Multiple risk factor interventions for primary prevention of coronary heart disease (Review)

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[Intervention Review]

Multiple risk factor interventions for primary prevention of coronary heart disease

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ABSTRACT

Background

Primary prevention programmes in many countries attempt to reduce mortality and morbidity due to coronary heart disease (CHD) through risk factor modification. It is widely believed that multiple risk factor intervention using counselling and educational methods is efficacious and cost-effective and should be expanded. Recent trials examining risk factor changes have cast considerable doubt on the effectiveness of these multiple risk factor interventions.

Objectives

To assess the effects of multiple risk factor intervention for reducing cardiovascular risk factors, total mortality, and mortality from CHD among adults without clinical evidence of established cardiovascular disease.

Search strategy

MEDLINE was searched for the original review to 1995. This was updated by searching the Cochrane Central Register of Controlled Trials on The Cochrane Library Issue 3 2001, MEDLINE(2000 to September 2001) and EMBASE (1998 to September 2001).

Selection criteria

Intervention studies using counselling or education to modify more than one cardiovascular risk factor in adults from general populations, occupational groups, or high risk groups. Trials of less than 6 months duration were excluded.

Data collection and analysis

Data were extracted by two reviewers independently. Investigators were contacted to obtain missing information.

Main results

A total of 39 trials were found of which ten reported clinical event data. In the ten trials with clinical event end-points, the pooled odds ratios for total and CHD mortality were 0.96 (95% confidence intervals (CI) 0.92 to 1.01) and 0.96 (95% CI 0.89 to 1.04) respectively. Net changes in systolic and diastolic blood pressure, and blood cholesterol were (weighted mean differences) -3.6 mmHg (95% CI -3.9 to -3.3 mmHg), -2.8 mmHg (95% CI -2.9 to -2.6 mmHg) and -0.07 mMol/l (95% CI -0.8 to -0.06 mMol/l) respectively. Odds of reduction in smoking prevalence was 20% (95% CI 8% to 31%). Statistical heterogeneity between the studies with respect to mortality and risk factor changes was due to trials focusing on hypertensive participants and those using considerable amounts of drug treatment.

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Authors' conclusions

The pooled effects suggest multiple risk factor intervention has no effect on mortality. However, a small, but potentially important, benefit of treatment (about a 10% reduction in CHD mortality) may have been missed. Risk factor changes were relatively modest, were related to the amount of pharmacological treatment used, and in some cases may have been over-estimated because of regression to the mean effects, lack of intention to treat analyses, habituation to blood pressure measurement, and use of self-reports of smoking. Interventions using personal or family counselling and education with or without pharmacological treatments appear to be more effective at achieving risk factor reduction and consequent reductions in mortality in high risk hypertensive populations. The evidence suggests that such interventions have limited utility in the general population.

PLAIN LANGUAGE SUMMARY

Multiple risk factor interventions for primary prevention of coronary heart disease

In many countries, there is enthusiasm for "Healthy Heart Programmes" that use counseling and educational methods to encourage people to reduce their risks for developing heart disease. These risk factors include high cholesterol, excessive salt intake, high blood pressure, excess weight, a high-fat diet, smoking, diabetes, and a sedentary lifestyle. This updated review of all relevant studies found that the approach of trying to reduce more than one risk factor - multiple risk factor intervention - advocated by these Programmes do result in small reductions in blood pressure, cholesterol, salt intake, weight loss, etc. Contrary to expectations, these lifestyle changes had little or no impact on the risk of heart attack or death. Possible explanations for this are that the small risk factor changes are not maintained long-term or are not real but caused by some of the studies being poorly conducted. This review is based on the findings from 39 trials conducted in several countries over the course of three decades. Its authors discourage more research on the topic: "Our methods of attempting behaviour change in the general population are very limited. Different approaches to behaviour change are needed and should be tested empirically before being widely promoted. For example, the availability of foods and better access to recreational and sporting facilities may have a greater impact on dietary and exercise patterns respectively, than health professional advice."

BACKGROUND

In apparently healthy and asymptomatic people, the incidence of cardiovascular disease is in part explained by the modifiable risk factors: serum total cholesterol and reduced high density lipoprotein (HDL) cholesterol, blood pressure, cigarette smoking and diabetes. Primary prevention programmes attempt to reduce coronary heart disease (CHD) mortality and morbidity through risk factor modification. While the identification of high risk individuals and treatment according to level of cardiac risk may be effective at an individual level, population strategies may be more effective in reducing the burden of cardiovascular disease (Emberson 2004). Recent findings suggest that increasingly effective drug treatments for high risk individuals and widespread implementation of population wide strategies of tobacco control and dietary changes is increasing the advantage of high risk approaches to prevention. (Jackson 2006)

In the UK, the National Service Framework for coronary heart disease promotes multiple risk factor counselling and health education (NSF-CHD 2000). In the USA, the AHA Guidelines for Primary Prevention of Cardiovascular Disease and Stroke: 2002 update identify areas for intervention based on the non-pharmacological treatment of established risk factors (AHA 2002). Similarly, the Third Joint Task Force of the European and other Societies recommend use of behavioural counselling for stopping smoking tobacco, making healthy food choices and increasing physical activity (ESC 2003).

Primary prevention programmes in many countries attempt to reduce mortality and morbidity due to coronary heart disease through risk factor modification (Canadian 1986; Kickbush 1988). Randomized controlled trials of the efficacy of multiple risk factor intervention using counselling and education in addition to, or instead of, pharmacological treatments to modify major cardiovascular risk factors have been carried out in primary care and in the work place. The findings of these trials have been equivocal; efficacy in reducing disease incidence appears to be associated with the degree of risk factor control achieved (Editorial I 1982; Editorial II 1982). Taken with evidence from quasi-experimen-

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tal studies, such as the North Karelia project (Puska 1976; Puska 1981) and the Stanford Heart Disease Prevention Programme (Farquhar 1977; Farquhar 1990; Fortmann 1993), it was widely believed that multiple risk factor intervention using counselling and educational methods was efficacious and cost-effective and should be expanded.

Along side this research health services have acted by developing health promotion as a specialty (Editorial 1984), organising the routine collection of data on cardiovascular risk factors in British primary care, and issuing primary prevention policy, for example the Health of the Nation strategy in England (DoH 1992). More recent trials examining risk factor changes have cast considerable doubt on the effectiveness of these multiple risk factor interventions (Stott 1994a; Stott 1994b) and even interventions specifically against smoking (COMMIT I 1995; COMMIT II 1995) prompting a review of the reasons for the frequent failure of such community experiments (Susser 1995). A new generation of population based interventions such as the Minnesota Heart Health Program (Luepker 1994), Heartbeat Wales (Tudor-Smith 1998), the Malmö preventive project (Berglund 2000) have cast further doubt on the value of such interventions.

Treatment of multiple risk factors by diet modification, promotion of physical activity, weight loss and smoking cessation has been evaluated in a number of randomised trials. Two previous reviews (McCormick 1988; Schoenberger 1990) of multiple risk factor intervention using counselling and education with or without pharmacological treatments were conducted prior to the publication of more recent trials, were not systematic in their coverage, and did not formally aggregate the findings through meta-analysis.

In a systematic review, fourteen randomised trials were identified up until April 1995. Meta-analyses suggested that although interventions achieved reductions in risk factors, these were small and were not translated into significant decreases in morbidity or mortality (Ebrahim 1997). Since this systematic review was published a number of trials of multiple risk factor interventions have been reported and update of the review is needed.

OBJECTIVES

To assess the effectiveness of multiple risk factor intervention using counselling and/or educational approaches with or without pharmacological interventions in:

a) reducing systolic and diastolic blood pressure;

b) reducing blood cholesterol levels;

c) reducing smoking rates;

d) reducing total mortality;

e) reducing CHD mortality;

among middle-aged (40+) adults.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials of at least 6 months duration with parallel group design. Trials may be randomized by individual or by group (e.g. family, workplace site).

Types of participants

Adults aged at least 40 years old.
General populations, workforce populations and high risk groups.
Participants without clinical evidence of cardiovascular diseases.

Types of interventions

Counselling or educational interventions, with or without pharmacological treatments, which aim to reduce more than one cardiovascular risk factor (i.e. blood pressure, smoking, total blood cholesterol, physical activity, diet).

Types of outcome measures

Total mortality, CHD mortality, net change in blood pressure, smoking and total blood cholesterol.

Search methods for identification of studies

MEDLINE was searched from 1966 to April 1995 using an RCT filter (Dickersin 1994,) together with relevant diagnostic terms (i.e. coronary heart disease and stroke) and text word searches for specific interventions (e.g. dietary change, smoking cessation, exercise, blood pressure control, prevention, cholesterol lowering). Searches of reference lists of papers, expert advice and use of citation searches. This was updated by searching the Cochrane Central Register of Controlled Trials (CENTRAL) on the Cochrane Library Issue 3 2001, MEDLINE (2000 to September 2001) and EMBASE (1998 to September 2001),using an RCT filter for MEDLINE (Dickersin 1994) and EMBASE (Lefebvre 1996). See additional tables for details of search strategies (Table 1; Table 2; Table 3; Table 4).
Strategy used for searching The Cochrane LIbrary:
#1 CARDIOVASCULAR DISEASES
#2 CORONARY DISEASE

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#3 cardiovascular
#4 (coronary near disease*)
#5 (heart near disease*)
#6 HYPERTENSION
#7 hypertension
#8 (atherosclerosis or arteriosclerosis)
#9 (hyperlipidaemia or hyperlipidemia)
#10 ARTERIOSCLEROSIS
#11 CHOLESTEROL
#12 HYPERLIPIDEMIA
#13 cholesterol
#14 (multiple next risk next factor*)
#15 (coronary next risk next factor*)
#16 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10)
#17 (#11 or #12 or #13 or #14 or #15)
#18 (#16 or #17)
#19 HEALTH EDUCATION
#20 HEALTH PROMOTION
#21 HEALTH BEHAVIOR
#22 PRIMARY PREVENTION
#23 COUNSELING
#24 counsel*
#25 (health near educat*)
#26 (patient near educat*)
#27 (education* near program*)
#28 (health near promotion*)
#29 (health near behaviour*)
#30 (health near behavior*)
#31 (primary next prevention)
#32 ((multiple next risk) near intervention*)
#33 (multifactor* near intervention*)
#34 (multifactor* near prevention)
#35 ((risk next factor*) near reduc*)
#36 ((risk next factor*) near manag*)
#37 ((risk next factor*) near intervent*)
#38 (lifestyle near intervention*)
#39 (lifestyle near advice)
#40 (life-style near intervention*)
#41 (life-style near advice)
#42 (life-style near alter*)
#43 (lifestyle near alter*)
#44 (lifestyle near educat*)
#45 (life-style near educat*)
#46 (life-style near chang*)
#47 (lifestyle near chang*)
#48 (behavior* near chang*)
#49 (behaviour* near chang*)
#50 ((health next care) near advice)
#51 (healthcare near advice)
#52 nonpharmacologic*
#53 non-pharmacologic*
#54 (#19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29)
#55 (#30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39)
#56 (#40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53)
#57 ((#54 or #55 or #56)
#58 (#18 and #57)

Data collection and analysis

For the original search titles and abstracts obtained through searches were checked by two reviewers. Each paper thought to be of possible relevance was obtained and read by each reviewer independently to determine whether it fitted specified inclusion criteria. Disagreements were discussed and resolved between the two reviewers. The results of the updated search were checked by one reviewer to eliminate those studies that were definitely not relevant to the review. Remaining records were checked by two reviewers independently. All papers that were thought to be of relevance were obtained and read by two reviewers independently. Disagreements were resolved by discussion or by consultation with a third reviewer. The main aspect of quality that was formally assessed was the adequacy of concealment of randomisation as other aspects (e.g. blinding) are of less relevance in non-pharmacological interventions. In addition, comparability of baseline characteristics and completeness of follow up were assessed.

Independent data abstraction was performed and chief investigators were contacted to provide additional relevant information where necessary.

For continuous variables, net changes were compared (i.e. control group minus intervention group differences) at the longest duration of follow up available and the standardised mean difference were examined using random and fixed effects model. Categorical variables (mortality rates) were expressed as odds ratios and fixed effect models used except where there was significant heterogeneity of effects.

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Details of the studies included in the review are shown in the table of characteristics of included studies.

Risk of bias in included studies

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The quality of the trials examined deserves comment. Very few of the published reports provided sufficient detail to replicate the intervention used, and in several trials the intervention varied between sites and over time. It is likely that the quality of the intervention, in terms of intensity and frequency, person carrying out activities, and the theoretical framework of behavioural change used will determine the impact of intervention. Losses to follow up were a particular problem as changes in risk factors cannot be assessed in an intention to treat analysis. Validation of smoking outcomes using biochemical assay of cotinine was only used in one trial.

Random allocation methods were not usually reported in the smaller trials and specific enquiries were not made of investigators. In the large trials, it is unlikely that the allocation method was suspect. Blinding of intervention allocation is not possible in lifestyle interventions and this inevitably raises the possibility of bias. Outcomes were usually assessed with knowledge of treatment allocation and this too makes biased assessment of some outcomes possible. It seems unlikely that lack of blinding had any effect on clinical event outcomes, but it is possible that participants randomised to a control or usual care group might have been more likely to take health preventive activity as they may have felt they were missing potential benefits. Lack of blinding in assessment of smoking histories may have resulted in a reporting bias with those allocated to interventions more likely to say they had stopped smoking. Validation of self-reported smoking outcomes using biochemical assay of serum thiocyanate was reported in three trials.

Effects of interventions

Details of the studies included in the review are shown in Table 1. A total of 39 trials of multiple risk factor intervention were found comprising 44 distinct study groups. This is more than double the 18 trials identified for the original review. Ten trials reported total or coronary heart disease mortality as outcomes but none of these were additional to those in the original review. One trial from the original review, the Swedish RIS study, reported extended mortality follow up. Only four trials were sufficiently large to have adequate power to show meaningful changes in total or coronary heart disease mortality. More recent trials focussed on the outcomes: blood pressure, serum cholesterol, physical activity, diet, control of diabetes and weight loss. In the original review eleven studies reported smoking habit as an outcome. Among the newly identified trials only a further three reported an outcome relating to smoking cessation.

In more recent trials the quality of reporting was noticeably improved. It was noted in the original review that few early trials provided sufficient detail to replicate the intervention used and that several studies reported interventions that varied between sites and over time.

In general, the trials compared an intervention comprising some form of counselling and education with control groups, which either received nothing or usual care. The type of behavioural intervention used was seldom reported. In the few studies reporting the type of intervention a Stages of Change model (Diclemente 1991; Prochaska 1983) and a person centred and self directed psychological approach (Meichenbaum 1993) were described. In trials included in the review, education and counselling targeted combinations of diet, exercise, weight loss, smoking cessation, diabetes management and use of medication.

With the exception of one study comprising men and women aged 60-85 years (Applegate 1992), the oldest subjects included in the trials were 75 years of age. The majority of trials randomised only middle-aged adults and some included younger adults. One trial was not included in analyses (Connell 1995) as losses to follow up were extremely high.

Sixty seven trials identified as involving multiple risk factor interventions were excluded from consideration for the following reasons: no risk factor changes measured and/or reported (n=9), non-random or inadequate allocation to intervention and control groups (n=21), no specific multiple risk factor intervention (n=3), control group received substantial intervention (n=17), follow up to 6 months was not reported (n=6), the mean age of participants was less than 40 (n=5), a substantial proportion of participants had heart disease (n=3), numbers in groups were not reported (n= 1), or baseline or follow up data were not provided (n=2). A large number of studies were set up in what was then the Soviet Union but it appears that allocation to intervention and control groups was not random although attempts to trace the investigators have been unsuccessful.

The trials with clinical end-points comprise approximately 903,000 patient years of observation and those with risk factor end-points had 303,000 patient-years of observation. The oldest subjects included in any of the trials were less than 74 years of age, with the majority of trials randomising only middle-aged adults.

Total mortality and coronary heart disease mortality

Ten trials reported total and coronary heart disease mortality outcomes. For total mortality there was a pooled odds ratio of 0.96 (95% CI 0.92 to 1.01) favouring intervention. With regard to coronary heart disease mortality the odds ratio favouring intervention was 0.96 (95% CI 0.89 to 1.04). Funnel plots suggested little evidence of small study bias in trials with these outcomes (Figure 1; Figure 2). Only the Hypertension Detection and Follow-up Program, Johns Hopkins Hypertension Trial and Swedish RIS reported significant effects on total mortality (HDFP trial, Johns Hopkins, Swedish RIS). The Johns Hopkins Hypertension Trial also showed a significant benefit for coronary heart disease mortality.

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Figure 1.

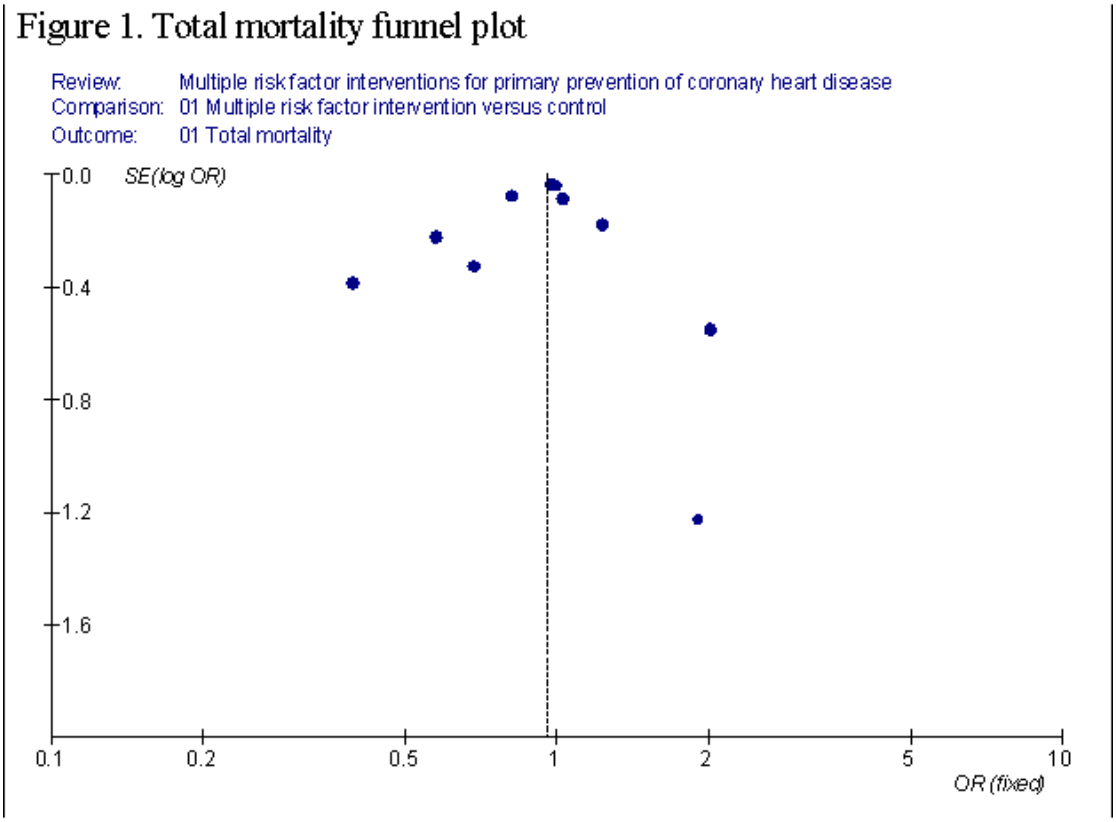

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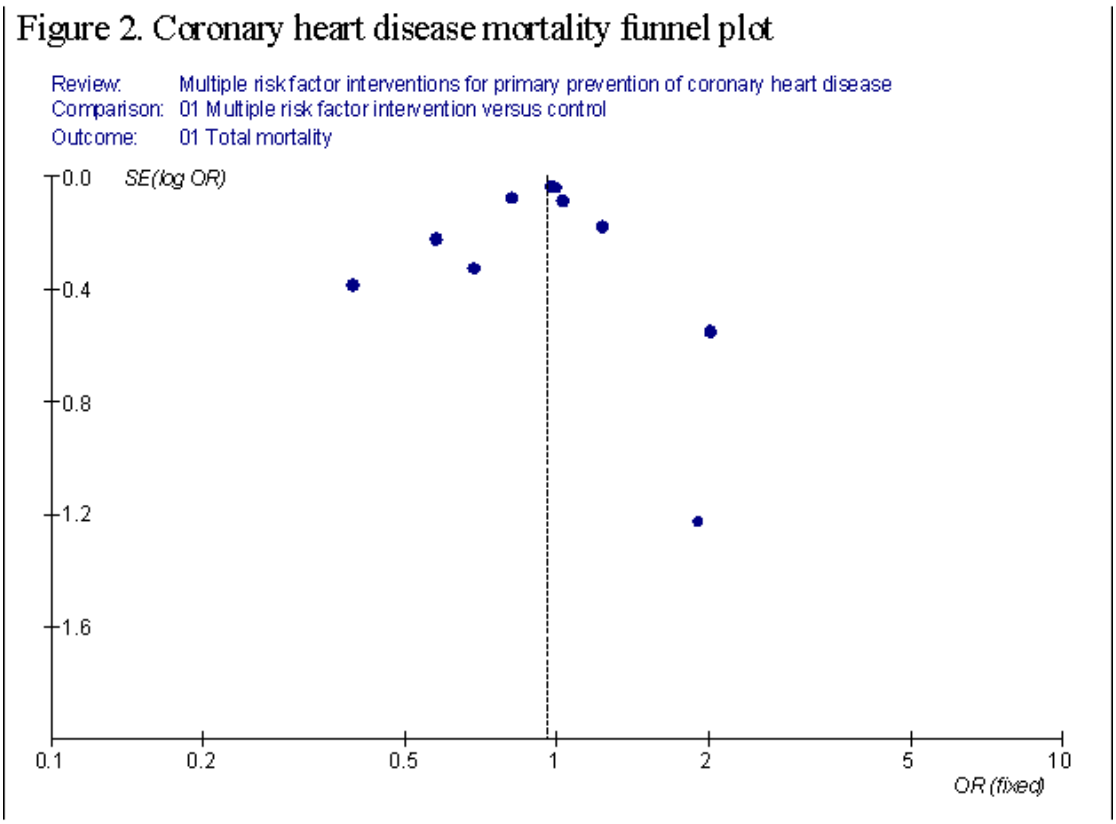
Figure 2.



Evidence of statistical heterogeneity was apparent in the pooled odds ratios for total mortality but not for coronary heart disease mortality when all studies were included. Removal of the trials including hypertensives (HDFP trial; Johns Hopkins) reduced the heterogeneity for total mortality. Including a term for interaction between treatment effect and baseline level of coronary heart disease risk calculated using either control group coronary heart disease risk or combined control and intervention group risk reduced heterogeneity between the trials to insignificant levels for total and coronary heart disease mortality.

Modelling the effects of age using the mean age of study participants and proportion of patients on antihypertensive treatment and cholesterol lowering drug treatment did not reveal any significant interactions between age, drug treatments and outcome. The significant interaction between intervention and level of coronary heart disease risk indicated that trials recruiting higher risk participants were more likely to demonstrate beneficial effects. This effect is explained by the inclusion of the two trials which studied hypertensive patients rather than general population or workforce subjects. It is impossible to separate this effect of baseline coronary heart disease risk from the benefits of pharmacological treatment of hypertension.

Non-fatal myocardial infarctions were reported in the WHO Factory Study, the Gothenberg Study and in the Oslo Study (WHO Factories; Gothenberg Study;The Oslo Study). The pooled odds ratio for non-fatal myocardial infarction in these three trials was 1.01 (95% CI 0.93 to 1.10).

Changes in risk factors

In all but five of the trials reporting systolic blood pressure as an outcome there was a tendency for reduced systolic blood pressure in intervention groups. Changes in blood pressure were small and slightly less in the updated compared with the original review. In 38 interventions reporting systolic blood pressure change, the weighted mean difference between intervention and control was -3.6 mm Hg (95% CI -3.9 to -3.3) in fixed effect analysis. For diastolic blood pressure the weighted mean difference was -2.8

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mm Hg (95% CI -2.9 to -2.6). For both outcomes there was no evidence of small study bias in the trials as shown by the funnel plots (Figure 3; Figure 4; Figure 5; Figure 6).

Figure 3.

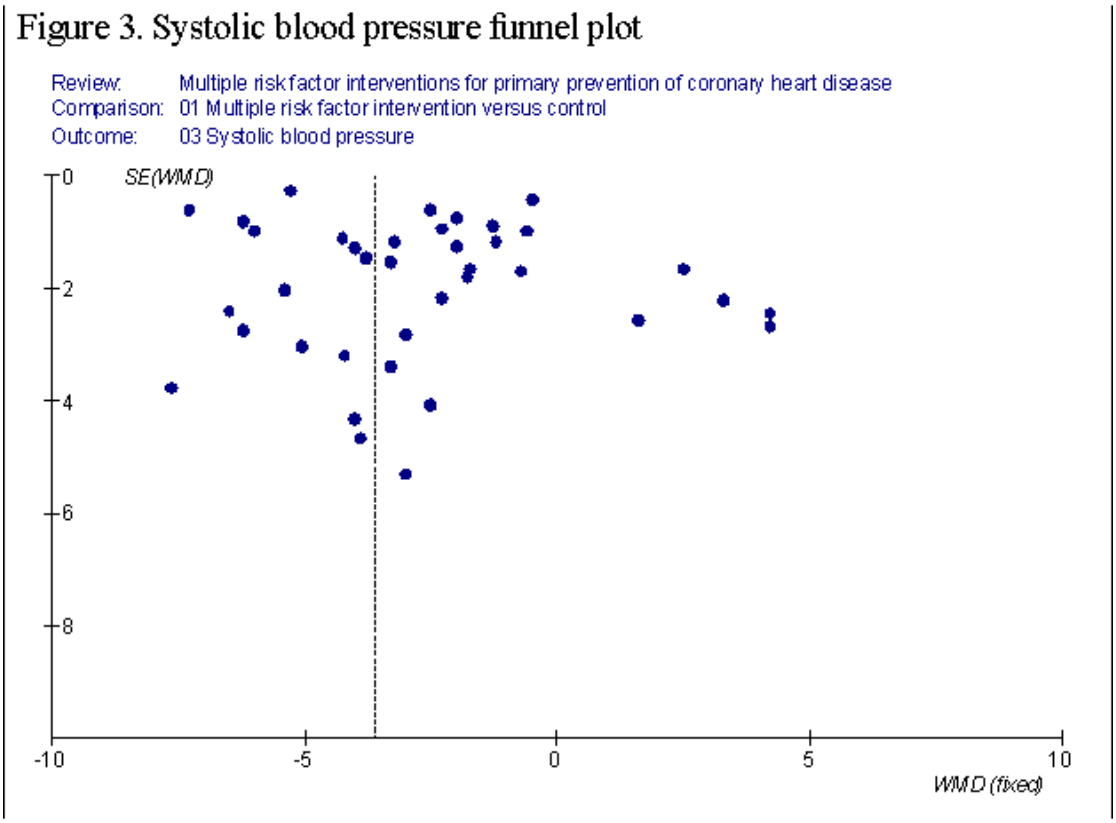

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Figure 4.

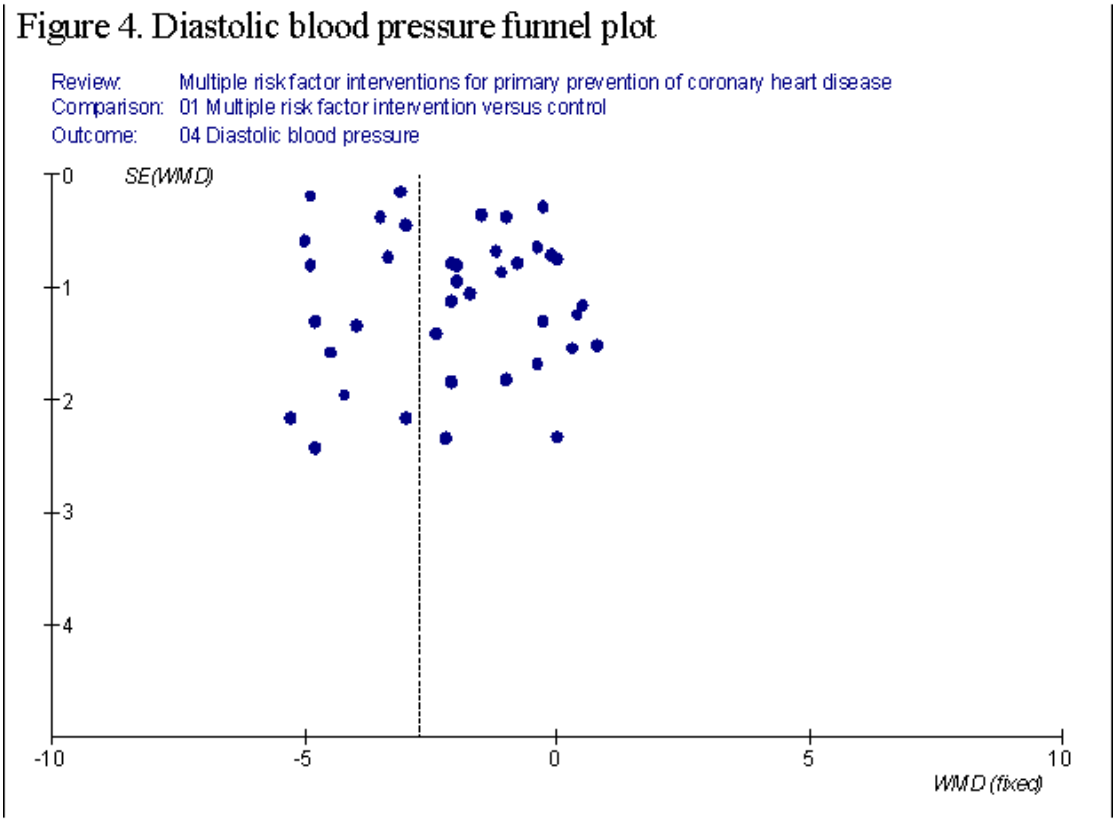

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Figure 5.

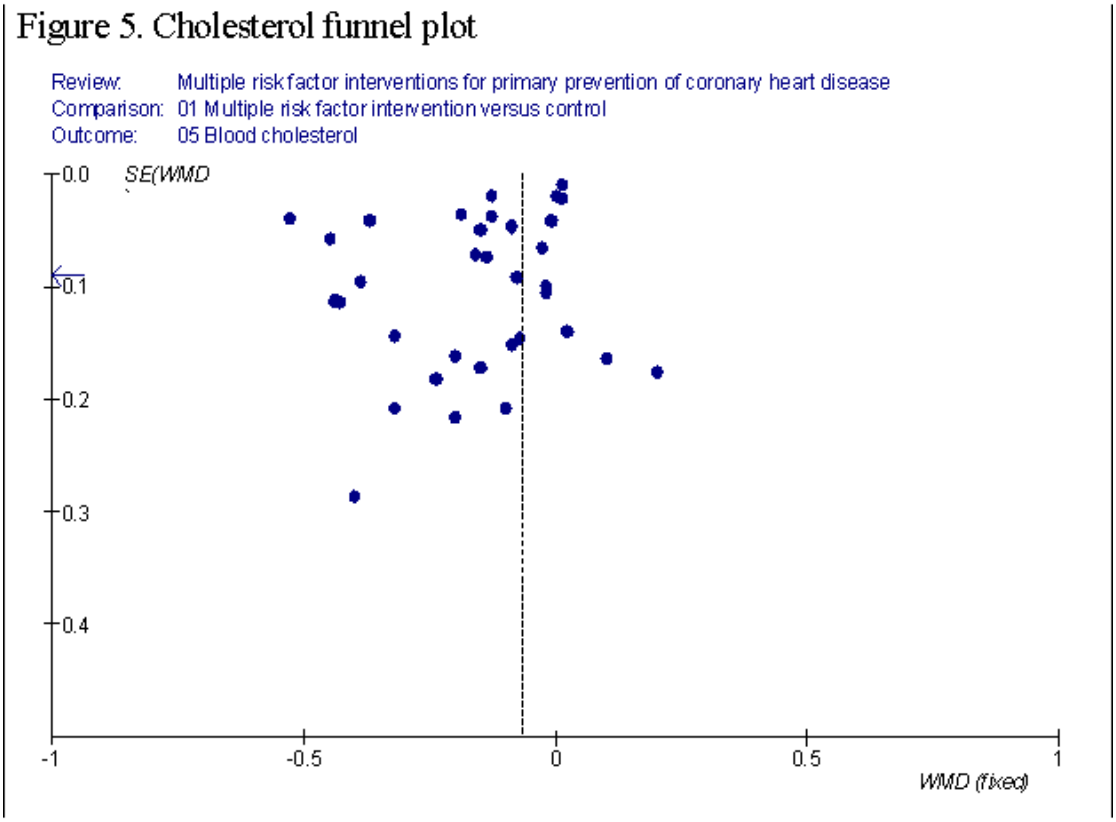

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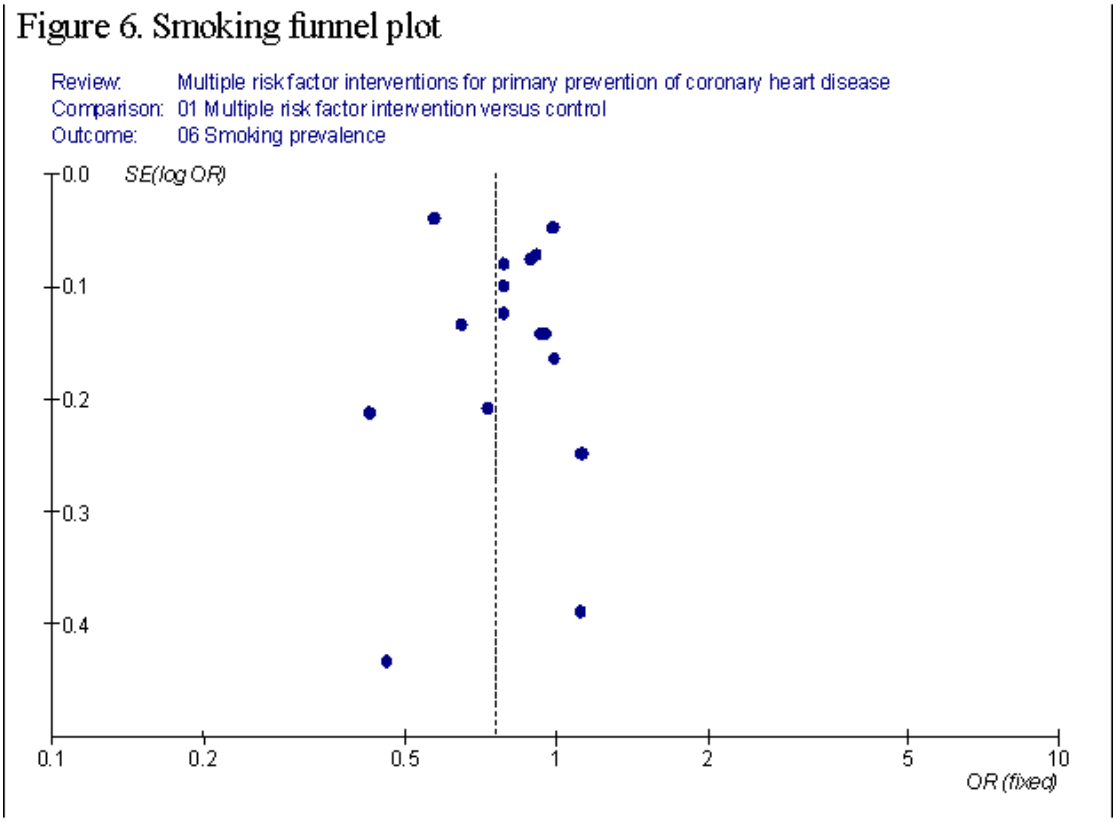
Figure 6.



The Multiple Risk Factor Intervention Trial, the Hypertension Detection and Follow Up Program, the WHO factories study, the Gothenburg study and the Finnish Businessmen study used antihypertensive drug therapy if indicated (Finnish men; Gothenberg Study; HDFP trial; MRFIT Study; WHO Factories). Exclusion of those trials in which a high proportion of participants were on pharmacological treatment (CELL Study; Gothenberg Study; Finnish men; HDFP trial; MRFIT Study; Perez-Stable prop) resulted in smaller, but still statistically significant, net reductions in blood pressure: systolic -2.7 mmHg (CI -3.9 to -3.3), diastolic -1.7 mmHg (CI -2.0 to -1.5).

Not all trials reported, or were able to provide data on, blood pressure at follow up. Investigators from the Oslo study stated that there were no changes observed (Hjerman I. personal communication, 1996).

Blood cholesterol

Blood cholesterol levels showed a small but highly significant fall (net difference -0.07 mmol/L, 95% CI -0.08 to -0.06 mmol/L). This was half the fall seen in the earlier review and may reflect more widespread use of cholesterol lowering medication in recent years. Substantial heterogeneity was apparent in this meta-analysis.

The Hypertension Detection & Follow-up Program reported no reduction in blood cholesterol levels but published quantitative data are not available (HDFP trial). The Finnish Businessmen Trial made substantial use of cholesterol lowering drugs (mainly probucol and clofibrate) which probably explains the larger reduction in blood cholesterol observed in this trial (Finnish men). In the FARIS trial there was a mean reduction in cholesterol of 3.0 mmol/L in men randomised to multifactorial intervention (FARIS men; FARIS women). This is probably a consequence of statin prescription being recommended after 3 months of intervention if cholesterol control was not adequate by lifestyle modification. Exclusion of these trials did not make a difference to the pooled fall observed.

Smoking

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Smoking prevalence showed an overall net reduction of 24%. Substantial heterogeneity was apparent and an odds reduction of 20% was observed in a random effects model. In the Hypertension Detection & Follow up Program quantitative data were not available but no changes in smoking rates were found (HDFP trial). Smoking rates fell particularly sharply in the Multiple Risk Factor Intervention Trial and in the Oslo Study which both used individual smoking advice given by a physician (MRFIT Study; The Oslo Study) and in the Change of Heart study where large baseline differences between groups were noted and losses to follow up were high (Change of Heart study). Validation of self-reported smoking rate reductions in the Multiple Risk Factor Intervention Trial by comparison with serum thiocyanate levels suggested that the improvement might be overestimated (MRFIT Study).

Heterogeneity of effects

Blood pressure, smoking, and blood cholesterol outcomes were subject to substantial heterogeneity. Random effects analyses were also conducted which showed similar pooled net effects but as the variation between trials is taken into account (which is large), confidence intervals were wider. The heterogeneity between trials is probably explained by differences in the use of both antihypertensive and cholesterol-lowering drugs, and the populations studied. Risk factor net changes were strongly correlated with the initial level of diastolic blood pressure, smoking and blood cholesterol but not systolic blood pressure. The sample size weighted correlation coefficients between initial level and magnitude of risk factor reduction for diastolic blood pressure, smoking and blood cholesterol were 0.73, p=0.006, 0.63, p=0.01 and 0.74, p=0.004 respectively. Those studies with the highest baseline diastolic blood pressure, smoking prevalence and blood cholesterol levels demonstrated larger intervention associated falls in these risk factors.

Cluster-randomisation

In meta-analysis the weighting given to trials with a cluster design may be over-estimated. In trials with cluster design analysed by individual or by cluster there was no evidence of overall benefit with regard to lowering of blood pressure or cholesterol. Benefits tended to be in trials with randomisation by individual.

DISCUSSION

Findings

As reported in the earlier review, multiple risk factor interventions comprising counselling, education and drug therapies were ineffective in achieving reductions in total or cardiovascular disease mortality when used in general or workforce populations of middle-aged adults. The pooled effects of intervention were statistically insignificant but a potentially useful benefit of treatment (about a 10% reduction in coronary heart disease mortality) may have been missed.

The risk factor changes associated with interventions were modest, but are probably optimistic estimates as changes could only be measured in those remaining in the trials. Habituation to blood pressure measurement, regression to the mean, and self-reports of smoking will also tend to exaggerate the changes observed. It is, however, not possible to separate participants' level of risk from the use of anti-hypertensives in the present set of trials, as studies with high-risk participants tended to be the ones which included participants with high levels of anti-hypertensive drug use. Furthermore, there are many problems in relating trial outcome to a risk measure which is itself dependent on the outcome in meta-analysis (Egger 1995). Therefore our conclusions on these issues can only be tentative.

Heterogeneity of intervention effects is apparent. This is probably caused by two factors: the participants included in the trials, and the use of pharmacological treatments. Hypertensives, at highest risk, were more likely to benefit from counselling and education, and effective drugs. These findings suggest that targeting of current health promotion activities to high risk individuals might be of more value than more general health promotion for everyone.

The interventions used

The benefits of drug treatments for lowering blood pressure and cholesterol are clear (Collins 1994; Davey Smith 1993; CTT 2005). However, those people at highest risk of disease in both hypertension control (Mulrow 1995) and cholesterol lowering (Davey Smith 1993) benefit most. Treatment of low risk populations may result in small treatment benefits being outweighed by small treatment risks (Davey Smith 1994) which may have occurred in both the Multiple Risk Factor Intervention Trial and the Finnish businessmen's trial (Finnish men; MRFIT Study). There were strong associations between baseline levels of risk factors and net falls experienced, suggesting that intervention may be more effective in populations with particularly adverse risk factor profiles.

More intensive interventions might be expected to produce better effects although those used in many of the trials would far exceed what is feasible in routine practice. A meta-analysis of dietary modifications found that increasing intensity of dietary intervention was associated with greater falls in blood cholesterol levels in high risk participants (Brunner 1997). In the Minnesota Heart Health Programme, a non-randomised community trial of intensive health promotion, both risk-factor and mortality changes showed virtually no difference between intervention and control communities (Luepker 1996). The continued enthusiasm for health promotion practices given the failure of these community intervention trials is curious, especially given the huge resources which have been put into them.

Latency of effects

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It is possible that benefits cannot be detected in the early stages but emerge over time. Longer term follow up of the Multiple Risk Factor Intervention Trial participants has demonstrated increased divergence between control and intervention group mortality rates (MRFITRG 1990) which has also been found in the Tromso Family Trial (Professor S. Knutson, personal communication). However, evidence from pharmacological trials suggests benefits from reduction of blood pressure and blood cholesterol are observed within two to four years (Collins 1994; Scandanavian 1994). The effects of giving up smoking vary depending on the clinical outcome considered: stroke risk falls rapidly after stopping (Wannamethee 1995), but coronary heart disease risk may be less reversible (Ben-Shlomo 1994; Cook 1986).

Evidence of benefit

The quasi-experimental North Karelia study has been very influential in supporting multiple risk factor intervention. Examination of the trends in both risk factors (Puska 1985; Vartiainen 1994) and coronary heart disease mortality (Valkonen 1992) observed in North Karelia and comparison regions show similar patterns occurring at the same time, suggesting that the interventions in North Karelia were not instrumental in causing the improvements observed (Ebrahim 2001). Indeed, the North Karelia and similar projects may be viewed as effects, or epiphenomena, of the very high coronary heart disease mortality rates experienced in many countries in the 1960s.

In secondary prevention following myocardial infarction and angina, trials of multiple and single risk factor interventions have suggested substantial benefits (Mullen 1992; Oldridge 1988; O'Connor 1989). It is probable that intervention aimed at lifestyle modification following myocardial infarction is effective because participants are much more likely to change their behaviours.

Limitations of randomised controlled trials

The interventions reviewed were essentially individual or family approaches. Randomised controlled trials impose limitations on the nature of interventions that may be tested and are of more value in examining high risk rather than population and social approaches to prevention (Rose 1992).

Policy implications

Health protection through national fiscal and legislative changes that aim to reduce smoking, dietary consumption of fats, "hidden" salt and calories, and increase facilities and opportunities for exercise should have a higher priority than health promotion interventions applied to general and workforce populations. It is essential that the current concepts and practices of multiple risk factor intervention, primarily through individual risk factor counselling, are not exported to poorer countries as the best policy option for dealing with existing and projected burdens of cardiovascular disease, as is currently happening (Pearson 1993). Health protection should be promoted as the mainstay of chronic disease prevention in poorer countries (Ebrahim 2001).

Implications for research

It is unlikely that any further large-scale multiple risk factor intervention trials will be mounted in high income countries in the future. It is also unlikely that uncontrolled or quasi-experimental study designs will produce more robust answers to questions of the effectiveness of multiple risk factor intervention by means of individual or family health information and advice.

Research on the effects and costs of health protection (i.e. fiscal and legislative approaches) and primary prevention would be of direct policy relevance, particularly in low and middle income countries.

Qualitative studies examining how participants perceived and responded to the advice and treatment given in these randomised controlled trials could be very helpful in shaping future interventions.

Our methods of attempting behaviour change in the general population are very limited. Different approaches to behaviour change are needed and should be tested empirically before being widely promoted. For example, the availability of foods and better access to recreational and sporting facilities may have a greater impact on dietary and exercise patterns respectively, than health professional advice. The effects of new approaches need to be examined in a wide range of people as it seems likely that the poor, socially excluded, specific ethnic groups and older people may all react in different ways.

AUTHORS' CONCLUSIONS

Implications for practice

The use of "health promotion" techniques of one-to-one or family orientated information and advice on a range of life-styles (exercise, smoking cessation, diet) given to people at relatively low risk of cardiovascular disease is not particularly effective in terms of reducing the risk of clinical events. The costs of such interventions are high and it seems likely that these resources and techniques may be better used in people at high risk of cardiovascular disease where evidence of effectiveness is much stronger.

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* *Indicates the major publication for the study*

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Aberg men

Methods	Primary care. Random allocation by health centre (centres paired according to size, number of doctors and personnel) . Unit of analysis was individual
Participants	Men and women on anti-hypertensive drugs aged 30-69 years N=159
Interventions	Group based video taped lifestyle counselling: Dietary change, stress management, increased physical activity. home blood pressure monitoring. Up to 8 group sessions.
Outcomes	No clinical event outcomes. Change in anti-hypertensive treatment, weight, hypertension, cholesterol, triglycerides, fasting glucose, life quality
Notes	All patients followed the same schedule for reduction and withdrawal of antihypertensive drugs. Concluded that intervention was effective in reducing hypertensive medication

Aberg women

Methods	Primary care. Random allocation by health centre (centres paired according to size, number of doctors and personnel) . Unit of analysis was individual
Participants	Men and women on anti-hypertensive drugs aged 30-69 years N=129
Interventions	Group based video taped lifestyle counselling: Dietary change, stress management, increased physical activity. home blood pressure monitoring. Up to 8 group sessions.
Outcomes	No clinical event outcomes. Change in anti-hypertensive treatment, weight, hypertension, cholesterol, triglycerides, fasting glucose, life quality
Notes	All patients followed the same schedule for reduction and withdrawal of antihypertensive drugs. Concluded that intervention was effective in reducing hypertensive medication

Abingdon

Methods	Primary care Random allocation by individual
Participants	Men and women, mean age 42 years (range 25-60) N=368

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Abingdon (*Continued*)

Interventions	Diet, weight control, smoking advice, exercise, alcohol advice carried out by nurse Duration 1 year
Outcomes	No clinical event outcomes Systolic blood pressure, diastolic blood pressure, blood cholesterol, smoking prevalence
Notes	Main focus was on dietary change, but despite self reported behaviour change, no changes in blood cholesterol found

Applegate 1992

Methods	Community screening and volunteers Randomisation by individual
Participants	Men and women aged 60-85 with mild diastolic hypertension and modestly overweight N=56
Interventions	Nutritionist supervised. Individual weight loss goals, exercise and diet self-monitoring with behavioural feedback. Duration 6 months
Outcomes	No clinical event outcomes. Weight, urinary sodium, systolic and diastolic blood pressure, waist-hip ratio, exercise
Notes	Reduction in weight and systolic blood pressure in those folowed up. Authors report good compliance with intervention. Authors conclusions: results indicate intervention will lower borderline or mild diastolic hypertension

Blumenthal 2000

Methods	Volunteers screened Randomisation by individual
Participants	Men and women aged 29+ with unmedicated high-normal blood pressure. Overweight and not performing regular aerobic exercise. N=79
Interventions	Exercise physiologist supervised exercise and behavioural intervention including diet. Duration 6 months
Outcomes	No clinical event outcomes Systolic and diastolic blood pressure, glucose tolerance, weight, exercise test
Notes	Another intervention group received only exercise intervention. Authors conclusions: Exercise alone reduced BP and the addition of behavioural weight loss programme enhanced this

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CELL Study

Methods	Primary care screening Randomisation of individuals in 2x3 factorial design
Participants	People with at least two risk factors in addition to moderately raised blood cholesterol Men and women, mean age 49 years (30-59) N=681
Interventions	Factor 1: Counselling on health problems and risk factor management, food purchasing, exercise vs. usual care Factor 2: Pravastatin vs. placebo vs control without drug Duration 1 year
Outcomes	Total mortality and CHD mortality Systolic blood pressure, diastolic blood pressure, blood cholesterol, smoking prevalence, exercise score
Notes	At one year counselling intervention main effects showed lower blood cholesterol and lower Framingham risk factor scores compared with groups not receiving counselling intervention. No significant differences in blood pressures, smoking prevalence, or exercise score

Change of Heart

Methods	General practice, cluster allocation by minimisation to balance for social deprivation, practice nurse hours and fundholding status. 20 practices. Unit of analysis was general practice
Participants	Men and women mean age 47 years with one or more cardiovascular risk factors. No treatment. N=883
Interventions	Nurse led stages of change behavioural counselling on smoking, diet, physical activity. 2 or 3 20 minute counselling sessions + telephone contact
Outcomes	No clinical event outcomes. Diet, exercise, smoking habits, blood pressure, cholesterol, weight, BMI Follow up 4 and 12 months
Notes	Based on stages of change model. Less smokers at baseline in intervention group (39%) than control (49%) Problems with recruitment and dropout - more recruited to intervention than control group - 59% of patients followed up at 12 months. Those at higher risk received more intensive treatment

Connell 1995

Methods	Worksite volunteers Randomisation by worksite. Unit of analysis was individual
Participants	Men and women age 19-67 N=1432
Interventions	Health risk assessment and individual health counselling Educational classes and self-help material Duration 1 year

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Outcomes	Total cholesterol, systolic and diastolic blood pressure, BMI, exercise frequency One year follow up
Notes	Large loss to follow up

Family Heart - men

Methods	Primary care Random allocation of households to intervention and control groups
Participants	Primary care screening, mean age 50 (40-59) N=3941
Interventions	Intensity of intervention depended on individual's level of risk. Nurse counselling on diet, weight, smoking, exercise, alcohol Duration 1 year
Outcomes	No clinical event outcomes Systolic blood pressure, diastolic blood pressure, blood cholesterol, smoking prevalence
Notes	Two control groups used: internal to study used for comparisons in this review. Drop outs were more likely to have high CVD risk factor levels. Overall predicted risk reduction of 12% achieved but thought to be too costly in practice - no cost-effectiveness analysis conducted however

Family Heart - women

Methods	Primary care Random allocation of households to intervention and control groups
Participants	Primary care: women age 50 (40-59) N=2619
Interventions	Intensity of intervention depended on level of individual's risk Nurse counselling on diet, weight control, smoking advice, exercise, alcohol Duration 1 year
Outcomes	No clinical event outcomes Systolic blood pressure, diastolic blood pressure, blood cholesterol, smoking prevalence
Notes	Two control groups used but internal control used in this review

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FARIS men

Methods	First degree relatives of AMI, CABG and PTCA patients Randomised by family.
Participants	Families of people with CHD event, age 18-69, N=442
Interventions	Individualised risk factor advice. 3 months dietary advice and lipid lowering medication if required
Outcomes	No clinical event outcomes Systolic blood pressure diastolic blood pressure, cholesterol, smoking, BMI and CVD risk
Notes	Results are for people without cardiovascular disease attending combined primary and secondary prevention clinic. Information on baseline and follow up smoking prevalence not available. No significant effect of intervention on smoking quit rate

FARIS women

Methods	First degree relatives of AMI, CABG and PTCA patients Randomised by family.
Participants	Families of people with CHD event, age 18-69, N=658
Interventions	Individualised risk factor advice. 3 months dietary advice and lipid lowering medication if required
Outcomes	No clinical event outcomes Systolic blood pressure diastolic blood pressure, cholesterol, smoking, BMI and CVD risk
Notes	Results are for people without cardiovascular disease attending combined primary and secondary prevention clinic. Information on baseline and follow up smoking prevalence not available. No significant effect of intervention on smoking quit rate

Finnish DPS

Methods	High risk groups identified from epidemiological surveys, opportunistic screening, volunteers. Randomisation by individual, stratified by sex, centre and OGTT result
Participants	Overweight or with family history of type 2 diabetes men and women aged 40-64 years with impaired glucose tolerance N=523
Interventions	Nutritionist delivered individual and group dietary advice. Weight goal established with physician and nutritionist and reguar assessment. Supervised exercise. Each person had 7 sessions in the first year and one session every 3 months subsequently

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Finnish DPS (*Continued*)

Outcomes	No clinical events outcomes. Development of diabetes, weight, diet, exercise, waist circumference, glucose, insulin, cholesterol, HDL, triglycerides, systolic and diastolic blood pressure. Follow up reported end of year 1
Notes	Study planned for 6 years, recruited 1993 to 1998. In March 2000 study stopped on basis of results regarding reduction in incidence in diabetes in treatment group

Finnish men

Methods	Volunteers recruited Randomisation by individual
Participants	Men only, mean age 48 years (40-58) High risk N = 1222
Interventions	Diet, smoking, exercise, antihypertensive drugs, cholesterol lowering drugs Duration 5 years
Outcomes	Total mortality, CHD mortality Systolic blood pressure, diastolic blood pressure, blood cholesterol, smoking prevalence
Notes	Large reductions in blood pressure and blood cholesterol achieved largely through drug treatments, reductions in smoking prevalence. Control group risk factors increased. CHD event rates higher in intervention group but stroke rates significantly lower. Concluded that adverse effects of drug treatment may explain lack of benefit

Given 1984

Methods	Primary care Selection of hypertensives by screening Randomisation of individuals
Participants	Men and women with hypertension on a prescribed regimen of diet or medication, mean age 47 years (18-65) N=86
Interventions	Educational handbook on risk, impact and benefits of controlling hypertension. Individual problem solving sessions on medication, diet and exercise. Duration 6 months
Outcomes	Systolic and diastolic blood pressure, weight, patient beliefs, symptom severity
Notes	Authors note reduction in diastolic blood pressure. Intervention affected patient beliefs

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Gothenberg Study

Methods	Population based Selection of high risk people by screening Randomisation of individuals
Participants	Men only, mean age 51 years (47-55) N=30,022
Interventions	Diet, smoking, antihypertensive drugs, cholesterol lowering drugs Duration 11.8 years
Outcomes	Total mortality, coronary heart disease mortality Systolic blood pressure, diastolic blood pressure, blood cholesterol, smoking prevalence
Notes	Large falls in risk factors occurred in both intervention and control groups. Concluded that other strategies in high risk men are required to have a major impact on incidence of disease in the general population

HDFP trial

Methods	Population screening Randomisation of individuals
Participants	Men and women, all hypertensives, age range 30-69 years N=10,940
Interventions	Stepped care: Antihypertensive drugs, diet, smoking advice, weight control, exercise vs. Referred care: usual primary care Duration 5 years
Outcomes	Total mortality, CHD mortality, Stroke mortality Non-fatal CHD and stroke events Diastolic blood pressure
Notes	No reductions in smoking prevalence of blood cholesterol (data not published) but significant reductions in blood pressure. Total mortality, CHD and stroke mortality significantly lower in intervention group. Benefits attributed to treatment of high blood pressure and sustained over prolonged follow up

Hellenius

Methods	Randomization of individuals in a 2x2 factorial design
Participants	Men only, mean age 46 years (35-60) Moderately raised CVD risk factors - already involved in a primary prevention programme N=158
Interventions	Diet and exercise advised Duration 6 months

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Hellenius (*Continued*)

Outcomes	No clinical event outcomes Systolic blood pressure, diastolic blood pressure, blood cholesterol Data also given on BMI, Waist/Hip ratio, HDL/LDL/VLDL cholesterol, tryglycerides, dietary intake, physical activity
Notes	Only data from control group (N=39) and diet and exercise group (N=39) used in this review

Iso

Methods	Community screening. Randomisation by individual using permuted block method, stratified by blood pressure
Participants	Untreated hypertensive men and women age 35-69 years N=111
Interventions	Physician, public health nurse and nutritionist led education, counselling and practical sessions. Individual goals for sodium intake, weight control, walking and alcohol intake. Duration 18 months
Outcomes	No clinical event outcomes. Urinary sodium and potassium, sodium reduction behaviours, alchohol intake, calcium intake, BMI, systolic and diastolic blood pressure
Notes	Intervention associated with reduced systolic blood pressure, reduction in sodium excretion, alcohol consumption. No change in BMI, diastoilc blood pressure. Greater use of anti-hypertensive medication in control group

Jalkanen 1991

Methods	Patients from hypertension clinic Randomisation of individuals
Participants	Men and women, mean age 49 years (range 35-59) With hypertension and overweight N=50
Interventions	Individually planned diet (1000-1500kcal per day) Advice on exercise and weight reduction, weekly meetings for 6 months then 3 weekly. Duration 12 months
Outcomes	No clinical events outcomes. Systolic and diastolic blood pressure, blood cholesterol, weight, food intake, urinary sodium and potassium
Notes	Intervention led to reduction in weight

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Johns Hopkins

Methods	Clinic attenders Randomisation by individual to a complex factorial design with 8 groups
Participants	Men and women, all hypertensives, mean age 54.1 years N=400
Interventions	Antihypertensive drugs, weight control, general health advice vs. no extra educational interventions Duration 5 years
Outcomes	Total and CHD mortality
Notes	Better control of blood pressure (but values not reported), weight and better adherence with treatment and appointments in intervention group. Concluded that educational programmes for hypertensive patients were beneficial

Lin 1996

Methods	Primary care screening 4 villages randomly assigned. Unit of analysis was individual
Participants	Men and women aged 40+ (mean 60) N=1102
Interventions	Home visits by public health nurse students aimed at weight reduction, physical activity, compliance with medication. Trained volunteers and community leaders involved. Education classes and speeches. Duration 6 months
Outcomes	No clinical events outcomes. Blood pressure, behavioural changes
Notes	Hypertensives received more intensive intervention

Lindahl 1999

Methods	Participants in health survey screened for abnormal glucose tolerance
Participants	Men and women with abnormal glucose tolerance and high BMI mean age 55 N=301
Interventions	One month stay in full-board wellness centre. Scheduled aerobic physical activity, stress management, diet modification, smoking cessation encouraged
Outcomes	No clinical events outcomes. Systolic and diastolic blood pressure, cholesterol, fibrinolysis, BMI, physical fitness, Follow up of 12 months
Notes	Not all participants were followed up Intense programme compared with usual care group

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Meland 1997

Methods	Primary care opportunistic screening. Randomisation by general practice (N=22). Unit of analysis was individual
Participants	Men aged 30-59 at high risk for CVD by infarction score N=127
Interventions	Counselling on health promotion and behaviour change. Self help and self monitoring. Duration 1 year
Outcomes	No clinical event outcome. Systolic and diastolic blood pressure, weight, resting pulse, cholesterol, lipid profile, smoking habit, thiocyanate, C-peptide
Notes	Kanfer and Gaelick (1986), and Meichenbaum (1986), person centred and self directed psychological approach. Self efficacy was related to exercise change

MRFIT Study

Methods	Worksite, population and volunteer screening Randomisation by individual
Participants	Men only, mean age 46 years (35-47) N=12,866
Interventions	Diet, smoking, weight, antihypertensive drugs Duration 6 years
Outcomes	Total mortality, coronary heart disease mortality Systolic blood pressure, diastolic blood pressure, blood cholesterol, smoking prevalence
Notes	Small reductions in blood cholesterol concentration. Large reductions in blood pressure and smoking rates. No significant reduction in disease events. Concluded that possibly effective in sub-groups but no net benefit because of potentially harmful effects of antihypertensive drugs used. Small benefits emerging after prolonged follow up

Nilsson 1992

Methods	Randomisation of hyperinsulinaemics by individual within cross-sectional study of treated hypertensives and normotensive controls
Participants	Men and women, mean age 56.1 years with hyperinsulinaemia but not diabetic N=59
Interventions	Group education and individual counselling on diet and physical activity by nurse, dieticianand physiotherapist. Duration 1 year
Outcomes	Systolic and diastolic blood pressure, blood cholesterol, LDL/HDL cholesterol ratio, weight, waist hip ratio, blood glucose, insulin, c-peptide, urate, glucose tolerance

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Nilsson 1992 (*Continued*)

Notes	63 randomised Intervention group had reduced weight, waist hip ratio, blood pressure and LDL/HDL ratio. Also dietary improvements. Controls informed of hyperinsulinaemic status

Nilsson 2001

Methods	Worksite screening Randomisation by individual
Participants	Men and women, mean age 50 years (range 28-65) N=89
Interventions	Multidisciplinary education and counselling. Weight reduction in obese, diet, physical activity, stress management, smoking cessation Duration 18 months
Outcomes	Risk scores, BMI, waist hip ratio, sick days, sedentary behaviour, heart rate, smoking, CHD risk factors, glucose, insulin, liver function, cortisol, dehydroepiandrosterone (DHEA)
Notes	128 randomised (Intervention group: 5 did not attend baseline, 16 dropouts or excluded for medical reasons at 12 months, 1 lost to followup at 18 month; control group corresponding figures 10, 5, 2 respectively)

Oldroyd

Methods	People with impaired glucose tolerance identified in research studies, hospital databases and by GPs. Randomisation by individual
Participants	Men and women aged 24-75 years with impaired glucose tolerance identified in 2 OGTT N=78
Interventions	Dietician and physiotherapist counselling on diet and physical activity. Targets set by Stages of Change. Duration 6 months
Outcomes	No clinical event outcomes. Diet, aerobic physical activity, glucose tolerance, insulin sensitivity, blood pressure, cholesterol, weight, BMI, waist hip ratio
Notes	Intervention group showed increased physical activity, decreased fat consumption but no change in glucose tolerance

Oslo Diet Exercise

Methods	Open, randomized 2x2 factorial design
Participants	Men and women, mean age 40 years N=219

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Oslo Diet Exercise (*Continued*)

Interventions	Diet advice and supervised endurance exercise programme Duration 1 year
Outcomes	No clinical event outcomes reported Systolic blood pressure, diastolic blood pressure, blood cholesterol Also measured haemostatic factors, BMI, body weight, waist hip ratio, aerobic capacity, thiocyanate, triglycerides, HDL/LDL cholesterol
Notes	Comparison used in this review is between the control group (N=43) and the diet+exercise group(N=65). Diet only and exercise only groups were not considered as single interventions

OXCHECK Study

Methods	Primary care practices in urban area Randomisation by household
Participants	Men and women, mean age 49 years (35-64) No risk screening N=11,090
Interventions	Diet, smoking advice, weight control, alcohol advice, exercise, protocols for management of high blood pressure and raised blood cholesterol vs. usual care. Duration 3 years
Outcomes	Total mortality and CHD mortality Systolic blood pressure, diastolic blood pressure, blood cholesterol, smoking prevalence, BMI
Notes	Changes in diet and small changes in blood cholesterol, blood pressure and body mass index. No effect on smoking prevalence. Concluded that primary prevention programmes were able to achieve benefits which were real but must be weighted against the costs in relation to other priorities. Study was not designed to examine mortality effects but those randomised to health checks in years 1 to 3 were considered to be intervention group and those randomised to checks in year 4 were the control group. Deaths up to year 4 were compared

Perez-Stable no prop

Methods	Volunteers screened Randomised by individual stratified for sex, diastolic blood pressure and weight
Participants	Men and women aged 18-59 Mild hypertension N=156
Interventions	Nutritionist, health educator, behavioural psychologist, general internist supervised Aerobic exercise, diet, relaxation 8 weekly meetings, subsequent meeting at 3 months

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Perez-Stable no prop (*Continued*)

Outcomes	No clinical event outcomes Systolic and diastolic blood pressure, cholesterol, physical activity, self-reported adverse effects dietary intake, weight, 24 hour uring (sodium, potassium) Follow up at 1 year
Notes	Four treatment arms other two had propanolol. Intervention did not promote persistent behaviour change.

Perez-Stable prop

Methods	Volunteers screened Randomised by individual stratified for sex, diastolic blood pressure and weight
Participants	Men and women aged 18-59 Mild hypertension on propanolol N=156
Interventions	Nutritionist, health educator, behavioural psychologist, general internist supervised Aerobic exercise, diet, relaxation. 8 weekly meetings, subsequent meeting at 3 months
Outcomes	No clinical event outcomes Systolic and diastolic blood pressure, cholesterol, physical activity, self-reported adverse effects, dietary intake, weight, 24 hour uring (sodium, potassium) Follow up at 1 year
Notes	Four treatment arms - other two did not have propanolol. Intervention did not promote persistent behaviour change.

Stamler 1989

Methods	Worksite screening. Randomisation of individuals
Participants	Volunteers from worksites, raised body weight, high pulse rate and DBP 80-89mmHg Men and women, mean age 37.5 (30-44) N=201
Interventions	Diet, weight control, exercise, alcohol Duration 5 years
Outcomes	No clinical event outcomes Systolic BP, diastolic BP
Notes	Small but significant reduction in blood pressure; other risk factors not reported. Volunteers who were thought unlikely to comply with intervention (eg. heavy drinkers, very obese) were excluded from the trial

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Stefanick men

Methods	Volunteers screened for HDL and LDL cholesterol Randomisation by individual
Participants	Men aged 30-64, HDL <45mg/dl, LDL 126-189mg/dl 126-209mg/dl N=98
Interventions	Individual diet counselling and group education. Weight loss groups. Supervised and home-based exercise. Duration 1 year
Outcomes	No clinical event outcomes. Diet assessment, body weight, exercise tests, CHD risk factors
Notes	Concluded that diet and aerobic exercise was effective in reducing LDL cholesterol

Stefanick women

Methods	Volunteers screened for HDL and LDL cholesterol Randomisation by individual
Participants	Post-menopausal women aged 45-64, HDL <60mg/dl, LDL N=89
Interventions	Individual diet counselling and group education. Weight loss groups. Supervised and home-based exercise. Duration 1 year
Outcomes	No clinical event outcomes. Diet assessment, body weight, exercise tests, CHD risk factors
Notes	Concluded that diet and aerobic exercise was effective in reducing LDL cholesterol

Swedish RIS

Methods	Clinic attending hypertensives Randomisation by individual after stratification by serum cholesterol, smoking habit and target organ damage
Participants	All men, age 50-72 years N=508
Interventions	Smoking advice + nicotine gum, dietary habits, weight control, spouse involved. Lipid lowering drugs used in needed. vs. usual care. All patients on antihypertensive medication Duration 6 years
Outcomes	Total mortality, CHD and stroke mortality Non-fatal myocardial infarction, stroke, new onsets of claudication and angina Systolic blood pressure, diastolic blood pressure, blood cholesterol, (HDL, LDL), smoking prevalence, body weight, BMI, blood glucose, heart rate, gGT, HbA1c

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Swedish RIS (*Continued*)

Notes	Significant reductions in blood cholesterol and smoking were achieved. No changes in diastolic blood pressure and HbA1c. Stroke incidence reduced in intervention group

Take Heart

Methods	Workplace screening. Matched pairs of worksites randomised. Unit of analysis was worksite
Participants	Men and women mean age 40 (17-73). N=1977
Interventions	Stage of change model used; motivational, educational, workplace environment and community reinforcement; focus on smoking and food choices. Duration 18 months
Outcomes	Smoking, blood cholesterol, dietary intake.
Notes	Despite documented implementation of interventions no evidence that changes in smoking, cholesterol concentration of dietary intakes were greater than improvements associated with secular trends observed in control sites. Large variation in rates of stopping smoking between sites suggested variable use and uptake of interventions

The Oslo Study

Methods	Population screening. Selected for raised blood cholesterol. Randomisation by individual.
Participants	Men only, mean age 45.2 (40-49). N=1232
Interventions	Diet and smoking Duration 5 years
Outcomes	Total mortality, CHD mortality, smoking prevalence, blood cholesterol
Notes	Reduction in smoking rates and blood cholesterol. Significant reduction in cardiovascular disease events. Concluded that advice to stop smoking and change eating habits reduces first myocardial infarctions and sudden deaths

Tromso men

Methods	Randomisation of individuals at high risk detected by primary care screening
Participants	Men and women, age 30-45 years N=1373
Interventions	Physician and dietician counselling of family, diet, smoking advice, exercise Duration 6 years

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Tromso men (*Continued*)

Outcomes	No clinical event outcomes Systolic blood pressure, diastolic blood pressure, blood cholesterol, smoking prevalence
Notes	Participants showed little interest in group meetings. Small significant reductions in blood cholesterol but no effects on smoking or blood pressure. Mortality and clinical event follow up is proceding in the trial and lead author has not yet published data

Tromso wives

Methods	Wives of the men randomised in the Tromso trial are considered to be a seperate trial. Randomisation therefore by husband
Participants	Women aged 30-45 N=809
Interventions	Physician and dietician counselling on diet, smoking, exercise Duration 6 years
Outcomes	No clinical event data Systolic blood pressure, diastolic blood pressure, blood cholesterol, smoking prevalence
Notes	Mortality data may be available in the future

Uusitupa

Methods	Diabetes clinic. Randomisation by individual
Participants	Newly diagnosed NIDDM, men and women aged 40-64 years N=86
Interventions	Education on weight reduction, diet, physical activity. Goals and regular monitoring. Duration 12 months
Outcomes	No clinical event data. Weight reduction, normoglycaemia, correction of dislipidaemias, blood pressure
Notes	Intervention and control received 3 months basic diabetes education before randomisation

WHLP

Methods	Volunteers recruited. Randomisation of individuals
Participants	Women aged 44-50 N=535
Interventions	Cognitive- behavioural programme with intensive group and individual guidance on diet, exercise and prevention of weight gain. Duration 4.5 years

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WHLP (*Continued*)

Outcomes	No clinical event outcomes Systolic blood pressure, diastolic blood pressure, blood LDL and HDL cholesterol
Notes	One accidental death. Participants were receptive to preventive approach and were successful in making initial lifestyle changes

WHO Factories

Methods	Worksites in Belgium, Italy, Poland, Spain, UK; randomisation by factory. Unit of analysis was factory
Participants	Men only, mean age 48.5 (40-59) N=63,732
Interventions	Diet, smoking, weight, exercise, antihypertensive drugs, mass media Control factories had usual occupational health service Duration 6 years
Outcomes	Mortality: cause specific blood pressure, blood cholesterol, smoking rates
Notes	Only small reductions in risk factors found. Spanish arm not included in event ascertainment. Belgium arm showed significant reduction in mortality and was written up seperately. Concluded that advice on risk factor reduction is effective to the extent that it is taken up and seems to be safe

Wing

Methods	Volunteers Randomisation by individual
Participants	Overweight men and women aged 40-55. Non diabetic but with 1 or 2 parents with type 2 diabetes. N=80
Interventions	Multidisciplinary led behavioural strategies. Group and individual education. Low calorie, low fat diet. Supervised walking and other activities. Duration 2 years
Outcomes	No clinical events outcomes. Eating and exercise behaviours, weight, incidence of diabetes, systolic blood pressure, diastolic blood pressure, cholesterol
Notes	

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Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Andersen 1999	Both groups received an intervention
Basler 1985	Non-random allocation
Blake 1987	No risk factor change measured or reported
Bruno 1983	Six month data not available
Burke 1999	Participants were younger adults
Cambien 1981	Participants were younger adults
Carlberg 1992	No risk factor data measured or reported
Crouch 1986	Control group received some elements of intervention
Da Qing 1997	No risk factor changes reported
Domarkene 1990	Non-random allocation
DPP 1999	Control group received some elements of intervention
Dunn 1997	Both groups recevied an exercise only intervention
Edye 1989	Non-random allocation
Fielding 1994	Control group received some elements of intervention
Fox 1996	Non-random allocation
Frommer 1990	Inadequate randomisation
Fuchs 1993	Both groups received an intervention
Fullard 1987	Non-random allocation
Gemson 1990	Control group received some elements of intervention
Gemson 1995	Control group received some elements of intervention
German 1994	Control group received some elements of intervention
Gomel 1993	Inadequate randomisation

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(*Continued*)

Gordon 1997	Control group received some elements of intervention
Hanlon 1995	Six month data not available
Haskell 1988	Secondary prevention
Hedberg 1998	Non-randomised allocation
Jula 1990	Inadequate randomisation
Kawakami 1999	Participants were younger adults
Ketola 2001	Mixed primary and secondary prevention
Knappe 1982	Inadequate randomisation
Kreuter 1996	Outcome is contemplation of quitting smoking
Lasater 1986	No risk factor changes measured or reported
Lauritzen 1995	Health screening only
Leighton 1990	Control group received some elements of intervention
Lindahl 1998	Uncontrolled study
Lovibond 1986	Control group received some elements of intervention
Macdonald 1990	RCT assessing simvastatin
Martinez-A 1990	No risk factor changes measured or reported
McCance 1985	Two month follow up
McCann 1997	Control group received some element of the intervention
Meimanaliev 1991	Non-random allocation
Miemanaliev 1993	Non-random allocation
Murray 1986	No control group baseline data available
Nikitin 1991	Non-random allocation
Nisbeth 2000	Participants were younger adults
Nolte 1997	Two month follow up

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(*Continued*)

Ostwald 1989	Control group received some element of the intervention
Patterson 1988	No risk factor changes measured or reported
Persson 1996	No 6 month follow up data available. After 6 months pharmacological treatment was provided to intervention group patients (67% on lipid-lowering drugs and 13% on antihypertensives at 1 year)
Pierce 1984	No risk factor change measured or reported
Reid 1995	Control group received some element of the intervention
Robson 1989	No risk factor changes measured or reported
Rosamond 2000	Non-random allocation
Rowland 1994	Non-random allocation
S-E London 1977	Intervention not characterised
Schwandt 1999	Children and families
Smith 1991	Non-random allocation
Steinbach 1982	Non-random allocation
TOMHS 1991	All participants received intervention
TONE 1998	Three month blood pressure follow up
Tsuyuki 1999	Secondary prevention
Velonakis 1999	Non-random allocation
Volozh 1991	Non-random allocation
WHP	Numbers in intervention and control group not reported
Wisewoman 1999	Control group received some element of the intervention
Working Well Trial	Baseline data only, no follow up
Wu 1999	Non-random allocation

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DATA AND ANALYSES

Comparison 1. Multiple risk factor intervention versus control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total mortality	9	125167	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.96 [0.92, 1.01]
2 Coronary heart disease mortality	9	125167	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.96 [0.89, 1.04]
3 Systolic blood pressure	38	53872	Mean Difference (IV, Fixed, 95% CI)	-3.62 [-3.93, -3.31]
4 Diastolic blood pressure	39	64859	Mean Difference (IV, Fixed, 95% CI)	-2.76 [-2.93, -2.59]
5 Blood cholesterol	35	66106	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.08, -0.06]
6 Smoking prevalence	15	48948	Odds Ratio (M-H, Random, 95% CI)	0.81 [0.70, 0.94]
7 Systolic blood pressure (individual analysis or cluster)	38	53872	Mean Difference (IV, Random, 95% CI)	-2.68 [-3.64, -1.72]
7.1 Cluster randomisation - analysis by cluster	2	19355	Mean Difference (IV, Random, 95% CI)	0.56 [-2.26, 3.38]
7.2 Individual randomisation	32	33157	Mean Difference (IV, Random, 95% CI)	-3.24 [-4.16, -2.31]
7.3 Cluster randomisation - analysis by individual	4	1360	Mean Difference (IV, Random, 95% CI)	0.03 [-3.28, 3.34]
8 Diastolic blood pressure (individual analysis or cluster)	39	65362	Mean Difference (IV, Random, 95% CI)	-2.01 [-2.63, -1.39]
8.1 Cluster randomisation - analysis by cluster	2	19348	Mean Difference (IV, Random, 95% CI)	-0.27 [-0.81, 0.27]
8.2 Individual randomisation	34	44619	Mean Difference (IV, Random, 95% CI)	-2.33 [-2.94, -1.72]
8.3 Cluster randomisation - analysis by individual	4	1395	Mean Difference (IV, Random, 95% CI)	-0.00 [-1.07, 1.07]
9 Cholesterol (individual analysis or cluster)	35	66106	Mean Difference (IV, Random, 95% CI)	-0.25 [-0.35, -0.15]
9.1 Cluster randomisation - analysis by cluster	2	18833	Mean Difference (IV, Random, 95% CI)	0.01 [-0.03, 0.05]
9.2 Individual randomisation	30	46775	Mean Difference (IV, Random, 95% CI)	-0.29 [-0.40, -0.18]
9.3 Cluster randomisation (analysis by individual)	3	498	Mean Difference (IV, Random, 95% CI)	0.06 [-0.15, 0.28]
10 Smoking prevalence (individual analysis or cluster)	15	48948	Odds Ratio (M-H, Random, 95% CI)	0.81 [0.70, 0.94]
10.1 Cluster randomisation - analysis by cluster	1	520	Odds Ratio (M-H, Random, 95% CI)	0.43 [0.28, 0.64]
10.2 Individual randomisation	12	29508	Odds Ratio (M-H, Random, 95% CI)	0.82 [0.70, 0.95]
10.3 Cluster randomisation - analysis by individual	2	18920	Odds Ratio (M-H, Random, 95% CI)	0.99 [0.90, 1.08]

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Analysis 1.1. Comparison 1 Multiple risk factor intervention versus control, Outcome 1 Total mortality.

Review: Multiple risk factor interventions for primary prevention of coronary heart disease

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 1 Total mortality

Study or subgroup	Intervention n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
CELL Study	2/339	1/320		0.0 %	1.84 [0.19, 17.80]
Finnish men	10/612	5/610		0.2 %	1.96 [0.71, 5.41]
Gothenberg Study	1293/10004	2636/20018		44.0 %	0.98 [0.91, 1.05]
HDFP trial	349/5485	419/5455		10.3 %	0.82 [0.71, 0.95]
Johns Hopkins	35/350	11/50		0.3 %	0.31 [0.12, 0.78]
MRFIT Study	265/6428	260/6438		7.3 %	1.02 [0.86, 1.22]
OXCHECK Study	146/8307	40/2783		2.0 %	1.21 [0.87, 1.70]
Swedish RIS	41/253	64/255		1.2 %	0.58 [0.38, 0.89]
WHO Factories	1325/30489	1186/26971		34.7 %	0.99 [0.91, 1.07]
Total (95% CI)	**62267**	**62900**		**100.0 %**	**0.96 [0.92, 1.01]**

Total events: 3466 (Intervention), 4622 (Control)

Heterogeneity: Chi^2 = 20.94, df = 8 (P = 0.01); I^2 =62%

Test for overall effect: Z = 1.54 (P = 0.12)

Test for subgroup differences: Not applicable

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Analysis 1.2. Comparison 1 Multiple risk factor intervention versus control, Outcome 2 Coronary heart disease mortality.

Review: Multiple risk factor interventions for primary prevention of coronary heart disease

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 2 Coronary heart disease mortality

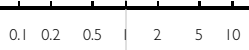
Study or subgroup	Intervention n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
CELL Study	2/339	1/320		0.1 %	1.84 [0.19, 17.80]
Finnish men	4/612	1/610		0.2 %	3.32 [0.57, 19.23]
Gothenberg Study	462/10004	923/20018		45.2 %	1.00 [0.89, 1.12]
HDFP trial	131/5485	148/5455		10.5 %	0.88 [0.69, 1.11]
Johns Hopkins	23/350	8/50		0.5 %	0.27 [0.09, 0.81]
MRFIT Study	115/6428	124/6438		9.0 %	0.93 [0.72, 1.20]
OXCHECK Study	52/8307	13/2783		1.9 %	1.31 [0.75, 2.30]
Swedish RIS	17/253	23/255		1.4 %	0.73 [0.38, 1.39]
WHO Factories	428/30489	398/26971		31.2 %	0.95 [0.83, 1.09]
Total (95% CI)	**62267**	**62900**		**100.0 %**	**0.96 [0.89, 1.04]**

Total events: 1234 (Intervention), 1639 (Control)

Heterogeneity: Chi^2 = 10.39, df = 8 (P = 0.24); I^2 =23%

Test for overall effect: Z = 0.98 (P = 0.33)

Test for subgroup differences: Not applicable



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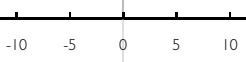
Analysis 1.3. Comparison 1 Multiple risk factor intervention versus control, Outcome 3 Systolic blood pressure.

Review: Multiple risk factor interventions for primary prevention of coronary heart disease

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 3 Systolic blood pressure

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Aberg men	79	3.3 (16.3)	80	1.7 (16.21)		0.4 %	1.60 [-3.45, 6.65]
Aberg women	114	4.4 (17.83)	80	0.2 (19.02)		0.3 %	4.20 [-1.10, 9.50]
Abingdon	167	-6.9 (14.6)	168	-5.2 (15.76)		0.9 %	-1.70 [-4.95, 1.55]
Applegate 1992	21	-8.7 (11.7)	26	-4.5 (9.7)		0.2 %	-4.20 [-10.44, 2.04]
Blumenthal 2000	46	-7.4 (9.31)	22	-0.9 (9.31)		0.4 %	-6.50 [-11.23, -1.77]
CELL Study	292	-1.2 (14.7)	310	0 (14.7)		1.7 %	-1.20 [-3.55, 1.15]
Change of Heart	165	4.3 (15.4)	339	1.8 (21.61)		0.9 %	2.50 [-0.79, 5.79]
Family Heart - men	1767	-7.3 (19.23)	2174	0 (19.23)		6.6 %	-7.30 [-8.51, -6.09]
Family Heart - women	1217	-6.2 (20.43)	1402	0 (20.43)		3.9 %	-6.20 [-7.77, -4.63]
FARIS men	219	-4.4 (15.38)	223	-0.6 (15.38)		1.2 %	-3.80 [-6.67, -0.93]
FARIS women	315	-3.9 (15.38)	343	-0.7 (15.38)		1.7 %	-3.20 [-5.55, -0.85]
Finnish DPS	256	-5 (14)	250	-1 (15)		1.5 %	-4.00 [-6.53, -1.47]
Finnish men	575	-10 (18)	580	-4 (16)		2.5 %	-6.00 [-7.96, -4.04]
Given 1984	62	-9.85 (12.7)	24	-4.79 (12.61)		0.3 %	-5.06 [-11.01, 0.89]
Gothenberg Study	1464	-2 (20)	1404	0 (20)		4.5 %	-2.00 [-3.46, -0.54]
Hellenius	39	-4 (12.6)	39	-1 (12.2)		0.3 %	-3.00 [-8.50, 2.50]
Iso	53	-13.2 (11.52)	55	-17.4 (14.02)		0.4 %	4.20 [-0.63, 9.03]
Jalkanen 1991	24	-8 (18.68)	25	-5 (18.33)		0.1 %	-3.00 [-13.37, 7.37]
Lin 1996	471	-1 (18.52)	426	1 (19.52)		1.5 %	-2.00 [-4.50, 0.50]
Lindahl 1999	93	-4.9 (19.3)	93	1.3 (18.3)		0.3 %	-6.20 [-11.61, -0.79]
Meland 1997	58	-4 (23.31)	52	0 (22.08)		0.1 %	-4.00 [-12.49, 4.49]
MRFIT Study	5740	-13.9 (13.23)	5633	-8.6 (15.27)		34.9 %	-5.30 [-5.83, -4.77]
Nilsson 1992	31	-7.7 (17.77)	32	-3.8 (19.3)		0.1 %	-3.90 [-13.06, 5.26]
Nilsson 2001	43	-3.7 (20.31)	46	-1.2 (17.9)		0.2 %	-2.50 [-10.48, 5.48]
Oldroyd	35	-7.9 (16.7)	32	-0.27 (14.3)		0.2 %	-7.63 [-15.06, -0.20]



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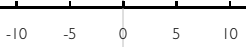
Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Oslo Diet Exercise	65	-5.9 (8.87)	43	-0.5 (11.15)		0.6 %	-5.40 [-9.37, -1.43]
OXCHECK Study	2205	-2.5 (19.3)	1916	0 (20.4)		6.5 %	-2.50 [-3.72, -1.28]
Perez-Stable no prop	72	-9 (12.99)	72	-6.7 (13.2)		0.5 %	-2.30 [-6.58, 1.98]
Perez-Stable prop	74	-8.3 (13.39)	73	-11.6 (13.3)		0.5 %	3.30 [-1.01, 7.61]
Stamler 1989	102	-2.6 (6.4)	99	-1.3 (6.1)		3.2 %	-1.30 [-3.03, 0.43]
Stefanick men	48	-3 (6.8)	46	0.3 (7.9)		1.1 %	-3.30 [-6.29, -0.31]
Stefanick women	43	-3.1 (8.4)	45	-2.4 (7.6)		0.9 %	-0.70 [-4.05, 2.65]
Swedish RIS	235	-2 (18.4)	227	-0.2 (20.5)		0.8 %	-1.80 [-5.36, 1.76]
Tromso men	525	0.5 (15.6)	535	1.1 (16.5)		2.6 %	-0.60 [-2.53, 1.33]
Tromso wives	422	-2.16 (15.8)	387	2.1 (16.5)		1.9 %	-4.26 [-6.49, -2.03]
WHLP	253	-3.5 (12.18)	267	-1.2 (9.21)		2.8 %	-2.30 [-4.16, -0.44]
WHO Factories	16949	2.67 (18.09)	1902	3.18 (18.14)		13.1 %	-0.51 [-1.37, 0.35]
Wing	32	-4.8 (15)	31	-1.5 (12)		0.2 %	-3.30 [-10.00, 3.40]
Total (95% CI)	**34371**		**19501**			**100.0 %**	**-3.62 [-3.93, -3.31]**

Heterogeneity: Chi^2 = 229.68, df = 37 (P<0.00001); I^2 =84%

Test for overall effect: Z = 22.84 (P < 0.00001)

Test for subgroup differences: Not applicable



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Analysis 1.4. Comparison 1 Multiple risk factor intervention versus control, Outcome 4 Diastolic blood pressure.

Review: Multiple risk factor interventions for primary prevention of coronary heart disease

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 4 Diastolic blood pressure

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Aberg men	79	2 (7.81)	80	1.6 (7.77)		0.5 %	0.40 [-2.02, 2.82]
Aberg women	114	1.3 (9.11)	115	0.8 (8.46)		0.5 %	0.50 [-1.78, 2.78]
Abingdon	167	-4.61 (9.29)	168	-2.9 (9.98)		0.7 %	-1.71 [-3.77, 0.35]
Applegate 1992	21	-6.8 (1.7)	26	-1.9 (3.6)		1.2 %	-4.90 [-6.46, -3.34]
Blumenthal 2000	46	-5.6 (7.56)	22	-1.4 (7.56)		0.2 %	-4.20 [-8.04, -0.36]
CELL Study	292	-0.1 (8.3)	310	0 (9.1)		1.5 %	-0.10 [-1.49, 1.29]
Change of Heart	165	0.7 (15.4)	338	1 (9.43)		0.4 %	-0.30 [-2.86, 2.26]
Family Heart - men	1767	-3.5 (11.43)	2174	0 (11.43)		5.5 %	-3.50 [-4.22, -2.78]
Family Heart - women	1217	-3 (11.33)	1402	0 (11.33)		3.7 %	-3.00 [-3.87, -2.13]
FARIS men	219	-1 (9.95)	223	1 (9.95)		0.8 %	-2.00 [-3.86, -0.14]
FARIS women	315	-1.1 (9.95)	343	-0.3 (9.95)		1.2 %	-0.80 [-2.32, 0.72]
Finnish DPS	256	-5 (9)	250	-3 (9)		1.1 %	-2.00 [-3.57, -0.43]
Finnish men	575	-8 (10)	580	-3 (10)		2.1 %	-5.00 [-6.15, -3.85]
Given 1984	62	-6.4 (6.99)	24	-2.42 (4.9)		0.4 %	-3.98 [-6.60, -1.36]
Gothenberg Study	1464	-1 (10)	1404	0 (10)		5.3 %	-1.00 [-1.73, -0.27]
HDFP trial	5485	-17 (10)	5455	-12.1 (10)		20.1 %	-4.90 [-5.27, -4.53]
Hellenius	39	-2 (7.7)	39	-1 (8.3)		0.2 %	-1.00 [-4.55, 2.55]
Iso	53	-5.1 (8.39)	55	-4.7 (9.06)		0.3 %	-0.40 [-3.69, 2.89]
Jalkanen 1991	24	-11 (9.16)	25	-11 (7)		0.1 %	0.0 [-4.58, 4.58]
Lin 1996	471	-2 (11)	426	-2 (11.53)		1.3 %	0.0 [-1.48, 1.48]
Lindahl 1999	93	-3.2 (9.6)	93	-0.8 (9.6)		0.4 %	-2.40 [-5.16, 0.36]
Meland 1997	58	-3 (11.66)	52	0 (11.04)		0.2 %	-3.00 [-7.24, 1.24]
MRFIT Study	5754	-10.2 (7.88)	5638	-7.1 (9.22)		28.3 %	-3.10 [-3.42, -2.78]
Nilsson 1992	31	-6.1 (6.2)	32	-4 (8.23)		0.2 %	-2.10 [-5.69, 1.49]
Nilsson 2001	43	-5.7 (10.71)	46	-0.4 (9.56)		0.2 %	-5.30 [-9.53, -1.07]

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Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Oldroyd	35	-2.9 (9.9)	32	1.9 (10)		0.1 %	-4.80 [-9.57, -0.03]
Oslo Diet Exercise	65	-5.2 (7.26)	43	-0.7 (8.52)		0.3 %	-4.50 [-7.60, -1.40]
OXCHECK Study	2205	-1.5 (11.6)	1916	0 (11.7)		5.5 %	-1.50 [-2.21, -0.79]
Perez-Stable no prop	72	-5 (9.09)	72	-5.8 (9.09)		0.3 %	0.80 [-2.17, 3.77]
Perez-Stable prop	74	-8.2 (9.66)	73	-8.5 (9.15)		0.3 %	0.30 [-2.74, 3.34]
Stamler 1989	102	-1.3 (4.7)	99	-0.1 (4.9)		1.6 %	-1.20 [-2.53, 0.13]
Stefanick men	48	-3 (6.6)	46	1.8 (6.1)		0.4 %	-4.80 [-7.37, -2.23]
Stefanick women	43	-2.7 (4.6)	45	-0.6 (5.9)		0.6 %	-2.10 [-4.30, 0.10]
Swedish RIS	235	-4.9 (9.1)	227	-3.8 (9.6)		1.0 %	-1.10 [-2.81, 0.61]
Tromso men	525	-4 (10.6)	535	-3.6 (10.5)		1.7 %	-0.40 [-1.67, 0.87]
Tromso wives	422	-2.13 (10.3)	387	1.23 (10.4)		1.4 %	-3.36 [-4.79, -1.93]
WHLP	253	-2.2 (10.48)	267	-0.09 (6.92)		1.2 %	-2.11 [-3.65, -0.57]
WHO Factories	16948	1.41 (12.29)	1897	1.68 (11.64)		9.1 %	-0.27 [-0.83, 0.29]
Wing	32	-0.2 (10.5)	31	2 (8)		0.1 %	-2.20 [-6.80, 2.40]
Total (95% CI)	**39869**		**24990**			**100.0 %**	**-2.76 [-2.93, -2.59]**

Heterogeneity: Chi^2 = 366.47, df = 38 (P<0.00001); I^2 =90%

Test for overall effect: Z = 32.22 (P < 0.00001)

Test for subgroup differences: Not applicable

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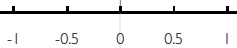
Analysis 1.5. Comparison 1 Multiple risk factor intervention versus control, Outcome 5 Blood cholesterol.

Review: Multiple risk factor interventions for primary prevention of coronary heart disease

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 5 Blood cholesterol

Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Aberg men	79	0.3 (1.1)	80	0.1 (1.1)		0.1 %	0.20 [-0.14, 0.54]
Aberg women	114	0.4 (1.35)	115	0.3 (1.1)		0.1 %	0.10 [-0.22, 0.42]
Abingdon	167	-0.2 (0.89)	166	-0.18 (0.9)		0.4 %	-0.02 [-0.21, 0.17]
CELL Study	292	-0.15 (0.56)	310	0 (0.65)		1.5 %	-0.15 [-0.25, -0.05]
Change of Heart	164	0.31 (0.82)	334	0.33 (1.54)		0.3 %	-0.02 [-0.23, 0.19]
Family Heart - men	1767	-0.13 (1.16)	2174	0 (1.16)		2.6 %	-0.13 [-0.20, -0.06]
Family Heart - women	1217	-0.09 (1.17)	1402	0 (1.17)		1.7 %	-0.09 [-0.18, 0.00]
FARIS men	219	-3 (0.94)	223	0.05 (0.94)		0.5 %	-3.05 [-3.23, -2.87]
FARIS women	315	-0.13 (0.94)	343	0.01 (0.94)		0.7 %	-0.14 [-0.28, 0.00]
Finnish DPS	256	-0.13 (0.73)	250	-0.1 (0.73)		0.9 %	-0.03 [-0.16, 0.10]
Finnish men	575	-0.4 (1)	580	0.05 (0.9)		1.1 %	-0.45 [-0.56, -0.34]
Gothenberg Study	1473	-0.01 (1.1)	1404	0 (1.1)		2.1 %	-0.01 [-0.09, 0.07]
HDFP trial	5485	-0.39 (1)	5455	-0.39 (1)		9.9 %	0.0 [-0.04, 0.04]
Hellenius	39	-0.45 (0.93)	39	-0.13 (0.9)		0.1 %	-0.32 [-0.73, 0.09]
Jalkanen 1991	24	-0.2 (1)	25	0.2 (1)		0.0 %	-0.40 [-0.96, 0.16]
Lindahl 1999	93	-0.21 (1.35)	93	-0.06 (0.96)		0.1 %	-0.15 [-0.49, 0.19]
Meland 1997	58	0.1 (1.17)	52	0.3 (1.1)		0.1 %	-0.20 [-0.62, 0.22]
MRFIT Study	5743	-0.43 (0.99)	5607	-0.3 (1.03)		10.0 %	-0.13 [-0.17, -0.09]
Nilsson 2001	43	-0.1 (0.9)	46	0 (1.05)		0.1 %	-0.10 [-0.51, 0.31]
Oldroyd	35	-0.16 (0.55)	32	-0.18 (0.59)		0.2 %	0.02 [-0.25, 0.29]
Oslo Diet Exercise	65	-0.48 (0.89)	43	-0.16 (0.59)		0.2 %	-0.32 [-0.60, -0.04]
OXCHECK Study	2205	-0.19 (1.1)	1916	0 (1.17)		2.9 %	-0.19 [-0.26, -0.12]
Perez-Stable no prop	69	-0.42 (1.15)	68	-0.18 (0.98)		0.1 %	-0.24 [-0.60, 0.12]
Perez-Stable prop	67	-0.32 (0.81)	67	-0.25 (0.86)		0.2 %	-0.07 [-0.35, 0.21]
Stefanick men	48	-0.54 (0.52)	46	-0.1 (0.56)		0.3 %	-0.44 [-0.66, -0.22]
Stefanick women	43	-0.46 (0.56)	45	-0.03 (0.51)		0.3 %	-0.43 [-0.65, -0.21]



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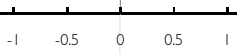
Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Swedish RIS	235	-0.78 (1.12)	227	-0.39 (0.92)		0.4 %	-0.39 [-0.58, -0.20]
Take Heart	1057	0.02 (0.2)	920	0.01 (0.18)		49.3 %	0.01 [-0.01, 0.03]
The Oslo Study	604	-0.92 (0.7)	628	-0.39 (0.7)		2.3 %	-0.53 [-0.61, -0.45]
Tromso men	525	-0.41 (1.15)	535	-0.25 (1.2)		0.7 %	-0.16 [-0.30, -0.02]
Tromso wives	422	0.06 (1.27)	387	0.14 (1.34)		0.4 %	-0.08 [-0.26, 0.10]
Uusitupa	38	-0.1 (0.31)	40	0.1 (0.97)		0.1 %	-0.20 [-0.52, 0.12]
WHLP	253	-0.34 (0.61)	267	0.03 (0.21)		2.2 %	-0.37 [-0.45, -0.29]
WHO Factories	16481	0.09 (0.89)	1854	0.08 (0.86)		8.1 %	0.01 [-0.03, 0.05]
Wing	32	0.09 (0.67)	31	0.18 (0.53)		0.2 %	-0.09 [-0.39, 0.21]
Total (95% CI)	**40302**		**25804**			**100.0 %**	**-0.07 [-0.08, -0.06]**

Heterogeneity: Chi^2 = 1536.07, df = 34 (P<0.00001); I^2 =98%

Test for overall effect: Z = 11.28 (P < 0.00001)

Test for subgroup differences: Not applicable



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Analysis 1.6. Comparison 1 Multiple risk factor intervention versus control, Outcome 6 Smoking prevalence.

Review: Multiple risk factor interventions for primary prevention of coronary heart disease

Comparison: 1 Multiple risk factor intervention versus control

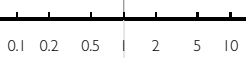
Outcome: 6 Smoking prevalence

Study or subgroup	Intervention n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Abingdon	46/168	42/167		4.6 %	1.12 [0.69, 1.83]
CELL Study	139/292	148/310		6.5 %	0.99 [0.72, 1.37]
Change of Heart	40/169	148/351		5.4 %	0.43 [0.28, 0.64]
Family Heart - men	337/1767	500/2174		8.4 %	0.79 [0.68, 0.92]
Family Heart - women	215/1217	301/1402		8.0 %	0.78 [0.65, 0.95]
Finnish men	125/575	131/580		7.0 %	0.95 [0.72, 1.26]
Gothenberg Study	691/1473	699/1404		8.5 %	0.89 [0.77, 1.03]
Meland 1997	35/58	30/52		2.7 %	1.12 [0.52, 2.39]
MRFIT Study	1847/5754	2554/5638		9.1 %	0.57 [0.53, 0.62]
Nilsson 2001	17/43	27/46		2.3 %	0.46 [0.20, 1.07]
OXCHECK Study	544/2205	506/1916		8.6 %	0.91 [0.79, 1.05]
Swedish RIS	55/253	70/255		5.5 %	0.73 [0.49, 1.10]
Tromso men	247/525	284/535		7.5 %	0.79 [0.62, 1.00]
Tromso wives	186/422	178/387		7.0 %	0.93 [0.70, 1.22]
WHO Factories	7910/16908	897/1902		9.0 %	0.98 [0.90, 1.08]
Total (95% CI)	**31829**	**17119**		**100.0 %**	**0.81 [0.70, 0.94]**

Total events: 12434 (Intervention), 6515 (Control)

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 113.62$, df = 14 (P<0.00001); $I^2 = 88\%$

Test for overall effect: Z = 2.77 (P = 0.0056)



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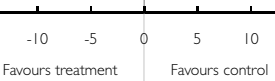
Analysis 1.7. Comparison 1 Multiple risk factor intervention versus control, Outcome 7 Systolic blood pressure (individual analysis or cluster).

Review: Multiple risk factor interventions for primary prevention of coronary heart disease

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 7 Systolic blood pressure (individual analysis or cluster)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Cluster randomisation - analysis by cluster							
Change of Heart	165	4.3 (15.4)	339	1.8 (21.61)		2.8 %	2.50 [-0.79, 5.79]
WHO Factories	16949	2.67 (18.09)	1902	3.18 (18.14)		4.1 %	-0.51 [-1.37, 0.35]
Subtotal (95% CI)	**17114**		**2241**			**6.9 %**	**0.56 [-2.26, 3.38]**
Heterogeneity: Tau² = 3.03; Chi² = 3.01, df = 1 (P = 0.08); I² =67%							
Test for overall effect: Z = 0.39 (P = 0.70)							
2 Individual randomisation							
Abingdon	167	-6.9 (14.6)	168	-5.2 (15.76)		2.8 %	-1.70 [-4.95, 1.55]
Applegate 1992	21	-8.7 (11.7)	26	-4.5 (9.7)		1.5 %	-4.20 [-10.44, 2.04]
Blumenthal 2000	46	-7.4 (9.31)	22	-0.9 (9.31)		2.1 %	-6.50 [-11.23, -1.77]
CELL Study	292	-1.2 (14.7)	310	0 (14.7)		3.4 %	-1.20 [-3.55, 1.15]
Family Heart - men	1767	-7.3 (19.23)	2174	0 (19.23)		3.9 %	-7.30 [-8.51, -6.09]
Family Heart - women	1217	-6.2 (20.43)	1402	0 (20.43)		3.8 %	-6.20 [-7.77, -4.63]
FARIS men	219	-4.4 (15.38)	223	-0.6 (15.38)		3.1 %	-3.80 [-6.67, -0.93]
FARIS women	315	-3.9 (15.38)	343	-0.7 (15.38)		3.4 %	-3.20 [-5.55, -0.85]
Finnish DPS	256	-5 (14)	250	-1 (15)		3.3 %	-4.00 [-6.53, -1.47]
Finnish men	575	-10 (18)	580	-4 (16)		3.6 %	-6.00 [-7.96, -4.04]
Given 1984	62	-9.85 (12.7)	24	-4.79 (12.61)		1.6 %	-5.06 [-11.01, 0.89]
Gothenberg Study	1464	-2 (20)	1404	0 (20)		3.8 %	-2.00 [-3.46, -0.54]
Hellenius	39	-4 (12.6)	39	-1 (12.2)		1.8 %	-3.00 [-8.50, 2.50]
Iso	53	-13.2 (11.52)	55	-17.4 (14.02)		2.0 %	4.20 [-0.63, 9.03]
Jalkanen 1991	24	-8 (18.68)	25	-5 (18.33)		0.7 %	-3.00 [-13.37, 7.37]
Lindahl 1999	93	-4.9 (19.3)	93	1.3 (18.3)		1.8 %	-6.20 [-11.61, -0.79]
MRFIT Study	5740	-13.9 (13.23)	5633	-8.6 (15.27)		4.2 %	-5.30 [-5.83, -4.77]
Nilsson 1992	31	-7.7 (17.77)	32	-3.8 (19.3)		0.9 %	-3.90 [-13.06, 5.26]
Nilsson 2001	43	-3.7 (20.31)	46	-1.2 (17.9)		1.1 %	-2.50 [-10.48, 5.48]



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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Oldroyd	35	-7.9 (16.7)	32	-0.27 (14.3)		1.2 %	-7.63 [-15.06, -0.20]
Oslo Diet Exercise	65	-5.9 (8.87)	43	-0.5 (11.15)		2.5 %	-5.40 [-9.37, -1.43]
OXCHECK Study	2205	-2.5 (19.3)	1916	0 (20.4)		3.9 %	-2.50 [-3.72, -1.28]
Perez-Stable no prop	72	-9 (12.99)	72	-6.7 (13.2)		2.3 %	-2.30 [-6.58, 1.98]
Perez-Stable prop	74	-8.3 (13.39)	73	-11.6 (13.3)		2.3 %	3.30 [-1.01, 7.61]
Stamler 1989	102	-2.6 (6.4)	99	-1.3 (6.1)		3.7 %	-1.30 [-3.03, 0.43]
Stefanick men	48	-3 (6.8)	46	0.3 (7.9)		3.0 %	-3.30 [-6.29, -0.31]
Stefanick women	43	-3.1 (8.4)	45	-2.4 (7.6)		2.8 %	-0.70 [-4.05, 2.65]
Swedish RIS	235	-2 (18.4)	227	-0.2 (20.5)		2.7 %	-1.80 [-5.36, 1.76]
Tromso men	525	0.5 (15.6)	535	1.1 (16.5)		3.6 %	-0.60 [-2.53, 1.33]
Tromso wives	422	-2.16 (15.8)	387	2.1 (16.5)		3.4 %	-4.26 [-6.49, -2.03]
WHLP	253	-3.5 (12.18)	267	-1.2 (9.21)		3.6 %	-2.30 [-4.16, -0.44]
Wing	32	-4.8 (15)	31	-1.5 (12)		1.4 %	-3.30 [-10.00, 3.40]
Subtotal (95% CI)	**16535**		**16622**			**85.1 %**	**-3.24 [-4.16, -2.31]**
Heterogeneity: Tau^2 = 4.03; Chi^2 = 138.58, df = 31 (P<0.00001); I^2 =78%							
Test for overall effect: Z = 6.88 (P < 0.00001)							
3 Cluster randomisation - analysis by individual							
Aberg men	79	3.3 (16.3)	80	1.7 (16.21)		1.9 %	1.60 [-3.45, 6.65]
Aberg women	114	4.4 (17.83)	80	0.2 (19.02)		1.8 %	4.20 [-1.10, 9.50]
Lin 1996	471	-1 (18.52)	426	1 (19.52)		3.3 %	-2.00 [-4.50, 0.50]
Meland 1997	58	-4 (23.31)	52	0 (22.08)		1.0 %	-4.00 [-12.49, 4.49]
Subtotal (95% CI)	**722**		**638**			**8.1 %**	**0.03 [-3.28, 3.34]**
Heterogeneity: Tau^2 = 5.26; Chi^2 = 5.70, df = 3 (P = 0.13); I^2 =47%							
Test for overall effect: Z = 0.02 (P = 0.98)							
Total (95% CI)	**34371**		**19501**			**100.0 %**	**-2.68 [-3.64, -1.72]**
Heterogeneity: Tau^2 = 5.73; Chi^2 = 229.68, df = 37 (P<0.00001); I^2 =84%							
Test for overall effect: Z = 5.45 (P < 0.00001)							

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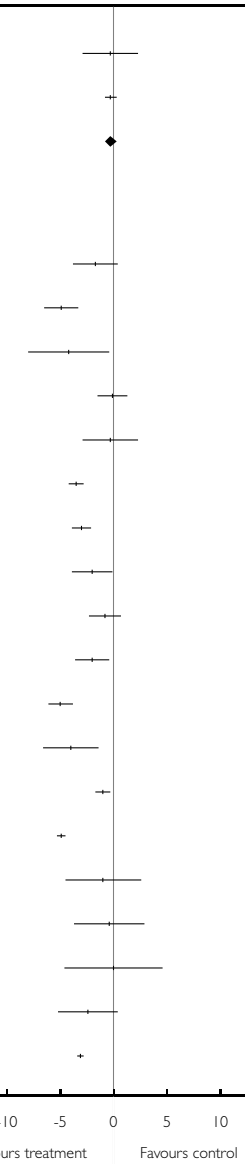
Analysis 1.8. Comparison 1 Multiple risk factor intervention versus control, Outcome 8 Diastolic blood pressure (individual analysis or cluster).

Review: Multiple risk factor interventions for primary prevention of coronary heart disease

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 8 Diastolic blood pressure (individual analysis or cluster)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Cluster randomisation - analysis by cluster							
Change of Heart	165	0.7 (15.4)	338	1 (9.43)		2.2 %	-0.30 [-2.86, 2.26]
WHO Factories	16948	1.41 (12.29)	1897	1.68 (11.64)		3.5 %	-0.27 [-0.83, 0.29]
Subtotal (95% CI)	**17113**		**2235**			**5.8 %**	**-0.27 [-0.81, 0.27]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.00$, df = 1 (P = 0.98); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.98 (P = 0.33)							
2 Individual randomisation							
Abingdon	167	-4.61 (9.29)	168	-2.9 (9.98)		2.6 %	-1.71 [-3.77, 0.35]
Applegate 1992	21	-6.8 (1.7)	26	-1.9 (3.6)		2.9 %	-4.90 [-6.46, -3.34]
Blumenthal 2000	46	-5.6 (7.56)	22	-1.4 (7.56)		1.5 %	-4.20 [-8.04, -0.36]
CELL Study	292	-0.1 (8.3)	310	0 (9.1)		3.1 %	-0.10 [-1.49, 1.29]
Change of Heart	165	0.7 (15.4)	338	1 (9.43)		2.2 %	-0.30 [-2.86, 2.26]
Family Heart - men	1767	-3.5 (11.43)	2174	0 (11.43)		3.4 %	-3.50 [-4.22, -2.78]
Family Heart - women	1217	-3 (11.33)	1402	0 (11.33)		3.4 %	-3.00 [-3.87, -2.13]
FARIS men	219	-1 (9.95)	223	1 (9.95)		2.7 %	-2.00 [-3.86, -0.14]
FARIS women	315	-1.1 (9.95)	343	-0.3 (9.95)		3.0 %	-0.80 [-2.32, 0.72]
Finnish DPS	256	-5 (9)	250	-3 (9)		2.9 %	-2.00 [-3.57, -0.43]
Finnish men	575	-8 (10)	580	-3 (10)		3.2 %	-5.00 [-6.15, -3.85]
Given 1984	62	-6.4 (6.99)	24	-2.42 (4.9)		2.2 %	-3.98 [-6.60, -1.36]
Gothenberg Study	1464	-1 (10)	1404	0 (10)		3.4 %	-1.00 [-1.73, -0.27]
HDFP trial	5485	-17 (10)	5455	-12.1 (10)		3.6 %	-4.90 [-5.27, -4.53]
Hellenius	39	-2 (7.7)	39	-1 (8.3)		1.7 %	-1.00 [-4.55, 2.55]
Iso	53	-5.1 (8.39)	55	-4.7 (9.06)		1.8 %	-0.40 [-3.69, 2.89]
Jalkanen 1991	24	-11 (9.16)	25	-11 (7)		1.2 %	0.0 [-4.58, 4.58]
Lindahl 1999	93	-3.2 (9.6)	93	-0.8 (9.6)		2.1 %	-2.40 [-5.16, 0.36]
MRFIT Study	5754	-10.2 (7.88)	5638	-7.1 (9.22)		3.6 %	-3.10 [-3.42, -2.78]



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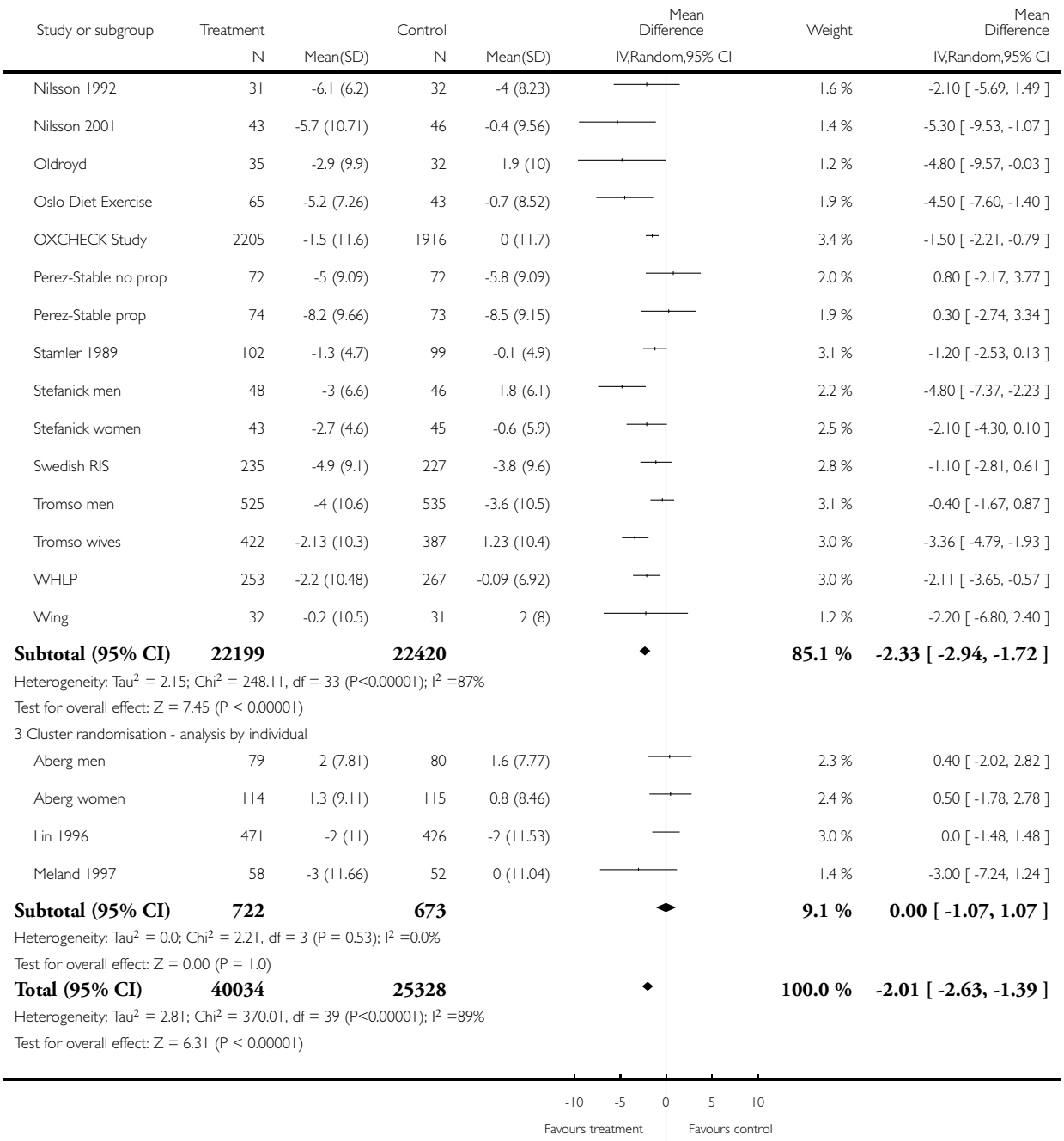

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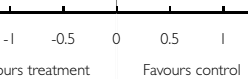
Analysis 1.9. Comparison 1 Multiple risk factor intervention versus control, Outcome 9 Cholesterol (individual analysis or cluster).

Review: Multiple risk factor interventions for primary prevention of coronary heart disease

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 9 Cholesterol (individual analysis or cluster)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Cluster randomisation - analysis by cluster							
Change of Heart	164	0.31 (0.82)	334	0.33 (1.54)		2.9 %	-0.02 [-0.23, 0.19]
WHO Factories	16481	0.09 (0.89)	1854	0.08 (0.86)		3.3 %	0.01 [-0.03, 0.05]
Subtotal (95% CI)	**16645**		**2188**			**6.2 %**	**0.01 [-0.03, 0.05]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.08$, df = 1 (P = 0.78); $I^2 = 0.0\%$							
Test for overall effect: Z = 0.43 (P = 0.67)							
2 Individual randomisation							
Abingdon	167	-0.2 (0.89)	166	-0.18 (0.9)		3.0 %	-0.02 [-0.21, 0.17]
CELL Study	292	-0.15 (0.56)	310	0 (0.65)		3.2 %	-0.15 [-0.25, -0.05]
Family Heart - men	1767	-0.13 (1.16)	2174	0 (1.16)		3.3 %	-0.13 [-0.20, -0.06]
Family Heart - women	1217	-0.09 (1.17)	1402	0 (1.17)		3.3 %	-0.09 [-0.18, 0.00]
FARIS men	219	-3 (0.94)	223	0.05 (0.94)		3.0 %	-3.05 [-3.23, -2.87]
FARIS women	315	-0.13 (0.94)	343	0.01 (0.94)		3.1 %	-0.14 [-0.28, 0.00]
Finnish DPS	256	-0.13 (0.73)	250	-0.1 (0.73)		3.2 %	-0.03 [-0.16, 0.10]
Finnish men	575	-0.4 (1)	580	0.05 (0.9)		3.2 %	-0.45 [-0.56, -0.34]
Gothenberg Study	1473	-0.01 (1.1)	1404	0 (1.1)		3.3 %	-0.01 [-0.09, 0.07]
HDFP trial	5485	-0.39 (1)	5455	-0.39 (1)		3.3 %	0.0 [-0.04, 0.04]
Hellenius	39	-0.45 (0.93)	39	-0.13 (0.9)		2.1 %	-0.32 [-0.73, 0.09]
Jalkanen 1991	24	-0.2 (1)	25	0.2 (1)		1.6 %	-0.40 [-0.96, 0.16]
Lindahl 1999	93	-0.21 (1.35)	93	-0.06 (0.96)		2.4 %	-0.15 [-0.49, 0.19]
MRFIT Study	5743	-0.43 (0.99)	5607	-0.3 (1.03)		3.3 %	-0.13 [-0.17, -0.09]
Nilsson 2001	43	-0.1 (0.9)	46	0 (1.05)		2.1 %	-0.10 [-0.51, 0.31]
Oldroyd	35	-0.16 (0.55)	32	-0.18 (0.59)		2.7 %	0.02 [-0.25, 0.29]
Oslo Diet Exercise	65	-0.48 (0.89)	43	-0.16 (0.59)		2.6 %	-0.32 [-0.60, -0.04]
OXCHECK Study	2205	-0.19 (1.1)	1916	0 (1.17)		3.3 %	-0.19 [-0.26, -0.12]
Perez-Stable no prop	69	-0.42 (1.15)	68	-0.18 (0.98)		2.3 %	-0.24 [-0.60, 0.12]



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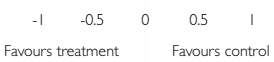
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Perez-Stable prop	67	-0.32 (0.81)	67	-0.25 (0.86)		2.6 %	-0.07 [-0.35, 0.21]
Stefanick men	48	-0.54 (0.52)	46	-0.1 (0.56)		2.9 %	-0.44 [-0.66, -0.22]
Stefanick women	43	-0.46 (0.56)	45	-0.03 (0.51)		2.9 %	-0.43 [-0.65, -0.21]
Swedish RIS	235	-0.78 (1.12)	227	-0.39 (0.92)		3.0 %	-0.39 [-0.58, -0.20]
Take Heart	1057	0.02 (0.2)	920	0.01 (0.18)		3.3 %	0.01 [-0.01, 0.03]
The Oslo Study	604	-0.92 (0.7)	628	-0.39 (0.7)		3.3 %	-0.53 [-0.61, -0.45]
Tromso men	525	-0.41 (1.15)	535	-0.25 (1.2)		3.1 %	-0.16 [-0.30, -0.02]
Tromso wives	422	0.06 (1.27)	387	0.14 (1.34)		3.0 %	-0.08 [-0.26, 0.10]
Uusitupa	38	-0.1 (0.31)	40	0.1 (0.97)		2.5 %	-0.20 [-0.52, 0.12]
WHLP	253	-0.34 (0.61)	267	0.03 (0.21)		3.3 %	-0.37 [-0.45, -0.29]
Wing	32	0.09 (0.67)	31	0.18 (0.53)		2.6 %	-0.09 [-0.39, 0.21]
Subtotal (95% CI)	**23406**		**23369**			**86.8 %**	**-0.29 [-0.40, -0.18]**
Heterogeneity: Tau^2 = 0.09; Chi^2 = 1517.13, df = 29 (P<0.00001); I^2 =98%							
Test for overall effect: Z = 5.04 (P < 0.00001)							
3 Cluster randomisation (analysis by individual)							
Aberg men	79	0.3 (1.1)	80	0.1 (1.1)		2.4 %	0.20 [-0.14, 0.54]
Aberg women	114	0.4 (1.35)	115	0.3 (1.1)		2.5 %	0.10 [-0.22, 0.42]
Meland 1997	58	0.1 (1.17)	52	0.3 (1.1)		2.1 %	-0.20 [-0.62, 0.22]
Subtotal (95% CI)	**251**		**247**			**6.9 %**	**0.06 [-0.15, 0.28]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 2.14, df = 2 (P = 0.34); I^2 =7%							
Test for overall effect: Z = 0.59 (P = 0.55)							
Total (95% CI)	**40302**		**25804**			**100.0 %**	**-0.25 [-0.35, -0.15]**
Heterogeneity: Tau^2 = 0.07; Chi^2 = 1536.07, df = 34 (P<0.00001); I^2 =98%							
Test for overall effect: Z = 4.95 (P < 0.00001)							



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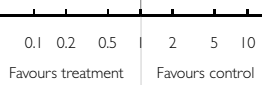
Analysis 1.10. Comparison 1 Multiple risk factor intervention versus control, Outcome 10 Smoking prevalence (individual analysis or cluster).

Review: Multiple risk factor interventions for primary prevention of coronary heart disease

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 10 Smoking prevalence (individual analysis or cluster)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
1 Cluster randomisation - analysis by cluster					
Change of Heart	40/169	148/351		5.4 %	0.43 [0.28, 0.64]
Subtotal (95% CI)	**169**	**351**		**5.4 %**	**0.43 [0.28, 0.64]**
Total events: 40 (Treatment), 148 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 4.06 (P = 0.000050)					
2 Individual randomisation					
Abingdon	46/168	42/167		4.6 %	1.12 [0.69, 1.83]
CELL Study	139/292	148/310		6.5 %	0.99 [0.72, 1.37]
Family Heart - men	337/1767	500/2174		8.4 %	0.79 [0.68, 0.92]
Family Heart - women	215/1217	301/1402		8.0 %	0.78 [0.65, 0.95]
Finnish men	125/575	131/580		7.0 %	0.95 [0.72, 1.26]
Gothenberg Study	691/1473	699/1404		8.5 %	0.89 [0.77, 1.03]
MRFIT Study	1847/5754	2554/5638		9.1 %	0.57 [0.53, 0.62]
Nilsson 2001	17/43	27/46		2.3 %	0.46 [0.20, 1.07]
OXCHECK Study	544/2205	506/1916		8.6 %	0.91 [0.79, 1.05]
Swedish RIS	55/253	70/255		5.5 %	0.73 [0.49, 1.10]
Tromso men	247/525	284/535		7.5 %	0.79 [0.62, 1.00]
Tromso wives	186/422	178/387		7.0 %	0.93 [0.70, 1.22]
Subtotal (95% CI)	**14694**	**14814**		**83.0 %**	**0.82 [0.70, 0.95]**
Total events: 4449 (Treatment), 5440 (Control)					
Heterogeneity: Tau^2 = 0.05; Chi^2 = 72.53, df = 11 (P<0.00001); I^2 =85%					
Test for overall effect: Z = 2.56 (P = 0.010)					
3 Cluster randomisation - analysis by individual					
Meland 1997	35/58	30/52		2.7 %	1.12 [0.52, 2.39]
WHO Factories	7910/16908	897/1902		9.0 %	0.98 [0.90, 1.08]
Subtotal (95% CI)	**16966**	**1954**		**11.6 %**	**0.99 [0.90, 1.08]**
Total events: 7945 (Treatment), 927 (Control)					



(*Continued . . .*)

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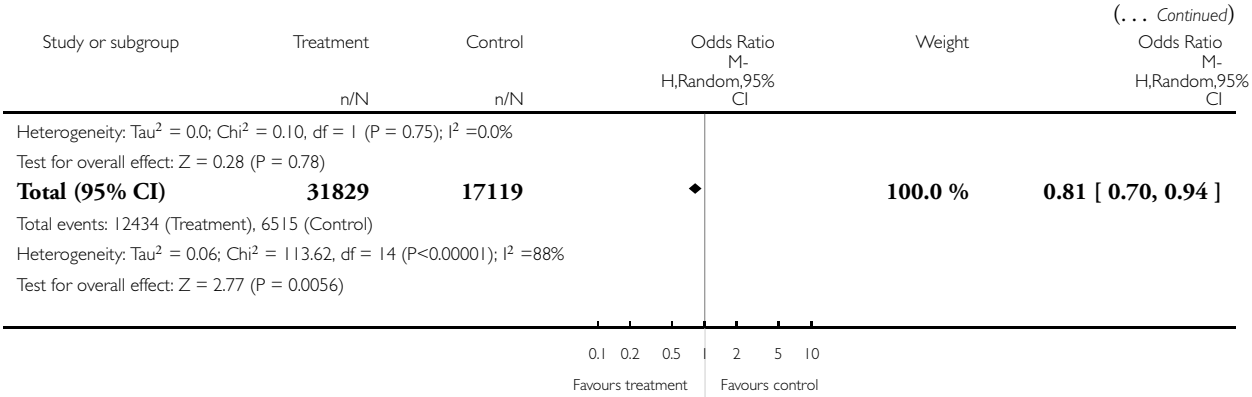
(. . . *Continued*)



ADDITIONAL TABLES

Table 1. MEDLINE search strategy April 1995

randomized controlled trial.pt.
randomized controlled trials/
random-allocation.sh.
double-blind-method.sh.
single-blind-method.sh.
1 or 2 or 3 or 4 or 5
clinical trials.pt.
clinical trials.sh.
clin$ near trial$.ti.
clin$ near trial$.ab.
placebo.sh.
placebo.tw.
random.tw.
7 or 8 or 9 or 10 or 11 or 12 or 13
limit 14 to human
coronary disease.sh.
cerebrovascular disorders.sh.

Table 2. CENTRAL search strategy Issue 3 2001

#1 CARDIOVASCULAR DISEASES
#2 CORONARY DISEASE
#3 cardiovascular

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Table 2. CENTRAL search strategy Issue 3 2001 (*Continued*)

#4 (coronary near disease*)
#5 (heart near disease*)
#6 HYPERTENSION
#7 hypertension
#8 (atherosclerosis or arteriosclerosis)
#9 (hyperlipidaemia or hyperlipidemia)
#10 ARTERIOSCLEROSIS
#11 CHOLESTEROL
#12 HYPERLIPIDEMIA
#13 cholesterol
#14 (multiple next risk next factor*)
#15 (coronary next risk next factor*)
#16 (#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10)
#17 (#11 or #12 or #13 or #14 or #15)
#18 (#16 or #17)
#19 HEALTH EDUCATION
#20 HEALTH PROMOTION
#21 HEALTH BEHAVIOR
#22 PRIMARY PREVENTION
#23 COUNSELING
#24 counsel*
#25 (health near educat*)
#26 (patient near educat*)
#27 (education* near program*)
#28 (health near promotion*)
#29 (health near behaviour*)
#30 (health near behavior*)
#31 (primary next prevention)
#32 ((multiple next risk) near intervention*)
#33 (multifactor* near intervention*)
#34 (multifactor* near prevention)
#35 ((risk next factor*) near reduc*)
#36 ((risk next factor*) near manag*)
#37 ((risk next factor*) near intervent*)
#38 (lifestyle near intervention*)
#39 (lifestyle near advice)
#40 (life-style near intervention*)
#41 (life-style near advice)
#42 (life-style near alter*)
#43 (lifestyle near alter*)
#44 (lifestyle near educat*)
#45 (life-style near educat*)
#46 (life-style near chang*)
#47 (lifestyle near chang*)
#48 (behavior* near chang*)
#49 (behaviour* near chang*)
#50 ((health next care) near advice)
#51 (healthcare near advice)
#52 nonpharmacologic*

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Table 2. CENTRAL search strategy Issue 3 2001 (*Continued*)

#53 non-pharmacologic*
#54 (#19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29)
#55 (#30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39)
#56 (#40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53)
#57 ((#54 or #55 or #56)
#58 (#18 and #57)

Table 3. MEDLINE search strategy September 2001

Database: Medline <Mid 1998 to August Week 2 2001>
Search Strategy:
---
1 cardiovascular diseases/
2 exp coronary disease/
3 hypertension/
4 exp Arteriosclerosis/
5 exp Hyperlipidemia/
6 (cardiovascular adj3 disease$).tw.
7 (cardiovascular adj3 (fit or fitness)).tw.
8 (Coronary adj3 disease$).tw.
9 heart disease$.tw.
10 hypertension.tw.
11 hyperlipid?emia.tw.
12 cholesterol.tw.
13 atherosclerosis.tw.
14 arteriosclerosis.tw.
15 coronary risk factor$.tw.
16 multiple risk factor$.tw.
17 cardiovascular risk factor$.tw.
18 or/1-17
19 health promotion/
20 exp health education/
21 exp health behavior/
22 exp counseling/
23 primary prevention/
24 (multifactor$ adj5 (intervent$ or prevent$)).tw.
25 ((lifestyle or life-style) adj3 (intervention$ or educat$ or advice$ or alter$ or change$)).tw.
26 ((lifestyle or life-style or behavio?r$) adj3 (intervention$ or educat$ or advice$ or alter$ or change$)).tw.
27 ((healthcare or health care) adj3 advice).tw.
28 primary prevention.tw.
29 (risk factor$ adj3 (reduc$ or manage$ or managing or intervent$ or program$)).tw.
30 (educat$ adj3 (program$ or patient$)).tw.
31 ((health or healthcare or health care) adj3 (educat$ or advice or promot$)).tw.
32 (nonpharmacologic$ or non-pharmacologic$).tw.
33 ((lifestyle or life style or life-style or behavio?r$ or risk factor$) adj3 modif$).tw.
34 or/19-33

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Table 3. MEDLINE search strategy September 2001 (*Continued*)

35 18 and 34
36 randomized controlled trial.pt.
37 controlled clinical trial.pt.
38 Randomized controlled trials/
39 random allocation.sh.
40 double blind method.sh.
41 single-blind method.sh.
42 or/36-41
43 (animal not human).sh.
44 42 not 43
45 clinical trial.pt.
46 exp Clinical trials/
47 (clin$ adj25 trial$).ti,ab.
48 ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab.
49 placebos.sh.
50 placebo$.ti,ab.
51 random$.ti,ab.
52 research design.sh.
53 or/45-52
54 53 not 43
55 54 not 44
56 44 or 54
57 35 and 56
58 limit 57 to yr=2000-2001

Table 4. EMBASE search strategy September 2001

Database: EMBASE <1996 to August Week 2 2001>
Search Strategy:
---
1 cardiovascular diseases/
2 exp coronary disease/
3 hypertension/
4 exp Arteriosclerosis/
5 exp Hyperlipidemia/
6 (cardiovascular adj3 disease$).tw.
7 (cardiovascular adj3 (fit or fitness)).tw.
8 (Coronary adj3 disease$).tw.
9 heart disease$.tw.
10 hypertension.tw.
11 hyperlipid?emia.tw.
12 cholesterol.tw.
13 atherosclerosis.tw.
14 arteriosclerosis.tw.
15 coronary risk factor$.tw.
16 multiple risk factor$.tw.

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Table 4. EMBASE search strategy September 2001 (*Continued*)

17 cardovascular risk factor$.tw.
18 or/1-17
19 health promotion/
20 exp health education/
21 exp health behavior/
22 exp counseling/
23 primary prevention/
24 (multifactor$ adj5 (intervent$ or prevent$)).tw.
25 ((lifestyle or life-style) adj3 (intervention$ or educat$ or advice$ or alter$ or change$)).tw.
26 ((lifestyle or life-style or behavio?r$) adj3 (intervention$ or educat$ or advice$ or alter$ or change$)).tw.
27 ((healthcare or health care) adj3 advice).tw.
28 primary prevention.tw.
29 (risk factor$ adj3 (reduc$ or manage$ or managing or intervent$ or program$)).tw.
30 (educat$ adj3 (program$ or patient$)).tw.
31 ((health or healthcare or health care) adj3 (educat$ or advice or promot$)).tw.
32 (nonpharmacologic$ or non-pharmacologic$).tw.
33 ((lifestyle or life style or life-style or behavio?r$ or risk factor$) adj3 modif$).tw.
34 or/19-33
35 18 and 34
36 cardiovascular disease/
37 exp ischemic heart disease/
38 (coronary adj3 disease$).tw.
39 heart disease$.tw.
40 Hypertension/
41 hypertension.tw.
42 (cardiovascular adj3 (disease$ or fit of fitness)).tw.
43 exp arteriosclerosis/
44 exp hyperlipidemia/
45 hyperlipid?emia.tw.
46 cholesterol.tw.
47 arteriosclero$.tw.
48 atherosclero$.tw.
49 coronary risk factor$.tw.
50 multiple risk factor$.tw.
51 cardiovascular risk factor$.tw.
52 or/36-51
53 exp health education/
54 exp health behavior/
55 primary prevention/
56 exp counseling/
57 (multifactor$ adj5 (intervent$ or prevent$)).tw.
58 ((life-style or life style or lifestyle or healthcare or health care) adj3 (intervention$ or educat$ or advice or alter$ or change$)).tw.
59 primary prevention.tw.
60 (risk factor$ adj3 (reduc$ or manage$ or managing or intervent$ or program$)).tw.
61 (educat$ adj3 (program$ or patient$)).tw.
62 (non pharmacologic$ or nonpharmacologic$).tw.
63 (risk factor$ adj3 modif$).tw.
64 ((lifestyle or life-style or life style) adj3 modif$).tw.
65 exp behavior therapy/

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Table 4. EMBASE search strategy September 2001 (*Continued*)

66 (behavi?r$ adj3 (intervention$ or program$ or modif$ or change$ or alter$)).tw.
67 (promot$ adj3 (health or healthcare or health care)).tw.
68 or/53-67
69 52 and 68
70 random$.tw.
71 randomized controlled trial/
72 trial$.tw.
73 compar$.tw.
74 follow-up.tw.
75 blind$.tw.
76 double blind procedure/
77 placebo$.tw.
78 placebo/
79 doubl$.tw.
80 nonhuman/ not human/
81 exp child/ not exp adult/
82 or/70-79
83 82 and 69
84 83 not (80 or 81)

WHAT'S NEW

Last assessed as up-to-date: 17 August 2006.

Date	Event	Description
9 September 2008	Amended	Converted to new review format.

HISTORY

Review first published: Issue 2, 1999

Date	Event	Description
18 August 2006	New citation required and conclusions have changed	Substantive amendment

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CONTRIBUTIONS OF AUTHORS

G Davey Smith and S Ebrahim wrote the original review.

For the update:

A Beswick selected studies, extracted data, performed analysis, and co-wrote the review

M Burke ran searches, selected studies and extracted data

S Ebrahim selected studies, analysed data and co-wrote the review

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- MRC Health Services Research Collaboration, UK.
- Systematic Reviews Training Unit, University of London, UK.
- Department of Social Medicine, University of Bristol, UK.
- Department of Epidemiology & Population Health, London School of Hygeine & Tropical Medicine, UK.

External sources

- NHS Centre for Reviews & Dissemination, University of York, UK.
- Health Education Authority, London, UK.

INDEX TERMS

Medical Subject Headings (MeSH)

Coronary Disease [mortality; *prevention & control]; Patient Education as Topic; Randomized Controlled Trials as Topic; Risk Factors

MeSH check words

Humans

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