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

Ebrahim S, Taylor F, Ward K, Beswick A, Burke M, Davey Smith G

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[Intervention Review]

Multiple risk factor interventions for primary prevention of coronary heart disease

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ABSTRACT

Background

Multiple risk factor interventions using counselling and educational methods assumed to be efficacious and cost-effective in reducing coronary heart disease (CHD) mortality and morbidity and that they should be expanded. Trials examining risk factor changes have cast doubt on the effectiveness of these interventions.

Objectives

To assess the effects of multiple risk factor interventions for reducing total mortality, fatal and non-fatal events from CHD and cardiovascular risk factors among adults assumed to be without prior clinical evidence CHD..

Search strategy

We updated the original search BY SEARCHING CENTRAL (2006, Issue 2), MEDLINE (2000 to June 2006) and EMBASE (1998 to June 2006), and checking bibliographies.

Selection criteria

Randomised controlled trials of more than six months duration using counselling or education to modify more than one cardiovascular risk factor in adults from general populations, occupational groups or specific risk factors (i.e. diabetes, hypertension, hyperlipidaemia, obesity).

Data collection and analysis

Two authors extracted data independently. We expressed categorical variables as odds ratios (OR) with 95% confidence intervals (CI). Where studies published subsequent follow-up data on mortality and event rates, we updated these data.

Main results

We found 55 trials (163,471 participants) with a median duration of 12 month follow up. Fourteen trials (139,256 participants) with reported clinical event endpoints, the pooled ORs for total and CHD mortality were 1.00 (95% CI 0.96 to 1.05) and 0.99 (95% CI 0.92 to 1.07), respectively. Total mortality and combined fatal and non-fatal cardiovascular events showed benefits from intervention

when confined to trials involving people with hypertension (16 trials) and diabetes (5 trials): OR 0.78 (95% CI 0.68 to 0.89) and OR 0.71 (95% CI 0.61 to 0.83), respectively. Net changes (weighted mean differences) in systolic and diastolic blood pressure (53 trials) and blood cholesterol (50 trials) were -2.71 mmHg (95% CI -3.49 to -1.93), -2.13 mmHg (95% CI -2.67 to -1.58) and -0.24 mmol/l (95% CI -0.32 to -0.16), respectively. The OR for reduction in smoking prevalence (20 trials) was 0.87 (95% CI 0.75 to 1.00). Marked heterogeneity (I^2 > 85%) for all risk factor analyses was not explained by co-morbidities, allocation concealment, use of antihypertensive or cholesterol-lowering drugs, or by age of trial.

Authors' conclusions

Interventions using counselling and education aimed at behaviour change do not reduce total or CHD mortality or clinical events in general populations but may be effective in reducing mortality in high-risk hypertensive and diabetic populations. Risk factor declines were modest but owing to marked unexplained heterogeneity between trials, the pooled estimates are of dubious validity. Evidence suggests that health promotion interventions have limited use in general populations.

PLAIN LANGUAGE SUMMARY

Multiple risk factor interventions for coronary heart disease

In many countries, there is enthusiasm for 'healthy heart programmes' that use counselling 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 review is an update of all relevant randomised trials that have evaluated an intervention that aimed to reduce more than one risk factor (multiple risk factor intervention) in people without evidence of cardiovascular disease. The findings are from 55 trials of between six months and 12 years duration conducted in several countries over the course of four decades. The median duration of follow up was 12 months (with a range of six months to 12 years). Multiple risk factor intervention does result in small reductions in risk factors including blood pressure, cholesterol and smoking. Contrary to expectations, multiple risk factor interventions had little or no impact on the risk of coronary heart disease mortality or morbidity. This could be because these small risk factor changes were not maintained in the long term. Alternatively, the small reductions in risk factors may be caused by biases in some of the studies. The methods of attempting behaviour change in the general population are limited and do not appear to be effective. Different approaches to behaviour change are needed and should be tested empirically before being widely promoted, particularly in developing countries where cardiovascular disease rates are rising. Further trials may be warranted.

BACKGROUND

As the incidence of cardiovascular disease is largely explained by modifiable risk factors (serum cholesterol and reduced high-density lipoprotein (HDL) cholesterol, blood pressure and cigarette smoking), reducing risk factors through health promotion focusing on lifestyles is a logical way of preventing disease. Randomised controlled trials of the effectiveness 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 workplace. The findings of these trials have been equivocal; effectiveness in reducing cardiovascular disease incidence appears to be associated with the degree of risk factor control achieved (Editorial 1982a; Editorial 1982b; Appel 2004). Taken with evidence from quasi-experimental 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 is widely believed that multiple risk factor intervention using counselling and educational methods is both effective and cost-effective and should be expanded. Recently this idea has been extended to people with diabetes (Davey Smith 2005; Sartorelli 2005) and hypertension (Pickering 2003; Little 2004; Svetkey 2005).

In many countries multiple risk factor counselling and health education is embodied in guidelines produced by professional groups (NSF-CHD 2000; AHA 2002; NSF-CHD 2006; European Task Force 2007) and government (Kickbush 1988; NSF-CHD 2000; Muto 2001) recommending use of behavioural counselling for stopping smoking tobacco, making healthy food choices and increasing physical activity.

Alongside the guidelines, health services have acted by developing health promotion as a specialty (Editorial 1984) and in the UK extra payments are now made for the routine collection of data on cardiovascular risk factors in primary care, and issuing of primary prevention policy (NSF-CHD 2000).

Non-systematic reviews have promoted the notion that multiple risk factor intervention is effective (McCormick 1988; Schoenberger 1990). However, a systematic review of the randomised trial evidence involving almost a million person-years of observation, using Cochrane Collaboration methodology, demonstrated no impact of multiple risk factor intervention on coronary heart disease mortality (Ebrahim 1997). Since this systematic review was published in 1997 more randomised trials and community evaluations have been published, predominantly with disappointing findings (Tudor-Smith 1998; Berglund 2000; Pickering 2004). A recent non-systematic review has again claimed benefits for multiple risk factor intervention (Daviglus 2006). With the rising burden of cardiovascular diseases in developing countries, there has been a strong view that multiple risk factor intervention should be the cornerstone of primary prevention (Ebrahim 2008; Vartiainen 2009), although it is acknowledged that interpretation of the findings from the randomised trials makes this problematic in poor countries (Ebrahim 2001; Lim 2007). In view of the continued policy importance of multiple risk factor intervention a further update of the review was needed to incorporate several new trials.

OBJECTIVES

To assess the effectiveness of multiple risk factor intervention using counselling or educational approaches (or both) aimed at behaviour change, with or without pharmacological interventions, in adults assumed to be without prior clinical evidence of heart attacks, stroke or peripheral vascular disease in reducing:

1. total (all-cause), CHD and stroke mortality;
2. non-fatal CHD and stroke events;
3. systolic and diastolic blood pressure;
4. blood cholesterol levels; and
5. smoking rates.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) of at least six months duration of follow up with parallel-group design. Trials could be randomised by individual or by group (e.g. family, workplace site).

Types of participants

We included trials which recruited an adult population whose mean age was 35 or above.
General populations included workforce populations and high-risk groups (hypertension, obesity, hyperlipidaemia, type 2 diabetes or a combination of these) as well as subjects that did not have a high risk of developing CHD. We excluded trials where the percentage of participants with evidence of CHD was more than 25%.

Types of interventions

A health promotion activity to achieve behaviour change; more specifically counselling or educational interventions, with or without pharmacological treatments, which aim to alter more than one cardiovascular risk factor (i.e. diet, reduce blood pressure, smoking, total blood cholesterol or increase physical activity).

Types of outcome measures

Primary outcomes

Total (all-cause) mortality, fatal CHD and fatal stroke events.

Secondary outcomes

Non-fatal CHD (including myocardial infarction, unstable angina, need for coronary bypass grafting and or percutaneous coronary intervention) and stroke events requiring hospital admission, net change in blood pressure, total blood cholesterol and smoking.

Search methods for identification of studies

For the original review we searched MEDLINE from 1966 to April 1995 using a RCT filter (Dickersin 1994) (see Appendix 3). We checked reference lists of identified papers, sought expert advice and undertook citation searches.
We updated these searches by searching the Cochrane Central Register of Controlled Trials (CENTRAL) in *The Cochrane Library* (2006, Issue 2), MEDLINE (2000 to June 2006) and EMBASE (1998 to June 2006), using a RCT filter for MEDLINE (Dickersin 1994) and EMBASE (Lefebvre 1996) (see Appendix 1 and Appendix 2). Reports of RCTs from MEDLINE and EMBASE are added to CENTRAL on a regular basis; to avoid duplication of effort we did not search earlier years of these databases.

We checked references of identified studies and made searches for additional follow-up papers if the studies published up until 2006 did not provide all of the data required for the review. We applied no language restrictions.

Data collection and analysis

For the searches in 1997 and in 2006, two review authors checked all titles and abstracts obtained through the searches independently to eliminate studies that were definitely not relevant to the review. In the 2001 update, one review author checked the results of searches and eliminated all those definitely not relevant to the review. Two review authors checked the remaining papers independently. For all versions, two review authors obtained and read each paper thought to be of possible relevance to determine whether it fitted the specified inclusion criteria. We discussed disagreements and resolved them with a third review author.

Two review authors performed independent data abstraction using a data extraction form and resolved disagreements by discussion or by consultation with a third review author. We contacted chief investigators to provide additional relevant information where necessary.

We attempted to contact study authors. However, when information was not available from trialists, we assumed missing data to occur at random.

The main aspects of quality which were formally assessed included the adequacy of concealment of randomisation, comparability of baseline characteristics, blinding of outcome assessors and completeness of follow up. It was not possible to include blinding of intervention allocation since this is not possible in lifestyle interventions.

For continuous variables (i.e. blood pressure, blood cholesterol) we used mean differences with 95% confidence intervals (CI) to ascertain net changes (i.e. control group minus intervention group differences). We used the longest duration of follow up that was reported in the primary publications. For studies where subsequent follow-up data were published, we did not update data on continuous variables since it was considered likely that long-term findings would reflect attrition bias, effects of co-treatments with drugs and possibly publication bias (publication of positive findings). Similarly, we used smoking levels from the primary publication of the trial and did not use any subsequent published follow-up data in analyses.

We expressed categorical variables (e.g. mortality, clinical event rates and smoking) as odds ratios (OR) with 95% CI. We used fixed-effect models except in instances where there was significant heterogeneity of effects, where we applied a random-effects model. For studies where subsequent follow-up data on mortality and event rates were published, we updated these data in the review. We applied intention-to-treat analysis to these outcomes.

We quantified statistical heterogeneity using the I^2 statistic which describes the percentage of total variation across studies that is due to heterogeneity rather than sampling error (Higgins 2008). We summarised the findings using a fixed-effect model unless there was significant heterogeneity (I^2 statistic > 75%) in which case we applied a random-effects model. In case of significant heterogeneity we sought to identify and explain possible causes by exploring the effect of participant, drug treatment, era of study and study design characteristics.

We confined subgroup analysis to co-morbidity (diabetes, hypertension, hyperlipidaemia and obesity and one other co-morbidity (e.g. obesity and diabetes), no co-morbidity), and evidence of prescribed drug treatment (prescribed medication during trial and no prescribed medication or drug treatment not stated).

We used meta-regression methods to examine the effects of age and blood pressure and cholesterol-lowering drug treatments on outcomes. We also examined the effect of level of coronary heart disease risk using the control group incidence rates to determine whether trials recruiting higher-risk participants were more likely to demonstrate beneficial effects.

We confined sensitivity analysis to method of randomisation (cluster, cluster analysed as individual, individual), allocation of concealment (adequate, unclear, inadequate) and age of trial (publication of trial before 2000 and after 2000). We used funnel plots to ascertain publication bias for each outcome.

RESULTS

Description of studies

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

Results of the search

The updated search (2001 to 2006) resulted in 3926 references, after removal of duplicates. From these we excluded 3844 and obtained 82 full-text papers for further inspection. Of these we excluded 55 papers reporting on 50 studies. Thus in total, including studies already listed as excluded in previous versions of the review, we excluded 128 references, reporting on 117 studies (see Characteristics of excluded studies). One additional paper was a design paper for an ongoing study (Roderigues 2005)

Citation searching of included studies identified two further papers for these studies (Look AHEAD 2003; Toobert (MLP) 2005) thus we added 29 papers reporting on 16 studies to those studies already included in previous versions. In total we included 55 trials (reported in 91 papers). Details of these studies are shown in the table of Characteristics of included studies.

Included studies

We found a total of 55 trials of multiple risk factor intervention, comprising 61 distinct study groups; a dramatic increase on the 14 trials identified for the original review. The total number of patients recruited amounted to 163,471 with data on clinical endpoint for 139,256 participants. The trials with clinical endpoints comprised approximately 909,500 patient-years of observation and those with risk factor endpoints 321,000 patient-years of observation. The duration of follow up ranged from six months to 12 years; the median follow-up time was one year. Sixteen studies (with 17 arms) recruited patients with hypertension and five trials were of patients with diabetes.

Fourteen trials reported total or coronary heart disease mortality as outcomes and two trials from the original review (the Swedish RIS 1994 study and the WHLP 1998) 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 (HDFP trial 1970; MRFIT Study 1982; Gothenberg Study 1986; WHO Factories 1986). In the Rachmani 2005 trial the number of fatal and non-fatal clinical events outnumbered the number of participants recruited to the study. For the purpose of this review, we used the number of participants who experienced one or more events in this analysis. However, most recent trials did not include clinical event endpoints but focused on the following outcomes: blood pressure, serum cholesterol, physical activity, diet, control of diabetes and weight loss.

In general, the trials compared an intervention comprising some form of counselling and education with control groups, which either received usual care or nothing was described. The type and intensity of behavioural intervention used was seldom reported in the older trials. Very few studies reported the theoretical approach used to underpin the intervention. When stated, the Stages of Change model (Prochaska 1983; DiClemente 1991) was the most common approach used. A person-centred and self-directed psychological approach was used by one study (Meichenbaum 1993) and another one relied on a combination of social cognitive theory, goal systems theory and social ecological theory (Toobert (MLP) 2005). Most education and counselling intervention strategies targeted a combination of risk factors including diet, exercise, weight loss, salt intake, alcohol use, stress management, smoking cessation, adherence to medication or specific clinical regimens, particularly in patients with hypertension or diabetes.

Interventions included workshops, lectures, individual sessions, personal counselling, provision of written material, assignments, shopping tours and cooking sessions. Some studies required family members, partners or both to participate in the intervention. The intervention strategies were commonly provided by a variety of health professionals including physicians, nurses, nutritionists, dieticians, nurses, exercise trainers, cooks, psychotherapists and physiotherapists. The intensity varied and ranged from four to 54 sessions over periods of time ranging from two weeks to three years.

With the exception of two studies recruiting men and women over the age of 60 years (Applegate 1992; Garcia-Pena 2001), the oldest subjects included in the trials were 75 years of age. The majority of trials randomised only middle-aged adults, although younger adults were recruited by some studies. The mean age in all the trials was 50 years.

Few studies looked at quality of life (Oslo Diet Exercise; Toobert (MLP) 2005) and only one examined cost-effectiveness of the intervention; in this case a nurse-led intervention for elderly hypertensive patients (Garcia-Pena 2001).

Excluded studies

We excluded 116 trials identified as involving multiple risk factor interventions from consideration for the following reasons: no relevant risk factor changes measured and/or reported (n = 159), non-random allocation to intervention and control groups (n = 315), no specific multiple risk factor intervention (n = 6), control group received substantial intervention (n = 210), follow up to at least six months was not reported (n = 12), the mean age of participants was less than 35 (n = 88), over 25% of participants had CHD (n = 110), numbers in groups were not reported (n = 1), baseline or follow-up data were not provided (n = 6), or no comparable control group was identified (n = 6). A large number of older studies were set up in what was then the Soviet Union but it appeared that allocation to intervention and control groups was not random. Attempts to trace the investigators were unsuccessful. Three studies appeared suitable in the latest update but missing data precluded them from inclusion in the review update, as attempts to request data from the original authors were unsuccessful (Boylan 2003; Kisioglu 2004; Elliot 2007).

Risk of bias in included studies

The quality of the trials examined deserves comment. Very few of the older published trials 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 the intervention. One third of studies (n = 18) used an intention-to-treat analysis on both categorical and continuous variables. Some explained that the last available reported measurement was used for the final endpoint measurement. Of these 18 studies, the loss to follow up ranged from 1% to 42% (median 13%). As such, losses to follow up were a particular problem as changes in risk factors cannot be reliably assessed in an intention-to-treat analysis.

Random allocation methods were not usually reported. In only 13 out of 55 trials we considered the methods used as adequate and in nine they were inadequate. We made specific enquiries of investigators for the original review predominantly to obtain event

data but did not make these in this update as most of the new trials had measured clinical events. In the large trials it is unlikely that the allocation method was suspect but was simply inadequately reported.

Blinding of intervention allocation for the participants is not possible in lifestyle interventions and this inevitably raises the possibility of bias. Only 12 out of 55 trials blinded the assessors to treatment allocation. As such 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 may have 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 and or relying on self-reported smoking histories may have resulted in a reporting bias with those allocated to interventions more likely to say they had stopped smoking, as seen in previous studies (West 2007). Validation of self-reported smoking outcomes using biochemical assay of serum thiocyanate was reported in only three of the older trials and none of the new trials.

Effects of interventions

Total (all-cause), coronary heart disease (CHD) and stroke mortality

Total (all-cause) mortality

From the 14 studies that reported total mortality, there was no strong evidence of any reduction in the pooled analysis (RR 1.00; 95% CI 0.96 to 1.05) using a fixed-effect model (Analysis 1.1). Follow up of mortality ranged from six months to 12 years.

A significant reduction in all-cause mortality was seen in trials where patients were recruited with either hypertension or diabetes (RR 0.78; 95% 0.68 to 0.89) (Analysis 1.4) and in those trials where patients were being prescribed either antihypertensive or lipid-lowering drugs during the trial period (RR 0.86; 95% CI 0.78 to 0.96) (Analysis 1.5) using a fixed-effect model.

Coronary heart disease mortality

Eleven trials reported on coronary heart disease mortality; the pooled OR was 0.99 (95% CI 0.92 to 1.07) using a fixed-effect model (Analysis 1.8).

Stroke mortality

Six trials reported on stroke mortality (HDFP trial 1970; Finnish men 1985; Gothenberg Study 1986; Oslo Diet Antismoking; Swedish RIS 1994; Rachmani 2005). Only one of these trials reported a significant reduction in stroke mortality but the pooled relative risk favoured intervention (RR 0.75; 95% CI 0.60 to 0.95) (Analysis 1.15) using a fixed-effect model. This may be explained by better monitoring and adherence of drug treatment as five of the six trials were given drug treatment during the study.

For total and coronary heart disease mortality, funnel plots suggested no evidence of small study bias in trials (Figure 1; Figure 2). Evidence of significant statistical heterogeneity was not apparent in the pooled RR for total mortality, coronary heart disease mortality or stroke mortality.

Figure 1.

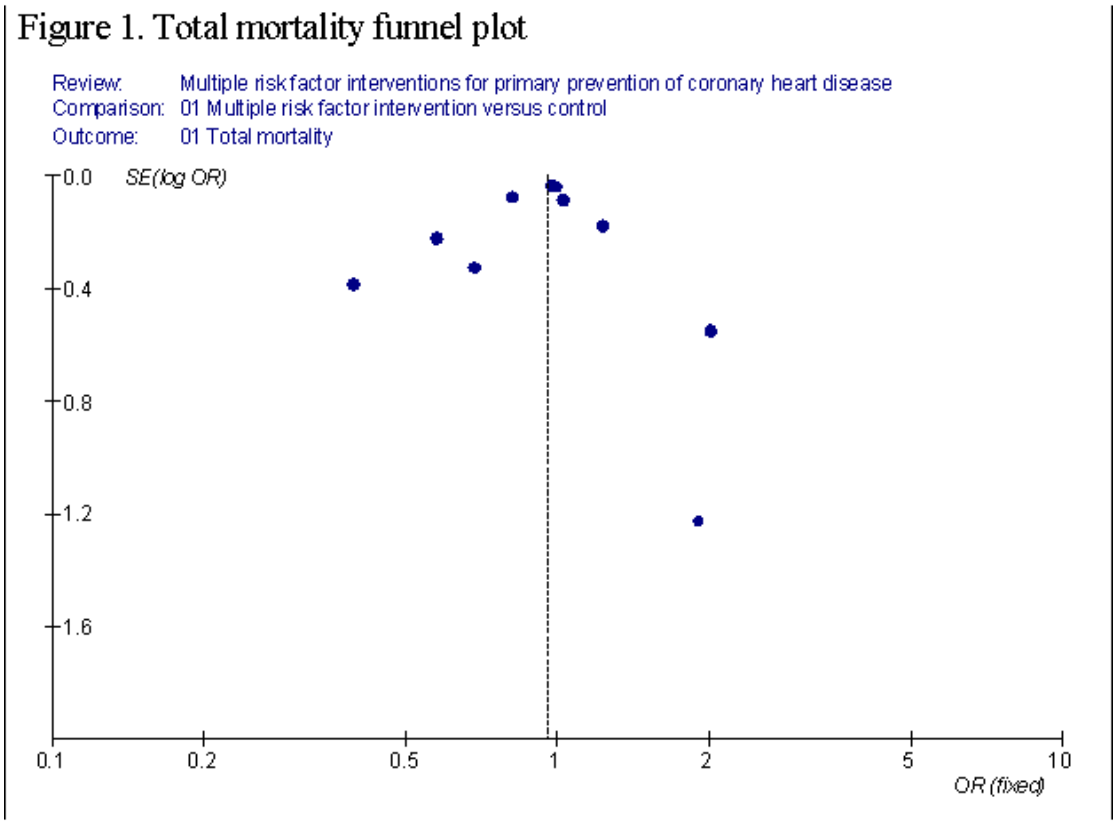
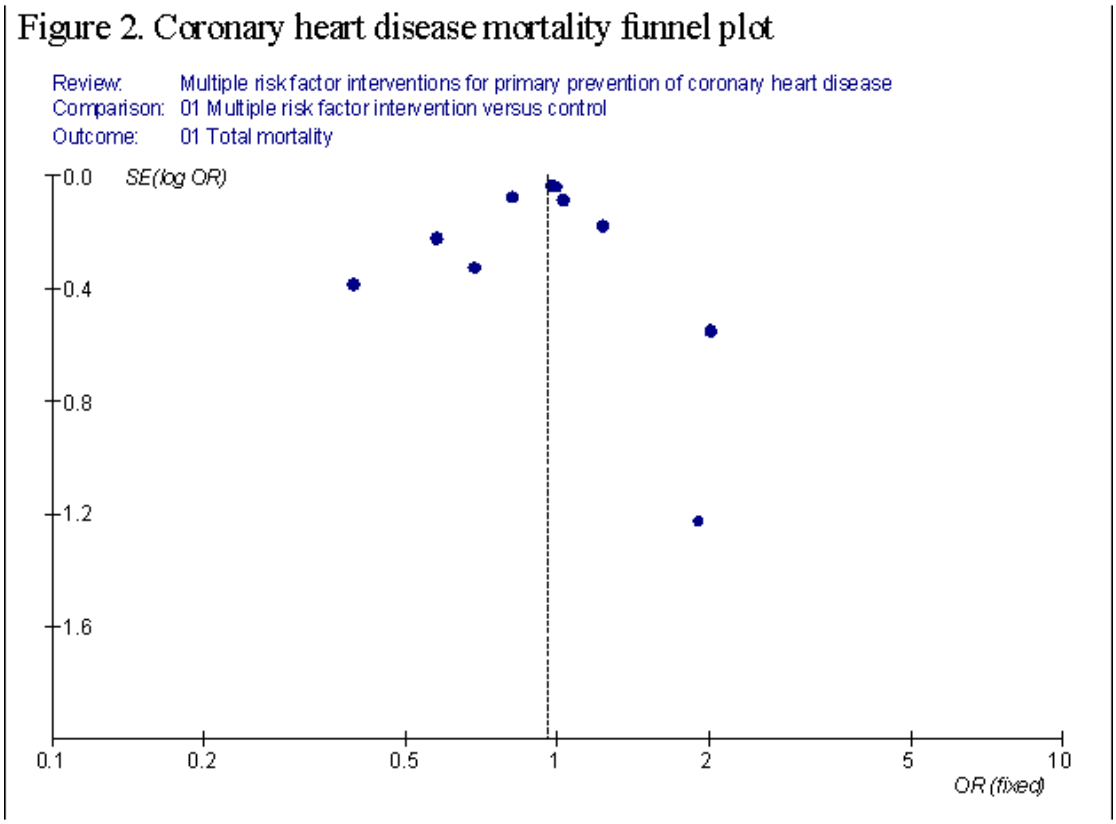


Figure 2.



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. There was a significant interaction between intervention and level of coronary heart disease risk estimated from control group incidence, indicating that trials recruiting higher-risk participants were more likely to demonstrate beneficial effects. This effect was 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.

Allocation concealment had little effect on total mortality although the trials with inadequate allocation concealment reported stronger evidence of an effect on total mortality, however this was driven by the HDFP trial of hypertensives (Analysis 1.3).

Fatal and non-fatal clinical events

Nine trials reported on fatal and non-fatal clinical events which required hospital admission (HDFP trial 1970; MRFIT Study 1982; Oslo Diet Antismoking; Finnish men 1985; Gothenberg Study 1986; WHO Factories 1986; Swedish RIS 1994; Garcia-Pena 2001; Rachmani 2005) and four trials reported on stroke events (Oslo Diet Antismoking; Gothenberg Study 1986; Swedish RIS 1994; Rachmani 2005). The follow-up period ranged from six months to 11.8 years.

All analyses showed considerable heterogeneity of effect (I^2 above 75%) so findings must be viewed with caution. Overall, a reduction in events was observed (RR 0.84; 95% CI 0.73 to 0.98) (Analysis 1.21) using a random-effects model. This effect was explained by inclusion of patients with either hypertension or diabetes in whom the combined event relative risk was 0.71 (95% CI 0.61 to 0.83) (Analysis 1.24). No effect was seen in participants without a co-morbidity.

Changes in risk factors

For all analyses of risk factor changes very high levels of heterogeneity of effect were found (I^2 between 85% and 97%). Although we applied random-effects, we cannot draw conclusions regarding the consistency of effects on risk factors. We explored this heterogeneity and it could not be attributed fully to the effects of pharmacological treatment or study design effects. There was some evidence of possible regression to the mean effects as risk factor net changes were strongly correlated with the initial level of blood pressure, smoking and blood cholesterol. 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. In other words, those studies with the highest baseline diastolic blood pressure, smoking prevalence and blood cholesterol levels demonstrated larger falls in these risk factors at follow up.

Systolic and diastolic blood pressure

For both systolic and diastolic blood pressure, 48 trials (53 arms) indicated a significant reduction favouring intervention. The weighted mean difference between intervention and control was -2.71 mm Hg (95% CI -3.49 to -1.93) for systolic blood pressure and -2.13 mm Hg (95% CI -2.67 to -1.58) for diastolic blood pressure using random-effects models (Analysis 1.36; Analysis 1.42). In total, 24 trials reported that patients were on medication for high blood pressure. When analysis of outcomes was confined to these trials, strong evidence of reductions in both systolic and diastolic remained. This was also seen when the analysis was confined to trials where no medication was prescribed (Analysis 1.39; Analysis 1.46).

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 (Hjermann I, personal communication, 1996). Overall, changes in blood pressure were small. 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 3.

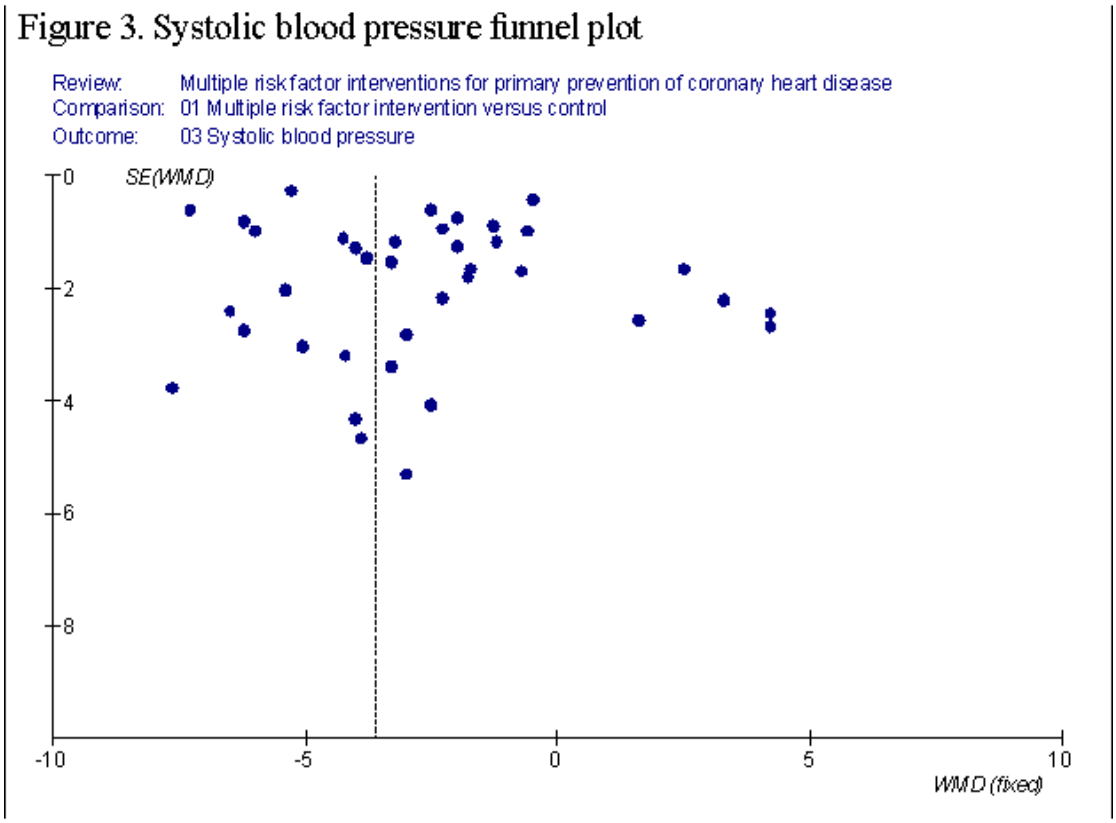
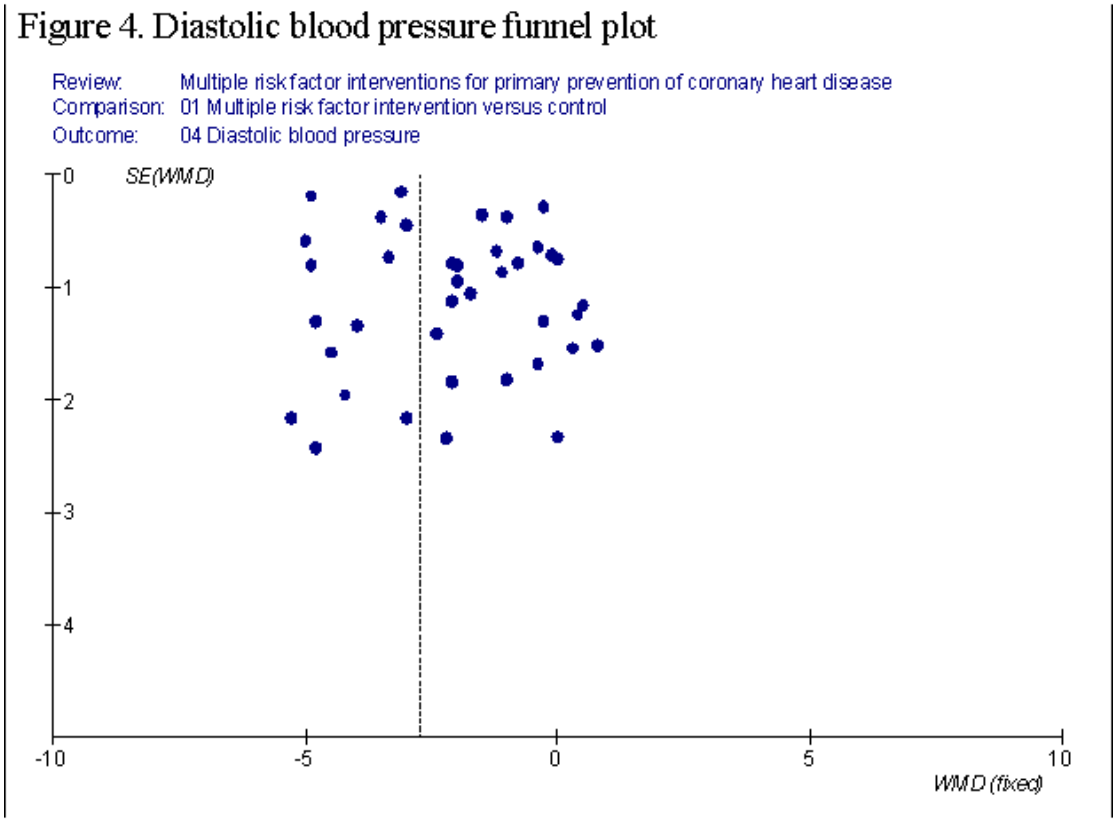


Figure 4.



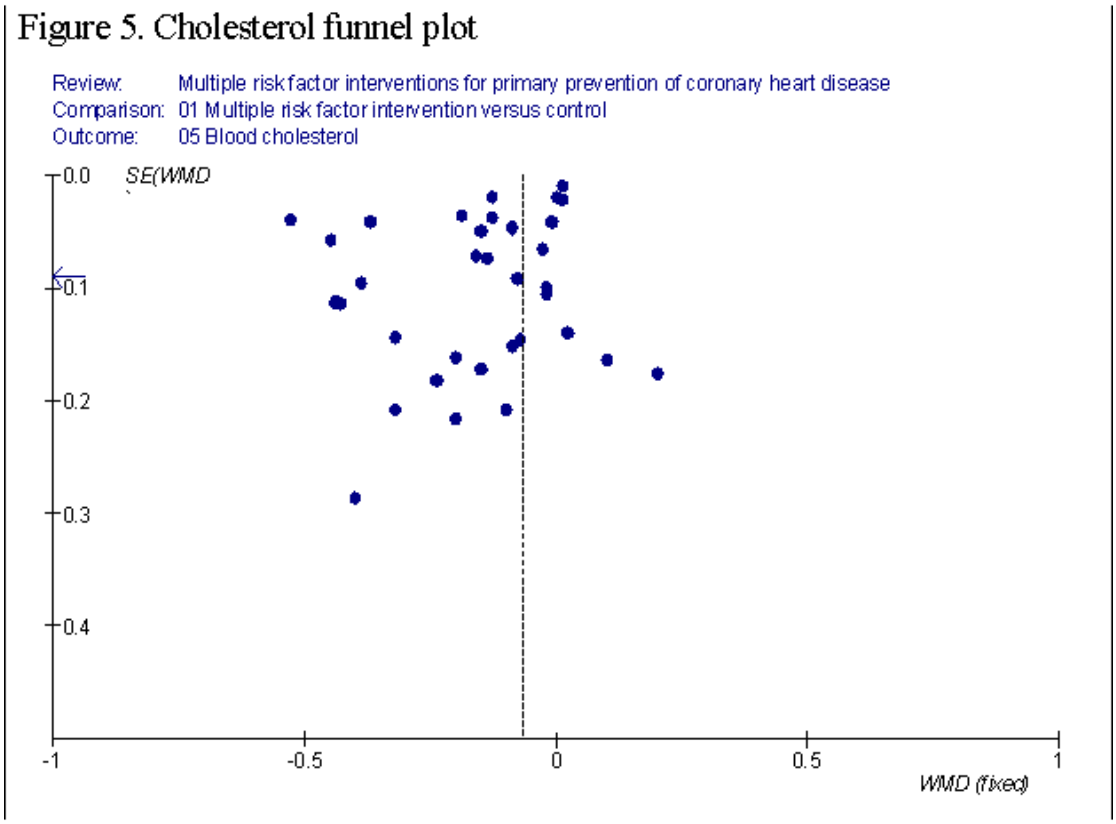
Both subgroup and sensitivity analysis had no effect in reducing heterogeneity or on the overall but inconsistent findings of a reduction in blood pressure.

Blood cholesterol

Forty-four trials (50 arms) reported blood cholesterol as an outcome. Blood cholesterol levels showed a small but highly significant fall (weighted mean net difference -0.07 mmol/L; 95% CI -0.08 to -0.06) (Analysis 1.49) using a random-effects model. This is a bigger effect on cholesterol-lowering than previously seen in the 2001 update of this review. Nineteen trials reported that patients were on cholesterol-lowering medication and when analysis was confined to this group the reduction in cholesterol was almost identical to the pooled result and was similar to that seen in those trials in which no cholesterol-lowering drugs were used (Analysis 1.53). Cholesterol levels were lower in the trials in which both antihypertensive and cholesterol-lowering drugs were used (-0.18 mmol/L; 95% CI -0.22 to -0.14 mmol/L).

Trials with inadequate concealment showed a non-significant reduction compared with those with adequate or unclear concealment (Analysis 1.51). Figure 5 shows no evidence of small study bias.

Figure 5.



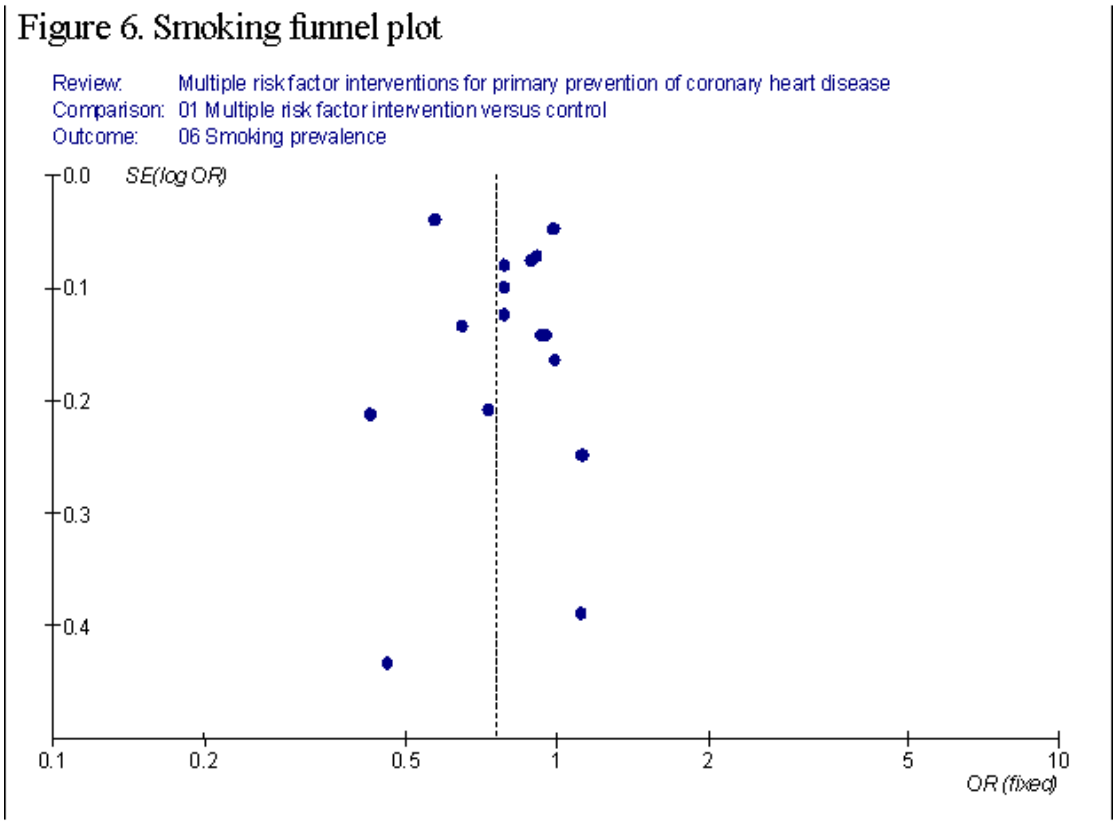
Smoking

Twenty studies reported on smoking prevalence. Pooled analysis indicated a non-significant reduction in smoking prevalence (RR 0.87; 95% CI 0.75 to 1.00) (Analysis 1.28). Most of the studies relied on self-reported smoking status at end of follow up. In the Hypertension Detection & Follow up Program quantitative data were not available but no changes in smoking rates were found (HDFP trial 1970). Smoking rates fell particularly sharply in the Multiple Risk Factor Intervention Trial and in the Change of Heart 1999 study. The former used individual smoking advice given by a physician (MRFIT Study 1982) and in the latter large baseline differences between groups were noted and losses to follow up were high (Change of Heart 1999). Validation of self-reported smoking rate reductions in the Multiple Risk Factor Intervention Trial (MRFIT Study 1982) by comparison with serum thiocyanate levels suggested that the improvement might be overestimated. None of the more recent trials indicated a significant reduction in smoking status.

Subgroup analysis indicated no change in the results in the other studies which had recruited a low number of participants with cardiovascular disease (CVD), where the risk reduction was 15% (RR 0.85; 95% CI 0.79 to 0.92) (Analysis 1.33) using a random-effects model.

Allocation concealment had no effect on the results. Figure 6 shows no evidence of small study bias.

Figure 6.



Sensitivity analysis

Age of trial

Age of trial did not have a significant effect on trial outcome other than fatal and non-fatal clinical events. Studies published before 2000 reported similar effect sizes compared with those published after 2000. Net differences were small: -0.45 mm Hg in systolic blood pressure, -0.49 mm Hg for diastolic blood pressure, 0.04 mmol/L in blood cholesterol (RR difference of -0.26 for total clinical events).

Cluster-randomisation

In meta-analysis the weighting given to trials with a cluster design may be over-estimated. Only one trial used a cluster design where analysis was confined to the clusters (Change of Heart 1999) and no benefits were demonstrated other than a 57% risk reduction in smoking prevalence (RR 0.43; 95% CI 0.28 to 0.64) (Analysis 1.29) using a random-effects model. In trials with a cluster design which provided analysis by individual significant benefits were observed in reductions of systolic and diastolic blood pressure and cholesterol (Analysis 1.36; Analysis 1.43; Analysis 1.50), all using a random-effects model. Overall benefits tended to be in trials with randomisation by individual.

Quality of life and economic costs

Oslo Diet Exercise used the General Health Questionnaire and found that exercise had a significant effect on enhancing self-esteem, competence and coping for the intervention group but that other quality of life dimensions remained unchanged. Toobert (MLP) 2005 used the Medical Outcomes, Short Form General Health questionnaires together with the Problem Areas in Diabetes scale. When the results were combined, quality of life did improve

for the intervention group particularly in enhancing competence in self-care. Garcia-Pena 2001 evaluated a programme whereby a nurse made weekly or fortnightly home visits to elderly patients with hypertension. In applying a cost-effectiveness analysis, the authors concluded that the reduction in blood pressure obtained may justify the small incremental cost of the intervention.

DISCUSSION

As reported in the earlier review, multiple risk factor interventions comprising counselling, education aimed at behaviour change and drug therapies for the primary prevention of coronary heart disease 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 8% reduction in coronary heart disease mortality) may have been missed despite the very large sample sizes in several of the trials. It is surprising that despite the continued popularity of these interventions no further large-scale randomised studies, powered to detect clinical event endpoints, have been carried out. Any coronary heart disease (CHD) mortality benefits of these multiple risk factor interventions was confined to those trials recruiting people with hypertension and diabetes. Similarly, benefits in stroke mortality were confined to those trials recruiting patients with hypertension and taking drug treatments. Such participants may well be more highly motivated to act on counselling and education interventions and may also benefit because they were more likely to adhere to their drug medications.

Our rationale for focusing on mortality outcomes rather than non-fatal event outcomes is that counting deaths and comparing them by random allocation group is unlikely to be biased, but once attribution of causes of death is involved there is some potential for bias to occur as events were not necessarily assigned causes blind to random allocation group, particularly in the older, large trials. Similar potential biases arise in counting and assigning causes to non-fatal events.

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. All risk factor change analyses were heterogeneous, making pooled estimates of effect questionable. Habituation to blood pressure measurement 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 antihypertensives in the present set of trials, as studies with high-risk participants tended to be the ones which included participants with high levels of antihypertensive 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). We are cautious in our interpretations of these risk factor changes because, if these effects were real, they would have been reflected in reductions in CHD mortality given the size of some of the trials. Furthermore, as the average duration of follow up was 12 months, the risk factor changes that were observed are unlikely to be mirrors of the broad secular trends occurring over much longer time periods. Our conclusions are that observed risk factor changes are likely to be over-estimates and are probably, in the main, due to bias in design and effects of pharmacological treatments.

Although we did observe weak evidence of benefits on combined fatal and non-fatal cardiovascular disease (CVD) events, this was explained by trials which included hypertensives and diabetics, supporting the conclusions based on the mortality findings. Heterogeneity of intervention effects on non-fatal clinical endpoints 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. We stand by our interpretation that these interventions are not beneficial in general populations. 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.

Our findings are relevant to middle-aged adults who are seen in general practice or occupational health practices. Although our inclusion criteria were focused on trials of primary prevention we found that some studies had recruited participants with some evidence of prior heart attack, stroke or peripheral vascular disease. These trials contribute important data to our analyses so we did not wish to exclude them but decided to reject trials that comprised more than 25% of participants with prior CVD events. These trials did not report findings by prior CVD and even if they had the comparisons would not be by randomisation as none of the trials deliberately set out to randomise patients with prior diseases. However, their inclusion in this review would tend to bias our findings towards finding positive effects of intervention given that these health promotion interventions appear to be more effective in people with established cardiovascular disease (Oldridge 1988; O'Connor 1989; Mullen 1992).

Although missing data could affect the conclusions of this review, we consider that the proportion of loss at follow up was not that substantial, and its impact on fatal events (primary outcomes) is perhaps lower than that observed for non-fatal events.

The interventions used

The benefits of drug treatments for lowering blood pressure and cholesterol are clear (Davey Smith 1993; Collins 1994; 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 (MRFIT Study 1982; Finnish men 1985). 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

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; Scandinavian 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 (Cook 1986; Ben-Shlomo 1994).

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 shows 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 (Oldridge 1988; O'Connor 1989; Mullen 1992). 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 (49 trials), family (three trials) or work site (three trials) 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).

Context

The majority of included trials (47%) were undertaken in Europe and in the USA (29%) whilst the remaining were undertaken in other countries including Australia, Japan, Brazil, Mexico, Israel and Taiwan. Over the past decades, whilst there has been a decline in deaths from heart disease and stroke in developed countries, especially in Europe and the US, increasing trends are being experienced in developing countries, particularly in India and China (Callow 2006). The US alone has experienced a decline in deaths from CHD by as much as 60% to 63% during 1965 to 1998 and a decline in cerebrovascular death by 59% to 63% during the same time period. In Europe similar trends have been observed: a decline in deaths from CHD of 30% to 32% and a decline in cerebrovascular death by 55% to 57% between 1965 and 1998 (Levi 2002). These declines have been attributed to lowering of risk factor distributions and better treatment (Bejot 2007; Ellekjaer 2007; Fang 2007). Our results must be viewed within the context of the falling trends seen in CHD and stroke deaths. Replication of these multiple risk factor intervention studies in countries where the cardiovascular disease is increasing should be a high research priority.

AUTHORS' CONCLUSIONS

Implications for practice

The use of 'health promotion' techniques for one-to-one, work site or family-orientated information and advice on a range of lifestyles (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 and those with established cardiovascular disease, where evidence of effectiveness is much stronger.

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 (Pearson 1993). Health protection should be promoted as the mainstay of chronic disease prevention in poorer countries (Ebrahim 2001; Asaria 2007).

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 about 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. 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 and in different contexts as it seems likely that the poor, socially excluded, specific ethnic groups and older people may all react in different ways and that interventions offered in developing countries where cardiovascular disease rates are increasing dramatically may be accepted more readily.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

Aberg 1989 F

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 antihypertensive drugs aged 30 to 69 years Mean age 55 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 antihypertensive 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 ITT used

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	Unclear

Aberg 1989 M

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 antihypertensive drugs aged 30 to 69 years Mean age 55 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 antihypertensive treatment, weight, hypertension, cholesterol, triglycerides, fasting glucose, life quality

Aberg 1989 M (*Continued*)

Notes	All patients followed the same schedule for reduction and withdrawal of antihypertensive drugs Concluded that intervention was effective in reducing hypertensive medication

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Abingdon 1990

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

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

ADAPT 2005

Methods	Screened volunteers on hypertensive drugs Individual randomisation
Participants	Men and women on hypertensive medication for at least 3 months with mean age 55 to 57 N = 241
Interventions	Facilitator provided individual counselling, interactive group workshops and handouts on lifestyle modification over 4 months
Outcomes	No clinical event outcomes Systolic and diastolic changes, total cholesterol at 3-year follow up

ADAPT 2005 (*Continued*)

Notes	42% loss to follow up ITT used No significant changes other than an increase in total cholesterol in usual care group

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Aldana (CHIP) 2005

Methods	Work site volunteers Random allocation by individual
Participants	Male and female employees mean age 46 N = 145
Interventions	Lectures on diet and exercise delivered by dieticians and medical staff
Outcomes	No clinical event outcomes Systolic and diastolic BP and total cholesterol at 6-month follow up
Notes	Unclear if ITT used Study focused on increasing health knowledge

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Applegate 1992

Methods	Community screening and volunteers Randomisation by individual
Participants	Men and women aged 60 to 85 (mean age 64 to 65) 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

Applegate 1992 (*Continued*)

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 followed up Authors report good compliance with intervention Authors conclusions: results indicate intervention will lower borderline or mild diastolic hypertension

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	D - Not used

Blumenthal 2000

Methods	Volunteers screened Randomisation by individual
Participants	Men and women aged 29+ (mean age 48) with un-medicated 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 ITT used

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Brekke 2005a

Methods	Screened volunteers of relatives of patients with type 2 diabetes individually randomised
Participants	Men and women mean age 42 with no diabetes N = 77
Interventions	Dietician delivered educational sessions on diet and exercise followed by group counselling for 4 months

Brekke 2005a (*Continued*)

Outcomes	No clinical event outcomes Dietary changes, smoking and total cholesterol at 1-year follow up
Notes	ITT not used Another intervention group received exercise only

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Cakir 2006

Methods	Individual randomisation in outpatient hypertension clinic
Participants	Men and women with hypertension mean age 55 to 57 N = 70
Interventions	Nurse delivered lifestyle modification programme on diet, exercise, smoking and stress management over a 3-month period
Outcomes	No clinical event outcomes Systolic and diastolic BP, smoking and total cholesterol at 6-month follow up
Notes	ITT not used Statistically significant results were obtained in lifestyle modification

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

CELL Study 1995

Methods	Primary care screening Randomisation of individuals in 2 x 3 factorial design
Participants	People with at least 2 risk factors in addition to moderately raised blood cholesterol Men and women, mean age 49 years (30 to 59) N = 681
Interventions	Factor 1: counselling on health problems and risk factor management, food purchasing, exercise versus usual care Factor 2: pravastatin versus placebo versus control without drug

CELL Study 1995 (*Continued*)

	Duration 1 year
Outcomes	Total mortality and CHD mortality Systolic blood pressure, diastolic blood pressure, blood cholesterol, smoking prevalence, exercise score
Notes	At 1 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

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Change of Heart 1999

Methods	General practice, cluster allocation by minimisation to balance for social deprivation, practice nurse hours and fund-holding status 20 practices Unit of analysis was general practice
Participants	Men and women mean age 47 years with 1 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 Fewer smokers at baseline in intervention group (39%) than control (49%) Problems with recruitment and drop-out - more recruited to intervention than control group - 59% of patients followed up at 12 months Those at higher risk received more intensive treatment

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	D - Not used

Connell 1995

Methods	Work site volunteers Randomisation by work site Unit of analysis was individual
Participants	Men and women age 19 to 67; mean age 39 N = 1432
Interventions	Health risk assessment and individual health counselling Educational classes and self-help material Duration 1 year
Outcomes	Total cholesterol, systolic and diastolic blood pressure, BMI, exercise frequency 1-year follow up
Notes	47% loss to follow up and no ITT used

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Esposito 2004

Methods	Obesity outpatient clinic individual randomisation
Participants	Obese men with erectile dysfunction and mean age of 43 N = 110
Interventions	Small group sessions on diet and physical exercise with individual counselling delivered by nutritionist and exercise trainer over a 2-year period
Outcomes	BMI, erectile dysfunction, total cholesterol, systolic and diastolic blood pressure at 2-year follow up
Notes	ITT used Emphasis on erectile dysfunction Significant changes observed in intervention group in BP and total cholesterol

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Family Heart 1994 M

Methods	Primary care Random allocation of households to intervention and control groups
Participants	Primary care screening, mean age 50 (40 to 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	2 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

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Family Heart 1994 F

Methods	Primary care Random allocation of households to intervention and control groups
Participants	Primary care: women age 50 (40 to 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	2 control groups used but internal control used in this review

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

FARIS 1997 F

Methods	First degree relatives of AMI, CABG and PTCA patients Randomised by family
Participants	Families of people with CHD event, age 18 to 69; mean age 61 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 ITT used

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

FARIS 1997 M

Methods	First degree relatives of AMI, CABG and PTCA patients Randomised by family
Participants	Families of people with CHD event, age 18 to 69, mean age 57 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 ITT used

Risk of bias

Item	Authors' judgement	Description

FARIS 1997 M (*Continued*)

Allocation concealment?	Unclear	B - Unclear

Finnish DPS 2001

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 to 64 years (mean age 52 to 53) with impaired glucose tolerance N = 523
Interventions	Nutritionist-delivered individual and group dietary advice Weight goal established with physician and nutritionist and regular assessment Supervised exercise Each person had 7 sessions in the first year and 1 session every 3 months subsequently
Outcomes	No clinical event 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 Significant reduction seen in total cholesterol and BMI in intervention group at 1 year and maintained at 3-year follow up

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	No	C - Inadequate

Finnish men 1985

Methods	Volunteers recruited Randomisation by individual
Participants	Men only, mean age 48 years (40 to 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

Finnish men 1985 (*Continued*)

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. ITT used

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Garcia-Pena 2001

Methods	Primary care individual randomisation
Participants	Men and women over the age of 60 with hypertension mean age 70 N = 718
Interventions	Fortnightly or monthly visits from nurse to advise on healthier lifestyles with individually negotiated targets over a 6-month period
Outcomes	Deaths, weight, sodium excretion, systolic and diastolic blood pressure at 6-month follow up
Notes	ITT not used BP was significantly reduced in the intervention group

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

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 to 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

Given 1984 (*Continued*)

Outcomes	Systolic and diastolic blood pressure, weight, patient beliefs, symptom severity	
Notes	Authors note reduction in diastolic blood pressure Intervention affected patient beliefs	
Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Gothenberg Study 1986

Methods	Population-based Selection of high-risk people by screening Randomisation of individuals	
Participants	Men only, mean age 51 years (47 to 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	
Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

HDFP trial 1970

Methods	Population screening Randomisation of individuals
Participants	Men and women, all hypertensives, age range 30 to 69 years (mean age 50) N = 10,940
Interventions	Stepped care: antihypertensive drugs, diet, smoking advice, weight control, exercise versus Referred care: usual primary care

HDFP trial 1970 (*Continued*)

	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 or 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 ITT used

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	No	C - Inadequate

Hellenius 1993

Methods	Randomisation of individuals in a 2 x 2 factorial design
Participants	Men only, mean age 46 years (35 to 60) Moderately raised CVD risk factors - already involved in a primary prevention programme N = 158
Interventions	Diet and exercise advised Duration 6 months
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, triglycerides, dietary intake, physical activity
Notes	Only data from control group (N = 39) and diet and exercise group (N = 39) used in this review

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Iso 1994

Methods	Community screening Randomisation by individual using permuted block method, stratified by blood pressure
Participants	Untreated hypertensive men and women age 35 to 69 years (mean age 58 to 59) 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, alcohol 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, diastolic blood pressure Greater use of antihypertensive medication in control group

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Iso 2002

Methods	Community screening Randomisation by individual
Participants	Hypercholesteraemic men and women men and women age 40 to 69 years (mean age 54 to 55) N = 104
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 12 months
Outcomes	No clinical event outcomes 8-year follow up of BMI and total cholesterol
Notes	20% loss to follow up ITT not used Significant reduction seen in total cholesterol in the intervention group

Risk of bias

Item	Authors' judgement	Description

Iso 2002 (*Continued*)

Allocation concealment?	Unclear	B - Unclear

Jalkanen 1991

Methods	Patients from hypertension clinic Randomisation of individuals
Participants	Men and women, mean age 49 years (range 35 to 59) With hypertension and overweight N = 50
Interventions	Individually planned diet (1000 to 1500 kcal 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

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	D - Not used

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 versus 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 ITT used 28% loss to follow up

Johns Hopkins (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Kastarinen 2002

Methods	Primary care Randomisation by individual
Participants	Hypertensive men and women mean age 54.3 N = 715
Interventions	Trained nurses provided counselling in behaviour modification in diet and exercise with individualised targets over 21 months
Outcomes	No clinical events outcomes. Smoking, systolic and diastolic blood pressure, blood cholesterol, weight, food intake, urinary sodium and potassium at 2 years
Notes	ITT used. Significant reductions in weight loss, alcohol consumption were seen in the intervention group.

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	No	C - Inadequate

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

Lin 1996 (*Continued*)

Notes	Hypertensives received more intensive intervention 35% loss to follow up

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

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	1-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

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Look AHEAD 2003

Methods	16 clinical diabetes centres screened and individually randomised diabetic patients
Participants	Diabetic men and women who were overweight aged 45 to 74 (mean age 59) N = 5145
Interventions	1-year programme of educational sessions on lifestyle modification (diet and exercise) plus support sessions delivered by counsellors, dieticians, behaviourists, exercise physiologists
Outcomes	No clinical events, weight loss, systolic and diastolic blood pressure, triglycerides, HDL cholesterol, urine albumin to creatinine ratio at one 1-year follow up

Look AHEAD 2003 (*Continued*)

Notes	ITT not used 9 deaths (4 in control group) but not explained Significant weight loss and reduction in blood pressure in intervention group was observed

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Mattila 2003

Methods	Work site screening (n = 45) Individual randomisation
Participants	Men and women with mean age of 49 and with hypertension N = 731
Interventions	1-year programme of practical training for lifestyle changes aimed at hypertension with group support Delivered by doctor, dietician, physiotherapist, cook and psychologist
Outcomes	No clinical events, smoking, weight loss, systolic and diastolic blood pressure, physical activity, BMI, HDL cholesterol, at 1-year follow up
Notes	ITT not used Significant reduction observed in BP in intervention group

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Meland 1997

Methods	Primary care opportunistic screening Randomisation by general practice (N = 22) Unit of analysis was individual
Participants	Men aged 30 to 59 (mean age 43 to 44) 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

Meland 1997 (*Continued*)

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

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	D - Not used

MRFIT Study 1982

Methods	Work site, population and volunteer screening Randomisation by individual
Participants	Men only, mean age 46 years (35 to 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 subgroups but no net benefit because of potentially harmful effects of antihypertensive drugs used Small benefits emerging after prolonged follow up ITT used

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Muto 2001

Methods	Work site screening Individual randomisation
Participants	Men with mean age of 42 and with at least 1 abnormality in BMI, BP, total cholesterol, triglycerides or fasting blood glucose N = 302
Interventions	6 health promotion seminars in health promotion and education, lectures in nutrition, exercise, stress Individual counselling offered, group discussion and self-education tools Programme delivered by dietician, doctors and exercise trainer over 18 months
Outcomes	BMI, BP, total cholesterol, triglycerides or fasting blood glucose at 6 and 18 months
Notes	ITT not used Significant reductions observed in intervention group in BMI, total cholesterol, triglycerides and systolic BP

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

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, dietician and 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
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

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Nilsson 2001

Methods	Work site screening Randomisation by individual
Participants	Men and women, mean age 50 years (range 28 to 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 drop-outs or excluded for medical reasons at 12 months, 1 lost to follow up at 18 months; control group corresponding figures 10, 5, 2 respectively) 30% loss to follow up

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Okayama 2004

Methods	Work site screening Individual randomisation
Participants	Men and women with mean age of 44 and 45 (range 30 to 64) with cholesterol levels of < 300 mg/dl N = 191
Interventions	Health professionals provided sessions on lifestyle behaviour modification and personalised plans were regularly reviewed Intervention lasted 6 months
Outcomes	BMI, cholesterol, triglycerides, apo-protein A1 and B at 6 months
Notes	ITT not used Significant reduction seen in cholesterol and BMI in both the intervention and control groups

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Oldroyd 2001

Methods	People with impaired glucose tolerance identified in research studies, hospital databases and by GPs Randomisation by individual
Participants	Men and women aged 24 to 75 (mean age 58) 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

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Oslo Diet Antismoking

Methods	Population screening Selected for raised blood cholesterol Randomisation by individual
Participants	Men only, mean age 45.2 (40 to 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 ITT used At 20-year follow up large loss to follow up

Risk of bias

Item	Authors' judgement	Description

Oslo Diet Antismoking (*Continued*)

Allocation concealment?	No	C - Inadequate

Oslo Diet Exercise

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

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

OXCHECK 1994

Methods	Primary care practices in urban area Randomisation by household
Participants	Men and women, mean age 49 years (35 to 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 versus 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

OXCHECK 1994 (*Continued*)

	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 ITT used

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Perez-Stable 1995 no prop

Methods	Volunteers screened Randomised by individual stratified for sex, diastolic blood pressure and weight
Participants	Men and women aged 18 to 59 (mean age 45) 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
Outcomes	No clinical event outcomes Systolic and diastolic BP, cholesterol, physical activity, self-reported adverse effects dietary intake, weight, 24-hour urine test (sodium, potassium) Follow up at 1 year
Notes	4 treatment arms; other 2 had propanolol Intervention did not promote persistent behaviour change ITT used

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Perez-Stable 1995 prop

Methods	Volunteers screened Randomised by individual stratified for sex, diastolic blood pressure and weight
Participants	Men and women aged 18 to 59 (mean age 46) Mild hypertension on propanolol N = 156

Perez-Stable 1995 prop (*Continued*)

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 BP diastolic BP pressure, cholesterol, physical activity, self-reported adverse effects, dietary intake, weight, 24-hour urine test (sodium, potassium) Follow up at 1 year
Notes	4 treatment arms; other 2 did not have propanolol Intervention did not promote persistent behaviour change

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Proper 2003

Methods	Block randomisation of municipal workplace units Individual randomisation within each unit
Participants	Male and female employees with mean age of 44 N = 299
Interventions	Trans-theoretical model used by physiotherapist who provided individual counselling sessions on diet, exercise, stress, smoking Individualised plans were drawn up and applied accordingly over a 9-month period
Outcomes	Physical activity, BMI, BP and cholesterol at 9 months
Notes	20% loss to follow up ITT not used Significant results observed with increased energy expenditure, reductions in BMI, cholesterol and diastolic BP

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Rachmani 2005

Methods	Diabetic outpatient clinic Individual randomisation
Participants	Men and women with type 2 diabetes, hypertension and hyperlipidaemia Mean age 59 (45 to 69) N = 165
Interventions	Primary care physician delivered initial teaching sessions and individual consultations on the importance of maintaining desired levels of BP, cholesterol and of drug compliance Patient-centred goals were defined Intervention group was encouraged to exercise Treatment length of 7 years
Outcomes	Clinical events, BP, cholesterol, urinary albumin, BMI, triglycerides and medications at 4 and 7.7 years follow up
Notes	ITT not used Significantly fewer patients in the intervention group had non-fatal CVD events at 7.7 years Improvements were also seen in BP and in cholesterol

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Sartorelli 2005

Methods	Primary care Randomised by individual
Participants	Overweight men and women aged 36 to 65 (mean age 45 to 46) n = 104
Interventions	3 individual counselling sessions by nutritionist on diet and exercise in 6 months
Outcomes	No clinical event outcomes Systolic and diastolic BP and total cholesterol at 1-year follow up
Notes	29% lost to follow up ITT used Significant reduction in diastolic BP at 1 year among intervention group

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Sone (JDCS) 2002

Methods	Diabetic centres Individuals randomised
Participants	Men and women with type 2 diabetes with a mean age of 59 N = 2205
Interventions	Nurse educators and physicians delivered programme of counselling, educational materials and patient-centred goal-setting over 3 years
Outcomes	No clinical event outcomes Systolic and diastolic BP, cholesterol, glycaemic control, diastolic BP at 3 years
Notes	ITT not used Small but significant improvements in glycaemic control

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Stamler 1989

Methods	Work site screening Randomisation of individuals
Participants	Volunteers from work sites, raised body weight, high pulse rate and diastolic BP 80 to 89 mmHg Men and women, mean age 37.5 (30 to 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 (e.g. heavy drinkers, very obese) were excluded from the trial

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Stefanick 1998 F

Methods	Volunteers screened for HDL and LDL cholesterol Randomisation by individual
Participants	Post-menopausal women aged 45 to 64 (mean age 57), HDL < 60 mg/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 ITT used

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Stefanick 1998 M

Methods	Volunteers screened for HDL and LDL cholesterol Randomisation by individual
Participants	Men aged 30 to 64, (mean age 48) HDL < 45 mg/dl, LDL 126 to 189 mg/dl 126 to 209 mg/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 ITT used

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Swedish RIS 1994

Methods	Clinic-attending hypertensives Randomisation by individual after stratification by serum cholesterol, smoking habit and target organ damage
Participants	All men, age 50 to 72 years (mean age 66) N = 508
Interventions	Smoking advice + nicotine gum, dietary habits, weight control, spouse involved Lipid-lowering drugs used in needed versus 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
Notes	Significant reductions in blood cholesterol and smoking were achieved No changes in diastolic blood pressure and HbA1c Stroke incidence reduced in intervention group 31% loss to follow up

Risk of bias

Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Take Heart 1995

Methods	Workplace screening Matched pairs of work sites randomised Unit of analysis was work site
Participants	Men and women mean age 40 (17 to 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

Take Heart 1995 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Toobert (MLP) 2005

Methods	Primary care setting, individual randomisation
Participants	Post-menopausal women with type 2 diabetes Mean age 61 N = 297
Interventions	Social cognitive, goal and ecological theory applied Dietician and physiologist delivered programme on diet, exercise, stress management and social support
Outcomes	BMI, blood pressure, diet and exercise modification, stress management, quality of life
Notes	ITT used Improvements seen in BMI and quality of life outcomes

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Unclear	B - Unclear

Tromso 1991 F

Methods	Wives of the men randomised in the Tromso trial are considered to be a separate trial Randomisation therefore by husband
Participants	Women aged 30 to 45 (mean age 40) 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 23% loss to follow up

Risk of bias

Tromso 1991 F (*Continued*)

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Tromso 1991 M

Methods	Randomisation of individuals at high risk detected by primary care screening
Participants	Men and women, age 30 to 45 years (mean age 40) N = 1373
Interventions	Physician and dietician counselling of family, diet, smoking advice, exercise Duration 6 years
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 proceeding in the trial and lead author has not yet published data

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

Uusitupa 1993

Methods	Diabetes clinic Randomisation by individual
Participants	Newly diagnosed NIDDM, men and women aged 40 to 64 years (mean age 53 to 54) N = 86
Interventions	Education on weight reduction, diet, physical activity Goals and regular monitoring Duration 12 months
Outcomes	No clinical event data Weight reduction, normocalcaemia, correction of dislipidaemias, blood pressure
Notes	Intervention and control received 3 months basic diabetes education before randomisation

Risk of bias

Uusitupa 1993 (*Continued*)

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

WHLP 1998

Methods	Volunteers recruited Randomisation of individuals
Participants	Women aged 44 to 50 (mean age 47) N = 535
Interventions	Cognitive-behavioural programme with intensive group and individual guidance on diet, exercise and prevention of weight gain Duration 4.5 years
Outcomes	No clinical event outcomes Systolic blood pressure, diastolic blood pressure, blood LDL and HDL cholesterol reported at 5 years
Notes	1 accidental death Participants were receptive to preventive approach and were successful in making long-term lifestyle changes

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	C - Inadequate

WHO Factories 1986

Methods	Work sites in Belgium, Italy, Poland, Spain, UK Randomisation by factory Unit of analysis was factory
Participants	Men only, mean age 48.5 (40 to 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 separately

WHO Factories 1986 (*Continued*)

	Concluded that advice on risk factor reduction is effective to the extent that it is taken up and seems to be safe

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Wing 1998

Methods	Volunteers Randomisation by individual
Participants	Overweight men and women aged 40 to 55 (mean age 45 to 46) 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	BMI, BP, cholesterol reductions and long-term behaviour changes were not achieved 26% loss to follow up

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

AMI: acute myocardial infarction
BMI: body mass index
BP: blood pressure
CABG: coronary artery bypass surgery
CHD: coronary heart disease
CVD: cardiovascular disease
HDL: high-density lipoprotein
ITT: intention-to-treat
LDL: low-density lipoprotein
NIDDM: non-insulin dependent diabetes mellitus

OGTT: oral glucose tolerance test
PTCA: percutaneous transluminal coronary angioplasty
VLDL: very low-density lipoprotein

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

Study	Reason for exclusion
Aldana (DPS) 2005	Both groups received an intervention
Andersen 1999	Both groups received an intervention
Bakx 1997	No multiple risk factor intervention
Basler 1985	Non-random allocation
Becker 2005	No comparable control group
Berg 2005	All groups received an intervention
Blake 1987	No risk factor change measured or reported
Boylan 2003	Relevant results not published. Data requested from author but nothing received.
Brekke 2005b	Follow up was less than 6 months
Bruckert 1999	Study was stopped prematurely
Bruno 1983	6-month data not available
Burke 2003	Participants were younger adults
Burke 1999	Participants were younger adults
Burke 2005	Inadequate randomisation
Cambien 1981	Participants were younger adults
Carlberg 1992	No risk factor data measured or reported
Cicek 2004	Inadequate randomisation
Crouch 1986	Control group received some elements of intervention
Da Qing 1997	No risk factor changes reported
Davey-Smith 2005	Follow up of MRFIT with no new relevant data

(*Continued*)

Domarkene 1990	Non-random allocation
DPP 1999	Control group received some elements of intervention
DPPRG 2002	No control group
Dunn 1997	Both groups received an exercise only intervention
Eberle 2003	Follow up of MRFIT with no new relevant data
Edye 1989	Non-random allocation
Elliot 2007	Relevant results not published. Data requested from author but nothing received.
Esposito 2003	Participants were young women
Ferro 2001	Not a randomised trial
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
Gaede 2003	More that 25% of patients recruited had CVD
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
Goldhaber-Fiebert 2003	Follow up was less than 6 months
Gomel 1993	Inadequate randomisation
Gordon 1997	Control group received some elements of intervention
Gordon 2002	More that 25% of patients recruited had CVD
Gump 2003	Follow up of MRFIT with no new relevant data
Gysan 2004	Cohort study

(*Continued*)

Hanlon 1995	6-month data not available
Haskell 1988	Secondary prevention
Hedberg 1998	Non-randomised allocation
Hopman-Rock	Drop-out replaced by recruits on reserve during the study
Huang 2001	Incomplete randomisation
Inter99 2003	Ongoing trial using quasi-randomised method
Jiang 2004	Community study
Jula 1990	Inadequate randomisation
Kamioka 2006	Control group received some elements of intervention
Karlehagen 2003	No comparable control group
Kawakami 1999	Participants were younger adults
Ketola 2001	Mixed primary and secondary prevention
Kisioglu 2004	Relevant results not published. Data requested from author but nothing received.
Knappe 1982	Inadequate randomisation
Ko 2004	Unclear if recruited patients had CVD. No response from author.
Kreuter 1996	Outcome is contemplation of quitting smoking
Lasater 1986	No risk factor changes measured or reported
Lauritzen 1995	Intervention was determined by patient choice
Leighton 1990	Control group received some elements of intervention
Lindahl 1998	Uncontrolled study
Little 2004	No results given for control group
Lovibond 1986	Control group received some elements of intervention
Macdonald 1990	RCT assessing simvastatin

(*Continued*)

Martinez-Amenos 1990	No risk factor changes measured or reported
McCance 1985	2-month follow up
McCann 1997	Control group received some element of the intervention
McMahon 2002	No control group
Meimanaliev 1991	Non-random allocation
Miemanaliev 1993	Non-random allocation
Miller 2002	Follow up was less than 6 months
Murray 1986	No control group baseline data available
Nieman 2002	Follow up was less than 6 months
Nikitin 1991	Non-random allocation
Nisbeth 2000	Participants were younger adults
Nolte 1997	2-month follow up
Olivarius 2001	More that 25% of patients recruited had CVD
Ostwald 1989	Control group received some element of the intervention
OXCHECK 2003	Follow-up data on patients that were not randomised
Parker 2005	Objective to test intraclass correlations - no relevant outcome data
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
Pora 2005	Not a randomised trial
PREMIER 2006	No comparable control group
Pritchard 2002	No comparable control group
Reid 1995	Control group received some element of the intervention

(*Continued*)

Robson 1989	No risk factor changes measured or reported
Rosamond 2000	Non-random allocation
Rothman 2004	No multiple risk factor intervention
Rowland 1994	Non-random allocation
S-E London 1977	Intervention not characterised
Sarraf-Zadegan 2003	Ongoing community study
Schwandt 1999	Children and families
Schwedes 2002	More that 25% of patients recruited had CVD
Smith 1991	Non-random allocation
Steinbach 1982	Non-random allocation
Strandberg 2001	82% of patients recruited had CVD
TOMHS 1991	All participants received intervention
TONE 1998	3-month blood pressure follow up
Tonstad 2005	Patients recruited were less than 40 years of age
Tsuyuki 1999	Secondary prevention
Van Elderen 2001	Patients recruited had CVD
Velonakis 1999	Non-random allocation
Volozh 1991	Non-random allocation
Wang 2002	Follow up was less than 6 months
WHP 1999	Numbers in intervention and control group not reported
Wisewoman 1999	Control group received some element of the intervention
Witmer 2004	Follow up was less than 6 months
Woollard 2003	Patients recruited had CVD
Working Well Trial	Baseline data only, no follow up

(*Continued*)

Wu 1999	Non-random allocation
Zimmerman 1996	A pilot study with no relevant results reported

CVD: cardiovascular disease
RCT: randomised controlled trial

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

Roderigues 2005

Trial name or title	-
Methods	Randomised clinical trial of an intensive intervention into lifestyle of patients with hyperfibrinogaenemia in primary prevention of cardiovascular pathology in primary health care
Participants	436 men and women aged 35 to 75
Interventions	Intensive counselling for lifestyle changes (smoking, diet, weight)
Outcomes	Quality of life, CVD events, modification of risk factors, plasm fibrinogen at 2 years
Starting date	2005
Contact information	-
Notes	-

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	14	139232	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.00 [0.96, 1.05]
2 Total mortality (individual analysis or cluster)	14	139232	Odds Ratio (M-H, Fixed, 95% CI)	1.00 [0.96, 1.05]
2.1 Individual	12	70355	Odds Ratio (M-H, Fixed, 95% CI)	0.95 [0.89, 1.00]
2.2 Cluster randomisation - analysis by individual	2	68877	Odds Ratio (M-H, Fixed, 95% CI)	1.12 [1.04, 1.22]
3 Total mortality (by allocation concealment)	14	139232	Odds Ratio (M-H, Fixed, 95% CI)	1.00 [0.96, 1.05]
3.1 Adequate allocation concealment	3	18729	Odds Ratio (M-H, Fixed, 95% CI)	1.02 [0.86, 1.21]
3.2 Inadequate allocation concealment	4	13388	Odds Ratio (M-H, Fixed, 95% CI)	0.82 [0.71, 0.94]
3.3 Unclear allocation concealment	7	107115	Odds Ratio (M-H, Fixed, 95% CI)	1.03 [0.98, 1.09]
4 Total mortality (by co-morbidity)	13	138010	Odds Ratio (M-H, Fixed, 95% CI)	1.00 [0.96, 1.05]
4.1 No co-morbidity	7	120158	Odds Ratio (M-H, Fixed, 95% CI)	1.04 [0.99, 1.09]
4.2 Co-morbidity (hypertension and diabetes)	6	17852	Odds Ratio (M-H, Fixed, 95% CI)	0.78 [0.68, 0.89]
5 Total mortality (by drug treatment)	13	139091	Odds Ratio (M-H, Fixed, 95% CI)	1.01 [0.96, 1.05]
5.1 No drug treatment	4	76589	Odds Ratio (M-H, Fixed, 95% CI)	1.12 [1.04, 1.21]
5.2 Antihypertensives OR lipid-lowering drugs	6	26113	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.78, 0.96]
5.3 Antihypertensives AND lipid-lowering drugs	3	36389	Odds Ratio (M-H, Fixed, 95% CI)	0.98 [0.92, 1.06]
6 Total mortality (by era)	14	139232	Odds Ratio (M-H, Fixed, 95% CI)	1.00 [0.96, 1.05]
6.1 Low rate of CVD	7	18818	Odds Ratio (M-H, Fixed, 95% CI)	0.93 [0.73, 1.18]
6.2 High Rate of CVD	7	120414	Odds Ratio (M-H, Fixed, 95% CI)	1.01 [0.96, 1.06]
7 Total mortality (by age of study)	14	139232	Odds Ratio (M-H, Fixed, 95% CI)	1.00 [0.96, 1.05]
7.1 Before 2000	11	133228	Odds Ratio (M-H, Fixed, 95% CI)	1.01 [0.96, 1.05]
7.2 After 2000	3	6004	Odds Ratio (M-H, Fixed, 95% CI)	0.90 [0.51, 1.60]
8 Coronary heart disease mortality	11	132564	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.99 [0.92, 1.07]
9 Coronary heart disease mortality (individual analysis or cluster)	11	132834	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.92, 1.07]
9.1 Individual	10	69102	Odds Ratio (M-H, Fixed, 95% CI)	0.96 [0.87, 1.05]
9.2 Cluster randomisation - analysis by individual	1	63732	Odds Ratio (M-H, Fixed, 95% CI)	1.08 [0.94, 1.23]
10 Coronary heart disease mortality (by allocation concealment)	11	132834	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.92, 1.07]
10.1 Adequate	1	12866	Odds Ratio (M-H, Fixed, 95% CI)	0.93 [0.72, 1.20]
10.2 Inadequate	3	12853	Odds Ratio (M-H, Fixed, 95% CI)	0.85 [0.67, 1.07]

10.3 Unclear	7	107115	Odds Ratio (M-H, Fixed, 95% CI)	1.02 [0.94, 1.11]
11 Coronary heart disease mortality (by co-morbidity)	11	132834	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.92, 1.07]
11.1 No co-morbidity	7	120845	Odds Ratio (M-H, Fixed, 95% CI)	1.02 [0.94, 1.11]
11.2 Co-morbidity (hypertension or diabetes)	4	11989	Odds Ratio (M-H, Fixed, 95% CI)	0.82 [0.66, 1.01]
12 Coronary heart disease (by drug treatment)	11	132834	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.92, 1.07]
12.1 No drug treatment	1	1232	Odds Ratio (M-H, Fixed, 95% CI)	0.44 [0.17, 1.15]
12.2 Antihypertensives OR lipid-lowering drugs	5	88079	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.89, 1.10]
12.3 Antihypertensives AND lipid-lowering drugs	5	43523	Odds Ratio (M-H, Fixed, 95% CI)	1.01 [0.90, 1.13]
13 Coronary heart disease (by era)	11	132834	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.92, 1.07]
13.1 Low rate of CVD	4	12420	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.66, 1.49]
13.2 High rate of CVD	7	120414	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.92, 1.07]
14 Coronary heart disease mortality (by study age)	11	132834	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.92, 1.07]
14.1 Before 2000	10	132693	Odds Ratio (M-H, Fixed, 95% CI)	0.99 [0.92, 1.07]
14.2 After 2000	1	141	Odds Ratio (M-H, Fixed, 95% CI)	0.57 [0.13, 2.50]
15 Stroke mortality	7	56931	Odds Ratio (M-H, Fixed, 95% CI)	0.75 [0.60, 0.95]
16 Stroke mortality (by allocation concealment)	7	56931	Odds Ratio (M-H, Fixed, 95% CI)	0.75 [0.60, 0.95]
16.1 Adequate	1	12866	Odds Ratio (M-H, Fixed, 95% CI)	1.18 [0.53, 2.64]
16.2 Inadequate	2	12172	Odds Ratio (M-H, Fixed, 95% CI)	0.58 [0.37, 0.91]
16.3 Unclear	4	31893	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.60, 1.05]
17 Stroke mortality (by co-morbidity)	7	56931	Odds Ratio (M-H, Fixed, 95% CI)	0.75 [0.60, 0.95]
17.1 No co-morbidity	4	45342	Odds Ratio (M-H, Fixed, 95% CI)	0.87 [0.66, 1.14]
17.2 Co-morbidity (hypertension or diabetes)	3	11589	Odds Ratio (M-H, Fixed, 95% CI)	0.54 [0.36, 0.83]
18 Stroke mortality (by drug treatment)	7	56931	Odds Ratio (M-H, Fixed, 95% CI)	0.75 [0.60, 0.95]
18.1 No drug treatment	1	1232	Odds Ratio (M-H, Fixed, 95% CI)	2.08 [0.19, 23.03]
18.2 Antihypertensives OR lipid-lowering drugs	3	23947	Odds Ratio (M-H, Fixed, 95% CI)	0.66 [0.45, 0.97]
18.3 Antihypertensives AND lipid-lowering drugs	3	31752	Odds Ratio (M-H, Fixed, 95% CI)	0.80 [0.60, 1.06]
19 Stroke mortality (by era)	7	56931	Odds Ratio (M-H, Fixed, 95% CI)	0.75 [0.60, 0.95]
19.1 Low rate of CVD	2	649	Odds Ratio (M-H, Fixed, 95% CI)	0.49 [0.17, 1.46]
19.2 High rate of CVD	5	56282	Odds Ratio (M-H, Fixed, 95% CI)	0.77 [0.61, 0.97]
20 Stroke mortality (by study age)	7	56931	Odds Ratio (M-H, Fixed, 95% CI)	0.75 [0.60, 0.95]
20.1 Before 2000	6	56790	Odds Ratio (M-H, Fixed, 95% CI)	0.76 [0.60, 0.95]
20.2 After 2000	1	141	Odds Ratio (M-H, Fixed, 95% CI)	0.65 [0.10, 4.00]
21 Fatal and non-fatal clinical events	9	121381	Odds Ratio (M-H, Random, 95% CI)	0.84 [0.73, 0.98]
22 Fatal and non-fatal clinical events (individual analysis or cluster)	9	121381	Odds Ratio (M-H, Fixed, 95% CI)	0.92 [0.88, 0.96]
22.1 Individual	8	57649	Odds Ratio (M-H, Fixed, 95% CI)	0.89 [0.84, 0.93]

22.2 Cluster randomisation - analysis by individual	1	63732	Odds Ratio (M-H, Fixed, 95% CI)	1.06 [0.97, 1.17]
23 Fatal and non-fatal clinical events (by allocation concealment)	9	121381	Odds Ratio (M-H, Fixed, 95% CI)	0.92 [0.88, 0.96]
23.1 Adequate	2	13584	Odds Ratio (M-H, Fixed, 95% CI)	0.82 [0.76, 0.88]
23.2 Inadequate	2	12172	Odds Ratio (M-H, Fixed, 95% CI)	0.73 [0.62, 0.86]
23.3 Unclear	5	95625	Odds Ratio (M-H, Fixed, 95% CI)	1.02 [0.96, 1.08]
24 Fatal and non-fatal clinical events (by co-morbidity)	9	121381	Odds Ratio (M-H, Fixed, 95% CI)	0.92 [0.88, 0.96]
24.1 No co-morbidity	5	109074	Odds Ratio (M-H, Fixed, 95% CI)	0.94 [0.90, 0.99]
24.2 Co-morbidity (hypertension or diabetes)	4	12307	Odds Ratio (M-H, Fixed, 95% CI)	0.71 [0.61, 0.83]
25 Fatal and non-fatal clinical events (by drug treatment)	9	121381	Odds Ratio (M-H, Fixed, 95% CI)	0.92 [0.88, 0.96]
25.1 No drug treatment	1	1232	Odds Ratio (M-H, Fixed, 95% CI)	0.57 [0.33, 0.97]
25.2 Antihypertensives OR lipid-lowering drugs	5	88397	Odds Ratio (M-H, Fixed, 95% CI)	0.88 [0.84, 0.93]
25.3 Antihypertensives AND lipid-lowering drugs	3	31752	Odds Ratio (M-H, Fixed, 95% CI)	1.00 [0.93, 1.08]
26 Fatal and non-fatal clinical events (by era)	9	121381	Odds Ratio (M-H, Fixed, 95% CI)	0.92 [0.88, 0.96]
26.1 Low rate of CVD	3	1367	Odds Ratio (M-H, Fixed, 95% CI)	0.60 [0.44, 0.84]
26.2 High Rate of CVD	6	120014	Odds Ratio (M-H, Fixed, 95% CI)	0.93 [0.89, 0.97]
27 Fatal and non-fatal clinical events (by age of study)	9	120011	Odds Ratio (M-H, Fixed, 95% CI)	0.93 [0.89, 0.97]
27.1 Before 2000	7	119152	Odds Ratio (M-H, Fixed, 95% CI)	0.94 [0.90, 0.98]
27.2 After 2000	2	859	Odds Ratio (M-H, Fixed, 95% CI)	0.46 [0.25, 0.85]
28 Smoking prevalence	20	51586	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.75, 1.00]
29 Smoking prevalence (individual analysis or cluster)	20	51586	Odds Ratio (M-H, Random, 95% CI)	0.87 [0.75, 1.00]
29.1 Cluster randomisation - analysis by cluster	1	520	Odds Ratio (M-H, Random, 95% CI)	0.43 [0.28, 0.64]
29.2 Individual randomisation	16	31506	Odds Ratio (M-H, Random, 95% CI)	0.89 [0.76, 1.04]
29.3 Cluster randomisation - analysis by individual	3	19560	Odds Ratio (M-H, Random, 95% CI)	0.98 [0.89, 1.07]
30 Smoking prevalence (by allocation concealment)	20	51586	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.76, 0.82]
30.1 Adequate allocation concealment	4	12136	Odds Ratio (M-H, Fixed, 95% CI)	0.58 [0.54, 0.63]
30.2 Inadequate allocation concealment	5	4365	Odds Ratio (M-H, Fixed, 95% CI)	1.03 [0.91, 1.17]
30.3 Unclear allocation concealment	11	35085	Odds Ratio (M-H, Fixed, 95% CI)	0.89 [0.84, 0.94]
31 Smoking prevalence (by co-morbidity)	15	49681	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.75, 0.82]
31.1 No co-morbidity	15	49681	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.75, 0.82]
32 Smoking prevalence (by drug treatment)	20	53491	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.76, 0.83]
32.1 No drug treatment	9	10724	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.78, 0.93]

32.2 Antihypertensives OR lipid-lowering drugs	6	31599	Odds Ratio (M-H, Fixed, 95% CI)	0.72 [0.68, 0.76]
32.3 Antihypertensives AND lipid-lowering drugs	5	9263	Odds Ratio (M-H, Fixed, 95% CI)	0.91 [0.83, 1.00]
32.4 Co-morbidity (hypertension or diabetes)	5	1905	Odds Ratio (M-H, Fixed, 95% CI)	0.89 [0.70, 1.12]
33 Smoking prevalence (by era)	20	51586	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.76, 0.82]
33.1 Low rate of CVD	15	16120	Odds Ratio (M-H, Fixed, 95% CI)	0.85 [0.79, 0.92]
33.2 High rate of CVD	5	35466	Odds Ratio (M-H, Fixed, 95% CI)	0.76 [0.72, 0.80]
34 Smoking prevalence (by age of study)	20	51586	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.76, 0.82]
34.1 Study before 2000	15	50166	Odds Ratio (M-H, Fixed, 95% CI)	0.79 [0.75, 0.82]
34.2 Study after 2000	5	1420	Odds Ratio (M-H, Fixed, 95% CI)	0.89 [0.68, 1.18]
35 Systolic blood pressure	53	64809	Mean Difference (IV, Fixed, 95% CI)	-3.38 [-3.63, -3.13]
36 Systolic blood pressure (individual analysis or cluster)	53	64809	Mean Difference (IV, Random, 95% CI)	-2.71 [-3.49, -1.93]
36.1 Cluster randomisation - analysis by cluster	1	504	Mean Difference (IV, Random, 95% CI)	2.5 [-0.79, 5.79]
36.2 Individual randomisation	45	38261	Mean Difference (IV, Random, 95% CI)	-2.99 [-3.87, -2.11]
36.3 Cluster randomisation - analysis by individual	7	26044	Mean Difference (IV, Random, 95% CI)	-1.79 [-3.54, -0.04]
37 Systolic blood pressure (by allocation concealment)	53	64809	Mean Difference (IV, Fixed, 95% CI)	-3.38 [-3.63, -3.13]
37.1 Adequate allocation concealment	14	18950	Mean Difference (IV, Fixed, 95% CI)	-4.32 [-4.69, -3.96]
37.2 Inadequate allocation concealment	9	4669	Mean Difference (IV, Fixed, 95% CI)	-2.03 [-2.84, -1.23]
37.3 Unclear allocation concealment	30	41190	Mean Difference (IV, Fixed, 95% CI)	-2.65 [-3.03, -2.26]
38 Systolic blood pressure (by co-morbidity)	53	64809	Mean Difference (IV, Fixed, 95% CI)	-3.38 [-3.63, -3.13]
38.1 No co-morbidity	29	52275	Mean Difference (IV, Fixed, 95% CI)	-3.70 [-4.01, -3.38]
38.2 Co-morbidity (hypertension or diabetes)	24	12534	Mean Difference (IV, Fixed, 95% CI)	-2.81 [-3.23, -2.38]
39 Systolic blood pressure (by drug treatment)	53	64809	Mean Difference (IV, Fixed, 95% CI)	-3.38 [-3.63, -3.13]
39.1 No drug treatment	29	15846	Mean Difference (IV, Fixed, 95% CI)	-2.74 [-3.19, -2.29]
39.2 Antihypertensives OR lipid-lowering drugs	17	34517	Mean Difference (IV, Fixed, 95% CI)	-3.89 [-4.28, -3.51]
39.3 Antihypertensives AND lipid-lowering drugs	7	14446	Mean Difference (IV, Fixed, 95% CI)	-3.31 [-3.81, -2.80]
40 Systolic blood pressure (by era)	53	64809	Mean Difference (IV, Fixed, 95% CI)	-3.38 [-3.63, -3.13]
40.1 Low rate of CVD	49	30562	Mean Difference (IV, Fixed, 95% CI)	-3.07 [-3.38, -2.75]
40.2 High rate of CVD	4	34247	Mean Difference (IV, Fixed, 95% CI)	-3.92 [-4.34, -3.51]
41 Systolic blood pressure (by age of study)	53	64809	Mean Difference (IV, Fixed, 95% CI)	-3.38 [-3.63, -3.13]
41.1 Study before 2000	36	53606	Mean Difference (IV, Fixed, 95% CI)	-3.59 [-3.90, -3.28]
41.2 Study after 2000	17	11203	Mean Difference (IV, Fixed, 95% CI)	-2.97 [-3.41, -2.54]
42 Diastolic blood pressure	53	75400	Mean Difference (IV, Fixed, 95% CI)	-2.41 [-2.55, -2.26]
43 Diastolic blood pressure (individual analysis or cluster)	53	75400	Mean Difference (IV, Random, 95% CI)	-2.13 [-2.67, -1.58]

43.1 Cluster randomisation - analysis by cluster	1	503	Mean Difference (IV, Random, 95% CI)	-0.30 [-2.86, 2.26]
43.2 Individual randomisation	46	49255	Mean Difference (IV, Random, 95% CI)	-2.36 [-2.94, -1.77]
43.3 Cluster randomisation - analysis by individual	6	25642	Mean Difference (IV, Random, 95% CI)	-0.79 [-1.42, -0.16]
44 Diastolic blood pressure (by allocation concealment)	53	75400	Mean Difference (IV, Fixed, 95% CI)	-2.41 [-2.55, -2.26]
44.1 Adequate concealment	14	18969	Mean Difference (IV, Fixed, 95% CI)	-2.38 [-2.60, -2.16]
44.2 Inadequate allocation concealment	10	15644	Mean Difference (IV, Fixed, 95% CI)	-3.70 [-4.01, -3.40]
44.3 Unclear allocation concealment	29	40787	Mean Difference (IV, Fixed, 95% CI)	-1.60 [-1.85, -1.35]
45 Diastolic blood pressure (by co-morbidity)	53	75400	Mean Difference (IV, Fixed, 95% CI)	-2.41 [-2.55, -2.26]
45.1 No co-morbidity	28	51891	Mean Difference (IV, Fixed, 95% CI)	-2.33 [-2.52, -2.13]
45.2 Co-morbidity (hypertension or diabetes)	25	23509	Mean Difference (IV, Fixed, 95% CI)	-2.51 [-2.73, -2.29]
46 Diastolic blood pressure (by drug treatment)	53	75400	Mean Difference (IV, Fixed, 95% CI)	-2.41 [-2.55, -2.26]
46.1 No drug treatment	28	15449	Mean Difference (IV, Fixed, 95% CI)	-2.09 [-2.40, -1.79]
46.2 Antihypertensives OR lipid-lowering drugs	18	45505	Mean Difference (IV, Fixed, 95% CI)	-3.05 [-3.25, -2.85]
46.3 Antihypertensives AND lipid-lowering drugs	7	14446	Mean Difference (IV, Fixed, 95% CI)	-1.41 [-1.70, -1.13]
47 Diastolic blood pressure (by era)	53	75400	Mean Difference (IV, Fixed, 95% CI)	-2.41 [-2.55, -2.26]
47.1 Low rate of CVD	48	30200	Mean Difference (IV, Fixed, 95% CI)	-1.70 [-1.90, -1.49]
47.2 High Rate of CVD	5	45200	Mean Difference (IV, Fixed, 95% CI)	-3.15 [-3.36, -2.94]
48 Diastolic blood pressure (by age of study)	53	75400	Mean Difference (IV, Fixed, 95% CI)	-2.41 [-2.55, -2.26]
48.1 Study before 2000	36	64197	Mean Difference (IV, Fixed, 95% CI)	-2.76 [-2.93, -2.59]
48.2 Study after 2000	17	11203	Mean Difference (IV, Fixed, 95% CI)	-1.38 [-1.67, -1.10]
49 Blood cholesterol	50	71776	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.08, -0.06]
50 Blood cholesterol (individual analysis or cluster)	50	71776	Mean Difference (IV, Random, 95% CI)	-0.24 [-0.32, -0.16]
50.1 Cluster randomisation - analysis by cluster	2	2475	Mean Difference (IV, Random, 95% CI)	0.01 [-0.01, 0.03]
50.2 Individual randomisation	43	49428	Mean Difference (IV, Random, 95% CI)	-0.28 [-0.39, -0.17]
50.3 Cluster randomisation (analysis by individual)	5	19873	Mean Difference (IV, Random, 95% CI)	0.01 [-0.03, 0.04]
51 Blood cholesterol (by allocation concealment)	50	71776	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.08, -0.06]
51.1 Adequate allocation concealment	12	13108	Mean Difference (IV, Fixed, 95% CI)	-0.16 [-0.19, -0.13]
51.2 Inadequate allocation concealment	11	16876	Mean Difference (IV, Fixed, 95% CI)	-0.13 [-0.16, -0.10]
51.3 Unclear allocation concealment	27	41792	Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.06, -0.03]
52 Blood cholesterol (by co-morbidity)	50	71776	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.08, -0.06]
52.1 No co-morbidity	34	55462	Mean Difference (IV, Fixed, 95% CI)	-0.08 [-0.09, -0.06]

52.2 Co-morbidity (hypertension and/or diabetes)	16	16314	Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.08, -0.03]
53 Blood cholesterol (by drug treatment)	50	71776	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.08, -0.06]
53.1 No drug treatment	31	19210	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.08, -0.05]
53.2 Antihypertensives OR lipid-lowering drugs	13	43070	Mean Difference (IV, Fixed, 95% CI)	-0.06 [-0.08, -0.04]
53.3 Antihypertensives AND lipid-lowering drug	6	9496	Mean Difference (IV, Fixed, 95% CI)	-0.18 [-0.22, -0.14]
54 Blood cholesterol (by era)	50	71776	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.08, -0.06]
54.1 Low rate of CVD	44	25887	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.08, -0.05]
54.2 High rate of CVD	6	45889	Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.11, -0.07]
55 Blood cholesterol (by age of study)	50	71776	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.08, -0.06]
55.1 Study before 2000	33	66040	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.08, -0.06]
55.2 Study after 2000	17	5736	Mean Difference (IV, Fixed, 95% CI)	-0.14 [-0.18, -0.10]

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 1995	2/339	1/342		0.0 %	1.97 [0.20, 18.99]
Finnish men 1985	10/612	5/610		0.2 %	1.96 [0.71, 5.41]
Garcia-Pena 2001	10/364	10/354		0.3 %	0.97 [0.40, 2.36]
Gothenberg Study 1986	1293/10004	2636/20018		43.3 %	0.98 [0.91, 1.05]
HDFP trial 1970	349/5485	419/5455		10.2 %	0.82 [0.71, 0.95]
Johns Hopkins	35/350	11/50		0.3 %	0.31 [0.12, 0.78]
Look AHEAD 2003	5/2570	4/2575		0.1 %	1.25 [0.34, 4.63]
MRFIT Study 1982	265/6428	260/6438		7.2 %	1.02 [0.86, 1.22]
Oslo Diet Antismoking	16/604	24/628		0.6 %	0.69 [0.37, 1.29]
OXCHECK 1994	146/8307	40/2783		2.0 %	1.21 [0.87, 1.70]
Rachmani 2005	9/71	12/70		0.3 %	0.70 [0.28, 1.78]
Swedish RIS 1994	41/253	64/255		1.2 %	0.58 [0.38, 0.89]
WHLP 1998	1/260	0/275		0.0 %	7.83 [0.16, 395.11]

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Study or subgroup	Intervention n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
WHO Factories 1986	1325/31873	1186/31859		34.4 %	1.12 [1.04, 1.21]
Total (95% CI)	**67520**	**71712**		**100.0 %**	**1.00 [0.96, 1.05]**
Total events: 3507 (Intervention), 4672 (Control)					
Heterogeneity: Chi^2 = 34.26, df = 13 (P = 0.001); I^2 =62%					
Test for overall effect: Z = 0.20 (P = 0.84)					

0.1 0.2 0.5 1 2 5 10

Analysis 1.2. Comparison 1 Multiple risk factor intervention versus control, Outcome 2 Total mortality (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: 2 Total mortality (individual analysis or cluster)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Individual					
CELL Study 1995	2/339	1/342		0.0 %	2.02 [0.18, 22.42]
Finnish men 1985	10/612	5/610		0.1 %	2.01 [0.68, 5.92]
Garcia-Pena 2001	10/364	10/354		0.3 %	0.97 [0.40, 2.36]
Gothenberg Study 1986	1293/10004	2636/20018		43.8 %	0.98 [0.91, 1.05]
HDFP trial 1970	349/5485	419/5455		11.3 %	0.82 [0.70, 0.95]
Johns Hopkins	35/350	11/50		0.5 %	0.39 [0.19, 0.84]
MRFIT Study 1982	265/6428	260/6438		7.1 %	1.02 [0.86, 1.22]
Oslo Diet Antismoking	16/604	24/628		0.7 %	0.68 [0.36, 1.30]
OXCHECK 1994	146/8307	40/2783		1.7 %	1.23 [0.86, 1.75]
Rachmani 2005	9/71	12/70		0.3 %	0.70 [0.28, 1.79]
Swedish RIS 1994	41/253	64/255		1.5 %	0.58 [0.37, 0.89]
WHLP 1998	1/260	0/275		0.0 %	3.18 [0.13, 78.53]
Subtotal (95% CI)	**33077**	**37278**		**67.3 %**	**0.95 [0.89, 1.00]**

0.1 0.2 0.5 1 2 5 10

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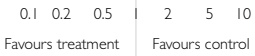
Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Total events: 2177 (Treatment), 3482 (Control)					
Heterogeneity: Chi² = 21.77, df = 11 (P = 0.03); I² =49%					
Test for overall effect: Z = 1.81 (P = 0.071)					
2 Cluster randomisation - analysis by individual					
Look AHEAD 2003	5/2570	4/2575		0.1 %	1.25 [0.34, 4.67]
WHO Factories 1986	1325/31873	1186/31859		32.6 %	1.12 [1.04, 1.22]
Subtotal (95% CI)	**34443**	**34434**		**32.7 %**	**1.12 [1.04, 1.22]**
Total events: 1330 (Treatment), 1190 (Control)					
Heterogeneity: Chi² = 0.03, df = 1 (P = 0.87); I² =0.0%					
Test for overall effect: Z = 2.83 (P = 0.0046)					
Total (95% CI)	**67520**	**71712**		**100.0 %**	**1.00 [0.96, 1.05]**
Total events: 3507 (Treatment), 4672 (Control)					
Heterogeneity: Chi² = 33.21, df = 13 (P = 0.002); I² =61%					
Test for overall effect: Z = 0.20 (P = 0.84)					

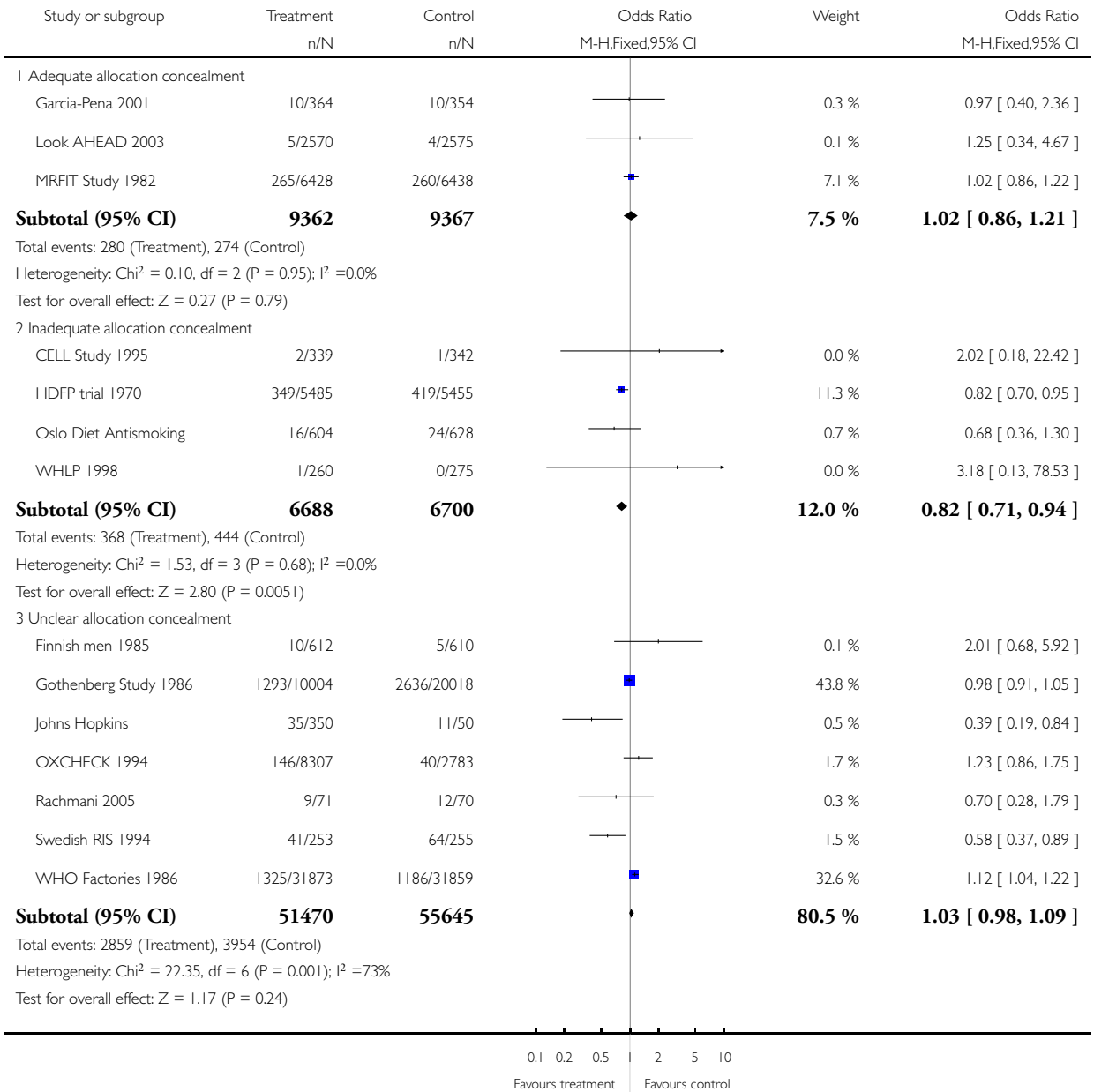


Analysis 1.3. Comparison 1 Multiple risk factor intervention versus control, Outcome 3 Total mortality (by allocation concealment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 3 Total mortality (by allocation concealment)



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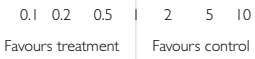
Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Total (95% CI)	**67520**	**71712**		**100.0 %**	**1.00 [0.96, 1.05]**
Total events: 3507 (Treatment), 4672 (Control)					
Heterogeneity: Chi^2 = 33.21, df = 13 (P = 0.002); I^2 =61%					
Test for overall effect: Z = 0.20 (P = 0.84)					



Analysis 1.4. Comparison 1 Multiple risk factor intervention versus control, Outcome 4 Total mortality (by co-morbidity).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 4 Total mortality (by co-morbidity)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 No co-morbidity					
CELL Study 1995	2/339	1/342		0.0 %	2.02 [0.18, 22.42]
Gothenberg Study 1986	1293/10004	2636/20018		43.9 %	0.98 [0.91, 1.05]
MRFIT Study 1982	265/6428	260/6438		7.1 %	1.02 [0.86, 1.22]
Oslo Diet Antismoking	16/604	24/628		0.7 %	0.68 [0.36, 1.30]
OXCHECK 1994	146/8307	40/2783		1.7 %	1.23 [0.86, 1.75]
WHLP 1998	1/260	0/275		0.0 %	3.18 [0.13, 78.53]
WHO Factories 1986	1325/31873	1186/31859		32.6 %	1.12 [1.04, 1.22]
Subtotal (95% CI)	**57815**	**62343**		**86.0 %**	**1.04 [0.99, 1.09]**
Total events: 3048 (Treatment), 4147 (Control)					
Heterogeneity: Chi^2 = 9.49, df = 6 (P = 0.15); I^2 =37%					
Test for overall effect: Z = 1.53 (P = 0.13)					
2 Co-morbidity (hypertension and diabetes)					
Garcia-Pena 2001	10/364	10/354		0.3 %	0.97 [0.40, 2.36]
HDFP trial 1970	349/5485	419/5455		11.3 %	0.82 [0.70, 0.95]
Johns Hopkins	35/350	11/50		0.5 %	0.39 [0.19, 0.84]

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Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Look AHEAD 2003	5/2570	4/2575		0.1 %	1.25 [0.34, 4.67]
Rachmani 2005	9/71	12/70		0.3 %	0.70 [0.28, 1.79]
Swedish RIS 1994	41/253	64/255		1.5 %	0.58 [0.37, 0.89]
Subtotal (95% CI)	**9093**	**8759**		**14.0 %**	**0.78 [0.68, 0.89]**
Total events: 449 (Treatment), 520 (Control)					
Heterogeneity: Chi^2 = 6.12, df = 5 (P = 0.29); I^2 =18%					
Test for overall effect: Z = 3.65 (P = 0.00026)					
Total (95% CI)	**66908**	**71102**		**100.0 %**	**1.00 [0.96, 1.05]**
Total events: 3497 (Treatment), 4667 (Control)					
Heterogeneity: Chi^2 = 31.61, df = 12 (P = 0.002); I^2 =62%					
Test for overall effect: Z = 0.14 (P = 0.89)					

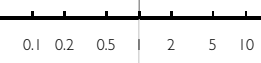
Analysis 1.5. Comparison 1 Multiple risk factor intervention versus control, Outcome 5 Total mortality (by drug treatment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 5 Total mortality (by drug treatment)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 No drug treatment					
Oslo Diet Antismoking	16/604	24/628		0.7 %	0.68 [0.36, 1.30]
OXCHECK 1994	146/8307	40/2783		1.7 %	1.23 [0.86, 1.75]
WHLP 1998	1/260	0/275		0.0 %	3.18 [0.13, 78.53]
WHO Factories 1986	1325/31873	1186/31859		32.7 %	1.12 [1.04, 1.22]
Subtotal (95% CI)	**41044**	**35545**		**35.0 %**	**1.12 [1.04, 1.21]**
Total events: 1488 (Treatment), 1250 (Control)					
Heterogeneity: Chi^2 = 2.92, df = 3 (P = 0.40); I^2 =0.0%					
Test for overall effect: Z = 2.86 (P = 0.0042)					
2 Antihypertensives OR lipid-lowering drugs					



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Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
CELL Study 1995	2/339	1/342		0.0 %	2.02 [0.18, 22.42]
Garcia-Pena 2001	10/364	10/354		0.3 %	0.97 [0.40, 2.36]
HDFP trial 1970	349/5485	419/5455		11.3 %	0.82 [0.70, 0.95]
Johns Hopkins	35/350	11/50		0.5 %	0.39 [0.19, 0.84]
MRFIT Study 1982	265/6428	260/6438		7.2 %	1.02 [0.86, 1.22]
Swedish RIS 1994	41/253	64/255		1.5 %	0.58 [0.37, 0.89]
Subtotal (95% CI)	**13219**	**12894**		**20.8 %**	**0.86 [0.78, 0.96]**
Total events: 702 (Treatment), 765 (Control)					
Heterogeneity: Chi^2 = 12.06, df = 5 (P = 0.03); I^2 =59%					
Test for overall effect: Z = 2.70 (P = 0.0070)					
3 Antihypertensives AND lipid-lowering drugs					
Finnish men 1985	10/612	5/610		0.1 %	2.01 [0.68, 5.92]
Gothenberg Study 1986	1293/10004	2636/20018		43.9 %	0.98 [0.91, 1.05]
Look AHEAD 2003	5/2570	4/2575		0.1 %	1.25 [0.34, 4.67]
Subtotal (95% CI)	**13186**	**23203**		**44.2 %**	**0.98 [0.92, 1.06]**
Total events: 1308 (Treatment), 2645 (Control)					
Heterogeneity: Chi^2 = 1.83, df = 2 (P = 0.40); I^2 =0.0%					
Test for overall effect: Z = 0.48 (P = 0.63)					
Total (95% CI)	**67449**	**71642**		**100.0 %**	**1.01 [0.96, 1.05]**
Total events: 3498 (Treatment), 4660 (Control)					
Heterogeneity: Chi^2 = 32.64, df = 12 (P = 0.001); I^2 =63%					
Test for overall effect: Z = 0.24 (P = 0.81)					

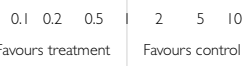
Analysis 1.6. Comparison 1 Multiple risk factor intervention versus control, Outcome 6 Total mortality (by era).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 6 Total mortality (by era)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Low rate of CVD					
CELL Study 1995	2/339	1/342		0.0 %	2.02 [0.18, 22.42]
Garcia-Pena 2001	10/364	10/354		0.3 %	0.97 [0.40, 2.36]
Look AHEAD 2003	5/2570	4/2575		0.1 %	1.25 [0.34, 4.67]
OXCHECK 1994	146/8307	40/2783		1.7 %	1.23 [0.86, 1.75]
Rachmani 2005	9/71	12/70		0.3 %	0.70 [0.28, 1.79]
Swedish RIS 1994	41/253	64/255		1.5 %	0.58 [0.37, 0.89]
WHLP 1998	1/260	0/275		0.0 %	3.18 [0.13, 78.53]
Subtotal (95% CI)	**12164**	**6654**		**4.0 %**	**0.93 [0.73, 1.18]**
Total events: 214 (Treatment), 131 (Control)					
Heterogeneity: Chi^2 = 8.45, df = 6 (P = 0.21); I^2 =29%					
Test for overall effect: Z = 0.59 (P = 0.56)					
2 High Rate of CVD					
Finnish men 1985	10/612	5/610		0.1 %	2.01 [0.68, 5.92]
Gothenberg Study 1986	1293/10004	2636/20018		43.8 %	0.98 [0.91, 1.05]
HDFP trial 1970	349/5485	419/5455		11.3 %	0.82 [0.70, 0.95]
Johns Hopkins	35/350	11/50		0.5 %	0.39 [0.19, 0.84]
MRFIT Study 1982	265/6428	260/6438		7.1 %	1.02 [0.86, 1.22]
Oslo Diet Antismoking	16/604	24/628		0.7 %	0.68 [0.36, 1.30]
WHO Factories 1986	1325/31873	1186/31859		32.6 %	1.12 [1.04, 1.22]
Subtotal (95% CI)	**55356**	**65058**		**96.0 %**	**1.01 [0.96, 1.06]**
Total events: 3293 (Treatment), 4541 (Control)					
Heterogeneity: Chi^2 = 24.31, df = 6 (P = 0.00046); I^2 =75%					
Test for overall effect: Z = 0.32 (P = 0.75)					
Total (95% CI)	**67520**	**71712**		**100.0 %**	**1.00 [0.96, 1.05]**
Total events: 3507 (Treatment), 4672 (Control)					
Heterogeneity: Chi^2 = 33.21, df = 13 (P = 0.002); I^2 =61%					
Test for overall effect: Z = 0.20 (P = 0.84)					

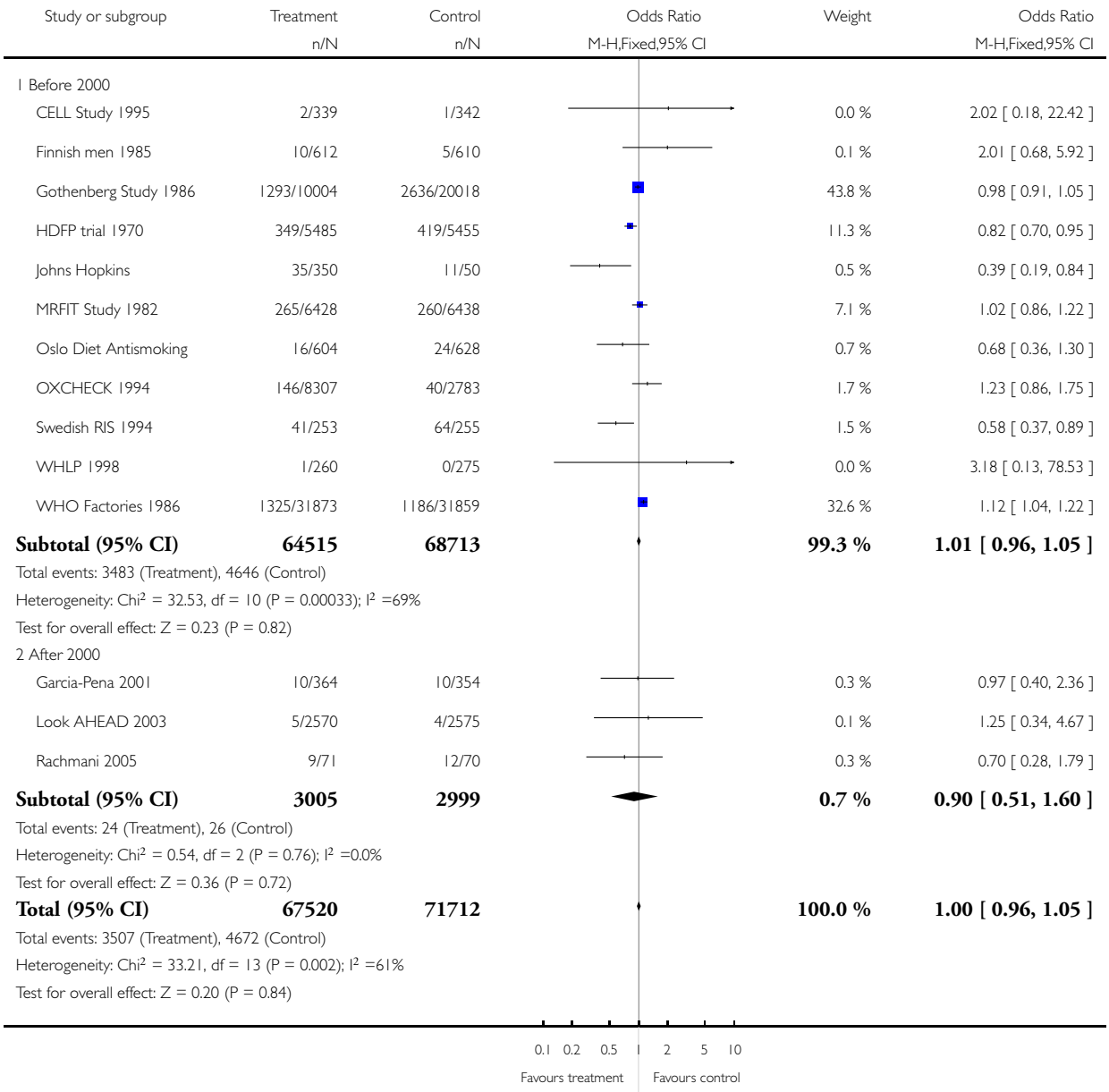


Analysis 1.7. Comparison 1 Multiple risk factor intervention versus control, Outcome 7 Total mortality (by age of study).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 7 Total mortality (by age of study)



Analysis 1.8. Comparison 1 Multiple risk factor intervention versus control, Outcome 8 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: 8 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 1995	2/339	1/342		0.1 %	1.97 [0.20, 18.99]
Finnish men 1985	4/612	1/610		0.2 %	3.32 [0.57, 19.23]
Gothenberg Study 1986	462/10004	923/20018		44.7 %	1.00 [0.89, 1.12]
HDFP trial 1970	131/5485	148/5455		10.3 %	0.88 [0.69, 1.11]
Johns Hopkins	23/350	8/50		0.5 %	0.27 [0.09, 0.81]
MRFIT Study 1982	115/6428	124/6438		8.9 %	0.93 [0.72, 1.20]
Oslo Diet Antismoking	6/604	14/628		0.7 %	0.46 [0.19, 1.12]
OXCHECK 1994	52/8307	13/2783		1.8 %	1.31 [0.75, 2.30]
Rachmani 2005	3/71	5/70		0.3 %	0.58 [0.14, 2.41]
Swedish RIS 1994	17/253	23/255		1.4 %	0.73 [0.38, 1.39]
WHO Factories 1986	428/31873	398/31589		31.0 %	1.07 [0.93, 1.22]
Total (95% CI)	**64326**	**68238**		**100.0 %**	**0.99 [0.92, 1.07]**

Total events: 1243 (Intervention), 1658 (Control)

Heterogeneity: Chi^2 = 15.17, df = 10 (P = 0.13); I^2 =34%

Test for overall effect: Z = 0.24 (P = 0.81)

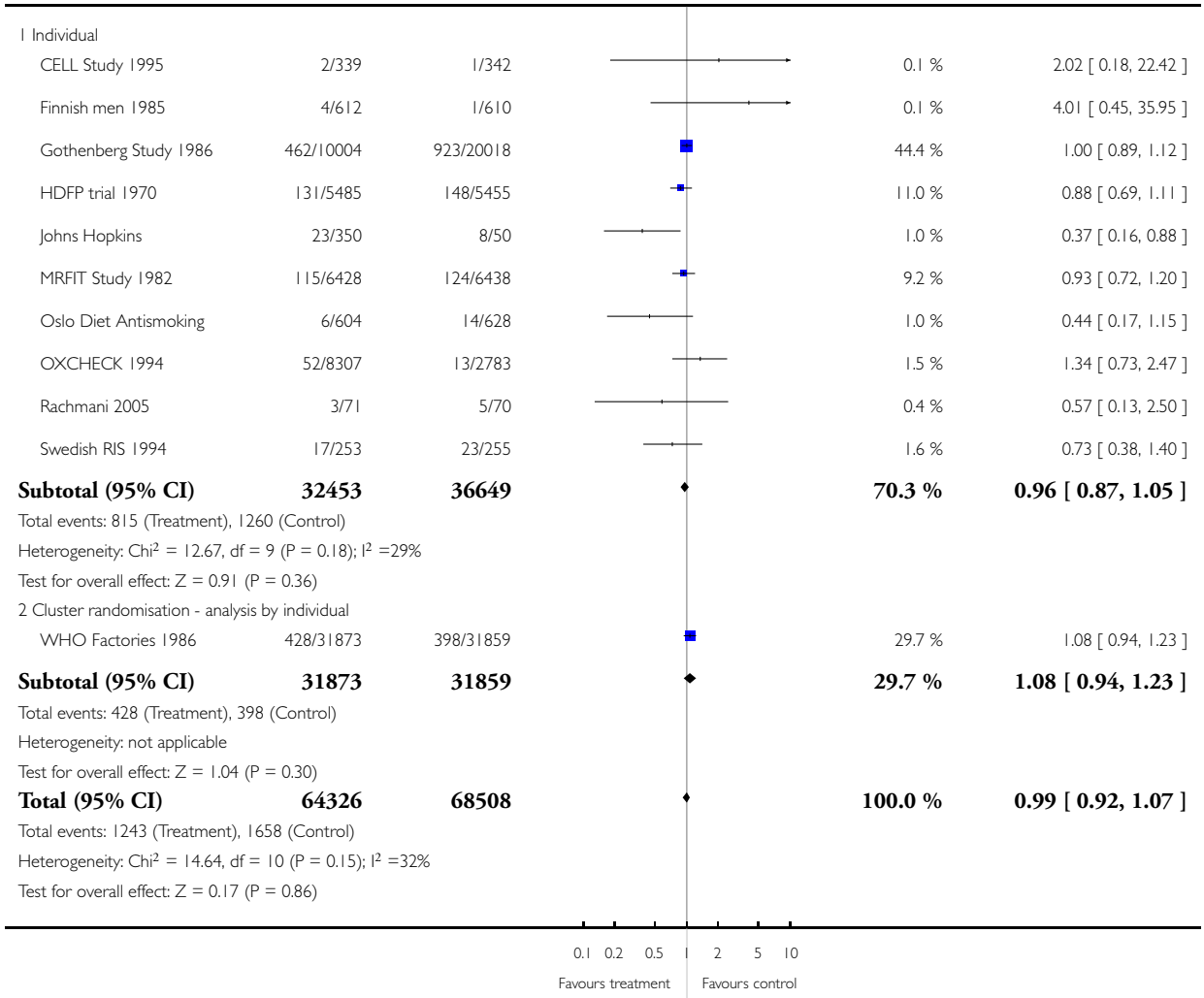
Analysis 1.9. Comparison 1 Multiple risk factor intervention versus control, Outcome 9 Coronary heart disease mortality (individual analysis or cluster).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 9 Coronary heart disease mortality (individual analysis or cluster)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Individual					
CELL Study 1995	2/339	1/342		0.1 %	2.02 [0.18, 22.42]
Finnish men 1985	4/612	1/610		0.1 %	4.01 [0.45, 35.95]
Gothenberg Study 1986	462/10004	923/20018		44.4 %	1.00 [0.89, 1.12]
HDFP trial 1970	131/5485	148/5455		11.0 %	0.88 [0.69, 1.11]
Johns Hopkins	23/350	8/50		1.0 %	0.37 [0.16, 0.88]
MRFIT Study 1982	115/6428	124/6438		9.2 %	0.93 [0.72, 1.20]
Oslo Diet Antismoking	6/604	14/628		1.0 %	0.44 [0.17, 1.15]
OXCHECK 1994	52/8307	13/2783		1.5 %	1.34 [0.73, 2.47]
Rachmani 2005	3/71	5/70		0.4 %	0.57 [0.13, 2.50]
Swedish RIS 1994	17/253	23/255		1.6 %	0.73 [0.38, 1.40]
Subtotal (95% CI)	**32453**	**36649**		**70.3 %**	**0.96 [0.87, 1.05]**
Total events: 815 (Treatment), 1260 (Control)					
Heterogeneity: Chi² = 12.67, df = 9 (P = 0.18); I² =29%					
Test for overall effect: Z = 0.91 (P = 0.36)					
2 Cluster randomisation - analysis by individual					
WHO Factories 1986	428/31873	398/31859		29.7 %	1.08 [0.94, 1.23]
Subtotal (95% CI)	**31873**	**31859**		**29.7 %**	**1.08 [0.94, 1.23]**
Total events: 428 (Treatment), 398 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.04 (P = 0.30)					
Total (95% CI)	**64326**	**68508**		**100.0 %**	**0.99 [0.92, 1.07]**
Total events: 1243 (Treatment), 1658 (Control)					
Heterogeneity: Chi² = 14.64, df = 10 (P = 0.15); I² =32%					
Test for overall effect: Z = 0.17 (P = 0.86)					

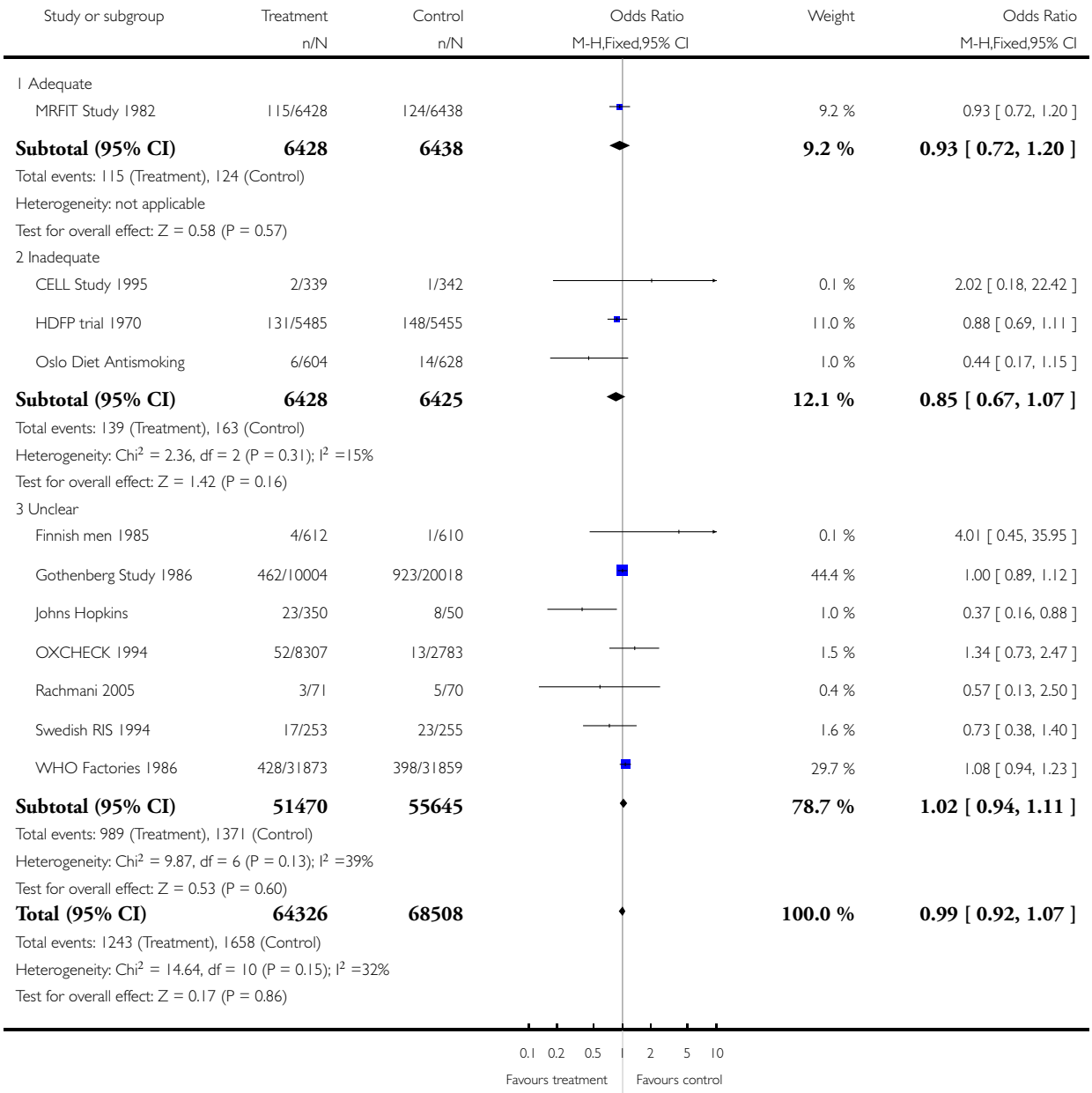


Analysis 1.10. Comparison 1 Multiple risk factor intervention versus control, Outcome 10 Coronary heart disease mortality (by allocation concealment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 10 Coronary heart disease mortality (by allocation concealment)



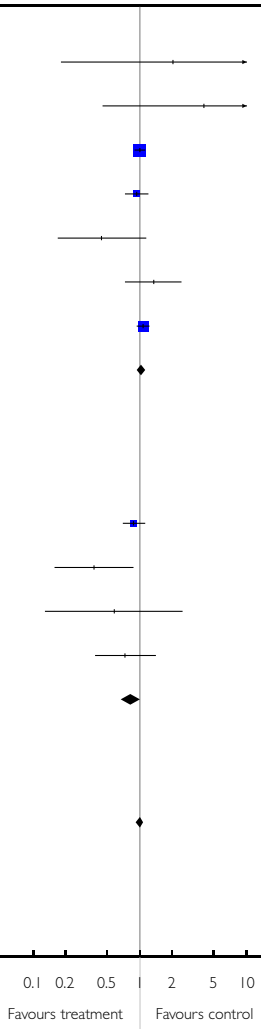
Analysis 1.11. Comparison 1 Multiple risk factor intervention versus control, Outcome 11 Coronary heart disease mortality (by co-morbidity).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 11 Coronary heart disease mortality (by co-morbidity)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 No co-morbidity					
CELL Study 1995	2/339	1/342		0.1 %	2.02 [0.18, 22.42]
Finnish men 1985	4/612	1/610		0.1 %	4.01 [0.45, 35.95]
Gothenberg Study 1986	462/10004	923/20018		44.4 %	1.00 [0.89, 1.12]
MRFIT Study 1982	115/6428	124/6438		9.2 %	0.93 [0.72, 1.20]
Oslo Diet Antismoking	6/604	14/628		1.0 %	0.44 [0.17, 1.15]
OXCHECK 1994	52/8307	13/2783		1.5 %	1.34 [0.73, 2.47]
WHO Factories 1986	428/31873	398/31859		29.7 %	1.08 [0.94, 1.23]
Subtotal (95% CI)	**58167**	**62678**		**86.1 %**	**1.02 [0.94, 1.11]**
Total events: 1069 (Treatment), 1474 (Control)					
Heterogeneity: Chi^2 = 6.72, df = 6 (P = 0.35); I^2 =11%					
Test for overall effect: Z = 0.52 (P = 0.60)					
2 Co-morbidity (hypertension or diabetes)					
HDFP trial 1970	131/5485	148/5455		11.0 %	0.88 [0.69, 1.11]
Johns Hopkins	23/350	8/50		1.0 %	0.37 [0.16, 0.88]
Rachmani 2005	3/71	5/70		0.4 %	0.57 [0.13, 2.50]
Swedish RIS 1994	17/253	23/255		1.6 %	0.73 [0.38, 1.40]
Subtotal (95% CI)	**6159**	**5830**		**13.9 %**	**0.82 [0.66, 1.01]**
Total events: 174 (Treatment), 184 (Control)					
Heterogeneity: Chi^2 = 3.92, df = 3 (P = 0.27); I^2 =23%					
Test for overall effect: Z = 1.86 (P = 0.064)					
Total (95% CI)	**64326**	**68508**		**100.0 %**	**0.99 [0.92, 1.07]**
Total events: 1243 (Treatment), 1658 (Control)					
Heterogeneity: Chi^2 = 14.64, df = 10 (P = 0.15); I^2 =32%					
Test for overall effect: Z = 0.17 (P = 0.86)					



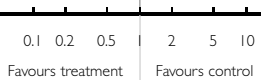
Analysis 1.12. Comparison 1 Multiple risk factor intervention versus control, Outcome 12 Coronary heart disease (by drug treatment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 12 Coronary heart disease (by drug treatment)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 No drug treatment					
Oslo Diet Antismoking	6/604	14/628		1.0 %	0.44 [0.17, 1.15]
Subtotal (95% CI)	**604**	**628**		**1.0 %**	**0.44 [0.17, 1.15]**
Total events: 6 (Treatment), 14 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.67 (P = 0.095)					
2 Antihypertensives OR lipid-lowering drugs					
HDFP trial 1970	131/5485	148/5455		11.0 %	0.88 [0.69, 1.11]
Johns Hopkins	23/350	8/50		1.0 %	0.37 [0.16, 0.88]
MRFIT Study 1982	115/6428	124/6438		9.2 %	0.93 [0.72, 1.20]
Rachmani 2005	3/71	5/70		0.4 %	0.57 [0.13, 2.50]
WHO Factories 1986	428/31873	398/31859		29.7 %	1.08 [0.94, 1.23]
Subtotal (95% CI)	**44207**	**43872**		**51.3 %**	**0.99 [0.89, 1.10]**
Total events: 700 (Treatment), 683 (Control)					
Heterogeneity: Chi^2 = 8.15, df = 4 (P = 0.09); I^2 =51%					
Test for overall effect: Z = 0.19 (P = 0.85)					
3 Antihypertensives AND lipid-lowering drugs					
CELL Study 1995	2/339	1/342		0.1 %	2.02 [0.18, 22.42]
Finnish men 1985	4/612	1/610		0.1 %	4.01 [0.45, 35.95]
Gothenberg Study 1986	462/10004	923/20018		44.4 %	1.00 [0.89, 1.12]
OXCHECK 1994	52/8307	13/2783		1.5 %	1.34 [0.73, 2.47]
Swedish RIS 1994	17/253	23/255		1.6 %	0.73 [0.38, 1.40]
Subtotal (95% CI)	**19515**	**24008**		**47.7 %**	**1.01 [0.90, 1.13]**
Total events: 537 (Treatment), 961 (Control)					
Heterogeneity: Chi^2 = 3.67, df = 4 (P = 0.45); I^2 =0.0%					
Test for overall effect: Z = 0.16 (P = 0.87)					
Total (95% CI)	**64326**	**68508**		**100.0 %**	**0.99 [0.92, 1.07]**
Total events: 1243 (Treatment), 1658 (Control)					
Heterogeneity: Chi^2 = 14.64, df = 10 (P = 0.15); I^2 =32%					
Test for overall effect: Z = 0.17 (P = 0.86)					



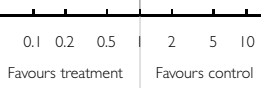
Analysis 1.13. Comparison 1 Multiple risk factor intervention versus control, Outcome 13 Coronary heart disease (by era).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 13 Coronary heart disease (by era)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Low rate of CVD					
CELL Study 1995	2/339	1/342		0.1 %	2.02 [0.18, 22.42]
OXCHECK 1994	52/8307	13/2783		1.5 %	1.34 [0.73, 2.47]
Rachmani 2005	3/71	5/70		0.4 %	0.57 [0.13, 2.50]
Swedish RIS 1994	17/253	23/255		1.6 %	0.73 [0.38, 1.40]
Subtotal (95% CI)	**8970**	**3450**		**3.5 %**	**0.99 [0.66, 1.49]**
Total events: 74 (Treatment), 42 (Control)					
Heterogeneity: Chi^2 = 2.69, df = 3 (P = 0.44); I^2 =0.0%					
Test for overall effect: Z = 0.03 (P = 0.98)					
2 High rate of CVD					
Finnish men 1985	4/612	1/610		0.1 %	4.01 [0.45, 35.95]
Gothenberg Study 1986	462/10004	923/20018		44.4 %	1.00 [0.89, 1.12]
HDFP trial 1970	131/5485	148/5455		11.0 %	0.88 [0.69, 1.11]
Johns Hopkins	23/350	8/50		1.0 %	0.37 [0.16, 0.88]
MRFIT Study 1982	115/6428	124/6438		9.2 %	0.93 [0.72, 1.20]
Oslo Diet Antismoking	6/604	14/628		1.0 %	0.44 [0.17, 1.15]
WHO Factories 1986	428/31873	398/31859		29.7 %	1.08 [0.94, 1.23]
Subtotal (95% CI)	**55356**	**65058**		**96.5 %**	**0.99 [0.92, 1.07]**
Total events: 1169 (Treatment), 1616 (Control)					
Heterogeneity: Chi^2 = 11.95, df = 6 (P = 0.06); I^2 =50%					
Test for overall effect: Z = 0.17 (P = 0.86)					
Total (95% CI)	**64326**	**68508**		**100.0 %**	**0.99 [0.92, 1.07]**
Total events: 1243 (Treatment), 1658 (Control)					
Heterogeneity: Chi^2 = 14.64, df = 10 (P = 0.15); I^2 =32%					
Test for overall effect: Z = 0.17 (P = 0.86)					



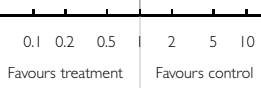
Analysis 1.14. Comparison 1 Multiple risk factor intervention versus control, Outcome 14 Coronary heart disease mortality (by study age).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 14 Coronary heart disease mortality (by study age)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Before 2000					
CELL Study 1995	2/339	1/342		0.1 %	2.02 [0.18, 22.42]
Finnish men 1985	4/612	1/610		0.1 %	4.01 [0.45, 35.95]
Gothenberg Study 1986	462/10004	923/20018		44.4 %	1.00 [0.89, 1.12]
HDFP trial 1970	131/5485	148/5455		11.0 %	0.88 [0.69, 1.11]
Johns Hopkins	23/350	8/50		1.0 %	0.37 [0.16, 0.88]
MRFIT Study 1982	115/6428	124/6438		9.2 %	0.93 [0.72, 1.20]
Oslo Diet Antismoking	6/604	14/628		1.0 %	0.44 [0.17, 1.15]
OXCHECK 1994	52/8307	13/2783		1.5 %	1.34 [0.73, 2.47]
Swedish RIS 1994	17/253	23/255		1.6 %	0.73 [0.38, 1.40]
WHO Factories 1986	428/31873	398/31859		29.7 %	1.08 [0.94, 1.23]
Subtotal (95% CI)	**64255**	**68438**		**99.6 %**	**0.99 [0.92, 1.07]**
Total events: 1240 (Treatment), 1653 (Control)					
Heterogeneity: Chi² = 14.11, df = 9 (P = 0.12); I² =36%					
Test for overall effect: Z = 0.13 (P = 0.89)					
2 After 2000					
Rachmani 2005	3/71	5/70		0.4 %	0.57 [0.13, 2.50]
Subtotal (95% CI)	**71**	**70**		**0.4 %**	**0.57 [0.13, 2.50]**
Total events: 3 (Treatment), 5 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.74 (P = 0.46)					
Total (95% CI)	**64326**	**68508**		**100.0 %**	**0.99 [0.92, 1.07]**
Total events: 1243 (Treatment), 1658 (Control)					
Heterogeneity: Chi² = 14.64, df = 10 (P = 0.15); I² =32%					
Test for overall effect: Z = 0.17 (P = 0.86)					



Analysis 1.15. Comparison 1 Multiple risk factor intervention versus control, Outcome 15 Stroke mortality.

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 15 Stroke mortality

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Finnish men 1985	0/612	1/610		0.8 %	0.33 [0.01, 8.16]
Gothenberg Study 1986	64/10004	154/20018		57.6 %	0.83 [0.62, 1.11]
HDFP trial 1970	29/5485	52/5455		29.3 %	0.55 [0.35, 0.87]
MRFIT Study 1982	13/6428	11/6438		6.2 %	1.18 [0.53, 2.64]
Oslo Diet Antismoking	2/604	1/628		0.6 %	2.08 [0.19, 23.03]
Rachmani 2005	2/71	3/70		1.7 %	0.65 [0.10, 4.00]
Swedish RIS 1994	3/253	7/255		3.9 %	0.43 [0.11, 1.66]
Total (95% CI)	**23457**	**33474**		**100.0 %**	**0.75 [0.60, 0.95]**

Total events: 113 (Treatment), 229 (Control)

Heterogeneity: $Chi^2 = 5.07$, df = 6 (P = 0.54); $I^2 = 0.0\%$

Test for overall effect: Z = 2.42 (P = 0.015)

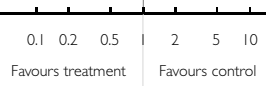
Analysis 1.16. Comparison 1 Multiple risk factor intervention versus control, Outcome 16 Stroke mortality (by allocation concealment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 16 Stroke mortality (by allocation concealment)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Adequate					
MRFIT Study 1982	13/6428	11/6438		6.2 %	1.18 [0.53, 2.64]
Subtotal (95% CI)	**6428**	**6438**		**6.2 %**	**1.18 [0.53, 2.64]**
Total events: 13 (Treatment), 11 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.41 (P = 0.68)					
2 Inadequate					
HDFP trial 1970	29/5485	52/5455		29.3 %	0.55 [0.35, 0.87]
Oslo Diet Antismoking	2/604	1/628		0.6 %	2.08 [0.19, 23.03]
Subtotal (95% CI)	**6089**	**6083**		**29.8 %**	**0.58 [0.37, 0.91]**
Total events: 31 (Treatment), 53 (Control)					
Heterogeneity: Chi^2 = 1.13, df = 1 (P = 0.29); I^2 =12%					
Test for overall effect: Z = 2.40 (P = 0.017)					
3 Unclear					
Finnish men 1985	0/612	1/610		0.8 %	0.33 [0.01, 8.16]
Gothenberg Study 1986	64/10004	154/20018		57.6 %	0.83 [0.62, 1.11]
Rachmani 2005	2/71	3/70		1.7 %	0.65 [0.10, 4.00]
Swedish RIS 1994	3/253	7/255		3.9 %	0.43 [0.11, 1.66]
Subtotal (95% CI)	**10940**	**20953**		**64.0 %**	**0.79 [0.60, 1.05]**
Total events: 69 (Treatment), 165 (Control)					
Heterogeneity: Chi^2 = 1.23, df = 3 (P = 0.75); I^2 =0.0%					
Test for overall effect: Z = 1.60 (P = 0.11)					
Total (95% CI)	**23457**	**33474**		**100.0 %**	**0.75 [0.60, 0.95]**
Total events: 113 (Treatment), 229 (Control)					
Heterogeneity: Chi^2 = 5.07, df = 6 (P = 0.54); I^2 =0.0%					
Test for overall effect: Z = 2.42 (P = 0.015)					



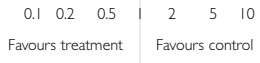
Analysis 1.17. Comparison 1 Multiple risk factor intervention versus control, Outcome 17 Stroke mortality (by co-morbidity).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 17 Stroke mortality (by co-morbidity)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 No co-morbidity					
Finnish men 1985	0/612	1/610		0.8 %	0.33 [0.01, 8.16]
Gothenberg Study 1986	64/10004	154/20018		57.6 %	0.83 [0.62, 1.11]
MRFIT Study 1982	13/6428	11/6438		6.2 %	1.18 [0.53, 2.64]
Oslo Diet Antismoking	2/604	1/628		0.6 %	2.08 [0.19, 23.03]
Subtotal (95% CI)	**17648**	**27694**		**65.2 %**	**0.87 [0.66, 1.14]**
Total events: 79 (Treatment), 167 (Control)					
Heterogeneity: Chi^2 = 1.52, df = 3 (P = 0.68); I^2 =0.0%					
Test for overall effect: Z = 1.02 (P = 0.31)					
2 Co-morbidity (hypertension or diabetes)					
HDFP trial 1970	29/5485	52/5455		29.3 %	0.55 [0.35, 0.87]
Rachmani 2005	2/71	3/70		1.7 %	0.65 [0.10, 4.00]
Swedish RIS 1994	3/253	7/255		3.9 %	0.43 [0.11, 1.66]
Subtotal (95% CI)	**5809**	**5780**		**34.8 %**	**0.54 [0.36, 0.83]**
Total events: 34 (Treatment), 62 (Control)					
Heterogeneity: Chi^2 = 0.16, df = 2 (P = 0.92); I^2 =0.0%					
Test for overall effect: Z = 2.85 (P = 0.0044)					
Total (95% CI)	**23457**	**33474**		**100.0 %**	**0.75 [0.60, 0.95]**
Total events: 113 (Treatment), 229 (Control)					
Heterogeneity: Chi^2 = 5.07, df = 6 (P = 0.54); I^2 =0.0%					
Test for overall effect: Z = 2.42 (P = 0.015)					

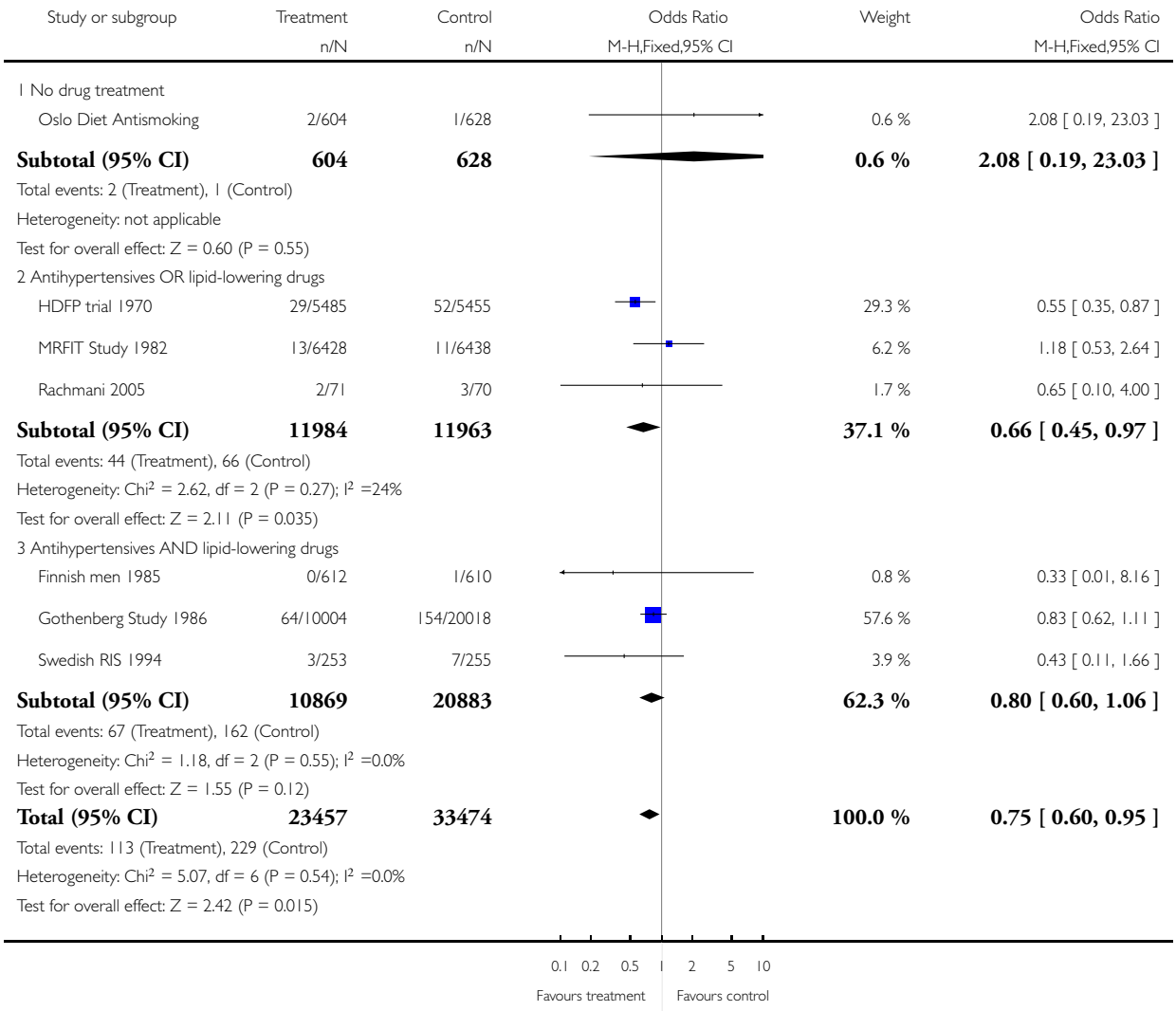


Analysis 1.18. Comparison 1 Multiple risk factor intervention versus control, Outcome 18 Stroke mortality (by drug treatment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 18 Stroke mortality (by drug treatment)



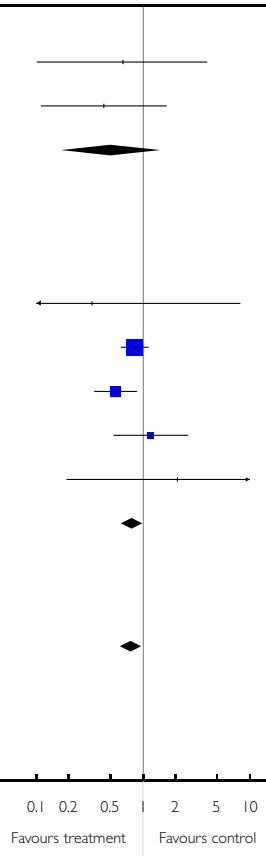
Analysis 1.19. Comparison 1 Multiple risk factor intervention versus control, Outcome 19 Stroke mortality (by era).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 19 Stroke mortality (by era)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Low rate of CVD					
Rachmani 2005	2/71	3/70		1.7 %	0.65 [0.10, 4.00]
Swedish RIS 1994	3/253	7/255		3.9 %	0.43 [0.11, 1.66]
Subtotal (95% CI)	**324**	**325**		**5.5 %**	**0.49 [0.17, 1.46]**
Total events: 5 (Treatment), 10 (Control)					
Heterogeneity: Chi^2 = 0.13, df = 1 (P = 0.72); I^2 =0.0%					
Test for overall effect: Z = 1.28 (P = 0.20)					
2 High rate of CVD					
Finnish men 1985	0/612	1/610		0.8 %	0.33 [0.01, 8.16]
Gothenberg Study 1986	64/10004	154/20018		57.6 %	0.83 [0.62, 1.11]
HDFP trial 1970	29/5485	52/5455		29.3 %	0.55 [0.35, 0.87]
MRFIT Study 1982	13/6428	11/6438		6.2 %	1.18 [0.53, 2.64]
Oslo Diet Antismoking	2/604	1/628		0.6 %	2.08 [0.19, 23.03]
Subtotal (95% CI)	**23133**	**33149**		**94.5 %**	**0.77 [0.61, 0.97]**
Total events: 108 (Treatment), 219 (Control)					
Heterogeneity: Chi^2 = 4.32, df = 4 (P = 0.36); I^2 =8%					
Test for overall effect: Z = 2.20 (P = 0.028)					
Total (95% CI)	**23457**	**33474**		**100.0 %**	**0.75 [0.60, 0.95]**
Total events: 113 (Treatment), 229 (Control)					
Heterogeneity: Chi^2 = 5.07, df = 6 (P = 0.54); I^2 =0.0%					
Test for overall effect: Z = 2.42 (P = 0.015)					



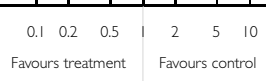
Analysis 1.20. Comparison 1 Multiple risk factor intervention versus control, Outcome 20 Stroke mortality (by study age).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 20 Stroke mortality (by study age)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Before 2000					
Finnish men 1985	0/612	1/610		0.8 %	0.33 [0.01, 8.16]
Gothenberg Study 1986	64/10004	154/20018		57.6 %	0.83 [0.62, 1.11]
HDFP trial 1970	29/5485	52/5455		29.3 %	0.55 [0.35, 0.87]
MRFIT Study 1982	13/6428	11/6438		6.2 %	1.18 [0.53, 2.64]
Oslo Diet Antismoking	2/604	1/628		0.6 %	2.08 [0.19, 23.03]
Swedish RIS 1994	3/253	7/255		3.9 %	0.43 [0.11, 1.66]
Subtotal (95% CI)	**23386**	**33404**		**98.3 %**	**0.76 [0.60, 0.95]**
Total events: 111 (Treatment), 226 (Control)					
Heterogeneity: Chi^2 = 5.04, df = 5 (P = 0.41); I^2 =1%					
Test for overall effect: Z = 2.38 (P = 0.017)					
2 After 2000					
Rachmani 2005	2/71	3/70		1.7 %	0.65 [0.10, 4.00]
Subtotal (95% CI)	**71**	**70**		**1.7 %**	**0.65 [0.10, 4.00]**
Total events: 2 (Treatment), 3 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.47 (P = 0.64)					
Total (95% CI)	**23457**	**33474**		**100.0 %**	**0.75 [0.60, 0.95]**
Total events: 113 (Treatment), 229 (Control)					
Heterogeneity: Chi^2 = 5.07, df = 6 (P = 0.54); I^2 =0.0%					
Test for overall effect: Z = 2.42 (P = 0.015)					



Analysis 1.21. Comparison 1 Multiple risk factor intervention versus control, Outcome 21 Fatal and non-fatal clinical events.

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

Comparison: 1 Multiple risk factor intervention versus control

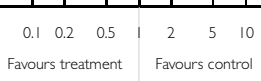
Outcome: 21 Fatal and non-fatal clinical events

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Finnish men 1985	19/612	17/610		4.0 %	1.12 [0.58, 2.17]
Garcia-Pena 2001	6/364	5/354		1.4 %	1.17 [0.35, 3.87]
Gothenberg Study 1986	1191/10004	2348/20018		20.3 %	1.02 [0.94, 1.10]
HDFP trial 1970	233/5485	306/5455		16.5 %	0.75 [0.63, 0.89]
MRFIT Study 1982	1786/6428	2063/6438		20.3 %	0.82 [0.76, 0.88]
Oslo Diet Antismoking	22/604	39/628		5.6 %	0.57 [0.33, 0.97]
Rachmani 2005	36/71	53/70		3.5 %	0.33 [0.16, 0.68]
Swedish RIS 1994	63/253	84/255		8.6 %	0.68 [0.46, 0.99]
WHO Factories 1986	927/31873	873/31859		19.7 %	1.06 [0.97, 1.17]
Total (95% CI)	**55694**	**65687**		**100.0 %**	**0.84 [0.73, 0.98]**

Total events: 4283 (Treatment), 5788 (Control)

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 45.16$, df = 8 ($P<0.00001$); $I^2 = 82\%$

Test for overall effect: Z = 2.29 (P = 0.022)



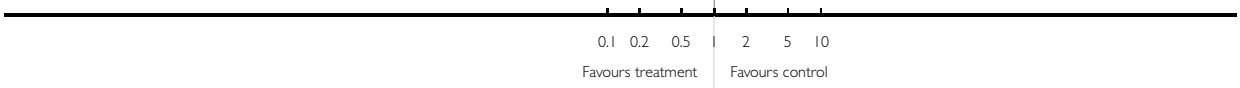
Analysis 1.22. Comparison 1 Multiple risk factor intervention versus control, Outcome 22 Fatal and non-fatal clinical events (individual analysis or cluster).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 22 Fatal and non-fatal clinical events (individual analysis or cluster)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Individual					
Finnish men 1985	19/612	17/610		0.4 %	1.12 [0.58, 2.17]
Garcia-Pena 2001	6/364	5/354		0.1 %	1.17 [0.35, 3.87]
Gothenberg Study 1986	1191/10004	2348/20018		33.2 %	1.02 [0.94, 1.10]
HDFP trial 1970	233/5485	306/5455		7.1 %	0.75 [0.63, 0.89]
MRFIT Study 1982	1786/6428	2063/6438		35.8 %	0.82 [0.76, 0.88]
Oslo Diet Antismoking	22/604	39/628		0.9 %	0.57 [0.33, 0.97]
Rachmani 2005	36/71	53/70		0.6 %	0.33 [0.16, 0.68]
Swedish RIS 1994	63/253	84/255		1.5 %	0.68 [0.46, 0.99]
Subtotal (95% CI)	**23821**	**33828**		**79.6 %**	**0.89 [0.84, 0.93]**
Total events: 3356 (Treatment), 4915 (Control)					
Heterogeneity: Chi^2 = 33.95, df = 7 (P = 0.00002); I^2 =79%					
Test for overall effect: Z = 4.74 (P < 0.00001)					
2 Cluster randomisation - analysis by individual					
WHO Factories 1986	927/31873	873/31859		20.4 %	1.06 [0.97, 1.17]
Subtotal (95% CI)	**31873**	**31859**		**20.4 %**	**1.06 [0.97, 1.17]**
Total events: 927 (Treatment), 873 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 1.28 (P = 0.20)					
Total (95% CI)	**55694**	**65687**		**100.0 %**	**0.92 [0.88, 0.96]**
Total events: 4283 (Treatment), 5788 (Control)					
Heterogeneity: Chi^2 = 45.16, df = 8 (P<0.00001); I^2 =82%					
Test for overall effect: Z = 3.60 (P = 0.00032)					



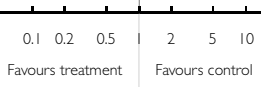
Analysis 1.23. Comparison 1 Multiple risk factor intervention versus control, Outcome 23 Fatal and non-fatal clinical events (by allocation concealment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 23 Fatal and non-fatal clinical events (by allocation concealment)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Adequate					
Garcia-Pena 2001	6/364	5/354		0.1 %	1.17 [0.35, 3.87]
MRFIT Study 1982	1786/6428	2063/6438		35.8 %	0.82 [0.76, 0.88]
Subtotal (95% CI)	**6792**	**6792**		**35.9 %**	**0.82 [0.76, 0.88]**
Total events: 1792 (Treatment), 2068 (Control)					
Heterogeneity: Chi^2 = 0.35, df = 1 (P = 0.56); I^2 =0.0%					
Test for overall effect: Z = 5.25 (P < 0.00001)					
2 Inadequate					
HDFP trial 1970	233/5485	306/5455		7.1 %	0.75 [0.63, 0.89]
Oslo Diet Antismoking	22/604	39/628		0.9 %	0.57 [0.33, 0.97]
Subtotal (95% CI)	**6089**	**6083**		**8.0 %**	**0.73 [0.62, 0.86]**
Total events: 255 (Treatment), 345 (Control)					
Heterogeneity: Chi^2 = 0.87, df = 1 (P = 0.35); I^2 =0.0%					
Test for overall effect: Z = 3.77 (P = 0.00017)					
3 Unclear					
Finnish men 1985	19/612	17/610		0.4 %	1.12 [0.58, 2.17]
Gothenberg Study 1986	1191/10004	2348/20018		33.2 %	1.02 [0.94, 1.10]
Rachmani 2005	36/71	53/70		0.6 %	0.33 [0.16, 0.68]
Swedish RIS 1994	63/253	84/255		1.5 %	0.68 [0.46, 0.99]
WHO Factories 1986	927/31873	873/31859		20.4 %	1.06 [0.97, 1.17]
Subtotal (95% CI)	**42813**	**52812**		**56.1 %**	**1.02 [0.96, 1.08]**
Total events: 2236 (Treatment), 3375 (Control)					
Heterogeneity: Chi^2 = 14.72, df = 4 (P = 0.01); I^2 =73%					
Test for overall effect: Z = 0.60 (P = 0.55)					
Total (95% CI)	**55694**	**65687**		**100.0 %**	**0.92 [0.88, 0.96]**
Total events: 4283 (Treatment), 5788 (Control)					
Heterogeneity: Chi^2 = 45.16, df = 8 (P<0.00001); I^2 =82%					
Test for overall effect: Z = 3.60 (P = 0.00032)					



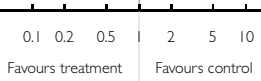
Analysis 1.24. Comparison 1 Multiple risk factor intervention versus control, Outcome 24 Fatal and non-fatal clinical events (by co-morbidity).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 24 Fatal and non-fatal clinical events (by co-morbidity)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 No co-morbidity					
Finnish men 1985	19/612	17/610		0.4 %	1.12 [0.58, 2.17]
Gothenberg Study 1986	1191/10004	2348/20018		33.2 %	1.02 [0.94, 1.10]
MRFIT Study 1982	1786/6428	2063/6438		35.8 %	0.82 [0.76, 0.88]
Oslo Diet Antismoking	22/604	39/628		0.9 %	0.57 [0.33, 0.97]
WHO Factories 1986	927/31873	873/31859		20.4 %	1.06 [0.97, 1.17]
Subtotal (95% CI)	**49521**	**59553**		**90.7 %**	**0.94 [0.90, 0.99]**
Total events: 3945 (Treatment), 5340 (Control)					
Heterogeneity: Chi^2 = 27.97, df = 4 (P = 0.00001); I^2 =86%					
Test for overall effect: Z = 2.46 (P = 0.014)					
2 Co-morbidity (hypertension or diabetes)					
Garcia-Pena 2001	6/364	5/354		0.1 %	1.17 [0.35, 3.87]
HDFP trial 1970	233/5485	306/5455		7.1 %	0.75 [0.63, 0.89]
Rachmani 2005	36/71	53/70		0.6 %	0.33 [0.16, 0.68]
Swedish RIS 1994	63/253	84/255		1.5 %	0.68 [0.46, 0.99]
Subtotal (95% CI)	**6173**	**6134**		**9.3 %**	**0.71 [0.61, 0.83]**
Total events: 338 (Treatment), 448 (Control)					
Heterogeneity: Chi^2 = 5.43, df = 3 (P = 0.14); I^2 =45%					
Test for overall effect: Z = 4.33 (P = 0.000015)					
Total (95% CI)	**55694**	**65687**		**100.0 %**	**0.92 [0.88, 0.96]**
Total events: 4283 (Treatment), 5788 (Control)					
Heterogeneity: Chi^2 = 45.16, df = 8 (P<0.00001); I^2 =82%					
Test for overall effect: Z = 3.60 (P = 0.00032)					

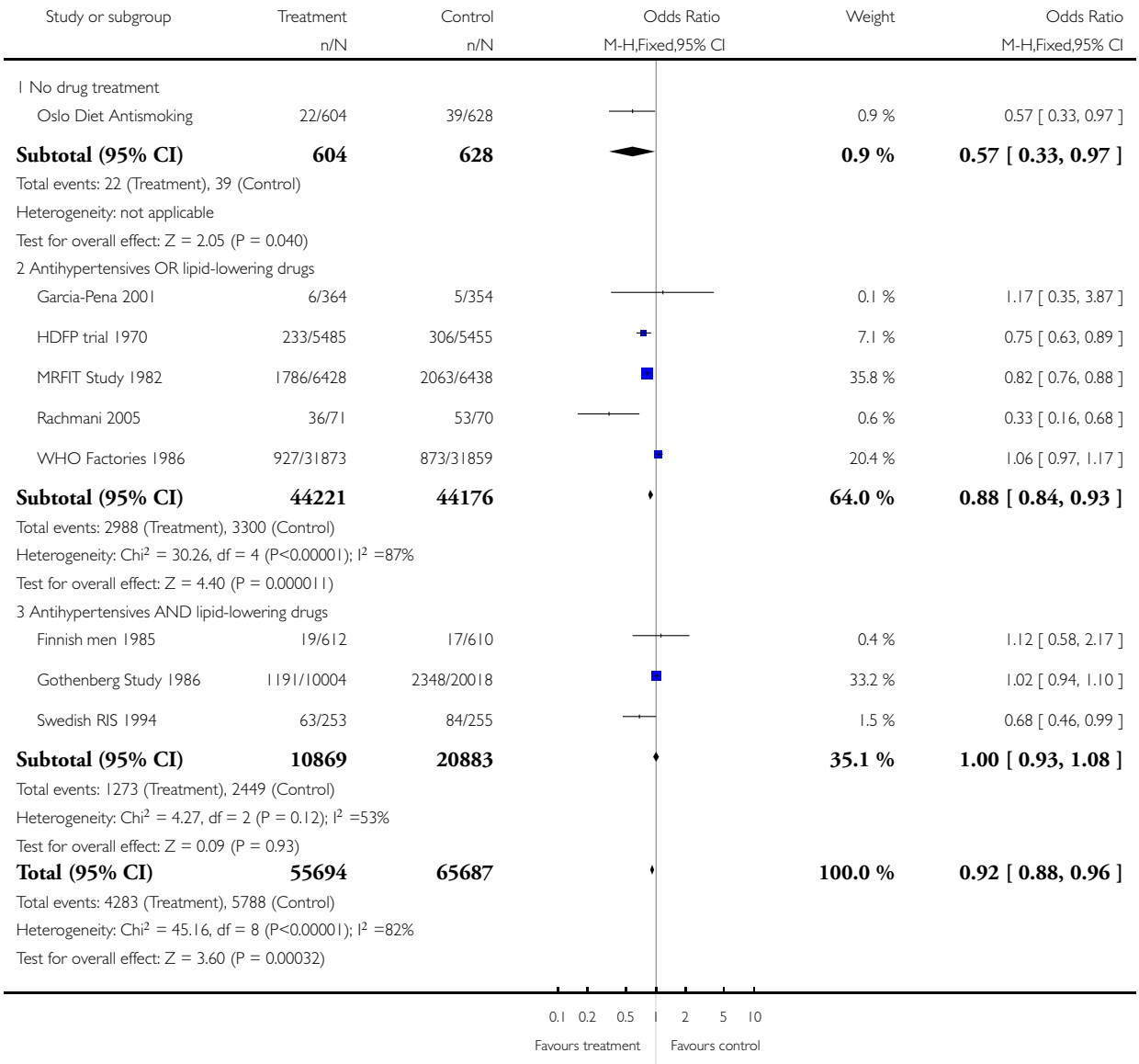


Analysis 1.25. Comparison 1 Multiple risk factor intervention versus control, Outcome 25 Fatal and non-fatal clinical events (by drug treatment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 25 Fatal and non-fatal clinical events (by drug treatment)



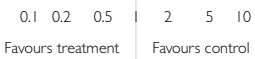
Analysis 1.26. Comparison 1 Multiple risk factor intervention versus control, Outcome 26 Fatal and non-fatal clinical events (by era).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 26 Fatal and non-fatal clinical events (by era)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Low rate of CVD					
Garcia-Pena 2001	6/364	5/354		0.1 %	1.17 [0.35, 3.87]
Rachmani 2005	36/71	53/70		0.6 %	0.33 [0.16, 0.68]
Swedish RIS 1994	63/253	84/255		1.5 %	0.68 [0.46, 0.99]
Subtotal (95% CI)	**688**	**679**		**2.3 %**	**0.60 [0.44, 0.84]**
Total events: 105 (Treatment), 142 (Control)					
Heterogeneity: Chi² = 4.22, df = 2 (P = 0.12); I² =53%					
Test for overall effect: Z = 3.04 (P = 0.0024)					
2 High Rate of CVD					
Finnish men 1985	19/612	17/610		0.4 %	1.12 [0.58, 2.17]
Gothenberg Study 1986	1191/10004	2348/20018		33.2 %	1.02 [0.94, 1.10]
HDFP trial 1970	233/5485	306/5455		7.1 %	0.75 [0.63, 0.89]
MRFIT Study 1982	1786/6428	2063/6438		35.8 %	0.82 [0.76, 0.88]
Oslo Diet Antismoking	22/604	39/628		0.9 %	0.57 [0.33, 0.97]
WHO Factories 1986	927/31873	873/31859		20.4 %	1.06 [0.97, 1.17]
Subtotal (95% CI)	**55006**	**65008**		**97.7 %**	**0.93 [0.89, 0.97]**
Total events: 4178 (Treatment), 5646 (Control)					
Heterogeneity: Chi² = 34.48, df = 5 (P<0.00001); I² =85%					
Test for overall effect: Z = 3.22 (P = 0.0013)					
Total (95% CI)	**55694**	**65687**		**100.0 %**	**0.92 [0.88, 0.96]**
Total events: 4283 (Treatment), 5788 (Control)					
Heterogeneity: Chi² = 45.16, df = 8 (P<0.00001); I² =82%					
Test for overall effect: Z = 3.60 (P = 0.00032)					



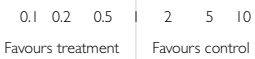
Analysis 1.27. Comparison 1 Multiple risk factor intervention versus control, Outcome 27 Fatal and non-fatal clinical events (by age of study).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 27 Fatal and non-fatal clinical events (by age of study)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Before 2000					
Finnish men 1985	19/612	17/610		0.4 %	1.12 [0.58, 2.17]
Gothenberg Study 1986	1191/10004	2348/20018		33.3 %	1.02 [0.94, 1.10]
HDFP trial 1970	233/5485	306/5455		7.1 %	0.75 [0.63, 0.89]
MRFIT Study 1982	1786/6428	2063/6438		36.0 %	0.82 [0.76, 0.88]
Oslo Diet Antismoking	22/604	39/628		0.9 %	0.57 [0.33, 0.97]
Swedish RIS 1994	63/253	84/255		1.5 %	0.68 [0.46, 0.99]
WHO Factories 1986	927/30489	873/31873		20.0 %	1.11 [1.01, 1.22]
Subtotal (95% CI)	**53875**	**65277**		**99.2 %**	**0.94 [0.90, 0.98]**
Total events: 4241 (Treatment), 5730 (Control)					
Heterogeneity: Chi^2 = 43.37, df = 6 (P<0.00001); I^2 =86%					
Test for overall effect: Z = 2.97 (P = 0.0029)					
2 After 2000					
Garcia-Pena 2001	6/364	5/354		0.1 %	1.17 [0.35, 3.87]
Rachmani 2005	36/71	53/70		0.6 %	0.33 [0.16, 0.68]
Subtotal (95% CI)	**435**	**424**		**0.8 %**	**0.46 [0.25, 0.85]**
Total events: 42 (Treatment), 58 (Control)					
Heterogeneity: Chi^2 = 3.16, df = 1 (P = 0.08); I^2 =68%					
Test for overall effect: Z = 2.50 (P = 0.012)					
Total (95% CI)	**54310**	**65701**		**100.0 %**	**0.93 [0.89, 0.97]**
Total events: 4283 (Treatment), 5788 (Control)					
Heterogeneity: Chi^2 = 51.59, df = 8 (P<0.00001); I^2 =84%					
Test for overall effect: Z = 3.15 (P = 0.0016)					



Analysis 1.28. Comparison 1 Multiple risk factor intervention versus control, Outcome 28 Smoking prevalence.

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

Comparison: 1 Multiple risk factor intervention versus control

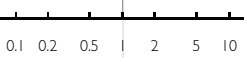
Outcome: 28 Smoking prevalence

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 1990	46/168	42/167		4.0 %	1.12 [0.69, 1.83]
Brekke 2005a	10/25	6/19		1.1 %	1.44 [0.41, 5.07]
Cakir 2006	8/30	6/30		1.2 %	1.45 [0.44, 4.86]
CELL Study 1995	139/292	148/310		5.4 %	0.99 [0.72, 1.37]
Change of Heart 1999	40/169	148/351		4.6 %	0.43 [0.28, 0.64]
Family Heart 1994 M	337/1767	500/2174		6.9 %	0.79 [0.68, 0.92]
Family Heart 1994 F	215/1217	301/1402		6.6 %	0.78 [0.65, 0.95]
Finnish men 1985	125/575	131/580		5.8 %	0.95 [0.72, 1.26]
Gothenberg Study 1986	691/1473	699/1404		7.0 %	0.89 [0.77, 1.03]
Kastarinen 2002	39/304	34/283		3.9 %	1.08 [0.66, 1.76]
Mattila 2003	52/331	57/309		4.6 %	0.82 [0.55, 1.24]
Meland 1997	35/58	30/52		2.4 %	1.12 [0.52, 2.39]
MRFIT Study 1982	1847/5754	2554/5638		7.4 %	0.57 [0.53, 0.62]
Nilsson 2001	17/43	27/46		2.0 %	0.46 [0.20, 1.07]
Oslo Diet Antismoking	236/604	214/628		6.2 %	1.24 [0.98, 1.57]
OXCHECK 1994	552/2205	506/1916		7.0 %	0.93 [0.81, 1.07]
Swedish RIS 1994	55/253	70/255		4.6 %	0.73 [0.49, 1.10]
Tromso 1991 F	208/422	212/462		6.0 %	1.15 [0.88, 1.49]
Tromso 1991 M	246/525	283/535		6.2 %	0.79 [0.62, 1.00]
WHO Factories 1986	7910/16908	897/1902		7.3 %	0.98 [0.90, 1.08]
Total (95% CI)	**33123**	**18463**		**100.0 %**	**0.87 [0.75, 1.00]**

Total events: 12808 (Intervention), 6865 (Control)

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 140.75$, df = 19 ($P<0.00001$); $I^2 = 87\%$

Test for overall effect: Z = 2.00 (P = 0.046)

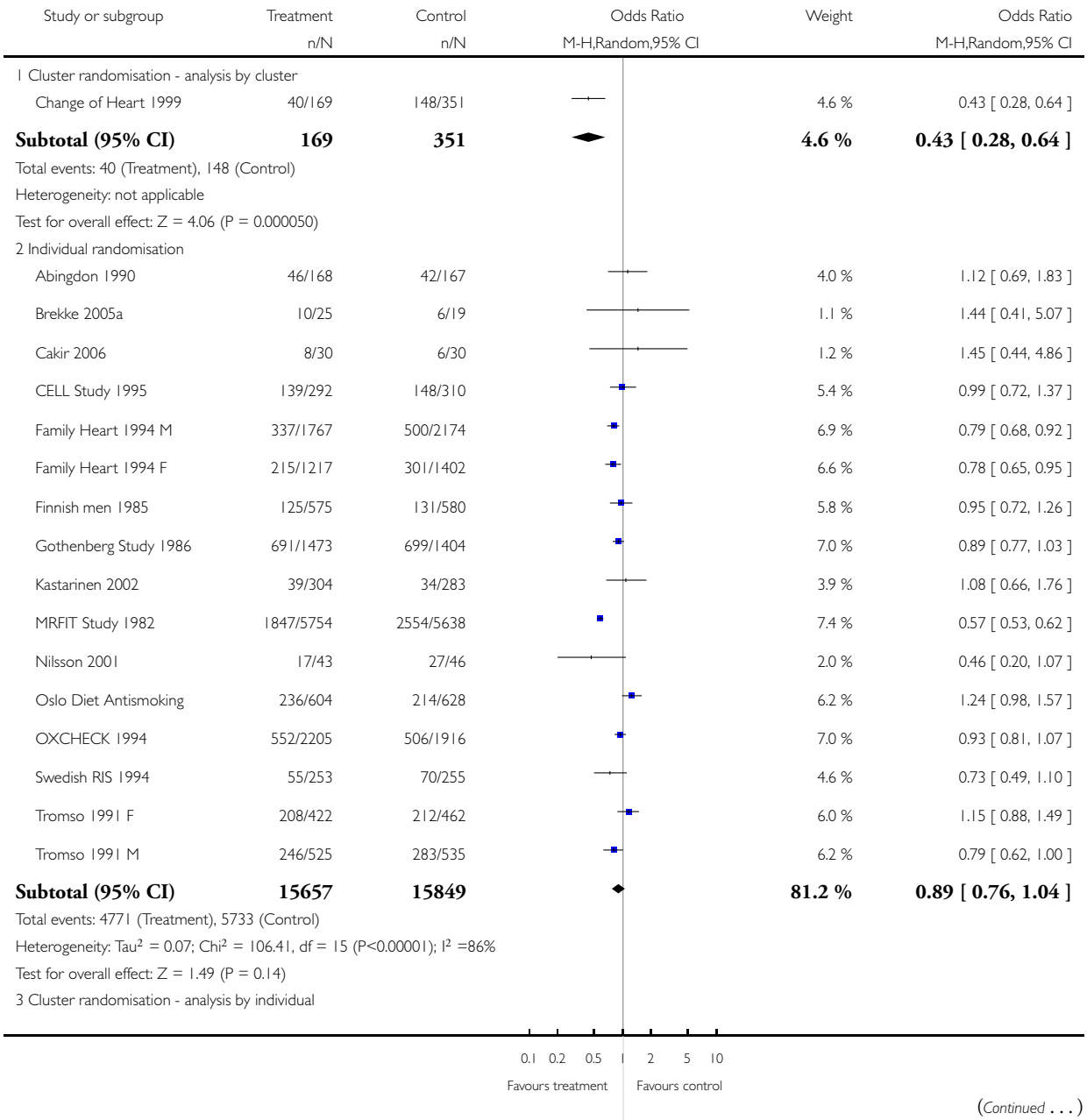


Analysis 1.29. Comparison 1 Multiple risk factor intervention versus control, Outcome 29 Smoking prevalence (individual analysis or cluster).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 29 Smoking prevalence (individual analysis or cluster)



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Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Mattila 2003	52/331	57/309		4.6 %	0.82 [0.55, 1.24]
Meland 1997	35/58	30/52		2.4 %	1.12 [0.52, 2.39]
WHO Factories 1986	7910/16908	897/1902		7.3 %	0.98 [0.90, 1.08]
Subtotal (95% CI)	**17297**	**2263**		**14.2 %**	**0.98 [0.89, 1.07]**
Total events: 7997 (Treatment), 984 (Control)					
Heterogeneity: Tau^2 = 0.0; Chi^2 = 0.80, df = 2 (P = 0.67); I^2 =0.0%					
Test for overall effect: Z = 0.47 (P = 0.64)					
Total (95% CI)	**33123**	**18463**		**100.0 %**	**0.87 [0.75, 1.00]**
Total events: 12808 (Treatment), 6865 (Control)					
Heterogeneity: Tau^2 = 0.07; Chi^2 = 140.75, df = 19 (P<0.00001); I^2 =87%					
Test for overall effect: Z = 2.00 (P = 0.046)					

Analysis 1.30. Comparison 1 Multiple risk factor intervention versus control, Outcome 30 Smoking prevalence (by allocation concealment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 30 Smoking prevalence (by allocation concealment)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Adequate allocation concealment					
Brekke 2005a	10/25	6/19		0.1 %	1.44 [0.41, 5.07]
Cakir 2006	8/30	6/30		0.1 %	1.45 [0.44, 4.86]
Mattila 2003	52/331	57/309		1.0 %	0.82 [0.55, 1.24]
MRFIT Study 1982	1847/5754	2554/5638		36.3 %	0.57 [0.53, 0.62]
Subtotal (95% CI)	**6140**	**5996**		**37.5 %**	**0.58 [0.54, 0.63]**
Total events: 1917 (Treatment), 2623 (Control)					
Heterogeneity: Chi^2 = 7.20, df = 3 (P = 0.07); I^2 =58%					
Test for overall effect: Z = 14.22 (P < 0.00001)					
2 Inadequate allocation concealment					

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Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
CELL Study 1995	139/292	148/310		1.6 %	0.99 [0.72, 1.37]
Kastarinen 2002	39/304	34/283		0.6 %	1.08 [0.66, 1.76]
Oslo Diet Antismoking	236/604	214/628		2.7 %	1.24 [0.98, 1.57]
Tromso 1991 F	208/422	212/462		2.1 %	1.15 [0.88, 1.49]
Tromso 1991 M	246/525	283/535		3.1 %	0.79 [0.62, 1.00]
Subtotal (95% CI)	**2147**	**2218**		**10.1 %**	**1.03 [0.91, 1.17]**
Total events: 868 (Treatment), 891 (Control)					
Heterogeneity: Chi^2 = 8.03, df = 4 (P = 0.09); I^2 =50%					
Test for overall effect: Z = 0.50 (P = 0.62)					
3 Unclear allocation concealment					
Abingdon 1990	46/168	42/167		0.6 %	1.12 [0.69, 1.83]
Change of Heart 1999	40/169	148/351		1.5 %	0.43 [0.28, 0.64]
Family Heart 1994 M	337/1767	500/2174		7.5 %	0.79 [0.68, 0.92]
Family Heart 1994 F	215/1217	301/1402		4.8 %	0.78 [0.65, 0.95]
Finnish men 1985	125/575	131/580		2.1 %	0.95 [0.72, 1.26]
Gothenberg Study 1986	691/1473	699/1404		7.9 %	0.89 [0.77, 1.03]
Meland 1997	35/58	30/52		0.3 %	1.12 [0.52, 2.39]
Nilsson 2001	17/43	27/46		0.3 %	0.46 [0.20, 1.07]
OXCHECK 1994	552/2205	506/1916		8.4 %	0.93 [0.81, 1.07]
Swedish RIS 1994	55/253	70/255		1.1 %	0.73 [0.49, 1.10]
WHO Factories 1986	7910/16908	897/1902		17.8 %	0.98 [0.90, 1.08]
Subtotal (95% CI)	**24836**	**10249**		**52.4 %**	**0.89 [0.84, 0.94]**
Total events: 10023 (Treatment), 3351 (Control)					
Heterogeneity: Chi^2 = 25.57, df = 10 (P = 0.004); I^2 =61%					
Test for overall effect: Z = 3.96 (P = 0.000076)					
Total (95% CI)	**33123**	**18463**		**100.0 %**	**0.79 [0.76, 0.82]**
Total events: 12808 (Treatment), 6865 (Control)					
Heterogeneity: Chi^2 = 140.75, df = 19 (P<0.00001); I^2 =87%					
Test for overall effect: Z = 10.93 (P < 0.00001)					

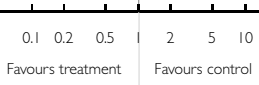
Analysis 1.31. Comparison 1 Multiple risk factor intervention versus control, Outcome 31 Smoking prevalence (by co-morbidity).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 31 Smoking prevalence (by co-morbidity)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 No co-morbidity					
Abingdon 1990	46/168	42/167		0.7 %	1.12 [0.69, 1.83]
Brekke 2005a	10/25	6/19		0.1 %	1.44 [0.41, 5.07]
CELL Study 1995	139/292	148/310		1.6 %	0.99 [0.72, 1.37]
Change of Heart 1999	40/169	148/351		1.6 %	0.43 [0.28, 0.64]
Family Heart 1994 M	337/1767	500/2174		7.8 %	0.79 [0.68, 0.92]
Family Heart 1994 F	215/1217	301/1402		4.9 %	0.78 [0.65, 0.95]
Finnish men 1985	125/575	131/580		2.2 %	0.95 [0.72, 1.26]
Gothenberg Study 1986	691/1473	699/1404		8.1 %	0.89 [0.77, 1.03]
MRFIT Study 1982	1847/5754	2554/5638		37.5 %	0.57 [0.53, 0.62]
Nilsson 2001	17/43	27/46		0.3 %	0.46 [0.20, 1.07]
Oslo Diet Antismoking	236/604	214/628		2.7 %	1.24 [0.98, 1.57]
OXCHECK 1994	552/2205	506/1916		8.7 %	0.93 [0.81, 1.07]
Tromso 1991 F	208/422	212/462		2.2 %	1.15 [0.88, 1.49]
Tromso 1991 M	246/525	283/535		3.2 %	0.79 [0.62, 1.00]
WHO Factories 1986	7910/16908	897/1902		18.4 %	0.98 [0.90, 1.08]
Total (95% CI)	**32147**	**17534**		**100.0 %**	**0.79 [0.75, 0.82]**
Total events: 12619 (Treatment), 6668 (Control)					
Heterogeneity: Chi^2 = 137.24, df = 14 (P<0.00001); I^2 =90%					
Test for overall effect: Z = 10.93 (P < 0.00001)					

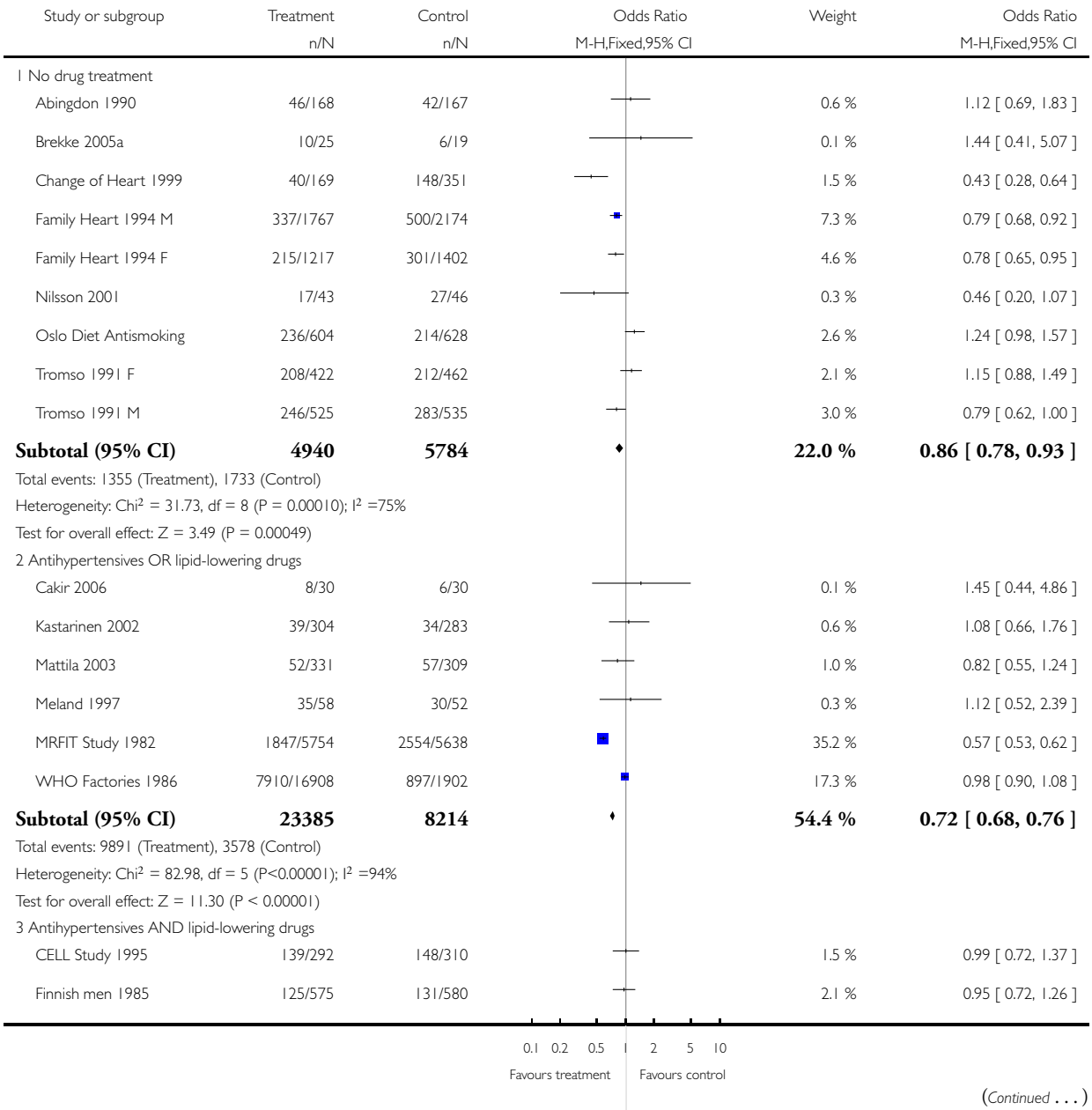


Analysis 1.32. Comparison 1 Multiple risk factor intervention versus control, Outcome 32 Smoking prevalence (by drug treatment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 32 Smoking prevalence (by drug treatment)



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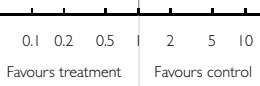
Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Gothenberg Study 1986	691/1473	699/1404		7.6 %	0.89 [0.77, 1.03]
OXCHECK 1994	552/2205	506/1916		8.2 %	0.93 [0.81, 1.07]
Swedish RIS 1994	55/253	70/255		1.1 %	0.73 [0.49, 1.10]
Subtotal (95% CI)	**4798**	**4465**		**20.5 %**	**0.91 [0.83, 1.00]**
Total events: 1562 (Treatment), 1554 (Control)					
Heterogeneity: Chi^2 = 1.64, df = 4 (P = 0.80); I^2 =0.0%					
Test for overall effect: Z = 2.03 (P = 0.043)					
4 Co-morbidity (hypertension or diabetes)					
Cakir 2006	8/30	6/30		0.1 %	1.45 [0.44, 4.86]
Kastarinen 2002	39/304	34/283		0.6 %	1.08 [0.66, 1.76]
Mattila 2003	52/331	57/309		1.0 %	0.82 [0.55, 1.24]
Meland 1997	35/58	30/52		0.3 %	1.12 [0.52, 2.39]
Swedish RIS 1994	55/253	70/255		1.1 %	0.73 [0.49, 1.10]
Subtotal (95% CI)	**976**	**929**		**3.1 %**	**0.89 [0.70, 1.12]**
Total events: 189 (Treatment), 197 (Control)					
Heterogeneity: Chi^2 = 2.56, df = 4 (P = 0.63); I^2 =0.0%					
Test for overall effect: Z = 1.03 (P = 0.30)					
Total (95% CI)	**34099**	**19392**		**100.0 %**	**0.79 [0.76, 0.83]**
Total events: 12997 (Treatment), 7062 (Control)					
Heterogeneity: Chi^2 = 144.19, df = 24 (P<0.00001); I^2 =83%					
Test for overall effect: Z = 10.94 (P < 0.00001)					



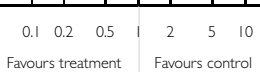
Analysis 1.33. Comparison 1 Multiple risk factor intervention versus control, Outcome 33 Smoking prevalence (by era).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 33 Smoking prevalence (by era)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Low rate of CVD					
Abingdon 1990	46/168	42/167		0.6 %	1.12 [0.69, 1.83]
Brekke 2005a	10/25	6/19		0.1 %	1.44 [0.41, 5.07]
Cakir 2006	8/30	6/30		0.1 %	1.45 [0.44, 4.86]
CELL Study 1995	139/292	148/310		1.6 %	0.99 [0.72, 1.37]
Change of Heart 1999	40/169	148/351		1.5 %	0.43 [0.28, 0.64]
Family Heart 1994 M	337/1767	500/2174		7.5 %	0.79 [0.68, 0.92]
Family Heart 1994 F	215/1217	301/1402		4.8 %	0.78 [0.65, 0.95]
Kastarinen 2002	39/304	34/283		0.6 %	1.08 [0.66, 1.76]
Mattila 2003	52/331	57/309		1.0 %	0.82 [0.55, 1.24]
Meland 1997	35/58	30/52		0.3 %	1.12 [0.52, 2.39]
Nilsson 2001	17/43	27/46		0.3 %	0.46 [0.20, 1.07]
OXCHECK 1994	552/2205	506/1916		8.4 %	0.93 [0.81, 1.07]
Swedish RIS 1994	55/253	70/255		1.1 %	0.73 [0.49, 1.10]
Tromso 1991 F	208/422	212/462		2.1 %	1.15 [0.88, 1.49]
Tromso 1991 M	246/525	283/535		3.1 %	0.79 [0.62, 1.00]
Subtotal (95% CI)	**7809**	**8311**		**33.2 %**	**0.85 [0.79, 0.92]**
Total events: 1999 (Treatment), 2370 (Control)					
Heterogeneity: Chi^2 = 26.77, df = 14 (P = 0.02); I^2 =48%					
Test for overall effect: Z = 4.30 (P = 0.000017)					
2 High rate of CVD					
Finnish men 1985	125/575	131/580		2.1 %	0.95 [0.72, 1.26]
Gothenberg Study 1986	691/1473	699/1404		7.9 %	0.89 [0.77, 1.03]
MRFIT Study 1982	1847/5754	2554/5638		36.3 %	0.57 [0.53, 0.62]
Oslo Diet Antismoking	236/604	214/628		2.7 %	1.24 [0.98, 1.57]
WHO Factories 1986	7910/16908	897/1902		17.8 %	0.98 [0.90, 1.08]
Subtotal (95% CI)	**25314**	**10152**		**66.8 %**	**0.76 [0.72, 0.80]**



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Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Total events: 10809 (Treatment), 4495 (Control)					
Heterogeneity: Chi² = 106.93, df = 4 (P<0.00001); I² =96%					
Test for overall effect: Z = 10.40 (P < 0.00001)					
Total (95% CI)	**33123**	**18463**		**100.0 %**	**0.79 [0.76, 0.82]**
Total events: 12808 (Treatment), 6865 (Control)					
Heterogeneity: Chi² = 140.75, df = 19 (P<0.00001); I² =87%					
Test for overall effect: Z = 10.93 (P < 0.00001)					

Analysis 1.34. Comparison 1 Multiple risk factor intervention versus control, Outcome 34 Smoking prevalence (by age of study).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 34 Smoking prevalence (by age of study)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
1 Study before 2000					
Abingdon 1990	46/168	42/167		0.6 %	1.12 [0.69, 1.83]
CELL Study 1995	139/292	148/310		1.6 %	0.99 [0.72, 1.37]
Change of Heart 1999	40/169	148/351		1.5 %	0.43 [0.28, 0.64]
Family Heart 1994 M	337/1767	500/2174		7.5 %	0.79 [0.68, 0.92]
Family Heart 1994 F	215/1217	301/1402		4.8 %	0.78 [0.65, 0.95]
Finnish men 1985	125/575	131/580		2.1 %	0.95 [0.72, 1.26]
Gothenberg Study 1986	691/1473	699/1404		7.9 %	0.89 [0.77, 1.03]
Meland 1997	35/58	30/52		0.3 %	1.12 [0.52, 2.39]
MRFIT Study 1982	1847/5754	2554/5638		36.3 %	0.57 [0.53, 0.62]
Oslo Diet Antismoking	236/604	214/628		2.7 %	1.24 [0.98, 1.57]
OXCHECK 1994	552/2205	506/1916		8.4 %	0.93 [0.81, 1.07]

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Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Swedish RIS 1994	55/253	70/255		1.1 %	0.73 [0.49, 1.10]
Tromso 1991 F	208/422	212/462		2.1 %	1.15 [0.88, 1.49]
Tromso 1991 M	246/525	283/535		3.1 %	0.79 [0.62, 1.00]
WHO Factories 1986	7910/16908	897/1902		17.8 %	0.98 [0.90, 1.08]
Subtotal (95% CI)	**32390**	**17776**		**97.8 %**	**0.79 [0.75, 0.82]**
Total events: 12682 (Treatment), 6735 (Control)					
Heterogeneity: Chi^2 = 135.72, df = 14 (P<0.00001); I^2 =90%					
Test for overall effect: Z = 10.94 (P < 0.00001)					
2 Study after 2000					
Brekke 2005a	10/25	6/19		0.1 %	1.44 [0.41, 5.07]
Cakir 2006	8/30	6/30		0.1 %	1.45 [0.44, 4.86]
Kastarinen 2002	39/304	34/283		0.6 %	1.08 [0.66, 1.76]
Mattila 2003	52/331	57/309		1.0 %	0.82 [0.55, 1.24]
Nilsson 2001	17/43	27/46		0.3 %	0.46 [0.20, 1.07]
Subtotal (95% CI)	**733**	**687**		**2.2 %**	**0.89 [0.68, 1.18]**
Total events: 126 (Treatment), 130 (Control)					
Heterogeneity: Chi^2 = 4.25, df = 4 (P = 0.37); I^2 =6%					
Test for overall effect: Z = 0.79 (P = 0.43)					
Total (95% CI)	**33123**	**18463**		**100.0 %**	**0.79 [0.76, 0.82]**
Total events: 12808 (Treatment), 6865 (Control)					
Heterogeneity: Chi^2 = 140.75, df = 19 (P<0.00001); I^2 =87%					
Test for overall effect: Z = 10.93 (P < 0.00001)					

Analysis 1.35. Comparison 1 Multiple risk factor intervention versus control, Outcome 35 Systolic blood pressure.

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 35 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 1989 F	114	4.4 (17.83)	80	0.2 (19.02)		0.2 %	4.20 [-1.10, 9.50]
Aberg 1989 M	79	3.3 (16.3)	80	1.7 (16.21)		0.3 %	1.60 [-3.45, 6.65]
Abingdon 1990	167	-6.9 (14.6)	168	-5.2 (15.76)		0.6 %	-1.70 [-4.95, 1.55]
ADAPT 2005	123	-1 (11.32)	118	1 (11.08)		0.8 %	-2.00 [-4.83, 0.83]
Aldana (CHIP) 2005	64	-5.9 (13.26)	79	-5.4 (14.36)		0.3 %	-0.50 [-5.04, 4.04]
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)		0.3 %	-6.50 [-11.23, -1.77]
Cakir 2006	30	-8.8 (5.2)	30	1.2 (5.3)		0.9 %	-10.00 [-12.66, -7.34]
CELL Study 1995	292	-1.2 (14.7)	310	0 (14.7)		1.2 %	-1.20 [-3.55, 1.15]
Change of Heart 1999	165	4.3 (15.4)	339	1.8 (21.61)		0.6 %	2.50 [-0.79, 5.79]
Connell 1995	141	-5 (13.26)	255	-3 (14.36)		0.8 %	-2.00 [-4.81, 0.81]
Esposito 2004	55	-3 (3.94)	55	-1 (7.75)		1.2 %	-2.00 [-4.30, 0.30]
Family Heart 1994 M	1767	-7.3 (19.23)	2174	0 (19.23)		4.4 %	-7.30 [-8.51, -6.09]
Family Heart 1994 F	1217	-6.2 (20.43)	1402	0 (20.43)		2.6 %	-6.20 [-7.77, -4.63]
FARIS 1997 F	315	-3.9 (15.38)	343	-0.7 (15.38)		1.2 %	-3.20 [-5.55, -0.85]
FARIS 1997 M	219	-4.4 (15.38)	223	-0.6 (15.38)		0.8 %	-3.80 [-6.67, -0.93]
Finnish DPS 2001	256	-5 (14)	250	-1 (15)		1.0 %	-4.00 [-6.53, -1.47]
Finnish men 1985	575	-10 (18)	580	-4 (16)		1.7 %	-6.00 [-7.96, -4.04]
Garcia-Pena 2001	345	-6.8 (7.41)	338	-3.5 (17.46)		1.6 %	-3.30 [-5.32, -1.28]
Given 1984	62	-9.85 (12.7)	24	-4.79 (12.61)		0.2 %	-5.06 [-11.01, 0.89]
Gothenberg Study 1986	1464	-2 (20)	1404	0 (20)		3.0 %	-2.00 [-3.46, -0.54]
Hellenius 1993	39	-4 (12.6)	39	-1 (12.2)		0.2 %	-3.00 [-8.50, 2.50]
Iso 1994	53	-13.2 (11.52)	55	-17.4 (14.02)		0.3 %	4.20 [-0.63, 9.03]
Jalkanen 1991	24	-8 (18.68)	25	-5 (18.33)		0.1 %	-3.00 [-13.37, 7.37]
Kastarinen 2002	360	-6.2 (5.66)	355	-4.2 (16)		2.1 %	-2.00 [-3.76, -0.24]
Lin 1996	471	-1 (18.52)	426	1 (19.52)		1.0 %	-2.00 [-4.50, 0.50]

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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
Lindahl 1999	93	-4.9 (19.3)	93	1.3 (18.3)		0.2 %	-6.20 [-11.61, -0.79]
Look AHEAD 2003	2496	-6.8 (14.13)	2463	-2.8 (10.53)		13.3 %	-4.00 [-4.69, -3.31]
Mattila 2003	331	-2.1 (12.53)	309	0 (12.56)		1.7 %	-2.10 [-4.05, -0.15]
Meland 1997	58	-4 (23.31)	52	0 (22.08)		0.1 %	-4.00 [-12.49, 4.49]
MRFIT Study 1982	5740	-13.9 (13.23)	5633	-8.6 (15.27)		23.2 %	-5.30 [-5.83, -4.77]
Muto 2001	152	0.5 (11.9)	150	2.9 (13.5)		0.8 %	-2.40 [-5.27, 0.47]
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)		0.1 %	-2.50 [-10.48, 5.48]
Oldroyd 2001	35	-7.9 (16.7)	32	-0.27 (14.3)		0.1 %	-7.63 [-15.06, -0.20]
Oslo Diet Exercise	65	-5.9 (8.87)	43	-0.5 (11.15)		0.4 %	-5.40 [-9.37, -1.43]
OXCHECK 1994	2205	-2.5 (19.3)	1916	0 (20.4)		4.3 %	-2.50 [-3.72, -1.28]
Perez-Stable 1995 no prop	72	-9 (12.99)	72	-6.7 (13.2)		0.4 %	-2.30 [-6.58, 1.98]
Perez-Stable 1995 prop	74	-8.3 (13.39)	73	-11.6 (13.3)		0.3 %	3.30 [-1.01, 7.61]
Proper 2003	75	-4.1 (4.25)	116	-5.2 (15.26)		0.7 %	1.10 [-1.84, 4.04]
Rachmani 2005	71	-20 (4.75)	70	-12 (6.54)		1.8 %	-8.00 [-9.89, -6.11]
Sartorelli 2005	51	-0.8 (12.3)	53	3.1 (13)		0.3 %	-3.90 [-8.76, 0.96]
Sone (JDCS) 2002	990	1 (4.24)	983	1 (15.52)		6.3 %	0.0 [-1.01, 1.01]
Stamler 1989	102	-2.6 (6.4)	99	-1.3 (6.1)		2.1 %	-1.30 [-3.03, 0.43]
Stefanick 1998 F	43	-3.1 (8.4)	45	-2.4 (7.6)		0.6 %	-0.70 [-4.05, 2.65]
Stefanick 1998 M	48	-3 (6.8)	46	0.3 (7.9)		0.7 %	-3.30 [-6.29, -0.31]
Swedish RIS 1994	235	-2 (18.4)	227	-0.2 (20.5)		0.5 %	-1.80 [-5.36, 1.76]
Toobert (MLP) 2005	163	-1.85 (4.81)	116	-2.18 (14.41)		0.9 %	0.33 [-2.39, 3.05]
Tromso 1991 F	422	-2.16 (15.8)	387	2.1 (16.5)		1.3 %	-4.26 [-6.49, -2.03]
Tromso 1991 M	525	0.5 (15.6)	535	1.1 (16.5)		1.7 %	-0.60 [-2.53, 1.33]
WHLP 1998	253	-3.5 (12.18)	267	-1.2 (9.21)		1.8 %	-2.30 [-4.16, -0.44]
WHO Factories 1986	16949	2.67 (18.09)	1902	3.18 (18.14)		8.7 %	-0.51 [-1.37, 0.35]
Wing 1998	32	-4.8 (15)	31	-1.5 (12)		0.1 %	-3.30 [-10.00, 3.40]
Total (95% CI)	**39818**		**24991**			**100.0 %**	**-3.38 [-3.63, -3.13]**

Heterogeneity: Chi^2 = 350.61, df = 52 (P<0.00001); I^2 =85%

Test for overall effect: Z = 26.16 (P < 0.00001)

Analysis 1.36. Comparison 1 Multiple risk factor intervention versus control, Outcome 36 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: 36 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 1999	165	4.3 (15.4)	339	1.8 (21.61)		1.9 %	2.50 [-0.79, 5.79]
Subtotal (95% CI)	**165**		**339**			**1.9 %**	**2.50 [-0.79, 5.79]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.49 (P = 0.14)							
2 Individual randomisation							
Aberg 1989 F	114	4.4 (17.83)	80	0.2 (19.02)		1.2 %	4.20 [-1.10, 9.50]
Aberg 1989 M	79	3.3 (16.3)	80	1.7 (16.21)		1.3 %	1.60 [-3.45, 6.65]
Abingdon 1990	167	-6.9 (14.6)	168	-5.2 (15.76)		1.9 %	-1.70 [-4.95, 1.55]
ADAPT 2005	123	-1 (11.32)	118	1 (11.08)		2.1 %	-2.00 [-4.83, 0.83]
Aldana (CHIP) 2005	64	-5.9 (13.26)	79	-5.4 (14.36)		1.4 %	-0.50 [-5.04, 4.04]
Applegate 1992	21	-8.7 (11.7)	26	-4.5 (9.7)		1.0 %	-4.20 [-10.44, 2.04]
Blumenthal 2000	46	-7.4 (9.31)	22	-0.9 (9.31)		1.4 %	-6.50 [-11.23, -1.77]
Cakir 2006	30	-8.8 (5.2)	30	1.2 (5.3)		2.1 %	-10.00 [-12.66, -7.34]
CELL Study 1995	292	-1.2 (14.7)	310	0 (14.7)		2.3 %	-1.20 [-3.55, 1.15]
Esposito 2004	55	-3 (3.94)	55	-1 (7.75)		2.3 %	-2.00 [-4.30, 0.30]
Family Heart 1994 M	1767	-7.3 (19.23)	2174	0 (19.23)		2.7 %	-7.30 [-8.51, -6.09]
Family Heart 1994 F	1217	-6.2 (20.43)	1402	0 (20.43)		2.6 %	-6.20 [-7.77, -4.63]
FARIS 1997 F	315	-3.9 (15.38)	343	-0.7 (15.38)		2.3 %	-3.20 [-5.55, -0.85]
FARIS 1997 M	219	-4.4 (15.38)	223	-0.6 (15.38)		2.1 %	-3.80 [-6.67, -0.93]
Finnish DPS 2001	256	-5 (14)	250	-1 (15)		2.2 %	-4.00 [-6.53, -1.47]
Finnish men 1985	575	-10 (18)	580	-4 (16)		2.4 %	-6.00 [-7.96, -4.04]
Garcia-Pena 2001	345	-6.8 (7.41)	338	-3.5 (17.46)		2.4 %	-3.30 [-5.32, -1.28]
Given 1984	62	-9.85 (12.7)	24	-4.79 (12.61)		1.1 %	-5.06 [-11.01, 0.89]
Gothenberg Study 1986	1464	-2 (20)	1404	0 (20)		2.6 %	-2.00 [-3.46, -0.54]
Hellenius 1993	39	-4 (12.6)	39	-1 (12.2)		1.2 %	-3.00 [-8.50, 2.50]

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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
Iso 1994	53	-13.2 (11.52)	55	-17.4 (14.02)		1.4 %	4.20 [-0.63, 9.03]
Jalkanen 1991	24	-8 (18.68)	25	-5 (18.33)		0.5 %	-3.00 [-13.37, 7.37]
Kastarinen 2002	360	-6.2 (5.66)	355	-4.2 (16)		2.5 %	-2.00 [-3.76, -0.24]
Lindahl 1999	93	-4.9 (19.3)	93	1.3 (18.3)		1.2 %	-6.20 [-11.61, -0.79]
MRFIT Study 1982	5740	-13.9 (13.23)	5633	-8.6 (15.27)		2.8 %	-5.30 [-5.83, -4.77]
Muto 2001	152	0.5 (11.9)	150	2.9 (13.5)		2.1 %	-2.40 [-5.27, 0.47]
Nilsson 1992	31	-7.7 (17.77)	32	-3.8 (19.3)		0.6 %	-3.90 [-13.06, 5.26]
Nilsson 2001	43	-3.7 (20.31)	46	-1.2 (17.9)		0.7 %	-2.50 [-10.48, 5.48]
Oldroyd 2001	35	-7.9 (16.7)	32	-0.27 (14.3)		0.8 %	-7.63 [-15.06, -0.20]
Oslo Diet Exercise	65	-5.9 (8.87)	43	-0.5 (11.15)		1.6 %	-5.40 [-9.37, -1.43]
OXCHECK 1994	2205	-2.5 (19.3)	1916	0 (20.4)		2.7 %	-2.50 [-3.72, -1.28]
Perez-Stable 1995 no prop	72	-9 (12.99)	72	-6.7 (13.2)		1.5 %	-2.30 [-6.58, 1.98]
Perez-Stable 1995 prop	74	-8.3 (13.39)	73	-11.6 (13.3)		1.5 %	3.30 [-1.01, 7.61]
Rachmani 2005	71	-20 (4.75)	70	-12 (6.54)		2.4 %	-8.00 [-9.89, -6.11]
Sartorelli 2005	51	-0.8 (12.3)	53	3.1 (13)		1.3 %	-3.90 [-8.76, 0.96]
Sone (JDCS) 2002	990	1 (4.24)	983	1 (15.52)		2.7 %	0.0 [-1.01, 1.01]
Stamler 1989	102	-2.6 (6.4)	99	-1.3 (6.1)		2.5 %	-1.30 [-3.03, 0.43]
Stefanick 1998 F	43	-3.1 (8.4)	45	-2.4 (7.6)		1.9 %	-0.70 [-4.05, 2.65]
Stefanick 1998 M	48	-3 (6.8)	46	0.3 (7.9)		2.0 %	-3.30 [-6.29, -0.31]
Swedish RIS 1994	235	-2 (18.4)	227	-0.2 (20.5)		1.8 %	-1.80 [-5.36, 1.76]
Toobert (MLP) 2005	163	-1.85 (4.81)	116	-2.18 (14.41)		2.1 %	0.33 [-2.39, 3.05]
Tromso 1991 F	422	-2.16 (15.8)	387	2.1 (16.5)		2.3 %	-4.26 [-6.49, -2.03]
Tromso 1991 M	525	0.5 (15.6)	535	1.1 (16.5)		2.4 %	-0.60 [-2.53, 1.33]
WHLP 1998	253	-3.5 (12.18)	267	-1.2 (9.21)		2.5 %	-2.30 [-4.16, -0.44]
Wing 1998	32	-4.8 (15)	31	-1.5 (12)		0.9 %	-3.30 [-10.00, 3.40]
Subtotal (95% CI)	**19132**		**19129**			**83.2 %**	**-2.99 [-3.87, -2.11]**
Heterogeneity: Tau² = 5.99; Chi² = 273.25, df = 44 (P<0.00001); I² =84%							
Test for overall effect: Z = 6.66 (P < 0.00001)							
3 Cluster randomisation - analysis by individual							
Connell 1995	141	-5 (13.26)	255	-3 (14.36)		2.1 %	-2.00 [-4.81, 0.81]
Lin 1996	471	-1 (18.52)	426	1 (19.52)		2.2 %	-2.00 [-4.50, 0.50]
Look AHEAD 2003	2496	-6.8 (14.13)	2463	-2.8 (10.53)		2.8 %	-4.00 [-4.69, -3.31]
Mattila 2003	331	-2.1 (12.53)	309	0 (12.56)		2.4 %	-2.10 [-4.05, -0.15]

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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
Meland 1997	58	-4 (23.31)	52	0 (22.08)		0.6 %	-4.00 [-12.49, 4.49]
Proper 2003	75	-4.1 (4.25)	116	-5.2 (15.26)		2.0 %	1.10 [-1.84, 4.04]
WHO Factories 1986	16949	2.67 (18.09)	1902	3.18 (18.14)		2.8 %	-0.51 [-1.37, 0.35]
Subtotal (95% CI)	**20521**		**5523**			**14.9 %**	**-1.79 [-3.54, -0.04]**
Heterogeneity: Tau^2 = 3.91; Chi^2 = 44.87, df = 6 (P<0.00001); I^2 =87%							
Test for overall effect: Z = 2.00 (P = 0.045)							
Total (95% CI)	**39818**		**24991**			**100.0 %**	**-2.71 [-3.49, -1.93]**
Heterogeneity: Tau^2 = 5.49; Chi^2 = 350.61, df = 52 (P<0.00001); I^2 =85%							
Test for overall effect: Z = 6.84 (P < 0.00001)							

Analysis 1.37. Comparison 1 Multiple risk factor intervention versus control, Outcome 37 Systolic blood pressure (by allocation concealment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 37 Systolic blood pressure (by allocation concealment)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Adequate allocation concealment							
ADAPT 2005	123	-1 (11.32)	118	1 (11.08)		0.8 %	-2.00 [-4.83, 0.83]
Aldana (CHIP) 2005	64	-5.9 (13.26)	79	-5.4 (14.36)		0.3 %	-0.50 [-5.04, 4.04]
Cakir 2006	30	-8.8 (5.2)	30	1.2 (5.3)		0.9 %	-10.00 [-12.66, -7.34]
Esposito 2004	55	-3 (3.94)	55	-1 (7.75)		1.2 %	-2.00 [-4.30, 0.30]
Garcia-Pena 2001	345	-6.8 (7.41)	338	-3.5 (17.46)		1.6 %	-3.30 [-5.32, -1.28]
Look AHEAD 2003	2496	-6.8 (14.13)	2463	-2.8 (10.53)		13.3 %	-4.00 [-4.69, -3.31]
Mattila 2003	331	-2.1 (12.53)	309	0 (12.56)		1.7 %	-2.10 [-4.05, -0.15]
MRFIT Study 1982	5740	-13.9 (13.23)	5633	-8.6 (15.27)		23.2 %	-5.30 [-5.83, -4.77]
Oldroyd 2001	35	-7.9 (16.7)	32	-0.27 (14.3)		0.1 %	-7.63 [-15.06, -0.20]

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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Perez-Stable 1995 no prop	72	-9 (12.99)	72	-6.7 (13.2)		0.4 %	-2.30 [-6.58, 1.98]
Perez-Stable 1995 prop	74	-8.3 (13.39)	73	-11.6 (13.3)		0.3 %	3.30 [-1.01, 7.61]
Stamler 1989	102	-2.6 (6.4)	99	-1.3 (6.1)		2.1 %	-1.30 [-3.03, 0.43]
Stefanick 1998 F	43	-3.1 (8.4)	45	-2.4 (7.6)		0.6 %	-0.70 [-4.05, 2.65]
Stefanick 1998 M	48	-3 (6.8)	46	0.3 (7.9)		0.7 %	-3.30 [-6.29, -0.31]
Subtotal (95% CI)	**9558**		**9392**			**47.3 %**	**-4.32 [-4.69, -3.96]**
Heterogeneity: Chi² = 77.21, df = 13 (P<0.00001); I² =83%							
Test for overall effect: Z = 23.02 (P < 0.00001)							
2 Inadequate allocation concealment							
Aberg 1989 F	114	4.4 (17.83)	80	0.2 (19.02)		0.2 %	4.20 [-1.10, 9.50]
Aberg 1989 M	79	3.3 (16.3)	80	1.7 (16.21)		0.3 %	1.60 [-3.45, 6.65]
CELL Study 1995	292	-1.2 (14.7)	310	0 (14.7)		1.2 %	-1.20 [-3.55, 1.15]
Finnish DPS 2001	256	-5 (14)	250	-1 (15)		1.0 %	-4.00 [-6.53, -1.47]
Kastarinen 2002	360	-6.2 (5.66)	355	-4.2 (16)		2.1 %	-2.00 [-3.76, -0.24]
Sartorelli 2005	51	-0.8 (12.3)	53	3.1 (13)		0.3 %	-3.90 [-8.76, 0.96]
Tromso 1991 F	422	-2.16 (15.8)	387	2.1 (16.5)		1.3 %	-4.26 [-6.49, -2.03]
Tromso 1991 M	525	0.5 (15.6)	535	1.1 (16.5)		1.7 %	-0.60 [-2.53, 1.33]
WHLP 1998	253	-3.5 (12.18)	267	-1.2 (9.21)		1.8 %	-2.30 [-4.16, -0.44]
Subtotal (95% CI)	**2352**		**2317**			**9.8 %**	**-2.03 [-2.84, -1.23]**
Heterogeneity: Chi² = 16.69, df = 8 (P = 0.03); I² =52%							
Test for overall effect: Z = 4.94 (P < 0.00001)							
3 Unclear allocation concealment							
Abingdon 1990	167	-6.9 (14.6)	168	-5.2 (15.76)		0.6 %	-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)		0.3 %	-6.50 [-11.23, -1.77]
Change of Heart 1999	165	4.3 (15.4)	339	1.8 (21.61)		0.6 %	2.50 [-0.79, 5.79]
Connell 1995	141	-5 (13.26)	255	-3 (14.36)		0.8 %	-2.00 [-4.81, 0.81]
Family Heart 1994 M	1767	-7.3 (19.23)	2174	0 (19.23)		4.4 %	-7.30 [-8.51, -6.09]
Family Heart 1994 F	1217	-6.2 (20.43)	1402	0 (20.43)		2.6 %	-6.20 [-7.77, -4.63]
FARIS 1997 F	315	-3.9 (15.38)	343	-0.7 (15.38)		1.2 %	-3.20 [-5.55, -0.85]
FARIS 1997 M	219	-4.4 (15.38)	223	-0.6 (15.38)		0.8 %	-3.80 [-6.67, -0.93]
Finnish men 1985	575	-10 (18)	580	-4 (16)		1.7 %	-6.00 [-7.96, -4.04]
Given 1984	62	-9.85 (12.7)	24	-4.79 (12.61)		0.2 %	-5.06 [-11.01, 0.89]
Gothenberg Study 1986	1464	-2 (20)	1404	0 (20)		3.0 %	-2.00 [-3.46, -0.54]

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Favours treatment Favours control

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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Hellenius 1993	39	-4 (12.6)	39	-1 (12.2)		0.2 %	-3.00 [-8.50, 2.50]
Iso 1994	53	-13.2 (11.52)	55	-17.4 (14.02)		0.3 %	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)		1.0 %	-2.00 [-4.50, 0.50]
Lindahl 1999	93	-4.9 (19.3)	93	1.3 (18.3)		0.2 %	-6.20 [-11.61, -0.79]
Meland 1997	58	-4 (23.31)	52	0 (22.08)		0.1 %	-4.00 [-12.49, 4.49]
Muto 2001	152	0.5 (11.9)	150	2.9 (13.5)		0.8 %	-2.40 [-5.27, 0.47]
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)		0.1 %	-2.50 [-10.48, 5.48]
Oslo Diet Exercise	65	-5.9 (8.87)	43	-0.5 (11.15)		0.4 %	-5.40 [-9.37, -1.43]
OXCHECK 1994	2205	-2.5 (19.3)	1916	0 (20.4)		4.3 %	-2.50 [-3.72, -1.28]
Proper 2003	75	-4.1 (4.25)	116	-5.2 (15.26)		0.7 %	1.10 [-1.84, 4.04]
Rachmani 2005	71	-20 (4.75)	70	-12 (6.54)		1.8 %	-8.00 [-9.89, -6.11]
Sone (JDCS) 2002	990	1 (4.24)	983	1 (15.52)		6.3 %	0.0 [-1.01, 1.01]
Swedish RIS 1994	235	-2 (18.4)	227	-0.2 (20.5)		0.5 %	-1.80 [-5.36, 1.76]
Toobert (MLP) 2005	163	-1.85 (4.81)	116	-2.18 (14.41)		0.9 %	0.33 [-2.39, 3.05]
WHO Factories 1986	16949	2.67 (18.09)	1902	3.18 (18.14)		8.7 %	-0.51 [-1.37, 0.35]
Wing 1998	32	-4.8 (15)	31	-1.5 (12)		0.1 %	-3.30 [-10.00, 3.40]
Subtotal (95% CI)	**27908**		**13282**			**42.9 %**	**-2.65 [-3.03, -2.26]**
Heterogeneity: Chi² = 206.96, df = 29 (P<0.00001); I² =86%							
Test for overall effect: Z = 13.41 (P < 0.00001)							
Total (95% CI)	**39818**		**24991**			**100.0 %**	**-3.38 [-3.63, -3.13]**
Heterogeneity: Chi² = 350.61, df = 52 (P<0.00001); I² =85%							
Test for overall effect: Z = 26.16 (P < 0.00001)							
Test for subgroup differences: Chi² = 49.74, df = 2 (P = 0.00), I² =96%							

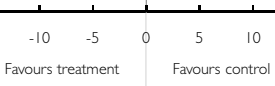
Analysis 1.38. Comparison 1 Multiple risk factor intervention versus control, Outcome 38 Systolic blood pressure (by co-morbidity).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 38 Systolic blood pressure (by co-morbidity)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 No co-morbidity							
Abingdon 1990	167	-6.9 (14.6)	168	-5.2 (15.76)		0.6 %	-1.70 [-4.95, 1.55]
Aldana (CHIP) 2005	64	-5.9 (13.26)	79	-5.4 (14.36)		0.3 %	-0.50 [-5.04, 4.04]
CELL Study 1995	292	-1.2 (14.7)	310	0 (14.7)		1.2 %	-1.20 [-3.55, 1.15]
Change of Heart 1999	165	4.3 (15.4)	339	1.8 (21.61)		0.6 %	2.50 [-0.79, 5.79]
Connell 1995	141	-5 (13.26)	255	-3 (14.36)		0.8 %	-2.00 [-4.81, 0.81]
Esposito 2004	55	-3 (3.94)	55	-1 (7.75)		1.2 %	-2.00 [-4.30, 0.30]
Family Heart 1994 M	1767	-7.3 (19.23)	2174	0 (19.23)		4.4 %	-7.30 [-8.51, -6.09]
Family Heart 1994 F	1217	-6.2 (20.43)	1402	0 (20.43)		2.6 %	-6.20 [-7.77, -4.63]
FARIS 1997 F	315	-3.9 (15.38)	343	-0.7 (15.38)		1.2 %	-3.20 [-5.55, -0.85]
FARIS 1997 M	219	-4.4 (15.38)	223	-0.6 (15.38)		0.8 %	-3.80 [-6.67, -0.93]
Finnish DPS 2001	256	-5 (14)	250	-1 (15)		1.0 %	-4.00 [-6.53, -1.47]
Finnish men 1985	575	-10 (18)	580	-4 (16)		1.7 %	-6.00 [-7.96, -4.04]
Gothenberg Study 1986	1464	-2 (20)	1404	0 (20)		3.0 %	-2.00 [-3.46, -0.54]
Hellenius 1993	39	-4 (12.6)	39	-1 (12.2)		0.2 %	-3.00 [-8.50, 2.50]
Lindahl 1999	93	-4.9 (19.3)	93	1.3 (18.3)		0.2 %	-6.20 [-11.61, -0.79]
MRFIT Study 1982	5740	-13.9 (13.23)	5633	-8.6 (15.27)		23.2 %	-5.30 [-5.83, -4.77]
Muto 2001	152	0.5 (11.9)	150	2.9 (13.5)		0.8 %	-2.40 [-5.27, 0.47]
Nilsson 2001	43	-3.7 (20.31)	46	-1.2 (17.9)		0.1 %	-2.50 [-10.48, 5.48]
Oldroyd 2001	35	-7.9 (16.7)	32	-0.27 (14.3)		0.1 %	-7.63 [-15.06, -0.20]
OXCHECK 1994	2205	-2.5 (19.3)	1916	0 (20.4)		4.3 %	-2.50 [-3.72, -1.28]
Proper 2003	75	-4.1 (4.25)	116	-5.2 (15.26)		0.7 %	1.10 [-1.84, 4.04]
Sartorelli 2005	51	-0.8 (12.3)	53	3.1 (13)		0.3 %	-3.90 [-8.76, 0.96]
Stefanick 1998 F	43	-3.1 (8.4)	45	-2.4 (7.6)		0.6 %	-0.70 [-4.05, 2.65]
Stefanick 1998 M	48	-3 (6.8)	46	0.3 (7.9)		0.7 %	-3.30 [-6.29, -0.31]



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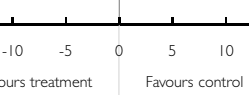
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Tromso 1991 F	422	-2.16 (15.8)	387	2.1 (16.5)		1.3 %	-4.26 [-6.49, -2.03]
Tromso 1991 M	525	0.5 (15.6)	535	1.1 (16.5)		1.7 %	-0.60 [-2.53, 1.33]
WHLP 1998	253	-3.5 (12.18)	267	-1.2 (9.21)		1.8 %	-2.30 [-4.16, -0.44]
WHO Factories 1986	16949	2.67 (18.09)	1902	3.18 (18.14)		8.7 %	-0.51 [-1.37, 0.35]
Wing 1998	32	-4.8 (15)	31	-1.5 (12)		0.1 %	-3.30 [-10.00, 3.40]
Subtotal (95% CI)	**33402**		**18873**			**64.2 %**	**-3.70 [-4.01, -3.38]**
Heterogeneity: Chi² = 200.26, df = 28 (P<0.00001); I² =86%							
Test for overall effect: Z = 22.94 (P < 0.00001)							
2 Co-morbidity (hypertension or diabetes)							
Aberg 1989 F	114	4.4 (17.83)	80	0.2 (19.02)		0.2 %	4.20 [-1.10, 9.50]
Aberg 1989 M	79	3.3 (16.3)	80	1.7 (16.21)		0.3 %	1.60 [-3.45, 6.65]
ADAPT 2005	123	-1 (11.32)	118	1 (11.08)		0.8 %	-2.00 [-4.83, 0.83]
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)		0.3 %	-6.50 [-11.23, -1.77]
Cakir 2006	30	-8.8 (5.2)	30	1.2 (5.3)		0.9 %	-10.00 [-12.66, -7.34]
Garcia-Pena 2001	345	-6.8 (7.41)	338	-3.5 (17.46)		1.6 %	-3.30 [-5.32, -1.28]
Given 1984	62	-9.85 (12.7)	24	-4.79 (12.61)		0.2 %	-5.06 [-11.01, 0.89]
Iso 1994	53	-13.2 (11.52)	55	-17.4 (14.02)		0.3 %	4.20 [-0.63, 9.03]
Jalkanen 1991	24	-8 (18.68)	25	-5 (18.33)		0.1 %	-3.00 [-13.37, 7.37]
Kastarinen 2002	360	-6.2 (5.66)	355	-4.2 (16)		2.1 %	-2.00 [-3.76, -0.24]
Lin 1996	471	-1 (18.52)	426	1 (19.52)		1.0 %	-2.00 [-4.50, 0.50]
Look AHEAD 2003	2496	-6.8 (14.13)	2463	-2.8 (10.53)		13.3 %	-4.00 [-4.69, -3.31]
Mattila 2003	331	-2.1 (12.53)	309	0 (12.56)		1.7 %	-2.10 [-4.05, -0.15]
Meland 1997	58	-4 (23.31)	52	0 (22.08)		0.1 %	-4.00 [-12.49, 4.49]
Nilsson 1992	31	-7.7 (17.77)	32	-3.8 (19.3)		0.1 %	-3.90 [-13.06, 5.26]
Oslo Diet Exercise	65	-5.9 (8.87)	43	-0.5 (11.15)		0.4 %	-5.40 [-9.37, -1.43]
Perez-Stable 1995 no prop	72	-9 (12.99)	72	-6.7 (13.2)		0.4 %	-2.30 [-6.58, 1.98]
Perez-Stable 1995 prop	74	-8.3 (13.39)	73	-11.6 (13.3)		0.3 %	3.30 [-1.01, 7.61]
Rachmani 2005	71	-20 (4.75)	70	-12 (6.54)		1.8 %	-8.00 [-9.89, -6.11]
Sone (JDCS) 2002	990	1 (4.24)	983	1 (15.52)		6.3 %	0.0 [-1.01, 1.01]
Stamler 1989	102	-2.6 (6.4)	99	-1.3 (6.1)		2.1 %	-1.30 [-3.03, 0.43]
Swedish RIS 1994	235	-2 (18.4)	227	-0.2 (20.5)		0.5 %	-1.80 [-5.36, 1.76]
Toobert (MLP) 2005	163	-1.85 (4.81)	116	-2.18 (14.41)		0.9 %	0.33 [-2.39, 3.05]



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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Subtotal (95% CI)	**6416**		**6118**		♦	**35.8 %**	**-2.81 [-3.23, -2.38]**
Heterogeneity: Chi² = 139.41, df = 23 (P<0.00001); I² =84%							
Test for overall effect: Z = 13.00 (P < 0.00001)							
Total (95% CI)	**39818**		**24991**		♦	**100.0 %**	**-3.38 [-3.63, -3.13]**
Heterogeneity: Chi² = 350.61, df = 52 (P<0.00001); I² =85%							
Test for overall effect: Z = 26.16 (P < 0.00001)							
Test for subgroup differences: Chi² = 10.93, df = 1 (P = 0.00), I² =91%							

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Favours treatment Favours control

Analysis 1.39. Comparison 1 Multiple risk factor intervention versus control, Outcome 39 Systolic blood pressure (by drug treatment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 39 Systolic blood pressure (by drug treatment)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 No drug treatment							
Abingdon 1990	167	-6.9 (14.6)	168	-5.2 (15.76)		0.6 %	-1.70 [-4.95, 1.55]
Aldana (CHIP) 2005	64	-5.9 (13.26)	79	-5.4 (14.36)		0.3 %	-0.50 [-5.04, 4.04]
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)		0.3 %	-6.50 [-11.23, -1.77]
Change of Heart 1999	165	4.3 (15.4)	339	1.8 (21.61)		0.6 %	2.50 [-0.79, 5.79]
Connell 1995	141	-5 (13.26)	255	-3 (14.36)		0.8 %	-2.00 [-4.81, 0.81]
Esposito 2004	55	-3 (3.94)	55	-1 (7.75)		1.2 %	-2.00 [-4.30, 0.30]
Family Heart 1994 M	1767	-7.3 (19.23)	2174	0 (19.23)		4.4 %	-7.30 [-8.51, -6.09]
Family Heart 1994 F	1217	-6.2 (20.43)	1402	0 (20.43)		2.6 %	-6.20 [-7.77, -4.63]
FARIS 1997 F	315	-3.9 (15.38)	343	-0.7 (15.38)		1.2 %	-3.20 [-5.55, -0.85]
FARIS 1997 M	219	-4.4 (15.38)	223	-0.6 (15.38)		0.8 %	-3.80 [-6.67, -0.93]

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Favours treatment Favours control

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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Finnish DPS 2001	256	-5 (14)	250	-1 (15)		1.0 %	-4.00 [-6.53, -1.47]
Hellenius 1993	39	-4 (12.6)	39	-1 (12.2)		0.2 %	-3.00 [-8.50, 2.50]
Iso 1994	53	-13.2 (11.52)	55	-17.4 (14.02)		0.3 %	4.20 [-0.63, 9.03]
Lindahl 1999	93	-4.9 (19.3)	93	1.3 (18.3)		0.2 %	-6.20 [-11.61, -0.79]
Muto 2001	152	0.5 (11.9)	150	2.9 (13.5)		0.8 %	-2.40 [-5.27, 0.47]
Nilsson 2001	43	-3.7 (20.31)	46	-1.2 (17.9)		0.1 %	-2.50 [-10.48, 5.48]
Oldroyd 2001	35	-7.9 (16.7)	32	-0.27 (14.3)		0.1 %	-7.63 [-15.06, -0.20]
Perez-Stable 1995 no prop	72	-9 (12.99)	72	-6.7 (13.2)		0.4 %	-2.30 [-6.58, 1.98]
Proper 2003	75	-4.1 (4.25)	116	-5.2 (15.26)		0.7 %	1.10 [-1.84, 4.04]
Sartorelli 2005	51	-0.8 (12.3)	53	3.1 (13)		0.3 %	-3.90 [-8.76, 0.96]
Sone (JDCS) 2002	990	1 (4.24)	983	1 (15.52)		6.3 %	0.0 [-1.01, 1.01]
Stamler 1989	102	-2.6 (6.4)	99	-1.3 (6.1)		2.1 %	-1.30 [-3.03, 0.43]
Stefanick 1998 F	43	-3.1 (8.4)	45	-2.4 (7.6)		0.6 %	-0.70 [-4.05, 2.65]
Stefanick 1998 M	48	-3 (6.8)	46	0.3 (7.9)		0.7 %	-3.30 [-6.29, -0.31]
Tromso 1991 F	422	-2.16 (15.8)	387	2.1 (16.5)		1.3 %	-4.26 [-6.49, -2.03]
Tromso 1991 M	525	0.5 (15.6)	535	1.1 (16.5)		1.7 %	-0.60 [-2.53, 1.33]
WHLP 1998	253	-3.5 (12.18)	267	-1.2 (9.21)		1.8 %	-2.30 [-4.16, -0.44]
Wing 1998	32	-4.8 (15)	31	-1.5 (12)		0.1 %	-3.30 [-10.00, 3.40]
Subtotal (95% CI)	**7461**		**8385**		◆	**31.8 %**	**-2.74 [-3.19, -2.29]**
Heterogeneity: Chi² = 147.04, df = 28 (P<0.00001); I² =81%							
Test for overall effect: Z = 11.94 (P < 0.00001)							
2 Antihypertensives OR lipid-lowering drugs							
Aberg 1989 F	114	4.4 (17.83)	80	0.2 (19.02)		0.2 %	4.20 [-1.10, 9.50]
Aberg 1989 M	79	3.3 (16.3)	80	1.7 (16.21)		0.3 %	1.60 [-3.45, 6.65]
ADAPT 2005	123	-1 (11.32)	118	1 (11.08)		0.8 %	-2.00 [-4.83, 0.83]
Cakir 2006	30	-8.8 (5.2)	30	1.2 (5.3)		0.9 %	-10.00 [-12.66, -7.34]
Garcia-Pena 2001	345	-6.8 (7.41)	338	-3.5 (17.46)		1.6 %	-3.30 [-5.32, -1.28]
Given 1984	62	-9.85 (12.7)	24	-4.79 (12.61)		0.2 %	-5.06 [-11.01, 0.89]
Jalkanen 1991	24	-8 (18.68)	25	-5 (18.33)		0.1 %	-3.00 [-13.37, 7.37]
Kastarinen 2002	360	-6.2 (5.66)	355	-4.2 (16)		2.1 %	-2.00 [-3.76, -0.24]
Lin 1996	471	-1 (18.52)	426	1 (19.52)		1.0 %	-2.00 [-4.50, 0.50]
Mattila 2003	331	-2.1 (12.53)	309	0 (12.56)		1.7 %	-2.10 [-4.05, -0.15]
Meland 1997	58	-4 (23.31)	52	0 (22.08)		0.1 %	-4.00 [-12.49, 4.49]

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Favours treatment Favours control

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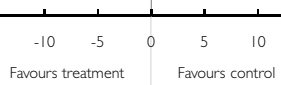
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
MRFIT Study 1982	5740	-13.9 (13.23)	5633	-8.6 (15.27)		23.2 %	-5.30 [-5.83, -4.77]
Nilsson 1992	31	-7.7 (17.77)	32	-3.8 (19.3)		0.1 %	-3.90 [-13.06, 5.26]
Oslo Diet Exercise	65	-5.9 (8.87)	43	-0.5 (11.15)		0.4 %	-5.40 [-9.37, -1.43]
Perez-Stable 1995 prop	74	-8.3 (13.39)	73	-11.6 (13.3)		0.3 %	3.30 [-1.01, 7.61]
Rachmani 2005	71	-20 (4.75)	70	-12 (6.54)		1.8 %	-8.00 [-9.89, -6.11]
WHO Factories 1986	16949	2.67 (18.09)	1902	3.18 (18.14)		8.7 %	-0.51 [-1.37, 0.35]
Subtotal (95% CI)	**24927**		**9590**			**43.4 %**	**-3.89 [-4.28, -3.51]**
Heterogeneity: Chi² = 162.36, df = 16 (P<0.00001); I² =90%							
Test for overall effect: Z = 19.85 (P < 0.00001)							
3 Antihypertensives AND lipid-lowering drugs							
CELL Study 1995	292	-1.2 (14.7)	310	0 (14.7)		1.2 %	-1.20 [-3.55, 1.15]
Finnish men 1985	575	-10 (18)	580	-4 (16)		1.7 %	-6.00 [-7.96, -4.04]
Gothenberg Study 1986	1464	-2 (20)	1404	0 (20)		3.0 %	-2.00 [-3.46, -0.54]
Look AHEAD 2003	2496	-6.8 (14.13)	2463	-2.8 (10.53)		13.3 %	-4.00 [-4.69, -3.31]
OXCHECK 1994	2205	-2.5 (19.3)	1916	0 (20.4)		4.3 %	-2.50 [-3.72, -1.28]
Swedish RIS 1994	235	-2 (18.4)	227	-0.2 (20.5)		0.5 %	-1.80 [-5.36, 1.76]
Toobert (MLP) 2005	163	-1.85 (4.81)	116	-2.18 (14.41)		0.9 %	0.33 [-2.39, 3.05]
Subtotal (95% CI)	**7430**		**7016**			**24.9 %**	**-3.31 [-3.81, -2.80]**
Heterogeneity: Chi² = 26.43, df = 6 (P = 0.00018); I² =77%							
Test for overall effect: Z = 12.76 (P < 0.00001)							
Total (95% CI)	**39818**		**24991**			**100.0 %**	**-3.38 [-3.63, -3.13]**
Heterogeneity: Chi² = 350.61, df = 52 (P<0.00001); I² =85%							
Test for overall effect: Z = 26.16 (P < 0.00001)							
Test for subgroup differences: Chi² = 14.78, df = 2 (P = 0.00), I² =86%							



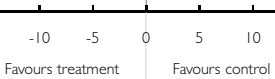
Analysis 1.40. Comparison 1 Multiple risk factor intervention versus control, Outcome 40 Systolic blood pressure (by era).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 40 Systolic blood pressure (by era)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Low rate of CVD							
Aberg 1989 F	114	4.4 (17.83)	80	0.2 (19.02)		0.2 %	4.20 [-1.10, 9.50]
Aberg 1989 M	79	3.3 (16.3)	80	1.7 (16.21)		0.3 %	1.60 [-3.45, 6.65]
Abingdon 1990	167	-6.9 (14.6)	168	-5.2 (15.76)		0.6 %	-1.70 [-4.95, 1.55]
ADAPT 2005	123	-1 (11.32)	118	1 (11.08)		0.8 %	-2.00 [-4.83, 0.83]
Aldana (CHIP) 2005	64	-5.9 (13.26)	79	-5.4 (14.36)		0.3 %	-0.50 [-5.04, 4.04]
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)		0.3 %	-6.50 [-11.23, -1.77]
Cakir 2006	30	-8.8 (5.2)	30	1.2 (5.3)		0.9 %	-10.00 [-12.66, -7.34]
CELL Study 1995	292	-1.2 (14.7)	310	0 (14.7)		1.2 %	-1.20 [-3.55, 1.15]
Change of Heart 1999	165	4.3 (15.4)	339	1.8 (21.61)		0.6 %	2.50 [-0.79, 5.79]
Connell 1995	141	-5 (13.26)	255	-3 (14.36)		0.8 %	-2.00 [-4.81, 0.81]
Esposito 2004	55	-3 (3.94)	55	-1 (7.75)		1.2 %	-2.00 [-4.30, 0.30]
Family Heart 1994 M	1767	-7.3 (19.23)	2174	0 (19.23)		4.4 %	-7.30 [-8.51, -6.09]
Family Heart 1994 F	1217	-6.2 (20.43)	1402	0 (20.43)		2.6 %	-6.20 [-7.77, -4.63]
FARIS 1997 F	315	-3.9 (15.38)	343	-0.7 (15.38)		1.2 %	-3.20 [-5.55, -0.85]
FARIS 1997 M	219	-4.4 (15.38)	223	-0.6 (15.38)		0.8 %	-3.80 [-6.67, -0.93]
Finnish DPS 2001	256	-5 (14)	250	-1 (15)		1.0 %	-4.00 [-6.53, -1.47]
Garcia-Pena 2001	345	-6.8 (7.41)	338	-3.5 (17.46)		1.6 %	-3.30 [-5.32, -1.28]
Given 1984	62	-9.85 (12.7)	24	-4.79 (12.61)		0.2 %	-5.06 [-11.01, 0.89]
Hellenius 1993	39	-4 (12.6)	39	-1 (12.2)		0.2 %	-3.00 [-8.50, 2.50]
Iso 1994	53	-13.2 (11.52)	55	-17.4 (14.02)		0.3 %	4.20 [-0.63, 9.03]
Jalkanen 1991	24	-8 (18.68)	25	-5 (18.33)		0.1 %	-3.00 [-13.37, 7.37]
Kastarinen 2002	360	-6.2 (5.66)	355	-4.2 (16)		2.1 %	-2.00 [-3.76, -0.24]
Lin 1996	471	-1 (18.52)	426	1 (19.52)		1.0 %	-2.00 [-4.50, 0.50]



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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Lindahl 1999	93	-4.9 (19.3)	93	1.3 (18.3)		0.2 %	-6.20 [-11.61, -0.79]
Look AHEAD 2003	2496	-6.8 (14.13)	2463	-2.8 (10.53)		13.3 %	-4.00 [-4.69, -3.31]
Mattila 2003	331	-2.1 (12.53)	309	0 (12.56)		1.7 %	-2.10 [-4.05, -0.15]
Meland 1997	58	-4 (23.31)	52	0 (22.08)		0.1 %	-4.00 [-12.49, 4.49]
Muto 2001	152	0.5 (11.9)	150	2.9 (13.5)		0.8 %	-2.40 [-5.27, 0.47]
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)		0.1 %	-2.50 [-10.48, 5.48]
Oldroyd 2001	35	-7.9 (16.7)	32	-0.27 (14.3)		0.1 %	-7.63 [-15.06, -0.20]
Oslo Diet Exercise	65	-5.9 (8.87)	43	-0.5 (11.15)		0.4 %	-5.40 [-9.37, -1.43]
OXCHECK 1994	2205	-2.5 (19.3)	1916	0 (20.4)		4.3 %	-2.50 [-3.72, -1.28]
Perez-Stable 1995 no prop	72	-9 (12.99)	72	-6.7 (13.2)		0.4 %	-2.30 [-6.58, 1.98]
Perez-Stable 1995 prop	74	-8.3 (13.39)	73	-11.6 (13.3)		0.3 %	3.30 [-1.01, 7.61]
Proper 2003	75	-4.1 (4.25)	116	-5.2 (15.26)		0.7 %	1.10 [-1.84, 4.04]
Rachmani 2005	71	-20 (4.75)	70	-12 (6.54)		1.8 %	-8.00 [-9.89, -6.11]
Sartorelli 2005	51	-0.8 (12.3)	53	3.1 (13)		0.3 %	-3.90 [-8.76, 0.96]
Sone (JDCS) 2002	990	1 (4.24)	983	1 (15.52)		6.3 %	0.0 [-1.01, 1.01]
Stamler 1989	102	-2.6 (6.4)	99	-1.3 (6.1)		2.1 %	-1.30 [-3.03, 0.43]
Stefanick 1998 F	43	-3.1 (8.4)	45	-2.4 (7.6)		0.6 %	-0.70 [-4.05, 2.65]
Stefanick 1998 M	48	-3 (6.8)	46	0.3 (7.9)		0.7 %	-3.30 [-6.29, -0.31]
Swedish RIS 1994	235	-2 (18.4)	227	-0.2 (20.5)		0.5 %	-1.80 [-5.36, 1.76]
Toobert (MLP) 2005	163	-1.85 (4.81)	116	-2.18 (14.41)		0.9 %	0.33 [-2.39, 3.05]
Tromso 1991 F	422	-2.16 (15.8)	387	2.1 (16.5)		1.3 %	-4.26 [-6.49, -2.03]
Tromso 1991 M	525	0.5 (15.6)	535	1.1 (16.5)		1.7 %	-0.60 [-2.53, 1.33]
WHLP 1998	253	-3.5 (12.18)	267	-1.2 (9.21)		1.8 %	-2.30 [-4.16, -0.44]
Wing 1998	32	-4.8 (15)	31	-1.5 (12)		0.1 %	-3.30 [-10.00, 3.40]
Subtotal (95% CI)	**15090**		**15472**			**63.5 %**	**-3.07 [-3.38, -2.75]**
Heterogeneity: Chi^2 = 242.51, df = 48 (P<0.00001); I^2 =80%							
Test for overall effect: Z = 18.91 (P < 0.00001)							
2 High rate of CVD							
Finnish men 1985	575	-10 (18)	580	-4 (16)		1.7 %	-6.00 [-7.96, -4.04]
Gothenberg Study 1986	1464	-2 (20)	1404	0 (20)		3.0 %	-2.00 [-3.46, -0.54]
MRFIT Study 1982	5740	-13.9 (13.23)	5633	-8.6 (15.27)		23.2 %	-5.30 [-5.83, -4.77]
WHO Factories 1986	16949	2.67 (18.09)	1902	3.18 (18.14)		8.7 %	-0.51 [-1.37, 0.35]

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Favours treatment Favours control

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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Subtotal (95% CI)	**24728**		**9519**			**36.5 %**	**-3.92 [-4.34, -3.51]**
Heterogeneity: Chi² = 97.87, df = 3 (P<0.00001); I² =97%							
Test for overall effect: Z = 18.36 (P < 0.00001)							
Total (95% CI)	**39818**		**24991**			**100.0 %**	**-3.38 [-3.63, -3.13]**
Heterogeneity: Chi² = 350.61, df = 52 (P<0.00001); I² =85%							
Test for overall effect: Z = 26.16 (P < 0.00001)							
Test for subgroup differences: Chi² = 10.24, df = 1 (P = 0.00), I² =90%							

Analysis 1.41. Comparison 1 Multiple risk factor intervention versus control, Outcome 41 Systolic blood pressure (by age of study).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 41 Systolic blood pressure (by age of study)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Study before 2000							
Aberg 1989 F	114	4.4 (17.83)	80	0.2 (19.02)		0.2 %	4.20 [-1.10, 9.50]
Aberg 1989 M	79	3.3 (16.3)	80	1.7 (16.21)		0.3 %	1.60 [-3.45, 6.65]
Abingdon 1990	167	-6.9 (14.6)	168	-5.2 (15.76)		0.6 %	-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)		0.3 %	-6.50 [-11.23, -1.77]
CELL Study 1995	292	-1.2 (14.7)	310	0 (14.7)		1.2 %	-1.20 [-3.55, 1.15]
Change of Heart 1999	165	4.3 (15.4)	339	1.8 (21.61)		0.6 %	2.50 [-0.79, 5.79]
Connell 1995	141	-5 (13.26)	255	-3 (14.36)		0.8 %	-2.00 [-4.81, 0.81]
Family Heart 1994 M	1767	-7.3 (19.23)	2174	0 (19.23)		4.4 %	-7.30 [-8.51, -6.09]
Family Heart 1994 F	1217	-6.2 (20.43)	1402	0 (20.43)		2.6 %	-6.20 [-7.77, -4.63]
FARIS 1997 F	315	-3.9 (15.38)	343	-0.7 (15.38)		1.2 %	-3.20 [-5.55, -0.85]

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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
FARIS 1997 M	219	-4.4 (15.38)	223	-0.6 (15.38)		0.8 %	-3.80 [-6.67, -0.93]
Finnish men 1985	575	-10 (18)	580	-4 (16)		1.7 %	-6.00 [-7.96, -4.04]
Given 1984	62	-9.85 (12.7)	24	-4.79 (12.61)		0.2 %	-5.06 [-11.01, 0.89]
Gothenberg Study 1986	1464	-2 (20)	1404	0 (20)		3.0 %	-2.00 [-3.46, -0.54]
Hellenius 1993	39	-4 (12.6)	39	-1 (12.2)		0.2 %	-3.00 [-8.50, 2.50]
Iso 1994	53	-13.2 (11.52)	55	-17.4 (14.02)		0.3 %	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)		1.0 %	-2.00 [-4.50, 0.50]
Lindahl 1999	93	-4.9 (19.3)	93	1.3 (18.3)		0.2 %	-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 1982	5740	-13.9 (13.23)	5633	-8.6 (15.27)		23.2 %	-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]
Oslo Diet Exercise	65	-5.9 (8.87)	43	-0.5 (11.15)		0.4 %	-5.40 [-9.37, -1.43]
OXCHECK 1994	2205	-2.5 (19.3)	1916	0 (20.4)		4.3 %	-2.50 [-3.72, -1.28]
Perez-Stable 1995 no prop	72	-9 (12.99)	72	-6.7 (13.2)		0.4 %	-2.30 [-6.58, 1.98]
Perez-Stable 1995 prop	74	-8.3 (13.39)	73	-11.6 (13.3)		0.3 %	3.30 [-1.01, 7.61]
Stamler 1989	102	-2.6 (6.4)	99	-1.3 (6.1)		2.1 %	-1.30 [-3.03, 0.43]
Stefanick 1998 F	43	-3.1 (8.4)	45	-2.4 (7.6)		0.6 %	-0.70 [-4.05, 2.65]
Stefanick 1998 M	48	-3 (6.8)	46	0.3 (7.9)		0.7 %	-3.30 [-6.29, -0.31]
Swedish RIS 1994	235	-2 (18.4)	227	-0.2 (20.5)		0.5 %	-1.80 [-5.36, 1.76]
Tromso 1991 F	422	-2.16 (15.8)	387	2.1 (16.5)		1.3 %	-4.26 [-6.49, -2.03]
Tromso 1991 M	525	0.5 (15.6)	535	1.1 (16.5)		1.7 %	-0.60 [-2.53, 1.33]
WHLP 1998	253	-3.5 (12.18)	267	-1.2 (9.21)		1.8 %	-2.30 [-4.16, -0.44]
WHO Factories 1986	16949	2.67 (18.09)	1902	3.18 (18.14)		8.7 %	-0.51 [-1.37, 0.35]
Wing 1998	32	-4.8 (15)	31	-1.5 (12)		0.1 %	-3.30 [-10.00, 3.40]
Subtotal (95% CI)	**34178**		**19428**			**66.1 %**	**-3.59 [-3.90, -3.28]**
Heterogeneity: Chi² = 229.64, df = 35 (P<0.00001); I² =85%							
Test for overall effect: Z = 22.58 (P < 0.00001)							
2 Study after 2000							
ADAPT 2005	123	-1 (11.32)	118	1 (11.08)		0.8 %	-2.00 [-4.83, 0.83]
Aldana (CHIP) 2005	64	-5.9 (13.26)	79	-5.4 (14.36)		0.3 %	-0.50 [-5.04, 4.04]
Cakir 2006	30	-8.8 (5.2)	30	1.2 (5.3)		0.9 %	-10.00 [-12.66, -7.34]
Esposito 2004	55	-3 (3.94)	55	-1 (7.75)		1.2 %	-2.00 [-4.30, 0.30]

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Favours treatment Favours control

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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Finnish DPS 2001	256	-5 (14)	250	-1 (15)		1.0 %	-4.00 [-6.53, -1.47]
Garcia-Pena 2001	345	-6.8 (7.41)	338	-3.5 (17.46)		1.6 %	-3.30 [-5.32, -1.28]
Kastarinen 2002	360	-6.2 (5.66)	355	-4.2 (16)		2.1 %	-2.00 [-3.76, -0.24]
Look AHEAD 2003	2496	-6.8 (14.13)	2463	-2.8 (10.53)		13.3 %	-4.00 [-4.69, -3.31]
Mattila 2003	331	-2.1 (12.53)	309	0 (12.56)		1.7 %	-2.10 [-4.05, -0.15]
Muto 2001	152	0.5 (11.9)	150	2.9 (13.5)		0.8 %	-2.40 [-5.27, 0.47]
Nilsson 2001	43	-3.7 (20.31)	46	-1.2 (17.9)		0.1 %	-2.50 [-10.48, 5.48]
Oldroyd 2001	35	-7.9 (16.7)	32	-0.27 (14.3)		0.1 %	-7.63 [-15.06, -0.20]
Proper 2003	75	-4.1 (4.25)	116	-5.2 (15.26)		0.7 %	1.10 [-1.84, 4.04]
Rachmani 2005	71	-20 (4.75)	70	-12 (6.54)		1.8 %	-8.00 [-9.89, -6.11]
Sartorelli 2005	51	-0.8 (12.3)	53	3.1 (13)		0.3 %	-3.90 [-8.76, 0.96]
Sone (JDCS) 2002	990	1 (4.24)	983	1 (15.52)		6.3 %	0.0 [-1.01, 1.01]
Toobert (MLP) 2005	163	-1.85 (4.81)	116	-2.18 (14.41)		0.9 %	0.33 [-2.39, 3.05]
Subtotal (95% CI)	**5640**		**5563**			**33.9 %**	**-2.97 [-3.41, -2.54]**
Heterogeneity: Chi^2 = 115.90, df = 16 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 13.41 (P < 0.00001)							
Total (95% CI)	**39818**		**24991**			**100.0 %**	**-3.38 [-3.63, -3.13]**
Heterogeneity: Chi^2 = 350.61, df = 52 (P<0.00001); I^2 =85%							
Test for overall effect: Z = 26.16 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 5.07, df = 1 (P = 0.02), I^2 =80%							

Analysis 1.42. Comparison 1 Multiple risk factor intervention versus control, Outcome 42 Diastolic blood pressure.

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 42 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 1989 F	114	1.3 (9.11)	115	0.8 (8.46)		0.4 %	0.50 [-1.78, 2.78]
Aberg 1989 M	79	2 (7.81)	80	1.6 (7.77)		0.4 %	0.40 [-2.02, 2.82]
Abingdon 1990	167	-4.61 (9.29)	168	-2.9 (9.98)		0.5 %	-1.71 [-3.77, 0.35]
ADAPT 2005	123	0 (8.49)	118	1 (8.31)		0.5 %	-1.00 [-3.12, 1.12]
Aldana (CHIP) 2005	64	-6.5 (8.76)	79	-3.8 (9.03)		0.2 %	-2.70 [-5.63, 0.23]
Applegate 1992	21	-6.8 (1.7)	26	-1.9 (3.6)		0.9 %	-4.90 [-6.46, -3.34]
Blumenthal 2000	46	-5.6 (7.56)	22	-1.4 (7.56)		0.1 %	-4.20 [-8.04, -0.36]
Cakir 2006	30	-6.9 (5.3)	30	1.6 (4.6)		0.3 %	-8.50 [-11.01, -5.99]
CELL Study 1995	292	-0.1 (8.3)	310	0 (9.1)		1.1 %	-0.10 [-1.49, 1.29]
Change of Heart 1999	165	0.7 (15.4)	338	1 (9.43)		0.3 %	-0.30 [-2.86, 2.26]
Esposito 2004	55	-4 (3.65)	55	0 (4.31)		1.0 %	-4.00 [-5.49, -2.51]
Family Heart 1994 M	1767	-3.5 (11.43)	2174	0 (11.43)		4.1 %	-3.50 [-4.22, -2.78]
Family Heart 1994 F	1217	-3 (11.33)	1402	0 (11.33)		2.8 %	-3.00 [-3.87, -2.13]
FARIS 1997 F	315	-1.1 (9.95)	343	-0.3 (9.95)		0.9 %	-0.80 [-2.32, 0.72]
FARIS 1997 M	219	-1 (9.95)	223	1 (9.95)		0.6 %	-2.00 [-3.86, -0.14]
Finnish DPS 2001	256	-5 (9)	250	-3 (9)		0.9 %	-2.00 [-3.57, -0.43]
Finnish men 1985	575	-8 (10)	580	-3 (10)		1.6 %	-5.00 [-6.15, -3.85]
Garcia-Pena 2001	345	-3.7 (9.5)	338	0 (9.85)		1.0 %	-3.70 [-5.15, -2.25]
Given 1984	62	-6.4 (6.99)	24	-2.42 (4.9)		0.3 %	-3.98 [-6.60, -1.36]
Gothenberg Study 1986	1464	-1 (10)	1404	0 (10)		4.0 %	-1.00 [-1.73, -0.27]
HDFP trial 1970	5485	-17 (10)	5455	-12.1 (10)		15.1 %	-4.90 [-5.27, -4.53]
Hellenius 1993	39	-2 (7.7)	39	-1 (8.3)		0.2 %	-1.00 [-4.55, 2.55]
Iso 1994	53	-5.1 (8.39)	55	-4.7 (9.06)		0.2 %	-0.40 [-3.69, 2.89]
Jalkanen 1991	24	-11 (9.17)	25	-11 (7)		0.1 %	0.0 [-4.58, 4.58]
Kastarinen 2002	360	-4.3 (9)	355	-3.2 (8)		1.4 %	-1.10 [-2.35, 0.15]
Lin 1996	471	-2 (11)	426	-2 (11.53)		1.0 %	0.0 [-1.48, 1.48]

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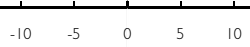
Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Lindahl 1999	93	-3.2 (9.6)	93	-0.8 (9.6)		0.3 %	-2.40 [-5.16, 0.36]
Look AHEAD 2003	2496	-3 (7.07)	2463	-1.8 (7.02)		13.8 %	-1.20 [-1.59, -0.81]
Mattila 2003	331	-1.6 (6.96)	309	-0.1 (7.17)		1.8 %	-1.50 [-2.60, -0.40]
Meland 1997	58	-3 (11.66)	52	0 (11.04)		0.1 %	-3.00 [-7.24, 1.24]
MRFIT Study 1982	5754	-10.2 (7.88)	5638	-7.1 (9.22)		21.4 %	-3.10 [-3.42, -2.78]
Muto 2001	152	0 (9.9)	150	2.3 (10.9)		0.4 %	-2.30 [-4.65, 0.05]
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)		0.1 %	-5.30 [-9.53, -1.07]
Oldroyd 2001	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)		0.2 %	-4.50 [-7.60, -1.40]
OXCHECK 1994	2205	-1.5 (11.6)	1916	0 (11.7)		4.2 %	-1.50 [-2.21, -0.79]
Perez-Stable 1995 no prop	72	-5 (9.09)	72	-5.8 (9.09)		0.2 %	0.80 [-2.17, 3.77]
Perez-Stable 1995 prop	74	-8.2 (9.66)	73	-8.5 (9.15)		0.2 %	0.30 [-2.74, 3.34]
Proper 2003	75	-3.5 (8.78)	116	-3.9 (9.25)		0.3 %	0.40 [-2.20, 3.00]
Rachmani 2005	71	-12 (2.16)	70	-7 (16.09)		0.1 %	-5.00 [-8.80, -1.20]
Sartorelli 2005	51	-1.3 (8.9)	53	3.5 (7.4)		0.2 %	-4.80 [-7.95, -1.65]
Sone (JDCS) 2002	990	-1 (9.54)	983	-2 (9.54)		3.0 %	1.00 [0.16, 1.84]
Stamler 1989	102	-1.3 (4.7)	99	-0.1 (4.9)		1.2 %	-1.20 [-2.53, 0.13]
Stefanick 1998 F	43	-2.7 (4.6)	45	-0.6 (5.9)		0.4 %	-2.10 [-4.30, 0.10]
Stefanick 1998 M	48	-3 (6.6)	46	1.8 (6.1)		0.3 %	-4.80 [-7.37, -2.23]
Swedish RIS 1994	235	-4.9 (9.1)	227	-3.8 (9.6)		0.7 %	-1.10 [-2.81, 0.61]
Toobert (MLP) 2005	163	-2.14 (9.15)	116	-0.44 (8.8)		0.5 %	-1.70 [-3.83, 0.43]
Tromso 1991 F	422	-2.13 (10.3)	387	1.23 (10.4)		1.0 %	-3.36 [-4.79, -1.93]
Tromso 1991 M	525	-4 (10.6)	535	-3.6 (10.5)		1.3 %	-0.40 [-1.67, 0.87]
WHLP 1998	253	-2.2 (10.48)	267	-0.09 (6.92)		0.9 %	-2.11 [-3.65, -0.57]
WHO Factories 1986	16948	1.41 (12.29)	1897	1.68 (11.64)		6.9 %	-0.27 [-0.83, 0.29]
Wing 1998	32	-0.2 (10.5)	31	2 (8)		0.1 %	-2.20 [-6.80, 2.40]
Total (95% CI)	**45175**		**30225**			**100.0 %**	**-2.41 [-2.55, -2.26]**

Heterogeneity: Chi^2 = 530.18, df = 52 (P<0.00001); I^2 =90%

Test for overall effect: Z = 32.38 (P < 0.00001)



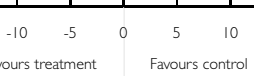
Analysis 1.43. Comparison 1 Multiple risk factor intervention versus control, Outcome 43 Diastolic blood pressure (individual analysis or cluster).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 43 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 1999	165	0.7 (15.4)	338	1 (9.43)		1.7 %	-0.30 [-2.86, 2.26]
Subtotal (95% CI)	**165**		**338**			**1.7 %**	**-0.30 [-2.86, 2.26]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.23 (P = 0.82)							
2 Individual randomisation							
Aberg 1989 F	114	1.3 (9.11)	115	0.8 (8.46)		1.8 %	0.50 [-1.78, 2.78]
Aberg 1989 M	79	2 (7.81)	80	1.6 (7.77)		1.7 %	0.40 [-2.02, 2.82]
Abingdon 1990	167	-4.61 (9.29)	168	-2.9 (9.98)		1.9 %	-1.71 [-3.77, 0.35]
ADAPT 2005	123	0 (8.49)	118	1 (8.31)		1.9 %	-1.00 [-3.12, 1.12]
Aldana (CHIP) 2005	64	-6.5 (8.76)	79	-3.8 (9.03)		1.5 %	-2.70 [-5.63, 0.23]
Applegate 1992	21	-6.8 (1.7)	26	-1.9 (3.6)		2.2 %	-4.90 [-6.46, -3.34]
Blumenthal 2000	46	-5.6 (7.56)	22	-1.4 (7.56)		1.2 %	-4.20 [-8.04, -0.36]
Cakir 2006	30	-6.9 (5.3)	30	1.6 (4.6)		1.7 %	-8.50 [-11.01, -5.99]
CELL Study 1995	292	-0.1 (8.3)	310	0 (9.1)		2.3 %	-0.10 [-1.49, 1.29]
Esposito 2004	55	-4 (3.65)	55	0 (4.31)		2.2 %	-4.00 [-5.49, -2.51]
Family Heart 1994 M	1767	-3.5 (11.43)	2174	0 (11.43)		2.5 %	-3.50 [-4.22, -2.78]
Family Heart 1994 F	1217	-3 (11.33)	1402	0 (11.33)		2.5 %	-3.00 [-3.87, -2.13]
FARIS 1997 F	315	-1.1 (9.95)	343	-0.3 (9.95)		2.2 %	-0.80 [-2.32, 0.72]
FARIS 1997 M	219	-1 (9.95)	223	1 (9.95)		2.0 %	-2.00 [-3.86, -0.14]
Finnish DPS 2001	256	-5 (9)	250	-3 (9)		2.2 %	-2.00 [-3.57, -0.43]
Finnish men 1985	575	-8 (10)	580	-3 (10)		2.4 %	-5.00 [-6.15, -3.85]
Garcia-Pena 2001	345	-3.7 (9.5)	338	0 (9.85)		2.2 %	-3.70 [-5.15, -2.25]
Given 1984	62	-6.4 (6.99)	24	-2.42 (4.9)		1.7 %	-3.98 [-6.60, -1.36]
Gothenberg Study 1986	1464	-1 (10)	1404	0 (10)		2.5 %	-1.00 [-1.73, -0.27]
HDFP trial 1970	5485	-17 (10)	5455	-12.1 (10)		2.6 %	-4.90 [-5.27, -4.53]



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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
Hellenius 1993	39	-2 (7.7)	39	-1 (8.3)		1.3 %	-1.00 [-4.55, 2.55]
Iso 1994	53	-5.1 (8.39)	55	-4.7 (9.06)		1.4 %	-0.40 [-3.69, 2.89]
Jalkanen 1991	24	-11 (9.17)	25	-11 (7)		0.9 %	0.0 [-4.58, 4.58]
Kastarinen 2002	360	-4.3 (9)	355	-3.2 (8)		2.3 %	-1.10 [-2.35, 0.15]
Lindahl 1999	93	-3.2 (9.6)	93	-0.8 (9.6)		1.6 %	-2.40 [-5.16, 0.36]
MRFIT Study 1982	5754	-10.2 (7.88)	5638	-7.1 (9.22)		2.6 %	-3.10 [-3.42, -2.78]
Muto 2001	152	0 (9.9)	150	2.3 (10.9)		1.8 %	-2.30 [-4.65, 0.05]
Nilsson 1992	31	-6.1 (6.2)	32	-4 (8.23)		1.2 %	-2.10 [-5.69, 1.49]
Nilsson 2001	43	-5.7 (10.71)	46	-0.4 (9.56)		1.0 %	-5.30 [-9.53, -1.07]
Oldroyd 2001	35	-2.9 (9.9)	32	1.9 (10)		0.9 %	-4.80 [-9.57, -0.03]
Oslo Diet Exercise	65	-5.2 (7.26)	43	-0.7 (8.52)		1.4 %	-4.50 [-7.60, -1.40]
OXCHECK 1994	2205	-1.5 (11.6)	1916	0 (11.7)		2.5 %	-1.50 [-2.21, -0.79]
Perez-Stable 1995 no prop	72	-5 (9.09)	72	-5.8 (9.09)		1.5 %	0.80 [-2.17, 3.77]
Perez-Stable 1995 prop	74	-8.2 (9.66)	73	-8.5 (9.15)		1.5 %	0.30 [-2.74, 3.34]
Rachmani 2005	71	-12 (2.16)	70	-7 (16.09)		1.2 %	-5.00 [-8.80, -1.20]
Sartorelli 2005	51	-1.3 (8.9)	53	3.5 (7.4)		1.4 %	-4.80 [-7.95, -1.65]
Sone (JDCS) 2002	990	-1 (9.54)	983	-2 (9.54)		2.5 %	1.00 [0.16, 1.84]
Stamler 1989	102	-1.3 (4.7)	99	-0.1 (4.9)		2.3 %	-1.20 [-2.53, 0.13]
Stefanick 1998 F	43	-2.7 (4.6)	45	-0.6 (5.9)		1.9 %	-2.10 [-4.30, 0.10]
Stefanick 1998 M	48	-3 (6.6)	46	1.8 (6.1)		1.7 %	-4.80 [-7.37, -2.23]
Swedish RIS 1994	235	-4.9 (9.1)	227	-3.8 (9.6)		2.1 %	-1.10 [-2.81, 0.61]
Toobert (MLP) 2005	163	-2.14 (9.15)	116	-0.44 (8.8)		1.9 %	-1.70 [-3.83, 0.43]
Tromso 1991 F	422	-2.13 (10.3)	387	1.23 (10.4)		2.2 %	-3.36 [-4.79, -1.93]
Tromso 1991 M	525	-4 (10.6)	535	-3.6 (10.5)		2.3 %	-0.40 [-1.67, 0.87]
WHLP 1998	253	-2.2 (10.48)	267	-0.09 (6.92)		2.2 %	-2.11 [-3.65, -0.57]
Wing 1998	32	-0.2 (10.5)	31	2 (8)		0.9 %	-2.20 [-6.80, 2.40]
Subtotal (95% CI)	**24631**		**24624**			**85.8 %**	**-2.36 [-2.94, -1.77]**
Heterogeneity: Tau² = 2.86; Chi² = 384.24, df = 45 (P<0.00001); I² =88%							
Test for overall effect: Z = 7.89 (P < 0.00001)							
3 Cluster randomisation - analysis by individual							
Lin 1996	471	-2 (11)	426	-2 (11.53)		2.2 %	0.0 [-1.48, 1.48]
Look AHEAD 2003	2496	-3 (7.07)	2463	-1.8 (7.02)		2.6 %	-1.20 [-1.59, -0.81]
Mattila 2003	331	-1.6 (6.96)	309	-0.1 (7.17)		2.4 %	-1.50 [-2.60, -0.40]

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Favours treatment Favours control

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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
Meland 1997	58	-3 (11.66)	52	0 (11.04)		1.0 %	-3.00 [-7.24, 1.24]
Proper 2003	75	-3.5 (8.78)	116	-3.9 (9.25)		1.7 %	0.40 [-2.20, 3.00]
WHO Factories 1986	16948	1.41 (12.29)	1897	1.68 (11.64)		2.6 %	-0.27 [-0.83, 0.29]
Subtotal (95% CI)	**20379**		**5263**			**12.5 %**	**-0.79 [-1.42, -0.16]**
Heterogeneity: $Tau^2 = 0.27$; $Chi^2 = 11.66$, df = 5 (P = 0.04); $I^2 = 57\%$							
Test for overall effect: Z = 2.46 (P = 0.014)							
Total (95% CI)	**45175**		**30225**			**100.0 %**	**-2.13 [-2.67, -1.58]**
Heterogeneity: $Tau^2 = 2.95$; $Chi^2 = 530.18$, df = 52 (P<0.00001); $I^2 = 90\%$							
Test for overall effect: Z = 7.60 (P < 0.00001)							

Analysis 1.44. Comparison 1 Multiple risk factor intervention versus control, Outcome 44 Diastolic blood pressure (by allocation concealment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 44 Diastolic blood pressure (by allocation concealment)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Adequate concealment							
ADAPT 2005	123	0 (8.49)	118	1 (8.31)		0.5 %	-1.00 [-3.12, 1.12]
Aldana (CHIP) 2005	64	-6.5 (8.76)	79	-3.8 (9.03)		0.2 %	-2.70 [-5.63, 0.23]
Cakir 2006	30	-6.9 (5.3)	30	1.6 (4.6)		0.3 %	-8.50 [-11.01, -5.99]
Esposito 2004	55	-4 (3.65)	55	0 (4.31)		1.0 %	-4.00 [-5.49, -2.51]
Garcia-Pena 2001	345	-3.7 (9.5)	338	0 (9.85)		1.0 %	-3.70 [-5.15, -2.25]
Look AHEAD 2003	2496	-3 (7.07)	2463	-1.8 (7.02)		13.8 %	-1.20 [-1.59, -0.81]
Mattila 2003	331	-1.6 (6.96)	309	-0.1 (7.17)		1.8 %	-1.50 [-2.60, -0.40]
MRFIT Study 1982	5754	-10.2 (7.88)	5638	-7.1 (9.22)		21.4 %	-3.10 [-3.42, -2.78]
Oldroyd 2001	35	-2.9 (9.9)	32	1.9 (10)		0.1 %	-4.80 [-9.57, -0.03]

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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Perez-Stable 1995 no prop	72	-5 (9.09)	72	-5.8 (9.09)		0.2 %	0.80 [-2.17, 3.77]
Perez-Stable 1995 prop	74	-8.2 (9.66)	73	-8.5 (9.15)		0.2 %	0.30 [-2.74, 3.34]
Stamler 1989	102	-1.3 (4.7)	99	-0.1 (4.9)		1.2 %	-1.20 [-2.53, 0.13]
Stefanick 1998 F	43	-2.7 (4.6)	45	-0.6 (5.9)		0.4 %	-2.10 [-4.30, 0.10]
Stefanick 1998 M	48	-3 (6.6)	46	1.8 (6.1)		0.3 %	-4.80 [-7.37, -2.23]
Subtotal (95% CI)	**9572**		**9397**			**42.5 %**	**-2.38 [-2.60, -2.16]**
Heterogeneity: Chi² = 104.37, df = 13 (P<0.00001); I² =88%							
Test for overall effect: Z = 20.86 (P < 0.00001)							
2 Inadequate allocation concealment							
Aberg 1989 F	114	1.3 (9.11)	115	0.8 (8.46)		0.4 %	0.50 [-1.78, 2.78]
Aberg 1989 M	79	2 (7.81)	80	1.6 (7.77)		0.4 %	0.40 [-2.02, 2.82]
CELL Study 1995	292	-0.1 (8.3)	310	0 (9.1)		1.1 %	-0.10 [-1.49, 1.29]
Finnish DPS 2001	256	-5 (9)	250	-3 (9)		0.9 %	-2.00 [-3.57, -0.43]
HDFP trial 1970	5485	-17 (10)	5455	-12.1 (10)		15.1 %	-4.90 [-5.27, -4.53]
Kastarinen 2002	360	-4.3 (9)	355	-3.2 (8)		1.4 %	-1.10 [-2.35, 0.15]
Sartorelli 2005	51	-1.3 (8.9)	53	3.5 (7.4)		0.2 %	-4.80 [-7.95, -1.65]
Tromso 1991 F	422	-2.13 (10.3)	387	1.23 (10.4)		1.0 %	-3.36 [-4.79, -1.93]
Tromso 1991 M	525	-4 (10.6)	535	-3.6 (10.5)		1.3 %	-0.40 [-1.67, 0.87]
WHLP 1998	253	-2.2 (10.48)	267	-0.09 (6.92)		0.9 %	-2.11 [-3.65, -0.57]
Subtotal (95% CI)	**7837**		**7807**			**22.7 %**	**-3.70 [-4.01, -3.40]**
Heterogeneity: Chi² = 141.14, df = 9 (P<0.00001); I² =94%							
Test for overall effect: Z = 23.73 (P < 0.00001)							
3 Unclear allocation concealment							
Abingdon 1990	167	-4.61 (9.29)	168	-2.9 (9.98)		0.5 %	-1.71 [-3.77, 0.35]
Applegate 1992	21	-6.8 (1.7)	26	-1.9 (3.6)		0.9 %	-4.90 [-6.46, -3.34]
Blumenthal 2000	46	-5.6 (7.56)	22	-1.4 (7.56)		0.1 %	-4.20 [-8.04, -0.36]
Change of Heart 1999	165	0.7 (15.4)	338	1 (9.43)		0.3 %	-0.30 [-2.86, 2.26]
Family Heart 1994 M	1767	-3.5 (11.43)	2174	0 (11.43)		4.1 %	-3.50 [-4.22, -2.78]
Family Heart 1994 F	1217	-3 (11.33)	1402	0 (11.33)		2.8 %	-3.00 [-3.87, -2.13]
FARIS 1997 F	315	-1.1 (9.95)	343	-0.3 (9.95)		0.9 %	-0.80 [-2.32, 0.72]
FARIS 1997 M	219	-1 (9.95)	223	1 (9.95)		0.6 %	-2.00 [-3.86, -0.14]
Finnish men 1985	575	-8 (10)	580	-3 (10)		1.6 %	-5.00 [-6.15, -3.85]
Given 1984	62	-6.4 (6.99)	24	-2.42 (4.9)		0.3 %	-3.98 [-6.60, -1.36]
Gothenberg Study 1986	1464	-1 (10)	1404	0 (10)		4.0 %	-1.00 [-1.73, -0.27]

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Favours treatment Favours control

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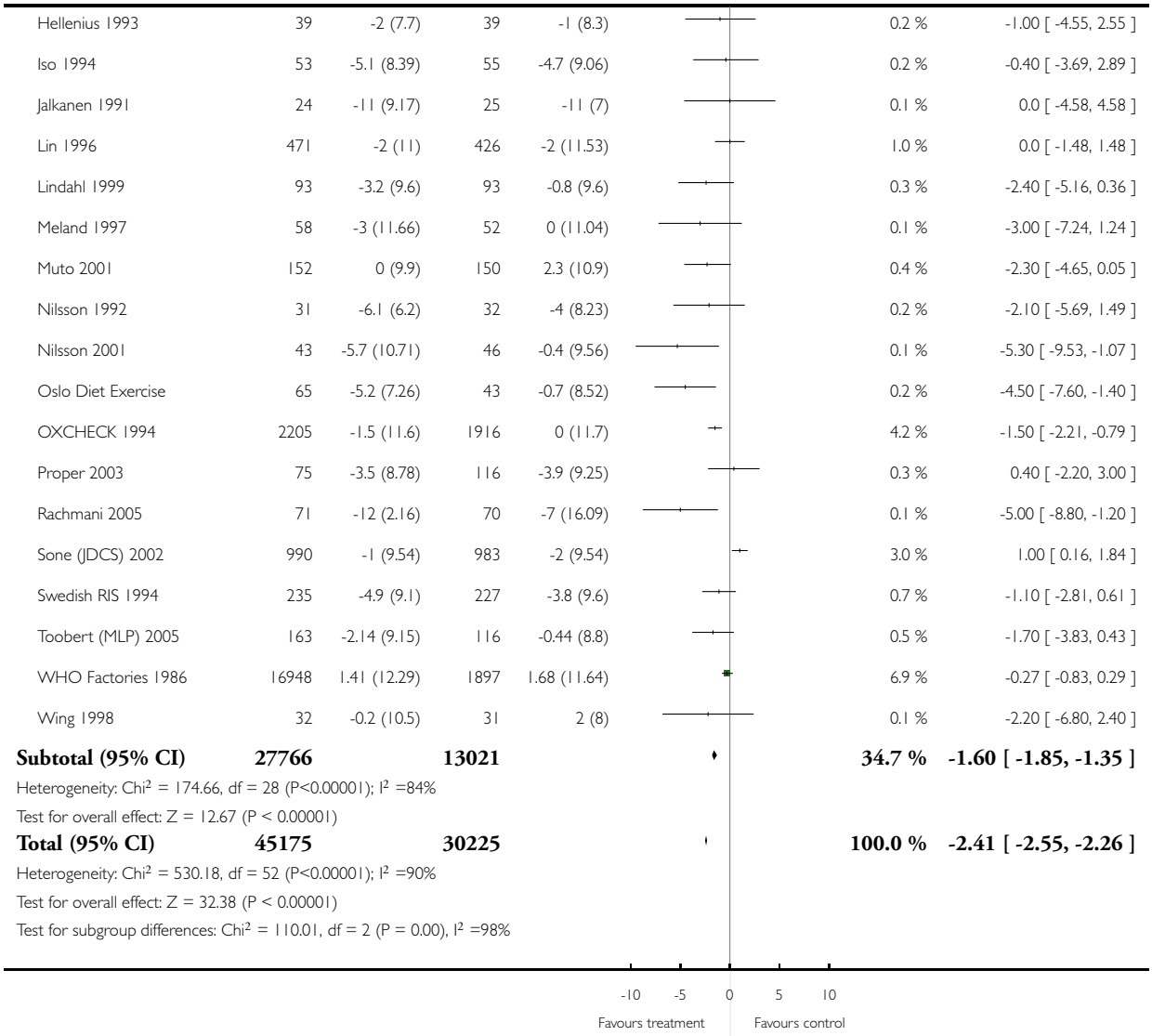
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Hellenius 1993	39	-2 (7.7)	39	-1 (8.3)		0.2 %	-1.00 [-4.55, 2.55]
Iso 1994	53	-5.1 (8.39)	55	-4.7 (9.06)		0.2 %	-0.40 [-3.69, 2.89]
Jalkanen 1991	24	-11 (9.17)	25	-11 (7)		0.1 %	0.0 [-4.58, 4.58]
Lin 1996	471	-2 (11)	426	-2 (11.53)		1.0 %	0.0 [-1.48, 1.48]
Lindahl 1999	93	-3.2 (9.6)	93	-0.8 (9.6)		0.3 %	-2.40 [-5.16, 0.36]
Meland 1997	58	-3 (11.66)	52	0 (11.04)		0.1 %	-3.00 [-7.24, 1.24]
Muto 2001	152	0 (9.9)	150	2.3 (10.9)		0.4 %	-2.30 [-4.65, 0.05]
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)		0.1 %	-5.30 [-9.53, -1.07]
Oslo Diet Exercise	65	-5.2 (7.26)	43	-0.7 (8.52)		0.2 %	-4.50 [-7.60, -1.40]
OXCHECK 1994	2205	-1.5 (11.6)	1916	0 (11.7)		4.2 %	-1.50 [-2.21, -0.79]
Proper 2003	75	-3.5 (8.78)	116	-3.9 (9.25)		0.3 %	0.40 [-2.20, 3.00]
Rachmani 2005	71	-12 (2.16)	70	-7 (16.09)		0.1 %	-5.00 [-8.80, -1.20]
Sone (JDCS) 2002	990	-1 (9.54)	983	-2 (9.54)		3.0 %	1.00 [0.16, 1.84]
Swedish RIS 1994	235	-4.9 (9.1)	227	-3.8 (9.6)		0.7 %	-1.10 [-2.81, 0.61]
Toobert (MLP) 2005	163	-2.14 (9.15)	116	-0.44 (8.8)		0.5 %	-1.70 [-3.83, 0.43]
WHO Factories 1986	16948	1.41 (12.29)	1897	1.68 (11.64)		6.9 %	-0.27 [-0.83, 0.29]
Wing 1998	32	-0.2 (10.5)	31	2 (8)		0.1 %	-2.20 [-6.80, 2.40]
Subtotal (95% CI)	**27766**		**13021**			**34.7 %**	**-1.60 [-1.85, -1.35]**
Heterogeneity: Chi² = 174.66, df = 28 (P<0.00001); I² =84%							
Test for overall effect: Z = 12.67 (P < 0.00001)							
Total (95% CI)	**45175**		**30225**			**100.0 %**	**-2.41 [-2.55, -2.26]**
Heterogeneity: Chi² = 530.18, df = 52 (P<0.00001); I² =90%							
Test for overall effect: Z = 32.38 (P < 0.00001)							
Test for subgroup differences: Chi² = 110.01, df = 2 (P = 0.00), I² =98%							



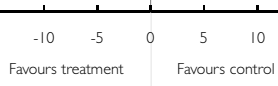
Analysis 1.45. Comparison 1 Multiple risk factor intervention versus control, Outcome 45 Diastolic blood pressure (by co-morbidity).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 45 Diastolic blood pressure (by co-morbidity)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 No co-morbidity							
Abingdon 1990	167	-4.61 (9.29)	168	-2.9 (9.98)		0.5 %	-1.71 [-3.77, 0.35]
Aldana (CHIP) 2005	64	-6.5 (8.76)	79	-3.8 (9.03)		0.2 %	-2.70 [-5.63, 0.23]
CELL Study 1995	292	-0.1 (8.3)	310	0 (9.1)		1.1 %	-0.10 [-1.49, 1.29]
Change of Heart 1999	165	0.7 (15.4)	338	1 (9.43)		0.3 %	-0.30 [-2.86, 2.26]
Esposito 2004	55	-4 (3.65)	55	0 (4.31)		1.0 %	-4.00 [-5.49, -2.51]
Family Heart 1994 M	1767	-3.5 (11.43)	2174	0 (11.43)		4.1 %	-3.50 [-4.22, -2.78]
Family Heart 1994 F	1217	-3 (11.33)	1402	0 (11.33)		2.8 %	-3.00 [-3.87, -2.13]
FARIS 1997 F	315	-1.1 (9.95)	343	-0.3 (9.95)		0.9 %	-0.80 [-2.32, 0.72]
FARIS 1997 M	219	-1 (9.95)	223	1 (9.95)		0.6 %	-2.00 [-3.86, -0.14]
Finnish DPS 2001	256	-5 (9)	250	-3 (9)		0.9 %	-2.00 [-3.57, -0.43]
Finnish men 1985	575	-8 (10)	580	-3 (10)		1.6 %	-5.00 [-6.15, -3.85]
Gothenberg Study 1986	1464	-1 (10)	1404	0 (10)		4.0 %	-1.00 [-1.73, -0.27]
Hellenius 1993	39	-2 (7.7)	39	-1 (8.3)		0.2 %	-1.00 [-4.55, 2.55]
Lindahl 1999	93	-3.2 (9.6)	93	-0.8 (9.6)		0.3 %	-2.40 [-5.16, 0.36]
MRFIT Study 1982	5754	-10.2 (7.88)	5638	-7.1 (9.22)		21.4 %	-3.10 [-3.42, -2.78]
Muto 2001	152	0 (9.9)	150	2.3 (10.9)		0.4 %	-2.30 [-4.65, 0.05]
Nilsson 2001	43	-5.7 (10.71)	46	-0.4 (9.56)		0.1 %	-5.30 [-9.53, -1.07]
Oldroyd 2001	35	-2.9 (9.9)	32	1.9 (10)		0.1 %	-4.80 [-9.57, -0.03]
OXCHECK 1994	2205	-1.5 (11.6)	1916	0 (11.7)		4.2 %	-1.50 [-2.21, -0.79]
Proper 2003	75	-3.5 (8.78)	116	-3.9 (9.25)		0.3 %	0.40 [-2.20, 3.00]
Sartorelli 2005	51	-1.3 (8.9)	53	3.5 (7.4)		0.2 %	-4.80 [-7.95, -1.65]
Stefanick 1998 F	43	-2.7 (4.6)	45	-0.6 (5.9)		0.4 %	-2.10 [-4.30, 0.10]
Stefanick 1998 M	48	-3 (6.6)	46	1.8 (6.1)		0.3 %	-4.80 [-7.37, -2.23]
Tromso 1991 F	422	-2.13 (10.3)	387	1.23 (10.4)		1.0 %	-3.36 [-4.79, -1.93]



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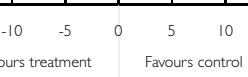
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Tromso 1991 M	525	-4 (10.6)	535	-3.6 (10.5)		1.3 %	-0.40 [-1.67, 0.87]
WHLP 1998	253	-2.2 (10.48)	267	-0.09 (6.92)		0.9 %	-2.11 [-3.65, -0.57]
WHO Factories 1986	16948	1.41 (12.29)	1897	1.68 (11.64)		6.9 %	-0.27 [-0.83, 0.29]
Wing 1998	32	-0.2 (10.5)	31	2 (8)		0.1 %	-2.20 [-6.80, 2.40]
Subtotal (95% CI)	**33274**		**18617**			**56.2 %**	**-2.33 [-2.52, -2.13]**
Heterogeneity: Chi² = 172.99, df = 27 (P<0.00001); I² =84%							
Test for overall effect: Z = 23.47 (P < 0.00001)							
2 Co-morbidity (hypertension or diabetes)							
Aberg 1989 F	114	1.3 (9.11)	115	0.8 (8.46)		0.4 %	0.50 [-1.78, 2.78]
Aberg 1989 M	79	2 (7.81)	80	1.6 (7.77)		0.4 %	0.40 [-2.02, 2.82]
ADAPT 2005	123	0 (8.49)	118	1 (8.31)		0.5 %	-1.00 [-3.12, 1.12]
Applegate 1992	21	-6.8 (1.7)	26	-1.9 (3.6)		0.9 %	-4.90 [-6.46, -3.34]
Blumenthal 2000	46	-5.6 (7.56)	22	-1.4 (7.56)		0.1 %	-4.20 [-8.04, -0.36]
Cakir 2006	30	-6.9 (5.3)	30	1.6 (4.6)		0.3 %	-8.50 [-11.01, -5.99]
Garcia-Pena 2001	345	-3.7 (9.5)	338	0 (9.85)		1.0 %	-3.70 [-5.15, -2.25]
Given 1984	62	-6.4 (6.99)	24	-2.42 (4.9)		0.3 %	-3.98 [-6.60, -1.36]
HDFP trial 1970	5485	-17 (10)	5455	-12.1 (10)		15.1 %	-4.90 [-5.27, -4.53]
Iso 1994	53	-5.1 (8.39)	55	-4.7 (9.06)		0.2 %	-0.40 [-3.69, 2.89]
Jalkanen 1991	24	-11 (9.17)	25	-11 (7)		0.1 %	0.0 [-4.58, 4.58]
Kastarinen 2002	360	-4.3 (9)	355	-3.2 (8)		1.4 %	-1.10 [-2.35, 0.15]
Lin 1996	471	-2 (11)	426	-2 (11.53)		1.0 %	0.0 [-1.48, 1.48]
Look AHEAD 2003	2496	-3 (7.07)	2463	-1.8 (7.02)		13.8 %	-1.20 [-1.59, -0.81]
Mattila 2003	331	-1.6 (6.96)	309	-0.1 (7.17)		1.8 %	-1.50 [-2.60, -0.40]
Meland 1997	58	-3 (11.66)	52	0 (11.04)		0.1 %	-3.00 [-7.24, 1.24]
Nilsson 1992	31	-6.1 (6.2)	32	-4 (8.23)		0.2 %	-2.10 [-5.69, 1.49]
Oslo Diet Exercise	65	-5.2 (7.26)	43	-0.7 (8.52)		0.2 %	-4.50 [-7.60, -1.40]
Perez-Stable 1995 no prop	72	-5 (9.09)	72	-5.8 (9.09)		0.2 %	0.80 [-2.17, 3.77]
Perez-Stable 1995 prop	74	-8.2 (9.66)	73	-8.5 (9.15)		0.2 %	0.30 [-2.74, 3.34]
Rachmani 2005	71	-12 (2.16)	70	-7 (16.09)		0.1 %	-5.00 [-8.80, -1.20]
Sone (JDCS) 2002	990	-1 (9.54)	983	-2 (9.54)		3.0 %	1.00 [0.16, 1.84]
Stamler 1989	102	-1.3 (4.7)	99	-0.1 (4.9)		1.2 %	-1.20 [-2.53, 0.13]
Swedish RIS 1994	235	-4.9 (9.1)	227	-3.8 (9.6)		0.7 %	-1.10 [-2.81, 0.61]
Toobert (MLP) 2005	163	-2.14 (9.15)	116	-0.44 (8.8)		0.5 %	-1.70 [-3.83, 0.43]



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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Subtotal (95% CI)	**11901**		**11608**			**43.8 %**	**-2.51 [-2.73, -2.29]**
Heterogeneity: Chi^2 = 355.70, df = 24 (P<0.00001); I^2 =93%							
Test for overall effect: Z = 22.35 (P < 0.00001)							
Total (95% CI)	**45175**		**30225**			**100.0 %**	**-2.41 [-2.55, -2.26]**
Heterogeneity: Chi^2 = 530.18, df = 52 (P<0.00001); I^2 =90%							
Test for overall effect: Z = 32.38 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 1.49, df = 1 (P = 0.22), I^2 =33%							

Analysis 1.46. Comparison 1 Multiple risk factor intervention versus control, Outcome 46 Diastolic blood pressure (by drug treatment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 46 Diastolic blood pressure (by drug treatment)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 No drug treatment							
Abingdon 1990	167	-4.61 (9.29)	168	-2.9 (9.98)		0.5 %	-1.71 [-3.77, 0.35]
Aldana (CHIP) 2005	64	-6.5 (8.76)	79	-3.8 (9.03)		0.2 %	-2.70 [-5.63, 0.23]
Applegate 1992	21	-6.8 (1.7)	26	-1.9 (3.6)		0.9 %	-4.90 [-6.46, -3.34]
Blumenthal 2000	46	-5.6 (7.56)	22	-1.4 (7.56)		0.1 %	-4.20 [-8.04, -0.36]
Change of Heart 1999	165	0.7 (15.4)	338	1 (9.43)		0.3 %	-0.30 [-2.86, 2.26]
Esposito 2004	55	-4 (3.65)	55	0 (4.31)		1.0 %	-4.00 [-5.49, -2.51]
Family Heart 1994 M	1767	-3.5 (11.43)	2174	0 (11.43)		4.1 %	-3.50 [-4.22, -2.78]
Family Heart 1994 F	1217	-3 (11.33)	1402	0 (11.33)		2.8 %	-3.00 [-3.87, -2.13]
FARIS 1997 F	315	-1.1 (9.95)	343	-0.3 (9.95)		0.9 %	-0.80 [-2.32, 0.72]
FARIS 1997 M	219	-1 (9.95)	223	1 (9.95)		0.6 %	-2.00 [-3.86, -0.14]
Finnish DPS 2001	256	-5 (9)	250	-3 (9)		0.9 %	-2.00 [-3.57, -0.43]

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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Hellenius 1993	39	-2 (7.7)	39	-1 (8.3)		0.2 %	-1.00 [-4.55, 2.55]
Iso 1994	53	-5.1 (8.39)	55	-4.7 (9.06)		0.2 %	-0.40 [-3.69, 2.89]
Lindahl 1999	93	-3.2 (9.6)	93	-0.8 (9.6)		0.3 %	-2.40 [-5.16, 0.36]
Muto 2001	152	0 (9.9)	150	2.3 (10.9)		0.4 %	-2.30 [-4.65, 0.05]
Nilsson 2001	43	-5.7 (10.71)	46	-0.4 (9.56)		0.1 %	-5.30 [-9.53, -1.07]
Oldroyd 2001	35	-2.9 (9.9)	32	1.9 (10)		0.1 %	-4.80 [-9.57, -0.03]
Perez-Stable 1995 no prop	72	-5 (9.09)	72	-5.8 (9.09)		0.2 %	0.80 [-2.17, 3.77]
Proper 2003	75	-3.5 (8.78)	116	-3.9 (9.25)		0.3 %	0.40 [-2.20, 3.00]
Sartorelli 2005	51	-1.3 (8.9)	53	3.5 (7.4)		0.2 %	-4.80 [-7.95, -1.65]
Sone (JDCS) 2002	990	-1 (9.54)	983	-2 (9.54)		3.0 %	1.00 [0.16, 1.84]
Stamler 1989	102	-1.3 (4.7)	99	-0.1 (4.9)		1.2 %	-1.20 [-2.53, 0.13]
Stefanick 1998 F	43	-2.7 (4.6)	45	-0.6 (5.9)		0.4 %	-2.10 [-4.30, 0.10]
Stefanick 1998 M	48	-3 (6.6)	46	1.8 (6.1)		0.3 %	-4.80 [-7.37, -2.23]
Tromso 1991 F	422	-2.13 (10.3)	387	1.23 (10.4)		1.0 %	-3.36 [-4.79, -1.93]
Tromso 1991 M	525	-4 (10.6)	535	-3.6 (10.5)		1.3 %	-0.40 [-1.67, 0.87]
WHLP 1998	253	-2.2 (10.48)	267	-0.09 (6.92)		0.9 %	-2.11 [-3.65, -0.57]
Wing 1998	32	-0.2 (10.5)	31	2 (8)		0.1 %	-2.20 [-6.80, 2.40]
Subtotal (95% CI)	**7320**		**8129**		♦	**22.7 %**	**-2.09 [-2.40, -1.79]**
Heterogeneity: Chi^2 = 126.35, df = 27 (P<0.00001); I^2 =79%							
Test for overall effect: Z = 13.41 (P < 0.00001)							
2 Antihypertensives OR lipid-lowering drugs							
Aberg 1989 F	114	1.3 (9.11)	115	0.8 (8.46)		0.4 %	0.50 [-1.78, 2.78]
Aberg 1989 M	79	2 (7.81)	80	1.6 (7.77)		0.4 %	0.40 [-2.02, 2.82]
ADAPT 2005	123	0 (8.49)	118	1 (8.31)		0.5 %	-1.00 [-3.12, 1.12]
Cakir 2006	30	-6.9 (5.3)	30	1.6 (4.6)		0.3 %	-8.50 [-11.01, -5.99]
Garcia-Pena 2001	345	-3.7 (9.5)	338	0 (9.85)		1.0 %	-3.70 [-5.15, -2.25]
Given 1984	62	-6.4 (6.99)	24	-2.42 (4.9)		0.3 %	-3.98 [-6.60, -1.36]
HDFP trial 1970	5485	-17 (10)	5455	-12.1 (10)		15.1 %	-4.90 [-5.27, -4.53]
Jalkanen 1991	24	-11 (9.17)	25	-11 (7)		0.1 %	0.0 [-4.58, 4.58]
Kastarinen 2002	360	-4.3 (9)	355	-3.2 (8)		1.4 %	-1.10 [-2.35, 0.15]
Lin 1996	471	-2 (11)	426	-2 (11.53)		1.0 %	0.0 [-1.48, 1.48]
Mattila 2003	331	-1.6 (6.96)	309	-0.1 (7.17)		1.8 %	-1.50 [-2.60, -0.40]
Meland 1997	58	-3 (11.66)	52	0 (11.04)		0.1 %	-3.00 [-7.24, 1.24]

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Favours treatment Favours control

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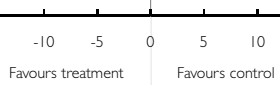
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
MRFIT Study 1982	5754	-10.2 (7.88)	5638	-7.1 (9.22)		21.4 %	-3.10 [-3.42, -2.78]
Nilsson 1992	31	-6.1 (6.2)	32	-4 (8.23)		0.2 %	-2.10 [-5.69, 1.49]
Oslo Diet Exercise	65	-5.2 (7.26)	43	-0.7 (8.52)		0.2 %	-4.50 [-7.60, -1.40]
Perez-Stable 1995 prop	74	-8.2 (9.66)	73	-8.5 (9.15)		0.2 %	0.30 [-2.74, 3.34]
Rachmani 2005	71	-12 (2.16)	70	-7 (16.09)		0.1 %	-5.00 [-8.80, -1.20]
WHO Factories 1986	16948	1.41 (12.29)	1897	1.68 (11.64)		6.9 %	-0.27 [-0.83, 0.29]
Subtotal (95% CI)	**30425**		**15080**			**51.4 %**	**-3.05 [-3.25, -2.85]**
Heterogeneity: Chi² = 271.87, df = 17 (P<0.00001); I² =94%							
Test for overall effect: Z = 29.40 (P < 0.00001)							
3 Antihypertensives AND lipid-lowering drugs							
CELL Study 1995	292	-0.1 (8.3)	310	0 (9.1)		1.1 %	-0.10 [-1.49, 1.29]
Finnish men 1985	575	-8 (10)	580	-3 (10)		1.6 %	-5.00 [-6.15, -3.85]
Gothenberg Study 1986	1464	-1 (10)	1404	0 (10)		4.0 %	-1.00 [-1.73, -0.27]
Look AHEAD 2003	2496	-3 (7.07)	2463	-1.8 (7.02)		13.8 %	-1.20 [-1.59, -0.81]
OXCHECK 1994	2205	-1.5 (11.6)	1916	0 (11.7)		4.2 %	-1.50 [-2.21, -0.79]
Swedish RIS 1994	235	-4.9 (9.1)	227	-3.8 (9.6)		0.7 %	-1.10 [-2.81, 0.61]
Toobert (MLP) 2005	163	-2.14 (9.15)	116	-0.44 (8.8)		0.5 %	-1.70 [-3.83, 0.43]
Subtotal (95% CI)	**7430**		**7016**			**25.9 %**	**-1.41 [-1.70, -1.13]**
Heterogeneity: Chi² = 43.19, df = 6 (P<0.00001); I² =86%							
Test for overall effect: Z = 9.65 (P < 0.00001)							
Total (95% CI)	**45175**		**30225**			**100.0 %**	**-2.41 [-2.55, -2.26]**
Heterogeneity: Chi² = 530.18, df = 52 (P<0.00001); I² =90%							
Test for overall effect: Z = 32.38 (P < 0.00001)							
Test for subgroup differences: Chi² = 88.77, df = 2 (P = 0.00), I² =98%							



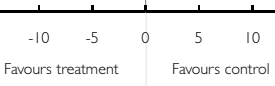
Analysis 1.47. Comparison 1 Multiple risk factor intervention versus control, Outcome 47 Diastolic blood pressure (by era).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 47 Diastolic blood pressure (by era)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Low rate of CVD							
Aberg 1989 F	114	1.3 (9.11)	115	0.8 (8.46)		0.4 %	0.50 [-1.78, 2.78]
Aberg 1989 M	79	2 (7.81)	80	1.6 (7.77)		0.4 %	0.40 [-2.02, 2.82]
Abingdon 1990	167	-4.61 (9.29)	168	-2.9 (9.98)		0.5 %	-1.71 [-3.77, 0.35]
ADAPT 2005	123	0 (8.49)	118	1 (8.31)		0.5 %	-1.00 [-3.12, 1.12]
Aldana (CHIP) 2005	64	-6.5 (8.76)	79	-3.8 (9.03)		0.2 %	-2.70 [-5.63, 0.23]
Applegate 1992	21	-6.8 (1.7)	26	-1.9 (3.6)		0.9 %	-4.90 [-6.46, -3.34]
Blumenthal 2000	46	-5.6 (7.56)	22	-1.4 (7.56)		0.1 %	-4.20 [-8.04, -0.36]
Cakir 2006	30	-6.9 (5.3)	30	1.6 (4.6)		0.3 %	-8.50 [-11.01, -5.99]
CELL Study 1995	292	-0.1 (8.3)	310	0 (9.1)		1.1 %	-0.10 [-1.49, 1.29]
Change of Heart 1999	165	0.7 (15.4)	338	1 (9.43)		0.3 %	-0.30 [-2.86, 2.26]
Esposito 2004	55	-4 (3.65)	55	0 (4.31)		1.0 %	-4.00 [-5.49, -2.51]
Family Heart 1994 M	1767	-3.5 (11.43)	2174	0 (11.43)		4.1 %	-3.50 [-4.22, -2.78]
Family Heart 1994 F	1217	-3 (11.33)	1402	0 (11.33)		2.8 %	-3.00 [-3.87, -2.13]
FARIS 1997 F	315	-1.1 (9.95)	343	-0.3 (9.95)		0.9 %	-0.80 [-2.32, 0.72]
FARIS 1997 M	219	-1 (9.95)	223	1 (9.95)		0.6 %	-2.00 [-3.86, -0.14]
Finnish DPS 2001	256	-5 (9)	250	-3 (9)		0.9 %	-2.00 [-3.57, -0.43]
Garcia-Pena 2001	345	-3.7 (9.5)	338	0 (9.85)		1.0 %	-3.70 [-5.15, -2.25]
Given 1984	62	-6.4 (6.99)	24	-2.42 (4.9)		0.3 %	-3.98 [-6.60, -1.36]
Hellenius 1993	39	-2 (7.7)	39	-1 (8.3)		0.2 %	-1.00 [-4.55, 2.55]
Iso 1994	53	-5.1 (8.39)	55	-4.7 (9.06)		0.2 %	-0.40 [-3.69, 2.89]
Jalkanen 1991	24	-11 (9.17)	25	-11 (7)		0.1 %	0.0 [-4.58, 4.58]
Kastarinen 2002	360	-4.3 (9)	355	-3.2 (8)		1.4 %	-1.10 [-2.35, 0.15]
Lin 1996	471	-2 (11)	426	-2 (11.53)		1.0 %	0.0 [-1.48, 1.48]
Lindahl 1999	93	-3.2 (9.6)	93	-0.8 (9.6)		0.3 %	-2.40 [-5.16, 0.36]



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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Look AHEAD 2003	2496	-3 (7.07)	2463	-1.8 (7.02)		13.8 %	-1.20 [-1.59, -0.81]
Mattila 2003	331	-1.6 (6.96)	309	-0.1 (7.17)		1.8 %	-1.50 [-2.60, -0.40]
Meland 1997	58	-3 (11.66)	52	0 (11.04)		0.1 %	-3.00 [-7.24, 1.24]
Muto 2001	152	0 (9.9)	150	2.3 (10.9)		0.4 %	-2.30 [-4.65, 0.05]
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)		0.1 %	-5.30 [-9.53, -1.07]
Oldroyd 2001	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)		0.2 %	-4.50 [-7.60, -1.40]
OXCHECK 1994	2205	-1.5 (11.6)	1916	0 (11.7)		4.2 %	-1.50 [-2.21, -0.79]
Perez-Stable 1995 no prop	72	-5 (9.09)	72	-5.8 (9.09)		0.2 %	0.80 [-2.17, 3.77]
Perez-Stable 1995 prop	74	-8.2 (9.66)	73	-8.5 (9.15)		0.2 %	0.30 [-2.74, 3.34]
Proper 2003	75	-3.5 (8.78)	116	-3.9 (9.25)		0.3 %	0.40 [-2.20, 3.00]
Rachmani 2005	71	-12 (2.16)	70	-7 (16.09)		0.1 %	-5.00 [-8.80, -1.20]
Sartorelli 2005	51	-1.3 (8.9)	53	3.5 (7.4)		0.2 %	-4.80 [-7.95, -1.65]
Sone (JDCS) 2002	990	-1 (9.54)	983	-2 (9.54)		3.0 %	1.00 [0.16, 1.84]
Stamler 1989	102	-1.3 (4.7)	99	-0.1 (4.9)		1.2 %	-1.20 [-2.53, 0.13]
Stefanick 1998 F	43	-2.7 (4.6)	45	-0.6 (5.9)		0.4 %	-2.10 [-4.30, 0.10]
Stefanick 1998 M	48	-3 (6.6)	46	1.8 (6.1)		0.3 %	-4.80 [-7.37, -2.23]
Swedish RIS 1994	235	-4.9 (9.1)	227	-3.8 (9.6)		0.7 %	-1.10 [-2.81, 0.61]
Toobert (MLP) 2005	163	-2.14 (9.15)	116	-0.44 (8.8)		0.5 %	-1.70 [-3.83, 0.43]
Tromso 1991 F	422	-2.13 (10.3)	387	1.23 (10.4)		1.0 %	-3.36 [-4.79, -1.93]
Tromso 1991 M	525	-4 (10.6)	535	-3.6 (10.5)		1.3 %	-0.40 [-1.67, 0.87]
WHLP 1998	253	-2.2 (10.48)	267	-0.09 (6.92)		0.9 %	-2.11 [-3.65, -0.57]
Wing 1998	32	-0.2 (10.5)	31	2 (8)		0.1 %	-2.20 [-6.80, 2.40]
Subtotal (95% CI)	**14949**		**15251**			**51.0 %**	**-1.70 [-1.90, -1.49]**
Heterogeneity: Chi^2 = 204.77, df = 47 (P<0.00001); I^2 =77%							
Test for overall effect: Z = 16.30 (P < 0.00001)							
2 High Rate of CVD							
Finnish men 1985	575	-8 (10)	580	-3 (10)		1.6 %	-5.00 [-6.15, -3.85]
Gothenberg Study 1986	1464	-1 (10)	1404	0 (10)		4.0 %	-1.00 [-1.73, -0.27]
HDFP trial 1970	5485	-17 (10)	5455	-12.1 (10)		15.1 %	-4.90 [-5.27, -4.53]
MRFIT Study 1982	5754	-10.2 (7.88)	5638	-7.1 (9.22)		21.4 %	-3.10 [-3.42, -2.78]
WHO Factories 1986	16948	1.41 (12.29)	1897	1.68 (11.64)		6.9 %	-0.27 [-0.83, 0.29]

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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Subtotal (95% CI)	**30226**		**14974**			**49.0 %**	**-3.15 [-3.36, -2.94]**
Heterogeneity: Chi² = 230.11, df = 4 (P<0.00001); I² =98%							
Test for overall effect: Z = 29.64 (P < 0.00001)							
Total (95% CI)	**45175**		**30225**			**100.0 %**	**-2.41 [-2.55, -2.26]**
Heterogeneity: Chi² = 530.18, df = 52 (P<0.00001); I² =90%							
Test for overall effect: Z = 32.38 (P < 0.00001)							
Test for subgroup differences: Chi² = 95.29, df = 1 (P = 0.0), I² =99%							

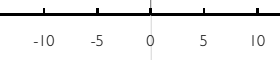
Analysis 1.48. Comparison 1 Multiple risk factor intervention versus control, Outcome 48 Diastolic blood pressure (by age of study).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 48 Diastolic blood pressure (by age of study)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Study before 2000							
Aberg 1989 F	114	1.3 (9.11)	115	0.8 (8.46)		0.4 %	0.50 [-1.78, 2.78]
Aberg 1989 M	79	2 (7.81)	80	1.6 (7.77)		0.4 %	0.40 [-2.02, 2.82]
Abingdon 1990	167	-4.61 (9.29)	168	-2.9 (9.98)		0.5 %	-1.71 [-3.77, 0.35]
Applegate 1992	21	-6.8 (1.7)	26	-1.9 (3.6)		0.9 %	-4.90 [-6.46, -3.34]
Blumenthal 2000	46	-5.6 (7.56)	22	-1.4 (7.56)		0.1 %	-4.20 [-8.04, -0.36]
CELL Study 1995	292	-0.1 (8.3)	310	0 (9.1)		1.1 %	-0.10 [-1.49, 1.29]
Change of Heart 1999	165	0.7 (15.4)	338	1 (9.43)		0.3 %	-0.30 [-2.86, 2.26]
Family Heart 1994 M	1767	-3.5 (11.43)	2174	0 (11.43)		4.1 %	-3.50 [-4.22, -2.78]
Family Heart 1994 F	1217	-3 (11.33)	1402	0 (11.33)		2.8 %	-3.00 [-3.87, -2.13]
FARIS 1997 F	315	-1.1 (9.95)	343	-0.3 (9.95)		0.9 %	-0.80 [-2.32, 0.72]
FARIS 1997 M	219	-1 (9.95)	223	1 (9.95)		0.6 %	-2.00 [-3.86, -0.14]



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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Finnish men 1985	575	-8 (10)	580	-3 (10)		1.6 %	-5.00 [-6.15, -3.85]
Given 1984	62	-6.4 (6.99)	24	-2.42 (4.9)		0.3 %	-3.98 [-6.60, -1.36]
Gothenberg Study 1986	1464	-1 (10)	1404	0 (10)		4.0 %	-1.00 [-1.73, -0.27]
HDFP trial 1970	5485	-17 (10)	5455	-12.1 (10)		15.1 %	-4.90 [-5.27, -4.53]
Hellenius 1993	39	-2 (7.7)	39	-1 (8.3)		0.2 %	-1.00 [-4.55, 2.55]
Iso 1994	53	-5.1 (8.39)	55	-4.7 (9.06)		0.2 %	-0.40 [-3.69, 2.89]
Jalkanen 1991	24	-11 (9.17)	25	-11 (7)		0.1 %	0.0 [-4.58, 4.58]
Lin 1996	471	-2 (11)	426	-2 (11.53)		1.0 %	0.0 [-1.48, 1.48]
Lindahl 1999	93	-3.2 (9.6)	93	-0.8 (9.6)		0.3 %	-2.40 [-5.16, 0.36]
Meland 1997	58	-3 (11.66)	52	0 (11.04)		0.1 %	-3.00 [-7.24, 1.24]
MRFIT Study 1982	5754	-10.2 (7.88)	5638	-7.1 (9.22)		21.4 %	-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]
Oslo Diet Exercise	65	-5.2 (7.26)	43	-0.7 (8.52)		0.2 %	-4.50 [-7.60, -1.40]
OXCHECK 1994	2205	-1.5 (11.6)	1916	0 (11.7)		4.2 %	-1.50 [-2.21, -0.79]
Perez-Stable 1995 no prop	72	-5 (9.09)	72	-5.8 (9.09)		0.2 %	0.80 [-2.17, 3.77]
Perez-Stable 1995 prop	74	-8.2 (9.66)	73	-8.5 (9.15)		0.2 %	0.30 [-2.74, 3.34]
Stamler 1989	102	-1.3 (4.7)	99	-0.1 (4.9)		1.2 %	-1.20 [-2.53, 0.13]
Stefanick 1998 F	43	-2.7 (4.6)	45	-0.6 (5.9)		0.4 %	-2.10 [-4.30, 0.10]
Stefanick 1998 M	48	-3 (6.6)	46	1.8 (6.1)		0.3 %	-4.80 [-7.37, -2.23]
Swedish RIS 1994	235	-4.9 (9.1)	227	-3.8 (9.6)		0.7 %	-1.10 [-2.81, 0.61]
Tromso 1991 F	422	-2.13 (10.3)	387	1.23 (10.4)		1.0 %	-3.36 [-4.79, -1.93]
Tromso 1991 M	525	-4 (10.6)	535	-3.6 (10.5)		1.3 %	-0.40 [-1.67, 0.87]
WHLP 1998	253	-2.2 (10.48)	267	-0.09 (6.92)		0.9 %	-2.11 [-3.65, -0.57]
WHO Factories 1986	16948	1.41 (12.29)	1897	1.68 (11.64)		6.9 %	-0.27 [-0.83, 0.29]
Wing 1998	32	-0.2 (10.5)	31	2 (8)		0.1 %	-2.20 [-6.80, 2.40]
Subtotal (95% CI)	**39535**		**24662**			**74.4 %**	**-2.76 [-2.93, -2.59]**
Heterogeneity: Chi² = 363.48, df = 35 (P<0.00001); I² =90%							
Test for overall effect: Z = 32.02 (P < 0.00001)							
2 Study after 2000							
ADAPT 2005	123	0 (8.49)	118	1 (8.31)		0.5 %	-1.00 [-3.12, 1.12]
Aldana (CHIP) 2005	64	-6.5 (8.76)	79	-3.8 (9.03)		0.2 %	-2.70 [-5.63, 0.23]
Cakir 2006	30	-6.9 (5.3)	30	1.6 (4.6)		0.3 %	-8.50 [-11.01, -5.99]
Esposito 2004	55	-4 (3.65)	55	0 (4.31)		1.0 %	-4.00 [-5.49, -2.51]

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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Finnish DPS 2001	256	-5 (9)	250	-3 (9)		0.9 %	-2.00 [-3.57, -0.43]
Garcia-Pena 2001	345	-3.7 (9.5)	338	0 (9.85)		1.0 %	-3.70 [-5.15, -2.25]
Kastarinen 2002	360	-4.3 (9)	355	-3.2 (8)		1.4 %	-1.10 [-2.35, 0.15]
Look AHEAD 2003	2496	-3 (7.07)	2463	-1.8 (7.02)		13.8 %	-1.20 [-1.59, -0.81]
Mattila 2003	331	-1.6 (6.96)	309	-0.1 (7.17)		1.8 %	-1.50 [-2.60, -0.40]
Muto 2001	152	0 (9.9)	150	2.3 (10.9)		0.4 %	-2.30 [-4.65, 0.05]
Nilsson 2001	43	-5.7 (10.71)	46	-0.4 (9.56)		0.1 %	-5.30 [-9.53, -1.07]
Oldroyd 2001	35	-2.9 (9.9)	32	1.9 (10)		0.1 %	-4.80 [-9.57, -0.03]
Proper 2003	75	-3.5 (8.78)	116	-3.9 (9.25)		0.3 %	0.40 [-2.20, 3.00]
Rachmani 2005	71	-12 (2.16)	70	-7 (16.09)		0.1 %	-5.00 [-8.80, -1.20]
Sartorelli 2005	51	-1.3 (8.9)	53	3.5 (7.4)		0.2 %	-4.80 [-7.95, -1.65]
Sone (JDCS) 2002	990	-1 (9.54)	983	-2 (9.54)		3.0 %	1.00 [0.16, 1.84]
Toobert (MLP) 2005	163	-2.14 (9.15)	116	-0.44 (8.8)		0.5 %	-1.70 [-3.83, 0.43]
Subtotal (95% CI)	**5640**		**5563**			**25.6 %**	**-1.38 [-1.67, -1.10]**
Heterogeneity: Chi^2 = 101.53, df = 16 (P<0.00001); I^2 =84%							
Test for overall effect: Z = 9.42 (P < 0.00001)							
Total (95% CI)	**45175**		**30225**			**100.0 %**	**-2.41 [-2.55, -2.26]**
Heterogeneity: Chi^2 = 530.18, df = 52 (P<0.00001); I^2 =90%							
Test for overall effect: Z = 32.38 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 65.17, df = 1 (P = 0.00), I^2 =98%							

Analysis 1.49. Comparison 1 Multiple risk factor intervention versus control, Outcome 49 Blood cholesterol.

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 49 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 1989 F	114	0.4 (1.35)	115	0.3 (1.1)		0.1 %	0.10 [-0.22, 0.42]
Aberg 1989 M	79	0.3 (1.1)	80	0.1 (1.1)		0.1 %	0.20 [-0.14, 0.54]
Abingdon 1990	167	-0.2 (0.89)	166	-0.18 (0.9)		0.3 %	-0.02 [-0.21, 0.17]
ADAPT 2005	123	0 (0.85)	118	1 (0.83)		0.3 %	-1.00 [-1.21, -0.79]
Aldana (CHIP) 2005	64	-0.02 (0.81)	79	0.35 (0.77)		0.2 %	-0.37 [-0.63, -0.11]
Brekke 2005a	25	0.37 (0.73)	19	0.24 (0.58)		0.1 %	0.13 [-0.26, 0.52]
Cakir 2006	30	-0.92 (0.92)	30	0.04 (0.5)		0.1 %	-0.96 [-1.33, -0.59]
CELL Study 1995	292	-0.15 (0.56)	310	0 (0.65)		1.4 %	-0.15 [-0.25, -0.05]
Change of Heart 1999	164	0.31 (0.82)	334	0.33 (1.54)		0.3 %	-0.02 [-0.23, 0.19]
Connell 1995	141	0.13 (0.81)	455	0.08 (0.77)		0.6 %	0.05 [-0.10, 0.20]
Esposito 2004	55	-0.29 (0.75)	55	0.05 (0.78)		0.2 %	-0.34 [-0.63, -0.05]
Family Heart 1994 M	1767	-0.13 (1.16)	2174	0 (1.16)		2.4 %	-0.13 [-0.20, -0.06]
Family Heart 1994 F	1217	-0.09 (1.17)	1402	0 (1.17)		1.6 %	-0.09 [-0.18, 0.00]
FARIS 1997 F	315	-0.13 (0.94)	343	0.01 (0.94)		0.6 %	-0.14 [-0.28, 0.00]
FARIS 1997 M	219	-3 (0.94)	223	0.05 (0.94)		0.4 %	-3.05 [-3.23, -2.87]
Finnish DPS 2001	256	-0.13 (0.73)	250	-0.1 (0.73)		0.8 %	-0.03 [-0.16, 0.10]
Finnish men 1985	575	-0.4 (1)	580	0.05 (0.9)		1.1 %	-0.45 [-0.56, -0.34]
Gothenberg Study 1986	1473	-0.01 (1.1)	1404	0 (1.1)		2.0 %	-0.01 [-0.09, 0.07]
HDFP trial 1970	5485	-0.39 (1)	5455	-0.39 (1)		9.2 %	0.0 [-0.04, 0.04]
Hellenius 1993	39	-0.45 (0.93)	39	-0.13 (0.9)		0.1 %	-0.32 [-0.73, 0.09]
Iso 2002	40	-0.11 (0.83)	43	-0.14 (0.83)		0.1 %	0.03 [-0.33, 0.39]
Jalkanen 1991	24	-0.2 (1)	25	0.2 (1)		0.0 %	-0.40 [-0.96, 0.16]
Kastarinen 2002	360	-0.03 (0.91)	355	0.07 (0.93)		0.7 %	-0.10 [-0.23, 0.03]
Lindahl 1999	93	-0.21 (1.35)	93	-0.06 (0.96)		0.1 %	-0.15 [-0.49, 0.19]
Mattila 2003	331	0 (0.93)	309	0 (0.45)		1.0 %	0.0 [-0.11, 0.11]
Meland 1997	58	0.1 (1.17)	52	0.3 (1.1)		0.1 %	-0.20 [-0.62, 0.22]

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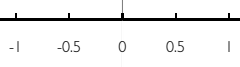
Study or subgroup	Intervention N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
MRFIT Study 1982	5743	-0.43 (0.99)	5607	-0.3 (1.03)		9.3 %	-0.13 [-0.17, -0.09]
Muto 2001	152	-0.17 (0.63)	150	0.12 (0.59)		0.7 %	-0.29 [-0.43, -0.15]
Nilsson 2001	43	-0.1 (0.9)	46	0 (1.05)		0.1 %	-0.10 [-0.51, 0.31]
Okayama 2004	96	-0.7 (0.72)	92	-0.48 (0.69)		0.3 %	-0.22 [-0.42, -0.02]
Oldroyd 2001	35	-0.16 (0.55)	32	-0.18 (0.59)		0.2 %	0.02 [-0.25, 0.29]
Oslo Diet Antismoking	604	-0.92 (0.7)	628	-0.39 (0.7)		2.1 %	-0.53 [-0.61, -0.45]
Oslo Diet Exercise	65	-0.48 (0.89)	43	-0.16 (0.59)		0.2 %	-0.32 [-0.60, -0.04]
OXCHECK 1994	2205	-0.19 (1.1)	1916	0 (1.17)		2.7 %	-0.19 [-0.26, -0.12]
Perez-Stable 1995 no prop	69	-0.42 (1.15)	68	-0.18 (0.98)		0.1 %	-0.24 [-0.60, 0.12]
Perez-Stable 1995 prop	67	-0.32 (0.81)	67	-0.25 (0.86)		0.2 %	-0.07 [-0.35, 0.21]
Proper 2003	75	-0.2 (1)	117	0 (0.9)		0.2 %	-0.20 [-0.48, 0.08]
Sartorelli 2005	51	-0.52 (1.2)	53	-0.28 (0.6)		0.1 %	-0.24 [-0.61, 0.13]
Sone (JDCS) 2002	990	-0.04 (0.84)	983	0.01 (0.89)		2.2 %	-0.05 [-0.13, 0.03]
Stefanick 1998 F	43	-0.46 (0.56)	45	-0.03 (0.51)		0.3 %	-0.43 [-0.65, -0.21]
Stefanick 1998 M	48	-0.54 (0.52)	46	-0.1 (0.56)		0.3 %	-0.44 [-0.66, -0.22]
Swedish RIS 1994	235	-0.78 (1.12)	227	-0.39 (0.92)		0.4 %	-0.39 [-0.58, -0.20]
Take Heart 1995	1057	0.02 (0.2)	920	0.01 (0.18)		45.9 %	0.01 [-0.01, 0.03]
Toobert (MLP) 2005	163	-0.1 (0.95)	116	-0.03 (0.99)		0.2 %	-0.07 [-0.30, 0.16]
Tromso 1991 F	422	0.06 (1.27)	387	0.14 (1.34)		0.4 %	-0.08 [-0.26, 0.10]
Tromso 1991 M	525	-0.41 (1.15)	535	-0.25 (1.2)		0.6 %	-0.16 [-0.30, -0.02]
Uusitupa 1993	38	-0.1 (0.31)	40	0.1 (0.97)		0.1 %	-0.20 [-0.52, 0.12]
WHLP 1998	253	-0.34 (0.61)	267	0.03 (0.21)		2.0 %	-0.37 [-0.45, -0.29]
WHO Factories 1986	16481	0.09 (0.89)	1854	0.08 (0.86)		7.5 %	0.01 [-0.03, 0.05]
Wing 1998	32	0.09 (0.67)	31	0.18 (0.53)		0.1 %	-0.09 [-0.39, 0.21]
Total (95% CI)	**42998**		**28778**			**100.0 %**	**-0.07 [-0.08, -0.06]**

Heterogeneity: Chi^2 = 1659.29, df = 49 (P<0.00001); I^2 =97%

Test for overall effect: Z = 12.57 (P < 0.00001)



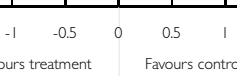
Analysis 1.50. Comparison 1 Multiple risk factor intervention versus control, Outcome 50 Blood cholesterol (individual analysis or cluster).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 50 Blood 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 1999	164	0.31 (0.82)	334	0.33 (1.54)		2.1 %	-0.02 [-0.23, 0.19]
Take Heart 1995	1057	0.02 (0.2)	920	0.01 (0.18)		2.4 %	0.01 [-0.01, 0.03]
Subtotal (95% CI)	**1221**		**1254**			**4.4 %**	**0.01 [-0.01, 0.03]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.08$, df = 1 (P = 0.78); $I^2 = 0.0\%$							
Test for overall effect: Z = 1.15 (P = 0.25)							
2 Individual randomisation							
Aberg 1989 F	114	0.4 (1.35)	115	0.3 (1.1)		1.7 %	0.10 [-0.22, 0.42]
Aberg 1989 M	79	0.3 (1.1)	80	0.1 (1.1)		1.7 %	0.20 [-0.14, 0.54]
Abingdon 1990	167	-0.2 (0.89)	166	-0.18 (0.9)		2.1 %	-0.02 [-0.21, 0.17]
ADAPT 2005	123	0 (0.85)	118	1 (0.83)		2.0 %	-1.00 [-1.21, -0.79]
Aldana (CHIP) 2005	64	-0.02 (0.81)	79	0.35 (0.77)		1.9 %	-0.37 [-0.63, -0.11]
Brekke 2005a	25	0.37 (0.73)	19	0.24 (0.58)		1.5 %	0.13 [-0.26, 0.52]
Cakir 2006	30	-0.92 (0.92)	30	0.04 (0.5)		1.6 %	-0.96 [-1.33, -0.59]
CELL Study 1995	292	-0.15 (0.56)	310	0 (0.65)		2.3 %	-0.15 [-0.25, -0.05]
Esposito 2004	55	-0.29 (0.75)	55	0.05 (0.78)		1.8 %	-0.34 [-0.63, -0.05]
Family Heart 1994 M	1767	-0.13 (1.16)	2174	0 (1.16)		2.3 %	-0.13 [-0.20, -0.06]
Family Heart 1994 F	1217	-0.09 (1.17)	1402	0 (1.17)		2.3 %	-0.09 [-0.18, 0.00]
FARIS 1997 F	315	-0.13 (0.94)	343	0.01 (0.94)		2.2 %	-0.14 [-0.28, 0.00]
FARIS 1997 M	219	-3 (0.94)	223	0.05 (0.94)		2.1 %	-3.05 [-3.23, -2.87]
Finnish DPS 2001	256	-0.13 (0.73)	250	-0.1 (0.73)		2.3 %	-0.03 [-0.16, 0.10]
Finnish men 1985	575	-0.4 (1)	580	0.05 (0.9)		2.3 %	-0.45 [-0.56, -0.34]
Gothenberg Study 1986	1473	-0.01 (1.1)	1404	0 (1.1)		2.3 %	-0.01 [-0.09, 0.07]
HDFP trial 1970	5485	-0.39 (1)	5455	-0.39 (1)		2.4 %	0.0 [-0.04, 0.04]
Hellenius 1993	39	-0.45 (0.93)	39	-0.13 (0.9)		1.5 %	-0.32 [-0.73, 0.09]
Iso 2002	40	-0.11 (0.83)	43	-0.14 (0.83)		1.6 %	0.03 [-0.33, 0.39]



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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
Jalkanen 1991	24	-0.2 (1)	25	0.2 (1)		1.1 %	-0.40 [-0.96, 0.16]
Kastarinen 2002	360	-0.03 (0.91)	355	0.07 (0.93)		2.2 %	-0.10 [-0.23, 0.03]
Lindahl 1999	93	-0.21 (1.35)	93	-0.06 (0.96)		1.7 %	-0.15 [-0.49, 0.19]
MRFIT Study 1982	5743	-0.43 (0.99)	5607	-0.3 (1.03)		2.4 %	-0.13 [-0.17, -0.09]
Muto 2001	152	-0.17 (0.63)	150	0.12 (0.59)		2.2 %	-0.29 [-0.43, -0.15]
Nilsson 2001	43	-0.1 (0.9)	46	0 (1.05)		1.5 %	-0.10 [-0.51, 0.31]
Okayama 2004	96	-0.7 (0.72)	92	-0.48 (0.69)		2.1 %	-0.22 [-0.42, -0.02]
Oldroyd 2001	35	-0.16 (0.55)	32	-0.18 (0.59)		1.9 %	0.02 [-0.25, 0.29]
Oslo Diet Antismoking	604	-0.92 (0.7)	628	-0.39 (0.7)		2.3 %	-0.53 [-0.61, -0.45]
Oslo Diet Exercise	65	-0.48 (0.89)	43	-0.16 (0.59)		1.9 %	-0.32 [-0.60, -0.04]
OXCHECK 1994	2205	-0.19 (1.1)	1916	0 (1.17)		2.3 %	-0.19 [-0.26, -0.12]
Perez-Stable 1995 no prop	69	-0.42 (1.15)	68	-0.18 (0.98)		1.6 %	-0.24 [-0.60, 0.12]
Perez-Stable 1995 prop	67	-0.32 (0.81)	67	-0.25 (0.86)		1.8 %	-0.07 [-0.35, 0.21]
Sartorelli 2005	51	-0.52 (1.2)	53	-0.28 (0.6)		1.6 %	-0.24 [-0.61, 0.13]
Sone (JDCS) 2002	990	-0.04 (0.84)	983	0.01 (0.89)		2.3 %	-0.05 [-0.13, 0.03]
Stefanick 1998 F	43	-0.46 (0.56)	45	-0.03 (0.51)		2.0 %	-0.43 [-0.65, -0.21]
Stefanick 1998 M	48	-0.54 (0.52)	46	-0.1 (0.56)		2.0 %	-0.44 [-0.66, -0.22]
Swedish RIS 1994	235	-0.78 (1.12)	227	-0.39 (0.92)		2.1 %	-0.39 [-0.58, -0.20]
Toobert (MLP) 2005	163	-0.1 (0.95)	116	-0.03 (0.99)		2.0 %	-0.07 [-0.30, 0.16]
Tromso 1991 F	422	0.06 (1.27)	387	0.14 (1.34)		2.1 %	-0.08 [-0.26, 0.10]
Tromso 1991 M	525	-0.41 (1.15)	535	-0.25 (1.2)		2.2 %	-0.16 [-0.30, -0.02]
Uusitupa 1993	38	-0.1 (0.31)	40	0.1 (0.97)		1.7 %	-0.20 [-0.52, 0.12]
WHLP 1998	253	-0.34 (0.61)	267	0.03 (0.21)		2.3 %	-0.37 [-0.45, -0.29]
Wing 1998	32	0.09 (0.67)	31	0.18 (0.53)		1.8 %	-0.09 [-0.39, 0.21]
Subtotal (95% CI)	**24691**		**24737**			**85.4 %**	**-0.28 [-0.39, -0.17]**
Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 1405.58$, df = 42 (P<0.00001); $I^2 = 97\%$							
Test for overall effect: Z = 5.05 (P < 0.00001)							
3 Cluster randomisation (analysis by individual)							
Connell 1995	141	0.13 (0.81)	455	0.08 (0.77)		2.2 %	0.05 [-0.10, 0.20]
Mattila 2003	331	0 (0.93)	309	0 (0.45)		2.3 %	0.0 [-0.11, 0.11]
Meland 1997	58	0.1 (1.17)	52	0.3 (1.1)		1.4 %	-0.20 [-0.62, 0.22]
Proper 2003	75	-0.2 (1)	117	0 (0.9)		1.9 %	-0.20 [-0.48, 0.08]
WHO Factories 1986	16481	0.09 (0.89)	1854	0.08 (0.86)		2.4 %	0.01 [-0.03, 0.05]

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Favours treatment Favours control

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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
Subtotal (95% CI)	**17086**		**2787**			**10.1 %**	**0.01 [-0.03, 0.04]**
Heterogeneity: Tau² = 0.0; Chi² = 3.37, df = 4 (P = 0.50); I² =0.0%							
Test for overall effect: Z = 0.32 (P = 0.75)							
Total (95% CI)	**42998**		**28778**			**100.0 %**	**-0.24 [-0.32, -0.16]**
Heterogeneity: Tau² = 0.07; Chi² = 1659.29, df = 49 (P<0.00001); I² =97%							
Test for overall effect: Z = 5.93 (P < 0.00001)							

Analysis 1.51. Comparison 1 Multiple risk factor intervention versus control, Outcome 51 Blood cholesterol (by allocation concealment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 51 Blood cholesterol (by allocation concealment)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Adequate allocation concealment							
ADAPT 2005	123	0 (0.85)	118	1 (0.83)		0.3 %	-1.00 [-1.21, -0.79]
Aldana (CHIP) 2005	64	-0.02 (0.81)	79	0.35 (0.77)		0.2 %	-0.37 [-0.63, -0.11]
Brekke 2005a	25	0.37 (0.73)	19	0.24 (0.58)		0.1 %	0.13 [-0.26, 0.52]
Cakir 2006	30	-0.92 (0.92)	30	0.04 (0.5)		0.1 %	-0.96 [-1.33, -0.59]
Esposito 2004	55	-0.29 (0.75)	55	0.05 (0.78)		0.2 %	-0.34 [-0.63, -0.05]
Mattila 2003	331	0 (0.93)	309	0 (0.45)		1.0 %	0.0 [-0.11, 0.11]
MRFIT Study 1982	5743	-0.43 (0.99)	5607	-0.3 (1.03)		9.3 %	-0.13 [-0.17, -0.09]
Oldroyd 2001	35	-0.16 (0.55)	32	-0.18 (0.59)		0.2 %	0.02 [-0.25, 0.29]
Perez-Stable 1995 no prop	69	-0.42 (1.15)	68	-0.18 (0.98)		0.1 %	-0.24 [-0.60, 0.12]
Perez-Stable 1995 prop	67	-0.32 (0.81)	67	-0.25 (0.86)		0.2 %	-0.07 [-0.35, 0.21]
Stefanick 1998 F	43	-0.46 (0.56)	45	-0.03 (0.51)		0.3 %	-0.43 [-0.65, -0.21]
Stefanick 1998 M	48	-0.54 (0.52)	46	-0.1 (0.56)		0.3 %	-0.44 [-0.66, -0.22]

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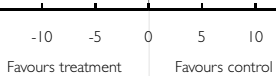
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Subtotal (95% CI)	**6633**		**6475**			**12.1 %**	**-0.16 [-0.19, -0.13]**
Heterogeneity: Chi^2 = 108.36, df = 11 (P<0.00001); I^2 =90%							
Test for overall effect: Z = 9.72 (P < 0.00001)							
2 Inadequate allocation concealment							
Aberg 1989 F	114	0.4 (1.35)	115	0.3 (1.1)		0.1 %	0.10 [-0.22, 0.42]
Aberg 1989 M	79	0.3 (1.1)	80	0.1 (1.1)		0.1 %	0.20 [-0.14, 0.54]
CELL Study 1995	292	-0.15 (0.56)	310	0 (0.65)		1.4 %	-0.15 [-0.25, -0.05]
Finnish DPS 2001	256	-0.13 (0.73)	250	-0.1 (0.73)		0.8 %	-0.03 [-0.16, 0.10]
HDFP trial 1970	5485	-0.39 (1)	5455	-0.39 (1)		9.2 %	0.0 [-0.04, 0.04]
Kastarinen 2002	360	-0.03 (0.91)	355	0.07 (0.93)		0.7 %	-0.10 [-0.23, 0.03]
Oslo Diet Antismoking	604	-0.92 (0.7)	628	-0.39 (0.7)		2.1 %	-0.53 [-0.61, -0.45]
Sartorelli 2005	51	-0.52 (1.2)	53	-0.28 (0.6)		0.1 %	-0.24 [-0.61, 0.13]
Tromso 1991 F	422	0.06 (1.27)	387	0.14 (1.34)		0.4 %	-0.08 [-0.26, 0.10]
Tromso 1991 M	525	-0.41 (1.15)	535	-0.25 (1.2)		0.6 %	-0.16 [-0.30, -0.02]
WHLP 1998	253	-0.34 (0.61)	267	0.03 (0.21)		2.0 %	-0.37 [-0.45, -0.29]
Subtotal (95% CI)	**8441**		**8435**			**17.6 %**	**-0.13 [-0.16, -0.10]**
Heterogeneity: Chi^2 = 191.07, df = 10 (P<0.00001); I^2 =95%							
Test for overall effect: Z = 9.47 (P < 0.00001)							
3 Unclear allocation concealment							
Abingdon 1990	167	-0.2 (0.89)	166	-0.18 (0.9)		0.3 %	-0.02 [-0.21, 0.17]
Change of Heart 1999	164	0.31 (0.82)	334	0.33 (1.54)		0.3 %	-0.02 [-0.23, 0.19]
Connell 1995	141	0.13 (0.81)	455	0.08 (0.77)		0.6 %	0.05 [-0.10, 0.20]
Family Heart 1994 M	1767	-0.13 (1.16)	2174	0 (1.16)		2.4 %	-0.13 [-0.20, -0.06]
Family Heart 1994 F	1217	-0.09 (1.17)	1402	0 (1.17)		1.6 %	-0.09 [-0.18, 0.00]
FARIS 1997 F	315	-0.13 (0.94)	343	0.01 (0.94)		0.6 %	-0.14 [-0.28, 0.00]
FARIS 1997 M	219	-3 (0.94)	223	0.05 (0.94)		0.4 %	-3.05 [-3.23, -2.87]
Finnish men 1985	575	-0.4 (1)	580	0.05 (0.9)		1.1 %	-0.45 [-0.56, -0.34]
Gothenberg Study 1986	1473	-0.01 (1.1)	1404	0 (1.1)		2.0 %	-0.01 [-0.09, 0.07]
Hellenius 1993	39	-0.45 (0.93)	39	-0.13 (0.9)		0.1 %	-0.32 [-0.73, 0.09]
Iso 2002	40	-0.11 (0.83)	43	-0.14 (0.83)		0.1 %	0.03 [-0.33, 0.39]
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]
Muto 2001	152	-0.17 (0.63)	150	0.12 (0.59)		0.7 %	-0.29 [-0.43, -0.15]



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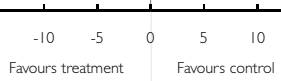
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Nilsson 2001	43	-0.1 (0.9)	46	0 (1.05)		0.1 %	-0.10 [-0.51, 0.31]
Okayama 2004	96	-0.7 (0.72)	92	-0.48 (0.69)		0.3 %	-0.22 [-0.42, -0.02]
Oslo Diet Exercise	65	-0.48 (0.89)	43	-0.16 (0.59)		0.2 %	-0.32 [-0.60, -0.04]
OXCHECK 1994	2205	-0.19 (1.1)	1916	0 (1.17)		2.7 %	-0.19 [-0.26, -0.12]
Proper 2003	75	-0.2 (1)	117	0 (0.9)		0.2 %	-0.20 [-0.48, 0.08]
Sone (JDCS) 2002	990	-0.04 (0.84)	983	0.01 (0.89)		2.2 %	-0.05 [-0.13, 0.03]
Swedish RIS 1994	235	-0.78 (1.12)	227	-0.39 (0.92)		0.4 %	-0.39 [-0.58, -0.20]
Take Heart 1995	1057	0.02 (0.2)	920	0.01 (0.18)		45.9 %	0.01 [-0.01, 0.03]
Toobert (MLP) 2005	163	-0.1 (0.95)	116	-0.03 (0.99)		0.2 %	-0.07 [-0.30, 0.16]
Uusitupa 1993	38	-0.1 (0.31)	40	0.1 (0.97)		0.1 %	-0.20 [-0.52, 0.12]
WHO Factories 1986	16481	0.09 (0.89)	1854	0.08 (0.86)		7.5 %	0.01 [-0.03, 0.05]
Wing 1998	32	0.09 (0.67)	31	0.18 (0.53)		0.1 %	-0.09 [-0.39, 0.21]
Subtotal (95% CI)	**27924**		**13868**			**70.3 %**	**-0.04 [-0.06, -0.03]**
Heterogeneity: Chi^2 = 1295.06, df = 26 (P<0.00001); I^2 =98%							
Test for overall effect: Z = 6.23 (P < 0.00001)							
Total (95% CI)	**42998**		**28778**			**100.0 %**	**-0.07 [-0.08, -0.06]**
Heterogeneity: Chi^2 = 1659.29, df = 49 (P<0.00001); I^2 =97%							
Test for overall effect: Z = 12.57 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 64.80, df = 2 (P = 0.00), I^2 =97%							



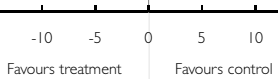
Analysis 1.52. Comparison 1 Multiple risk factor intervention versus control, Outcome 52 Blood cholesterol (by co-morbidity).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 52 Blood cholesterol (by co-morbidity)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 No co-morbidity							
Abingdon 1990	167	-0.2 (0.89)	166	-0.18 (0.9)		0.3 %	-0.02 [-0.21, 0.17]
Aldana (CHIP) 2005	64	-0.02 (0.81)	79	0.35 (0.77)		0.2 %	-0.37 [-0.63, -0.11]
Brekke 2005a	25	0.37 (0.73)	19	0.24 (0.58)		0.1 %	0.13 [-0.26, 0.52]
CELL Study 1995	292	-0.15 (0.56)	310	0 (0.65)		1.4 %	-0.15 [-0.25, -0.05]
Change of Heart 1999	164	0.31 (0.82)	334	0.33 (1.54)		0.3 %	-0.02 [-0.23, 0.19]
Connell 1995	141	0.13 (0.81)	455	0.08 (0.77)		0.6 %	0.05 [-0.10, 0.20]
Esposito 2004	55	-0.29 (0.75)	55	0.05 (0.78)		0.2 %	-0.34 [-0.63, -0.05]
Family Heart 1994 M	1767	-0.13 (1.16)	2174	0 (1.16)		2.4 %	-0.13 [-0.20, -0.06]
Family Heart 1994 F	1217	-0.09 (1.17)	1402	0 (1.17)		1.6 %	-0.09 [-0.18, 0.00]
FARIS 1997 F	315	-0.13 (0.94)	343	0.01 (0.94)		0.6 %	-0.14 [-0.28, 0.00]
FARIS 1997 M	219	-3 (0.94)	223	0.05 (0.94)		0.4 %	-3.05 [-3.23, -2.87]
Finnish DPS 2001	256	-0.13 (0.73)	250	-0.1 (0.73)		0.8 %	-0.03 [-0.16, 0.10]
Finnish men 1985	575	-0.4 (1)	580	0.05 (0.9)		1.1 %	-0.45 [-0.56, -0.34]
Gothenberg Study 1986	1473	-0.01 (1.1)	1404	0 (1.1)		2.0 %	-0.01 [-0.09, 0.07]
Hellenius 1993	39	-0.45 (0.93)	39	-0.13 (0.9)		0.1 %	-0.32 [-0.73, 0.09]
Iso 2002	40	-0.11 (0.83)	43	-0.14 (0.83)		0.1 %	0.03 [-0.33, 0.39]
Lindahl 1999	93	-0.21 (1.35)	93	-0.06 (0.96)		0.1 %	-0.15 [-0.49, 0.19]
MRFIT Study 1982	5743	-0.43 (0.99)	5607	-0.3 (1.03)		9.3 %	-0.13 [-0.17, -0.09]
Muto 2001	152	-0.17 (0.63)	150	0.12 (0.59)		0.7 %	-0.29 [-0.43, -0.15]
Nilsson 2001	43	-0.1 (0.9)	46	0 (1.05)		0.1 %	-0.10 [-0.51, 0.31]
Okayama 2004	96	-0.7 (0.72)	92	-0.48 (0.69)		0.3 %	-0.22 [-0.42, -0.02]
Oldroyd 2001	35	-0.16 (0.55)	32	-0.18 (0.59)		0.2 %	0.02 [-0.25, 0.29]
Oslo Diet Antismoking	604	-0.92 (0.7)	628	-0.39 (0.7)		2.1 %	-0.53 [-0.61, -0.45]
OXCHECK 1994	2205	-0.19 (1.1)	1916	0 (1.17)		2.7 %	-0.19 [-0.26, -0.12]



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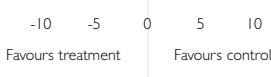
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Proper 2003	75	-0.2 (1)	117	0 (0.9)		0.2 %	-0.20 [-0.48, 0.08]
Sartorelli 2005	51	-0.52 (1.2)	53	-0.28 (0.6)		0.1 %	-0.24 [-0.61, 0.13]
Stefanick 1998 F	43	-0.46 (0.56)	45	-0.03 (0.51)		0.3 %	-0.43 [-0.65, -0.21]
Stefanick 1998 M	48	-0.54 (0.52)	46	-0.1 (0.56)		0.3 %	-0.44 [-0.66, -0.22]
Take Heart 1995	1057	0.02 (0.2)	920	0.01 (0.18)		45.9 %	0.01 [-0.01, 0.03]
Tromso 1991 F	422	0.06 (1.27)	387	0.14 (1.34)		0.4 %	-0.08 [-0.26, 0.10]
Tromso 1991 M	525	-0.41 (1.15)	535	-0.25 (1.2)		0.6 %	-0.16 [-0.30, -0.02]
WHLP 1998	253	-0.34 (0.61)	267	0.03 (0.21)		2.0 %	-0.37 [-0.45, -0.29]
WHO Factories 1986	16481	0.09 (0.89)	1854	0.08 (0.86)		7.5 %	0.01 [-0.03, 0.05]
Wing 1998	32	0.09 (0.67)	31	0.18 (0.53)		0.1 %	-0.09 [-0.39, 0.21]
Subtotal (95% CI)	**34767**		**20695**			**85.0 %**	**-0.08 [-0.09, -0.06]**
Heterogeneity: Chi^2 = 1526.68, df = 33 (P<0.00001); I^2 =98%							
Test for overall effect: Z = 12.09 (P < 0.00001)							
2 Co-morbidity (hypertension and/or diabetes)							
Aberg 1989 F	114	0.4 (1.35)	115	0.3 (1.1)		0.1 %	0.10 [-0.22, 0.42]
Aberg 1989 M	79	0.3 (1.1)	80	0.1 (1.1)		0.1 %	0.20 [-0.14, 0.54]
ADAPT 2005	123	0 (0.85)	118	1 (0.83)		0.3 %	-1.00 [-1.21, -0.79]
Cakir 2006	30	-0.92 (0.92)	30	0.04 (0.5)		0.1 %	-0.96 [-1.33, -0.59]
HDFP trial 1970	5485	-0.39 (1)	5455	-0.39 (1)		9.2 %	0.0 [-0.04, 0.04]
Jalkanen 1991	24	-0.2 (1)	25	0.2 (1)		0.0 %	-0.40 [-0.96, 0.16]
Kastarinen 2002	360	-0.03 (0.91)	355	0.07 (0.93)		0.7 %	-0.10 [-0.23, 0.03]
Mattila 2003	331	0 (0.93)	309	0 (0.45)		1.0 %	0.0 [-0.11, 0.11]
Meland 1997	58	0.1 (1.17)	52	0.3 (1.1)		0.1 %	-0.20 [-0.62, 0.22]
Oslo Diet Exercise	65	-0.48 (0.89)	43	-0.16 (0.59)		0.2 %	-0.32 [-0.60, -0.04]
Perez-Stable 1995 no prop	69	-0.42 (1.15)	68	-0.18 (0.98)		0.1 %	-0.24 [-0.60, 0.12]
Perez-Stable 1995 prop	67	-0.32 (0.81)	67	-0.25 (0.86)		0.2 %	-0.07 [-0.35, 0.21]
Sone (JDCS) 2002	990	-0.04 (0.84)	983	0.01 (0.89)		2.2 %	-0.05 [-0.13, 0.03]
Swedish RIS 1994	235	-0.78 (1.12)	227	-0.39 (0.92)		0.4 %	-0.39 [-0.58, -0.20]
Toobert (MLP) 2005	163	-0.1 (0.95)	116	-0.03 (0.99)		0.2 %	-0.07 [-0.30, 0.16]
Uusitupa 1993	38	-0.1 (0.31)	40	0.1 (0.97)		0.1 %	-0.20 [-0.52, 0.12]
Subtotal (95% CI)	**8231**		**8083**			**15.0 %**	**-0.06 [-0.08, -0.03]**
Heterogeneity: Chi^2 = 130.95, df = 15 (P<0.00001); I^2 =89%							
Test for overall effect: Z = 3.69 (P = 0.00023)							
Total (95% CI)	**42998**		**28778**			**100.0 %**	**-0.07 [-0.08, -0.06]**



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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Heterogeneity: Chi² = 1659.29, df = 49 (P<0.00001); I² =97%							
Test for overall effect: Z = 12.57 (P < 0.00001)							
Test for subgroup differences: Chi² = 1.65, df = 1 (P = 0.20), I² =39%							

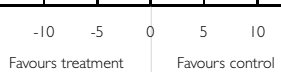
Analysis 1.53. Comparison 1 Multiple risk factor intervention versus control, Outcome 53 Blood cholesterol (by drug treatment).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 53 Blood cholesterol (by drug treatment)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 No drug treatment							
Abingdon 1990	167	-0.2 (0.89)	166	-0.18 (0.9)		0.3 %	-0.02 [-0.21, 0.17]
Aldana (CHIP) 2005	64	-0.02 (0.81)	79	0.35 (0.77)		0.2 %	-0.37 [-0.63, -0.11]
Brekke 2005a	25	0.37 (0.73)	19	0.24 (0.58)		0.1 %	0.13 [-0.26, 0.52]
Change of Heart 1999	164	0.31 (0.82)	334	0.33 (1.54)		0.3 %	-0.02 [-0.23, 0.19]
Connell 1995	141	0.13 (0.81)	455	0.08 (0.77)		0.6 %	0.05 [-0.10, 0.20]
Esposito 2004	55	-0.29 (0.75)	55	0.05 (0.78)		0.2 %	-0.34 [-0.63, -0.05]
Family Heart 1994 M	1767	-0.13 (1.16)	2174	0 (1.16)		2.4 %	-0.13 [-0.20, -0.06]
Family Heart 1994 F	1217	-0.09 (1.17)	1402	0 (1.17)		1.6 %	-0.09 [-0.18, 0.00]
FARIS 1997 F	315	-0.13 (0.94)	343	0.01 (0.94)		0.6 %	-0.14 [-0.28, 0.00]
FARIS 1997 M	219	-3 (0.94)	223	0.05 (0.94)		0.4 %	-3.05 [-3.23, -2.87]
Finnish DPS 2001	256	-0.13 (0.73)	250	-0.1 (0.73)		0.8 %	-0.03 [-0.16, 0.10]
Hellenius 1993	39	-0.45 (0.93)	39	-0.13 (0.9)		0.1 %	-0.32 [-0.73, 0.09]
Iso 2002	40	-0.11 (0.83)	43	-0.14 (0.83)		0.1 %	0.03 [-0.33, 0.39]
Lindahl 1999	93	-0.21 (1.35)	93	-0.06 (0.96)		0.1 %	-0.15 [-0.49, 0.19]



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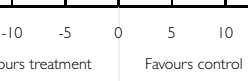
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Muto 2001	152	-0.17 (0.63)	150	0.12 (0.59)		0.7 %	-0.29 [-0.43, -0.15]
Nilsson 2001	43	-0.1 (0.9)	46	0 (1.05)		0.1 %	-0.10 [-0.51, 0.31]
Okayama 2004	96	-0.7 (0.72)	92	-0.48 (0.69)		0.3 %	-0.22 [-0.42, -0.02]
Oldroyd 2001	35	-0.16 (0.55)	32	-0.18 (0.59)		0.2 %	0.02 [-0.25, 0.29]
Oslo Diet Antismoking	604	-0.92 (0.7)	628	-0.39 (0.7)		2.1 %	-0.53 [-0.61, -0.45]
Perez-Stable 1995 no prop	69	-0.42 (1.15)	68	-0.18 (0.98)		0.1 %	-0.24 [-0.60, 0.12]
Proper 2003	75	-0.2 (1)	117	0 (0.9)		0.2 %	-0.20 [-0.48, 0.08]
Sartorelli 2005	51	-0.52 (1.2)	53	-0.28 (0.6)		0.1 %	-0.24 [-0.61, 0.13]
Sone (JDCS) 2002	990	-0.04 (0.84)	983	0.01 (0.89)		2.2 %	-0.05 [-0.13, 0.03]
Stefanick 1998 F	43	-0.46 (0.56)	45	-0.03 (0.51)		0.3 %	-0.43 [-0.65, -0.21]
Stefanick 1998 M	48	-0.54 (0.52)	46	-0.1 (0.56)		0.3 %	-0.44 [-0.66, -0.22]
Take Heart 1995	1057	0.02 (0.2)	920	0.01 (0.18)		45.9 %	0.01 [-0.01, 0.03]
Tromso 1991 F	422	0.06 (1.27)	387	0.14 (1.34)		0.4 %	-0.08 [-0.26, 0.10]
Tromso 1991 M	525	-0.41 (1.15)	535	-0.25 (1.2)		0.6 %	-0.16 [-0.30, -0.02]
Uusitupa 1993	38	-0.1 (0.31)	40	0.1 (0.97)		0.1 %	-0.20 [-0.52, 0.12]
WHLP 1998	253	-0.34 (0.61)	267	0.03 (0.21)		2.0 %	-0.37 [-0.45, -0.29]
Wing 1998	32	0.09 (0.67)	31	0.18 (0.53)		0.1 %	-0.09 [-0.39, 0.21]
Subtotal (95% CI)	**9095**		**10115**			**63.5 %**	**-0.07 [-0.08, -0.05]**
Heterogeneity: Chi^2 = 1442.67, df = 30 (P<0.00001); I^2 =98%							
Test for overall effect: Z = 9.24 (P < 0.00001)							
2 Antihypertensives OR lipid-lowering drugs							
Aberg 1989 F	114	0.4 (1.35)	115	0.3 (1.1)		0.1 %	0.10 [-0.22, 0.42]
Aberg 1989 M	79	0.3 (1.1)	80	0.1 (1.1)		0.1 %	0.20 [-0.14, 0.54]
ADAPT 2005	123	0 (0.85)	118	1 (0.83)		0.3 %	-1.00 [-1.21, -0.79]
Cakir 2006	30	-0.92 (0.92)	30	0.04 (0.5)		0.1 %	-0.96 [-1.33, -0.59]
HDFP trial 1970	5485	-0.39 (1)	5455	-0.39 (1)		9.2 %	0.0 [-0.04, 0.04]
Jalkanen 1991	24	-0.2 (1)	25	0.2 (1)		0.0 %	-0.40 [-0.96, 0.16]
Kastarinen 2002	360	-0.03 (0.91)	355	0.07 (0.93)		0.7 %	-0.10 [-0.23, 0.03]
Mattila 2003	331	0 (0.93)	309	0 (0.45)		1.0 %	0.0 [-0.11, 0.11]
Meland 1997	58	0.1 (1.17)	52	0.3 (1.1)		0.1 %	-0.20 [-0.62, 0.22]
MRFIT Study 1982	5743	-0.43 (0.99)	5607	-0.3 (1.03)		9.3 %	-0.13 [-0.17, -0.09]
Oslo Diet Exercise	65	-0.48 (0.89)	43	-0.16 (0.59)		0.2 %	-0.32 [-0.60, -0.04]
Perez-Stable 1995 prop	67	-0.32 (0.81)	67	-0.25 (0.86)		0.2 %	-0.07 [-0.35, 0.21]



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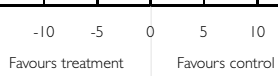
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
WHO Factories 1986	16481	0.09 (0.89)	1854	0.08 (0.86)		7.5 %	0.01 [-0.03, 0.05]
Subtotal (95% CI)	**28960**		**14110**			**28.8 %**	**-0.06 [-0.08, -0.04]**
Heterogeneity: Chi^2 = 141.75, df = 12 (P<0.00001); I^2 =92%							
Test for overall effect: Z = 5.28 (P < 0.00001)							
3 Antihypertensives AND lipid-lowering drug							
CELL Study 1995	292	-0.15 (0.56)	310	0 (0.65)		1.4 %	-0.15 [-0.25, -0.05]
Finnish men 1985	575	-0.4 (1)	580	0.05 (0.9)		1.1 %	-0.45 [-0.56, -0.34]
Gothenberg Study 1986	1473	-0.01 (1.1)	1404	0 (1.1)		2.0 %	-0.01 [-0.09, 0.07]
OXCHECK 1994	2205	-0.19 (1.1)	1916	0 (1.17)		2.7 %	-0.19 [-0.26, -0.12]
Swedish RIS 1994	235	-0.78 (1.12)	227	-0.39 (0.92)		0.4 %	-0.39 [-0.58, -0.20]
Toobert (MLP) 2005	163	-0.1 (0.95)	116	-0.03 (0.99)		0.2 %	-0.07 [-0.30, 0.16]
Subtotal (95% CI)	**4943**		**4553**			**7.7 %**	**-0.18 [-0.22, -0.14]**
Heterogeneity: Chi^2 = 46.59, df = 5 (P<0.00001); I^2 =89%							
Test for overall effect: Z = 8.54 (P < 0.00001)							
Total (95% CI)	**42998**		**28778**			**100.0 %**	**-0.07 [-0.08, -0.06]**
Heterogeneity: Chi^2 = 1659.29, df = 49 (P<0.00001); I^2 =97%							
Test for overall effect: Z = 12.57 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 28.28, df = 2 (P = 0.00), I^2 =93%							



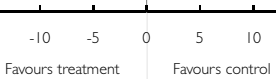
Analysis 1.54. Comparison 1 Multiple risk factor intervention versus control, Outcome 54 Blood cholesterol (by era).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 54 Blood cholesterol (by era)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Low rate of CVD							
Aberg 1989 F	114	0.4 (1.35)	115	0.3 (1.1)		0.1 %	0.10 [-0.22, 0.42]
Aberg 1989 M	79	0.3 (1.1)	80	0.1 (1.1)		0.1 %	0.20 [-0.14, 0.54]
Abingdon 1990	167	-0.2 (0.89)	166	-0.18 (0.9)		0.3 %	-0.02 [-0.21, 0.17]
ADAPT 2005	123	0 (0.85)	118	1 (0.83)		0.3 %	-1.00 [-1.21, -0.79]
Aldana (CHIP) 2005	64	-0.02 (0.81)	79	0.35 (0.77)		0.2 %	-0.37 [-0.63, -0.11]
Brekke 2005a	25	0.37 (0.73)	19	0.24 (0.58)		0.1 %	0.13 [-0.26, 0.52]
Cakir 2006	30	-0.92 (0.92)	30	0.04 (0.5)		0.1 %	-0.96 [-1.33, -0.59]
CELL Study 1995	292	-0.15 (0.56)	310	0 (0.65)		1.4 %	-0.15 [-0.25, -0.05]
Change of Heart 1999	164	0.31 (0.82)	334	0.33 (1.54)		0.3 %	-0.02 [-0.23, 0.19]
Connell 1995	141	0.13 (0.81)	455	0.08 (0.77)		0.6 %	0.05 [-0.10, 0.20]
Esposito 2004	55	-0.29 (0.75)	55	0.05 (0.78)		0.2 %	-0.34 [-0.63, -0.05]
Family Heart 1994 M	1767	-0.13 (1.16)	2174	0 (1.16)		2.4 %	-0.13 [-0.20, -0.06]
Family Heart 1994 F	1217	-0.09 (1.17)	1402	0 (1.17)		1.6 %	-0.09 [-0.18, 0.00]
FARIS 1997 F	315	-0.13 (0.94)	343	0.01 (0.94)		0.6 %	-0.14 [-0.28, 0.00]
FARIS 1997 M	219	-3 (0.94)	223	0.05 (0.94)		0.4 %	-3.05 [-3.23, -2.87]
Finnish DPS 2001	256	-0.13 (0.73)	250	-0.1 (0.73)		0.8 %	-0.03 [-0.16, 0.10]
Hellenius 1993	39	-0.45 (0.93)	39	-0.13 (0.9)		0.1 %	-0.32 [-0.73, 0.09]
Iso 2002	40	-0.11 (0.83)	43	-0.14 (0.83)		0.1 %	0.03 [-0.33, 0.39]
Jalkanen 1991	24	-0.2 (1)	25	0.2 (1)		0.0 %	-0.40 [-0.96, 0.16]
Kastarinen 2002	360	-0.03 (0.91)	355	0.07 (0.93)		0.7 %	-0.10 [-0.23, 0.03]
Lindahl 1999	93	-0.21 (1.35)	93	-0.06 (0.96)		0.1 %	-0.15 [-0.49, 0.19]
Mattila 2003	331	0 (0.93)	309	0 (0.45)		1.0 %	0.0 [-0.11, 0.11]
Meland 1997	58	0.1 (1.17)	52	0.3 (1.1)		0.1 %	-0.20 [-0.62, 0.22]
Muto 2001	152	-0.17 (0.63)	150	0.12 (0.59)		0.7 %	-0.29 [-0.43, -0.15]



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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Nilsson 2001	43	-0.1 (0.9)	46	0 (1.05)		0.1 %	-0.10 [-0.51, 0.31]
Okayama 2004	96	-0.7 (0.72)	92	-0.48 (0.69)		0.3 %	-0.22 [-0.42, -0.02]
Oldroyd 2001	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 1994	2205	-0.19 (1.1)	1916	0 (1.17)		2.7 %	-0.19 [-0.26, -0.12]
Perez-Stable 1995 no prop	69	-0.42 (1.15)	68	-0.18 (0.98)		0.1 %	-0.24 [-0.60, 0.12]
Perez-Stable 1995 prop	67	-0.32 (0.81)	67	-0.25 (0.86)		0.2 %	-0.07 [-0.35, 0.21]
Proper 2003	75	-0.2 (1)	117	0 (0.9)		0.2 %	-0.20 [-0.48, 0.08]
Sartorelli 2005	51	-0.52 (1.2)	53	-0.28 (0.6)		0.1 %	-0.24 [-0.61, 0.13]
Sone (JDCS) 2002	990	-0.04 (0.84)	983	0.01 (0.89)		2.2 %	-0.05 [-0.13, 0.03]
Stefanick 1998 F	43	-0.46 (0.56)	45	-0.03 (0.51)		0.3 %	-0.43 [-0.65, -0.21]
Stefanick 1998 M	48	-0.54 (0.52)	46	-0.1 (0.56)		0.3 %	-0.44 [-0.66, -0.22]
Swedish RIS 1994	235	-0.78 (1.12)	227	-0.39 (0.92)		0.4 %	-0.39 [-0.58, -0.20]
Take Heart 1995	1057	0.02 (0.2)	920	0.01 (0.18)		45.9 %	0.01 [-0.01, 0.03]
Toobert (MLP) 2005	163	-0.1 (0.95)	116	-0.03 (0.99)		0.2 %	-0.07 [-0.30, 0.16]
Tromso 1991 F	422	0.06 (1.27)	387	0.14 (1.34)		0.4 %	-0.08 [-0.26, 0.10]
Tromso 1991 M	525	-0.41 (1.15)	535	-0.25 (1.2)		0.6 %	-0.16 [-0.30, -0.02]
Uusitupa 1993	38	-0.1 (0.31)	40	0.1 (0.97)		0.1 %	-0.20 [-0.52, 0.12]
WHLP 1998	253	-0.34 (0.61)	267	0.03 (0.21)		2.0 %	-0.37 [-0.45, -0.29]
Wing 1998	32	0.09 (0.67)	31	0.18 (0.53)		0.1 %	-0.09 [-0.39, 0.21]
Subtotal (95% CI)	**12637**		**13250**			**68.8 %**	**-0.07 [-0.08, -0.05]**
Heterogeneity: Chi^2 = 1440.29, df = 43 (P<0.00001); I^2 =97%							
Test for overall effect: Z = 9.42 (P < 0.00001)							
2 High rate of CVD							
Finnish men 1985	575	-0.4 (1)	580	0.05 (0.9)		1.1 %	-0.45 [-0.56, -0.34]
Gothenberg Study 1986	1473	-0.01 (1.1)	1404	0 (1.1)		2.0 %	-0.01 [-0.09, 0.07]
HDFP trial 1970	5485	-0.39 (1)	5455	-0.39 (1)		9.2 %	0.0 [-0.04, 0.04]
MRFIT Study 1982	5743	-0.43 (0.99)	5607	-0.3 (1.03)		9.3 %	-0.13 [-0.17, -0.09]
Oslo Diet Antismoking	604	-0.92 (0.7)	628	-0.39 (0.7)		2.1 %	-0.53 [-0.61, -0.45]
WHO Factories 1986	16481	0.09 (0.89)	1854	0.08 (0.86)		7.5 %	0.01 [-0.03, 0.05]
Subtotal (95% CI)	**30361**		**15528**			**31.2 %**	**-0.09 [-0.11, -0.07]**
Heterogeneity: Chi^2 = 215.73, df = 5 (P<0.00001); I^2 =98%							
Test for overall effect: Z = 8.52 (P < 0.00001)							
Total (95% CI)	**42998**		**28778**			**100.0 %**	**-0.07 [-0.08, -0.06]**

-10 -5 0 5 10

Favours treatment Favours control

(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Heterogeneity: Chi² = 1659.29, df = 49 (P<0.00001); I² =97%							
Test for overall effect: Z = 12.57 (P < 0.00001)							
Test for subgroup differences: Chi² = 3.27, df = 1 (P = 0.07), I² =69%							

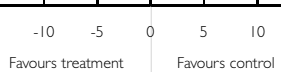
Analysis 1.55. Comparison 1 Multiple risk factor intervention versus control, Outcome 55 Blood cholesterol (by age of study).

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

Comparison: 1 Multiple risk factor intervention versus control

Outcome: 55 Blood cholesterol (by age of study)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Study before 2000							
Aberg 1989 F	114	0.4 (1.35)	115	0.3 (1.1)		0.1 %	0.10 [-0.22, 0.42]
Aberg 1989 M	79	0.3 (1.1)	80	0.1 (1.1)		0.1 %	0.20 [-0.14, 0.54]
Abingdon 1990	167	-0.2 (0.89)	166	-0.18 (0.9)		0.3 %	-0.02 [-0.21, 0.17]
CELL Study 1995	292	-0.15 (0.56)	310	0 (0.65)		1.4 %	-0.15 [-0.25, -0.05]
Change of Heart 1999	164	0.31 (0.82)	334	0.33 (1.54)		0.3 %	-0.02 [-0.23, 0.19]
Connell 1995	141	0.13 (0.81)	455	0.08 (0.77)		0.6 %	0.05 [-0.10, 0.20]
Family Heart 1994 M	1767	-0.13 (1.16)	2174	0 (1.16)		2.4 %	-0.13 [-0.20, -0.06]
Family Heart 1994 F	1217	-0.09 (1.17)	1402	0 (1.17)		1.6 %	-0.09 [-0.18, 0.00]
FARIS 1997 F	315	-0.13 (0.94)	343	0.01 (0.94)		0.6 %	-0.14 [-0.28, 0.00]
FARIS 1997 M	219	-3 (0.94)	223	0.05 (0.94)		0.4 %	-3.05 [-3.23, -2.87]
Finnish men 1985	575	-0.4 (1)	580	0.05 (0.9)		1.1 %	-0.45 [-0.56, -0.34]
Gothenberg Study 1986	1473	-0.01 (1.1)	1404	0 (1.1)		2.0 %	-0.01 [-0.09, 0.07]
HDFP trial 1970	5485	-0.39 (1)	5455	-0.39 (1)		9.2 %	0.0 [-0.04, 0.04]
Hellenius 1993	39	-0.45 (0.93)	39	-0.13 (0.9)		0.1 %	-0.32 [-0.73, 0.09]



(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
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 1982	5743	-0.43 (0.99)	5607	-0.3 (1.03)		9.3 %	-0.13 [-0.17, -0.09]
Oslo Diet Antismoking	604	-0.92 (0.7)	628	-0.39 (0.7)		2.1 %	-0.53 [-0.61, -0.45]
Oslo Diet Exercise	65	-0.48 (0.89)	43	-0.16 (0.59)		0.2 %	-0.32 [-0.60, -0.04]
OXCHECK 1994	2205	-0.19 (1.1)	1916	0 (1.17)		2.7 %	-0.19 [-0.26, -0.12]
Perez-Stable 1995 no prop	69	-0.42 (1.15)	68	-0.18 (0.98)		0.1 %	-0.24 [-0.60, 0.12]
Perez-Stable 1995 prop	67	-0.32 (0.81)	67	-0.25 (0.86)		0.2 %	-0.07 [-0.35, 0.21]
Stefanick 1998 F	43	-0.46 (0.56)	45	-0.03 (0.51)		0.3 %	-0.43 [-0.65, -0.21]
Stefanick 1998 M	48	-0.54 (0.52)	46	-0.1 (0.56)		0.3 %	-0.44 [-0.66, -0.22]
Swedish RIS 1994	235	-0.78 (1.12)	227	-0.39 (0.92)		0.4 %	-0.39 [-0.58, -0.20]
Take Heart 1995	1057	0.02 (0.2)	920	0.01 (0.18)		45.9 %	0.01 [-0.01, 0.03]
Tromso 1991 F	422	0.06 (1.27)	387	0.14 (1.34)		0.4 %	-0.08 [-0.26, 0.10]
Tromso 1991 M	525	-0.41 (1.15)	535	-0.25 (1.2)		0.6 %	-0.16 [-0.30, -0.02]
Uusitupa 1993	38	-0.1 (0.31)	40	0.1 (0.97)		0.1 %	-0.20 [-0.52, 0.12]
WHLP 1998	253	-0.34 (0.61)	267	0.03 (0.21)		2.0 %	-0.37 [-0.45, -0.29]
WHO Factories 1986	16481	0.09 (0.89)	1854	0.08 (0.86)		7.5 %	0.01 [-0.03, 0.05]
Wing 1998	32	0.09 (0.67)	31	0.18 (0.53)		0.1 %	-0.09 [-0.39, 0.21]
Subtotal (95% CI)	**40109**		**25931**			**92.6 %**	**-0.07 [-0.08, -0.06]**
Heterogeneity: Chi² = 1537.64, df = 32 (P<0.00001); I² =98%							
Test for overall effect: Z = 11.21 (P < 0.00001)							
2 Study after 2000							
ADAPT 2005	123	0 (0.85)	118	1 (0.83)		0.3 %	-1.00 [-1.21, -0.79]
Aldana (CHIP) 2005	64	-0.02 (0.81)	79	0.35 (0.77)		0.2 %	-0.37 [-0.63, -0.11]
Brekke 2005a	25	0.37 (0.73)	19	0.24 (0.58)		0.1 %	0.13 [-0.26, 0.52]
Cakir 2006	30	-0.92 (0.92)	30	0.04 (0.5)		0.1 %	-0.96 [-1.33, -0.59]
Esposito 2004	55	-0.29 (0.75)	55	0.05 (0.78)		0.2 %	-0.34 [-0.63, -0.05]
Finnish DPS 2001	256	-0.13 (0.73)	250	-0.1 (0.73)		0.8 %	-0.03 [-0.16, 0.10]
Iso 2002	40	-0.11 (0.83)	43	-0.14 (0.83)		0.1 %	0.03 [-0.33, 0.39]
Kastarinen 2002	360	-0.03 (0.91)	355	0.07 (0.93)		0.7 %	-0.10 [-0.23, 0.03]
Mattila 2003	331	0 (0.93)	309	0 (0.45)		1.0 %	0.0 [-0.11, 0.11]
Muto 2001	152	-0.17 (0.63)	150	0.12 (0.59)		0.7 %	-0.29 [-0.43, -0.15]

-10 -5 0 5 10

Favours treatment Favours control

(*Continued* . . .)

(. . . *Continued*)

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Nilsson 2001	43	-0.1 (0.9)	46	0 (1.05)		0.1 %	-0.10 [-0.51, 0.31]
Okayama 2004	96	-0.7 (0.72)	92	-0.48 (0.69)		0.3 %	-0.22 [-0.42, -0.02]
Oldroyd 2001	35	-0.16 (0.55)	32	-0.18 (0.59)		0.2 %	0.02 [-0.25, 0.29]
Proper 2003	75	-0.2 (1)	117	0 (0.9)		0.2 %	-0.20 [-0.48, 0.08]
Sartorelli 2005	51	-0.52 (1.2)	53	-0.28 (0.6)		0.1 %	-0.24 [-0.61, 0.13]
Sone (JDCS) 2002	990	-0.04 (0.84)	983	0.01 (0.89)		2.2 %	-0.05 [-0.13, 0.03]
Toobert (MLP) 2005	163	-0.1 (0.95)	116	-0.03 (0.99)		0.2 %	-0.07 [-0.30, 0.16]
Subtotal (95% CI)	**2889**		**2847**			**7.4 %**	**-0.14 [-0.18, -0.10]**
Heterogeneity: Chi^2 = 111.01, df = 16 (P<0.00001); I^2 =86%							
Test for overall effect: Z = 6.56 (P < 0.00001)							
Total (95% CI)	**42998**		**28778**			**100.0 %**	**-0.07 [-0.08, -0.06]**
Heterogeneity: Chi^2 = 1659.29, df = 49 (P<0.00001); I^2 =97%							
Test for overall effect: Z = 12.57 (P < 0.00001)							
Test for subgroup differences: Chi^2 = 10.64, df = 1 (P = 0.00), I^2 =91%							

APPENDICES

Appendix 1. Search strategies 2006

CENTRAL

#1 MeSH descriptor CARDIOVASCULAR DISEASES this term only
#2 MeSH descriptor CORONARY DISEASE explode all trees
#3 cardiovascular in All Text
#4 (coronary in All Text near/3 disease* in All Text)
#5 (heart in All Text near/3 disease* in All Text)
#6 MeSH descriptor HYPERTENSION this term only
#7 hypertension in All Text
#8 (atherosclerosis in All Text or arteriosclerosis in All Text)
#9 (hyperlipidaemia in All Text or hyperlipidemia in All Text)
#10 MeSH descriptor ARTERIOSCLEROSIS explode all trees
#11 MeSH descriptor CHOLESTEROL explode trees all trees
#12 MeSH descriptor HYPERLIPIDEMIA explode all trees
#13 cholesterol in All Text
#14 multiple next risk next factor* in All Text
#15 coronary next risk next factor* in All Text

#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 MeSH descriptor HEALTH EDUCATION explode all trees
#20 MeSH descriptor HEALTH PROMOTION explode all trees
#21 MeSH descriptor HEALTH BEHAVIOR explode all trees
#22 MeSH descriptor PRIMARY PREVENTION this term only
#23 MeSH descriptor COUNSELING this term only
#24 counsel* in All Text
#25 (health in All Text near/3 educat* in All Text)
#26 (patient in All Text near/3 educat* in All Text)
#27 (education* in All Text near/3 program* in All Text)
#28 (health in All Text near/3 promotion* in All Text)
#29 (health in All Text near/3 behaviour* in All Text)
#30 (health in All Text near/3 behavior* in All Text)
#31 primary next prevention in All Text
#32 (multiple next risk in All Text near/3 intervention* in All Text)
#33 (multifactor* in All Text near/3 intervention* in All Text)
#34 (multifactor* in All Text near/3 prevention in All Text)
#35 (risk next factor* in All Text near/3 reduc* in All Text)
#36 (risk next factor* in All Text near/3 manag* in All Text)
#37 (risk next factor* in All Text near/3 intervent* in All Text)
#38 (lifestyle in All Text near/3 intervention* in All Text)
#39 (lifestyle in All Text near/3 advice in All Text)
#40 (life-style in All Text near/3 intervention* in All Text)
#41 (life-style in All Text near/3 advice in All Text)
#42 (life-style in All Text near/3 alter* in All Text)
#43 (lifestyle in All Text near/3 alter* in All Text)
#44 (lifestyle in All Text near/3 educat* in All Text)
#45 (life-style in All Text near/3 educat* in All Text)
#46 (life-style in All Text near/3 chang* in All Text)
#47 (lifestyle in All Text near/3 chang* in All Text)
#48 (behavior* in All Text near/3 chang* in All Text)
#49 (behaviour* in All Text near/3 chang* in All Text)
#50 (health next care in All Text near/3 advice in All Text)
#51 (healthcare in All Text near/3 advice in All Text)
#52 nonpharmacologic* in All Text
#53 non-pharmacologic* in All Text
#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)

MEDLINE on Ovid

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
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 clinical trial.pt.
44 exp Clinical trials/
45 (clin$ adj25 trial$).ti,ab.
46 ((singl$ or doubl$ or trebl$ or tripl$) adj (blind$ or mask$)).ti,ab.
47 placebos.sh.
48 placebo$.ti,ab.
49 random$.ti,ab.
50 research design.sh.
51 or/43-50
52 exp animal/ not humans/
53 42 or 51
54 53 not 52
55 54 and 35

EMBASE on Ovid

1 cardiovascular disease/
2 exp ischemic heart disease/

3 (coronary adj3 disease$).tw.
4 heart disease$.tw.
5 Hypertension/
6 hypertension.tw.
7 (cardiovascular adj3 (disease$ or fit of fitness)).tw.
8 exp arteriosclerosis/
9 exp hyperlipidemia/
10 hyperlipid?emia.tw.
11 cholesterol.tw.
12 arteriosclero$.tw.
13 atherosclero$.tw.
14 coronary risk factor$.tw.
15 multiple risk factor$.tw.
16 cardiovascular risk factor$.tw.
17 or/1-16
18 exp health education/
19 exp health behavior/
20 primary prevention/
21 exp counseling/
22 (multifactor$ adj5 (intervent$ or prevent$)).tw.
23 ((life-style or life style or lifestyle or healthcare or health care) adj3 (intervention$ or educat$ or advice or alter$ or change$)).tw.
24 primary prevention.tw.
25 (risk factor$ adj3 (reduc$ or manage$ or managing or intervent$ or program$)).tw.
26 (educat$ adj3 (program$ or patient$)).tw.
27 (non pharmacologic$ or nonpharmacologic$).tw.
28 (risk factor$ adj3 modif$).tw.
29 ((lifestyle or life-style or life style) adj3 modif$).tw.
30 exp behavior therapy/
31 (behavi?r$ adj3 (intervention$ or program$ or modif$ or change$ or alter$)).tw.
32 (promot$ adj3 (health or healthcare or health care)).tw.
33 or/18-32
34 17 and 33
35 random$.ti,ab.
36 factorial$.ti,ab.
37 (crossover$ or cross over$ or cross-over$).ti,ab.
38 placebo$.ti,ab.
39 (double$ adj blind$).ti,ab.
40 (singl$ adj blind$).ti,ab.
41 assign$.ti,ab.
42 allocat$.ti,ab.
43 volunteer$.ti,ab.
44 Crossover Procedure/
45 Double Blind Procedure/
46 Randomized Controlled Trial/
47 Single Blind Procedure/
48 or/35-47
49 exp animal/
50 nonhuman/
51 exp animal experiment/
52 or/49-51
53 exp human/
54 52 not 53
55 48 not 54

56 55 and 34

Appendix 2. Search strategies 2001

MEDLINE on Ovid

<Mid 1998 to August Week 2 2001>
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
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

EMBASE on Ovid

<1996 to August Week 2 2001>
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$.tw.
17 cardovascular risk factor$.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/
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)

Appendix 3. Search strategy 1995

MEDLINE

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.

WHAT'S NEW

Last assessed as up-to-date: 21 December 2006.

Date	Event	Description
11 November 2010	New search has been performed	The search has been re-run to June 2006. We identified and included 16 trials from the updated search.
11 November 2010	New citation required and conclusions have changed	A total of 55 trials are included in this update. We applied the new criteria of including studies with at least six months follow up. New authors are introduced to this update.

HISTORY

Review first published: Issue 2, 1999

Date	Event	Description
1 October 2008	Amended	Converted to new review format.
16 February 2007	New search has been performed	Revised plain language summary.
18 August 2006	New citation required but conclusions have not changed	Substantive amendment: updated with a new search from 1995 to September 2001. An additional 21 trials were found and were incorporated into the earlier version of the review. The findings and conclusions are essentially unaltered from the previous review.

CONTRIBUTIONS OF AUTHORS

G. Davey Smith and S. Ebrahim wrote the original review.

For the first 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.

For the second update:

K. Ward selected studies, extracted data, performed analysis and co-wrote the review.

F. Taylor selected studies, extracted data, performed analysis and co-wrote the review.

M. Burke ran searches and selected studies.

S. Ebrahim selected studies 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