruit and vegetables themselves to increase consumption. Results from these two different types of interventions will be analysed separately. Advice can take many forms in that it may be written or verbal, involve a single or multiple contact and may be delivered by commercial organisations, health professionals or government organisations. Provision may include only one, or more fruit(s) and/or vegetable(s). If we find sufficient trials we will examine the effects of intensity and duration of the intervention. The present review is concerned with trials of the effect of such interventions in healthy populations or those who are at high risk of CVD to

investigate the effectiveness of fruit and vegetable consumption for the primary prevention of CVD.

How the intervention might work

Evidence from observational and experimental studies suggests that a high consumption of fruit and vegetables, that is more than 400g or more than five portions a day, is beneficial for the prevention and treatment of CVD (Ness 1997). However, the exact mechanisms by which increased fruit and vegetable consumption reduce CVD risk are not known. It may be due to fruit and vegetables containing protective elements including vitamins, minerals, antioxidants, micronutrients and phytochemicals (Department of Health 2010; Miller 2000; Van Duyn 2000). There are many potential mechanisms through which these protective elements can act to reduce blood pressure, reduce antioxidant stress, lower the serum level of low-density lipoprotein cholesterol and improve the regulation of hemostasis (Asgard 2007; Dauchet 2006; Suido 2002).

Why it is important to do this review

Many factors determine the intake of fruit and vegetables in adults (Pollard 2002). These include not only demographic and lifestyle factors but also sensory appeal, the media and availability (Anderson 1994; Brug 1995; Clark 1998; Lennernas 1997; Thompson 1999). Although studies investigating the factors that determine fruit and vegetable intake provide considerable information to aid in the development of interventions, they do not examine the effectiveness of interventions to increase fruit and vegetable consumption. Some systematic reviews have attempted to do this (Ammerman 2002; Brunner 2007; Contento 1995; Pomerleau 2005; Miller 2000a). Pomerleau et al. (Pomerleau 2005), for example, conducted a systematic review that investigated the effectiveness of interventions designed to promote the intake of fruit and vegetables. They found that the largest increase in fruit and vegetable consumption was for interventions that targeted high risk populations or those with a pre-existing disease, whilst a small increase of between 0.1 and 1.4 servings of fruit and vegetables a day was found for interventions promoting fruit and vegetable intake in healthy adults. This was similar to the findings of Brunner et al. (Brunner 2007) who found that dietary advice, when compared to no advice, increased the consumption of fruit and vegetables by 1.25 servings per day in healthy adults.

However, these systematic reviews do not always focus soley on the intake of fruit and vegetables (Brunner 2007; Contento 1995). For instance, the systematic review by Brunner (2007) investigated dietary advice in general and did not specifically examine interventions aimed at increasing fruit and vegetable consumption. What is more, the review by Brunner (2007) only considered interventions concerned with advice and did not investigate interventions involving the provision of foods. The systematic review by Pomerleau (2005) does not solely focus on CVD (Pomerleau 2005), other reviews include children (Burchett 2003; Miller 2000a) and many of these systematic reviews do not involve meta-analysis.

We are focusing our attention on adults since a Cochrane review is already being undertaken in assessing the evidence for interventions for increasing fruit and vegetable consumption in children aged up to five years (Wolfenden 2010). A comprehensive systematic review is

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therefore needed which thoroughly examines interventions providing advice to increase fruit and vegetable consumption and the provision of fruit and vegetables to increase consumption, in healthy adults or those with cardiovascular risk factors to determine their effectiveness in CVD prevention. This will provide guidance not only for national and international governments but also for local authorities, practitioners and members of the public.

OBJECTIVES

The primary objective is to determine the effectiveness of i) advice to increase fruit and vegetable consumption ii) the provision of fruit and vegetables to increase consumption, for the primary prevention of CVD.

METHODS

Criteria for considering studies for this review

Types of studies—Randomised Controlled Trials

Types of participants—Adults (people from the age of 18 onwards) of all ages from the general population and those who are at high risk of CVD due to the presence of major CVD risk factors such as smoking, dyslipidemia, diabetes or hypertension. Those who have had a myocardial infarction (MI), a stroke, undergone a revascularisation procedure (coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA)), have angina or angiographically defined CHD will be excluded.

Types of interventions—The interventions will include i) specific dietary advice to increase fruit and vegetable consumption or ii) the provision of fruit and vegetables (participants are provided with fruits and vegetables as part of the intervention) as a means to increase consumption.

Studies examining advice to increase fruit and vegetable intake will be examined separately from those investigating the provision of fruit and vegetables. Studies will also be stratified by baseline risk. If sufficient trials are available we will attempt to examine the “intensity” of the intervention by sub-grouping interventions by the number of fruit and vegetable components they contain and duration, and for interventions involving advice to increase fruit and vegetable consumption, by the number of scheduled personal contacts made with participants in the intervention arm, the support provided and duration. Multi-factorial dietary interventions studies will not be included in this review in order to avoid confounding.

In addition, we will also focus on follow-up periods of six months or more as these are the most relevant to public health interventions. Follow-up is considered to be the time elapsed since the start of the intervention. Trials will also only be considered where the comparison group is either no intervention or minimal intervention (e.g. leaflets with no person to person intervention or reinforcement).

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Types of outcome measures

Primary outcomes: Clinical outcomes (mortality (CVD and all-cause), non-fatal CVD endpoints (MI, CABG or PTCA, angiographically defined angina pectoris, stroke, carotid endarterectomy, peripheral arterial disease (PAD)).

Secondary outcomes: Changes in major CVD risk factors (blood pressure, blood lipids, type 2 diabetes), adverse events and costs.

Search methods for identification of studies

Electronic searches—The following electronic databases will be searched: the Cochrane Library (including the Cochrane Central Register of controlled Trials (CENTRAL) and NHS Centre for Reviews and Dissemination (CRD) databases Health Technology Assessment (HTA), Databse of Abstracts of Reviews of Effects (DARE) and NHS Economic Evaluation Database (NEED)), MEDLINE, EMBASE, the Web of Science (Conference Proceedings Citation Index - Science (CPCI-S)).

Medical Subject Headings (MsSH) or equivalent and text word terms will be use with searches designed in accordance with Cochrane Heart Group methods and guidance. There will be no language restrictions.

Searches will be tailored to individual databases. The search strategy for MEDLINE is shown in Appendix 1.

Searching other resources—Reference lists of reviews and retrieved articles will be checked for additional studies.

We will search the metaRegister of controlled trials (mRCT) (www.controlled-trials.com/mrct), Clinicaltrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (http://apps.who.int/trialsearch/) for ongoing trials and unpublished or part-published trials.

Citation searches will be performed on key articles. Google Scholar will also be used to search for further studies.

Experts in the field will be contacted for unpublished and ongoing trials and authors will be contacted where necessary for additional information.

Data collection and analysis

Selection of studies—The search strategy will identify titles and abstracts which will be reviewed by two reviewers (LH, EI). Potentially relevant references will then be retrieved. Following this initial screen, the full text reports of the potentially relevant studies will be obtained and two reviewers (LH, EI) will independently select relevant studies using predetermined inclusion criteria. In all cases, disagreements concerning study inclusion will be resolved by consensus with a third reviewer being consulted if disagreement persists.

Data extraction and management—Data extraction will be carried out independently by two reviewers (LH, EI) using a proforma and chief investigators will be contacted to provide additional relevant information if necessary.

The following details will be extracted from each study:

1. Study design.
2. Study setting.
3. Participant characteristics.
4. Intervention (advice or provision of fruit and vegetables, personnel, intensity, duration, follow up).
5. Comparison group (no intervention or details of minimal intervention).
6. Outcome data (outcome assessment, adverse effects).
7. Methodological quality (randomisation, blinding, attrition).

Disagreements about extracted data will be resolved by consensus and a third reviewer will be consulted if disagreement persists.

Assessment of risk of bias in included studies—Risk of bias will be assessed independently by two reviewers (LH, EI). This will be done by examining the quality of the random sequence generation and allocation concealment, description of drop-outs and withdrawals (including intention-to-treat analysis), blinding (participant, personnel and outcome assessment) and selective outcome reporting (Higgins 2011).

Measures of treatment effect—Data will be processed in accordance with the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Dichotomous outcomes will be expressed as relative risks (RR) and 95% confidence intervals (CI) will be calculated for each study. For continuous outcomes net changes will be compared (i.e. intervention group minus control group differences) and a weighted mean difference (WMD) or standardised mean difference (SMD) and 95% CI's calculated for each study.

Assessment of heterogeneity—For each outcome tests of heterogeneity will be conducted (using chi-squared test of heterogeneity and I^2 statistic). If no heterogeneity is present a fixed effect meta-analysis will be performed. If there is substantial heterogeneity the reviewers will look for possible explanations for this (e.g. intervention and participants). If the heterogeneity cannot be explained, the reviewers will consider the following options:

1. provide a narrative overview and not aggregate the studies at all;
2. use a random effects model with appropriate cautious interpretation.

Subgroup analysis and investigation of heterogeneity—Results will be stratified by i) advice to increase fruit and vegetable consumption and ii) the provision of fruit and vegetables to increase consumption. Trials will also be stratified by baseline risk; i.e. healthy participants versus participants at high risk.

If sufficient trials are available we will attempt to examine the "intensity" of the intervention by sub-grouping interventions by the number of fruit and vegetable components they contain and duration, and for interventions involving advice to increase fruit and vegetable consumption, by the number of scheduled personal contacts made with participants in the intervention arm, the support provided and duration.

Sensitivity analysis—We will carry out sensitivity analysis excluding studies of low methodological quality; i.e. trials with unclear or inadequate allocation concealment. Funnel plots and tests of asymmetry (Egger 1997) will be conducted to assess the possibility of publication bias. We will also examine the impact of "time and attention" given to participants in the intervention and control groups as a potential confounder in the relationship by excluding studies where the intervention group had more "time and attention" than the control group in a sensitivity analysis.

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Internal sources

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External sources

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Appendix 1. MEDLINE search strategy

MEDLINE OVID

The Cochrane sensitive maximising RCT filter has been applied to the search (Lefebvre C, Manheimer E, Glanville J. Chapter 6: Searching for studies. In: Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.)

1. exp Fruit/
2. exp Citrus/
3. exp Vegetables/
4. fruit*.tw.
5. vegetable*.tw.
6. orange*.tw.
7. apple*.tw.
8. (pear or pears).tw.

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9. (grape or grapes).tw.
10. banana*.tw.
11. (berry or berries).tw.
12. citrus.tw.
13. carrot*.tw.
14. greens.tw.
15. cabbage*.tw.
16. brassica*.tw.
17. blackberr*.tw.
18. blueberr*.tw.
19. cranberr*.tw.
20. guava*.tw.
21. kiwi*.tw.
22. lingonberr*.tw.
23. mango*.tw.
24. melon*.tw.
25. papaya*.tw.
26. pineapple*.tw.
27. raspberr*.tw.
28. strawberr*.tw.
29. tomato*.tw.
30. potato*.tw.
31. onion*.tw.
32. grapefruit*.tw.
33. mandarin*.tw.
34. satsuma*.tw.
35. tangerine*.tw.
36. (plum or plums).tw.
37. apricot*.tw.
38. (cherry or cherries).tw.
39. nectarine*.tw.
40. (peach or peaches).tw.

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41. celery.tw.
42. spinach*.tw.
43. (salad or salads).tw.
44. (pea or peas).tw.
45. (bean or beans).tw.
46. broccoli.tw.
47. cauliflower*.tw.
48. beetroot*.tw.
49. turnip*.tw.
50. rhubarb.tw.
51. legume*.tw.
52. cucumber*.tw.
53. leek*.tw.
54. aubergine*.tw.
55. pepper*.tw.
56. okra.tw.
57. pumpkin*.tw.
58. squash*.tw.
59. artichoke*.tw.
60. lettuce*.tw.
61. kale.tw.
62. chard.tw.
63. parsnip*.tw.
64. asparagus.tw.
65. fennel.tw.
66. chickpea*.tw.
67. five-a-day.tw.
68. 5-a-day.tw.
69. or/1-68
70. exp Cardiovascular Diseases/
71. cardio*.tw.
72. cardia*.tw.

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73. heart*.tw.

74. coronary*.tw.

75. angina*.tw.

76. ventric*.tw.

77. myocard*.tw.

78. pericard*.tw.

79. isch?em*.tw.

80. emboli*.tw.

81. arrhythmi*.tw.

82. thrombo*.tw.

83. atrial fibrillat*.tw.

84. tachycardi*.tw.

85. endocardi*.tw.

86. (sick adj sinus).tw.

87. exp Stroke/

88. (stroke or stokes).tw.

89. cerebrovasc*.tw.

90. cerebral vascular.tw.

91. apoplexy.tw.

92. (brain adj2 accident*).tw.

93. ((brain* or cerebral or lacunar) adj2 infarct*).tw.

94. exp Hypertension/

95. hypertensi*.tw.

96. peripheral arter* disease*.tw.

97. ((high or increased or elevated) adj2 blood pressure).tw.

98. exp Hyperlipidemias/

99. hyperlipid*.tw.

100. hyperlip?emia*.tw.

101. hypercholesterol*.tw.

102. hypercholester?emia*.tw.

103. hyperlipoprotein?emia*.tw.

104. hypertriglycerid?emia*.tw.

105. or/70-104

106. randomized controlled trial.pt.

107. controlled clinical trial.pt.

108. randomized.ab.

109. placebo.ab.

110. drug therapy.fs.

111. randomly.ab.

112. trial.ab.

113. groups.ab.

114. 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113

115. exp animals/ not humans.sh.

116. 114 not 115

117. 69 and 105 and 116

HISTORY

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* *Indicates the major publication for the study*