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Risk scoring for the primary prevention of cardiovascular disease (Review)

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[Intervention Review]

Risk scoring for the primary prevention of cardiovascular disease

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ABSTRACT

Background

The current paradigm for cardiovascular disease (CVD) emphasises absolute risk assessment to guide treatment decisions in primary prevention. Although the derivation and validation of multivariable risk assessment tools, or CVD risk scores, have attracted considerable attention, their effect on clinical outcomes is uncertain.

Objectives

To assess the effects of evaluating and providing CVD risk scores in adults without prevalent CVD on cardiovascular outcomes, risk factor levels, preventive medication prescribing, and health behaviours.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library (2016, Issue 2), MEDLINE Ovid (1946 to March week 1 2016), Embase (embase.com) (1974 to 15 March 2016), and Conference Proceedings Citation Index-Science (CPCI-S) (1990 to 15 March 2016). We imposed no language restrictions. We searched clinical trial registers in March 2016 and handsearched reference lists of primary studies to identify additional reports.

Selection criteria

We included randomised and quasi-randomised trials comparing the systematic provision of CVD risk scores by a clinician, healthcare professional, or healthcare system compared with usual care (i.e. no systematic provision of CVD risk scores) in adults without CVD.

Data collection and analysis

Three review authors independently selected studies, extracted data, and evaluated study quality. We used the Cochrane 'Risk of bias' tool to assess study limitations. The primary outcomes were: CVD events, change in CVD risk factor levels (total cholesterol, systolic blood pressure, and multivariable CVD risk), and adverse events. Secondary outcomes included: lipid-lowering and antihypertensive medication prescribing in higher-risk people. We calculated risk ratios (RR) for dichotomous data and mean differences (MD) or

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standardised mean differences (SMD) for continuous data using 95% confidence intervals. We used a fixed-effects model when heterogeneity (I^2) was at least 50% and a random-effects model for substantial heterogeneity (I^2 > 50%). We evaluated the quality of evidence using the GRADE framework.

Main results

We identified 41 randomised controlled trials (RCTs) involving 194,035 participants from 6422 reports. We assessed studies as having high or unclear risk of bias across multiple domains. Low-quality evidence evidence suggests that providing CVD risk scores may have little or no effect on CVD events compared with usual care (5.4% versus 5.3%; RR 1.01, 95% confidence interval (CI) 0.95 to 1.08; I^2 = 25%; 3 trials, N = 99,070). Providing CVD risk scores may reduce CVD risk factor levels by a small amount compared with usual care. Providing CVD risk scores reduced total cholesterol (MD −0.10 mmol/L, 95% CI −0.20 to 0.00; I^2 = 94%; 12 trials, N = 20,437, low-quality evidence), systolic blood pressure (MD −2.77 mmHg, 95% CI −4.16 to −1.38; I^2 = 93%; 16 trials, N = 32,954, low-quality evidence), and multivariable CVD risk (SMD −0.21, 95% CI −0.39 to −0.02; I^2 = 94%; 9 trials, N = 9549, low-quality evidence). Providing CVD risk scores may reduce adverse events compared with usual care, but results were imprecise (1.9% versus 2.7%; RR 0.72, 95% CI 0.49 to 1.04; I^2 = 0%; 4 trials, N = 4630, low-quality evidence). Compared with usual care, providing CVD risk scores may increase new or intensified lipid-lowering medications (15.7% versus 10.7%; RR 1.47, 95% CI 1.15 to 1.87; I^2 = 40%; 11 trials, N = 14,175, low-quality evidence) and increase new or increased antihypertensive medications (17.2% versus 11.4%; RR 1.51, 95% CI 1.08 to 2.11; I^2 = 53%; 8 trials, N = 13,255, low-quality evidence).

Authors' conclusions

There is uncertainty whether current strategies for providing CVD risk scores affect CVD events. Providing CVD risk scores may slightly reduce CVD risk factor levels and may increase preventive medication prescribing in higher-risk people without evidence of harm. There were multiple study limitations in the identified studies and substantial heterogeneity in the interventions, outcomes, and analyses, so readers should interpret results with caution. New models for implementing and evaluating CVD risk scores in adequately powered studies are needed to define the role of applying CVD risk scores in primary CVD prevention.

PLAIN LANGUAGE SUMMARY

Clinical effects of cardiovascular risk scores in people without cardiovascular disease

Review question

What is the evidence about the potential clinical benefits and harms of providing cardiovascular disease (CVD) risk scores in people without a history of heart disease or stroke?

Background

Cardiovascular disease (CVD) is a group of conditions that includes heart disease and stroke. CVD prevention guidelines emphasise the use of risk scores, equations that use clinical variables to estimate the chance of a first heart attack or stroke, to guide treatment decisions in the general population. While there has been much attention to developing different types of CVD risk scores, there is uncertainty about the effects of providing a CVD risk score in clinical practice.

The aim of this systematic review was to assess the effects of evaluating CVD risk scores in adults without a history of heart disease or stroke on cardiovascular outcomes, risk factor levels, preventive medication prescribing, and health behaviours.

Study characteristics

We searched scientific databases for randomised trials (clinical studies that randomly put people into different treatment groups) that systematically provided CVD risk scores or usual care to adults without a history of heart disease or stroke. The evidence is current to March 2016. Funding for the majority of trials came from government sources or pharmaceutical companies.

Key results

We identified 41 trials that included 194,035 participants. Many of the studies had limitations. Low-quality evidence suggests that providing CVD risk scores had little or no effect on the number of people who develop heart disease or stroke. Providing CVD risk scores may reduce CVD risk factor levels (like cholesterol, blood pressure, and multivariable CVD risk) by a small amount and may increase cholesterol-lowering and blood pressure-lowering medication prescribing in higher risk people. Providing CVD risk scores may reduce harms, but the results were imprecise.

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Quality of the evidence

There is low-quality evidence to guide the use of CVD risk scores in clinical practice. Studies had multiple limitations and used different methods to provide CVD risk scores. It is likely that further research will influence these results.

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SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

CVD risk scoring for the primary prevention of cardiovascular disease

Patient or population: adults without prevalent cardiovascular disease (primary cardiovascular disease prevention)
Setting: outpatient
Intervention: providing CVD risk scores
Comparison: not providing CVD risk scores/usual care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	N of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with not providing CVD risk scores/usual care	Risk with providing CVD risk scores				
CVD events follow-up: range 1-10 years	Study population		RR 1.01 (0.95 to 1.08)	99,070 (3 RCTs)	⊕⊕◯◯ Low[a,b]	-
	53 per 1000	54 per 1000 (51 to 58)				
Total cholesterol (mmol/L) follow-up: median 1 years	In the comparison group, the range of mean total cholesterol level was 5.1 to 6.6 mmol/L and the range of mean change from baseline in total cholesterol level was 0.09 lower to 0.14 mmol/L higher	The mean difference in total cholesterol in the intervention group was 0.10 mmol/L lower (0.20 lower to 0.00)	-	20,437 (12 RCTs)	⊕⊕◯◯ Low[c,d]	-
Systolic blood pressure (mmHg) follow-up: median 1 years	In the comparison group, the range of mean systolic blood pressure level was 124.1 to 159.0 mmHg and the range of mean	The mean difference in systolic blood pressure in the intervention group was 2.77 mmHg lower (4.16 lower to 1.38	-	32,954 (16 RCTs)	⊕⊕◯◯ Low[c,d]	-

	change from baseline in systolic blood pressure level was 5.3 lower to 1.0 higher mmHg	lower)				
Change in multivariable CVD risk (SD) follow-up: median 1 years	In the comparison group, the range of mean change from baseline in multivariable CVD risk was 5.3 lower to 0.77 higher SDs	The mean difference in multivariable CVD risk in the intervention group was 0.21 SDs lower (0.39 lower to 0.02 lower)	-	9549 (9 RCTs)	⊕⊕◯◯ Low[c,d]	Standardised mean differences were calculated for this outcome due to the use of different multivariable CVD risk scales. An effect size of ~0.20 SD units reflects a small effect
Investigator-defined adverse events follow-up: range 1 month to 1 year	Study population		RR 0.72 (0.49 to 1.04)	4630 (4 RCTs)	⊕⊕◯◯ Low[e,f]	Adverse events were defined heterogeneously by investigators and included some events that may have been due to newly prescribed medications rather than the provision of a CVD risk score itself
	27 per 1000	19 per 1000 (13 to 28)				
New/intensified lipid-lowering medication follow-up: median 6 months	Study population		RR 1.47 (1.15 to 1.87)	14,175 (11 RCTs)	⊕⊕◯◯ Low[d,e]	Prescribing rates in the comparison group varied among the included trials (range 4% to 22%). Median prescribing rate presented
	107 per 1000	157 per 1000 (123 to 200)				
New/intensified antihypertensive medication follow-up: median 1 years	Study population		RR 1.51 (1.08 to 2.11)	13,255 (8 RCTs)	⊕⊕◯◯ Low[d,e]	Prescribing rates in the comparison group varied among the included trials (range 0% to 27%). Median prescribing rate presented

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	114 per 1000	172 per 1000 (123 to 240)	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).
CI: confidence interval; **RCT**: randomised controlled trial; **RR**: risk ratio; **SD**: standard deviation.

GRADE Working Group grades of evidence
High quality: we are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect
Very low quality: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

[a] Downgraded due to study limitations, primarily driven by high risk of selection bias in Holt 2010 and high risk of reporting bias in Bucher 2010 and Jorgensen 2014.
[b] Downgraded due to imprecision; trials reported being underpowered for CVD events.
[c] Downgraded due to study limitations, primarily in the domains of attrition bias (missing data for follow-up risk factor levels) and other sources of bias (poor intervention fidelity, potential conflicts of interest).
[d] Downgraded due to heterogeneity in pooled estimates.
[e] Downgraded due to study limitations, primarily in the domains of attrition bias (missing data for medication prescribing in follow-up) and other sources of bias (poor intervention fidelity, potential conflicts of interest).
[f] Downgraded due to imprecision, because confidence interval includes 1 and sample size does not meet threshold for optimal information size.

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BACKGROUND

Description of the condition

Cardiovascular disease (CVD), which includes ischaemic heart disease and stroke, is the leading cause of mortality and disability worldwide (Murray 2012; Naghavi 2015). According to the Global Burden of Disease study, ischaemic heart disease and stroke accounted for 12.9 million deaths worldwide in 2013, or one in every four of the total (Naghavi 2015). CVD is also costly, and the World Economic Forum estimates that the direct cost attributable to CVD is USD 863 billion worldwide, with a projected rise of 22% by 2030 (Bloom 2011).

The incidence of CVD is largely explained by several modifiable risk factors, which include abnormal cholesterol, elevated blood pressure, diabetes mellitus, smoking, unhealthy diet, excessive alcohol intake, abdominal obesity, psychosocial stress, and lack of physical activity. These nine modifiable risk factors increase the risk of future CVD events and contribute to an estimated 90% of the population attributable risk fraction of ischaemic heart disease and stroke worldwide (O'Donnell 2010; Yusuf 2004). Prevention, treatment, and control of these risk factors before clinical manifestation are therefore primary targets of interventions to reduce the burden of CVD.

Description of the intervention

CVD events are often determined by the confluence of multiple, co-existing risk factors (Smith 2004). The multifactorial nature of CVD has led to the development and application of multivariable risk assessment tools, or CVD risk scores, to calculate CVD risk. CVD risk scores allow clinicians to integrate information from multiple CVD risk factors and quantitatively estimate a person's absolute risk for, or likelihood of experiencing, a CVD event during a defined period of time.

The first widely used multivariable CVD risk score was derived from the Framingham Heart Study in the USA (Anderson 1991; Wilson 1998). The Framingham risk score incorporated the effects of age, sex, systolic blood pressure, total cholesterol, high-density lipoprotein (HDL) cholesterol, smoking status, antihypertensive treatment status, and diabetes mellitus to estimate 10-year risk of coronary heart disease. During the past two decades, there has been widespread development of additional CVD risk scores such as the European Systematic COronary Risk Evaluation (SCORE) algorithm (Conroy 2003); the German Prospective Cardiovascular Munster (PROCAM) model (Assmann 2002); the UK QRISK and QRISK2 equations (Hippisley-Cox 2007; Hippisley-Cox 2008); the World Health Organization (WHO) risk chart (WHO 2007); the American College of Cardiology (ACC)/American Heart Association (AHA) 2013 Pooled Cohort risk equations (Goff 2014); and the Globorisk cardiovascular risk equation for use globally, including in low- and middle-income countries (Hajifathalian 2015). CVD prevention guidelines recommend use of these risk scores to guide treatment decisions for primary prevention in people who do not yet have clinical manifestations of CVD (Anderson 2013; NCEP 2002; NICE 2014; Piepoli 2016; Stone 2014; WHO 2007).

How the intervention might work

The current paradigm for CVD risk reduction in primary prevention matches the intensity of prevention efforts to a person's absolute risk for developing CVD (Bethesda 1996; Smith 2004). Risk-based prevention, therefore, directs treatments toward people at increased risk who derive greater benefit from treatment, while sparing people at lower risk for whom benefits may not outweigh the costs and harms of treatment. Qualitative assessment of CVD risk, however, is fraught with error, thereby providing a rationale for quantitative risk assessment tools (Grover 1995; Meland 1994; Pignone 2003; Van der Weijden 2008). Prevention guidelines in the USA, the UK, Europe, Canada, and the developing world promote the use of multivariable CVD risk scores to guide treatment decisions in primary prevention (Anderson 2013; NCEP 2002; NICE 2014; Piepoli 2016; Stone 2014; WHO 2007). The 2013 ACC/AHA Cholesterol Guidelines in the USA, described in Stone 2014, and the National Institute for Health and Care Excellence (NICE) recommendations for the prevention of CVD in the UK, laid out in NICE 2014, both advocate risk-based prevention strategies that incorporate multivariable CVD risk scores to estimate short- and long-term CVD risk, providing a quantitative framework to guide clinician-patient discussions regarding statins in primary prevention.

Analyses of randomised clinical trials (RCTs) provide empiric support for risk stratification by demonstrating that the absolute risk reduction from preventive medications is related more to the magnitude of pretreatment risk than the relative risk reduction associated with treating a single risk factor (BPLTTC 2014; CTT 2012; Jackson 2005). Therefore, use of CVD risk scores not only has the potential to effectively and efficiently direct preventive care to those in greatest need but may help maximise benefit of treatment in high-risk people and minimise harms of over-treatment in people at low risk. Additional purported benefits of CVD risk scores also include raising awareness of disease, improving communication between clinician and patient, and motivating adherence to recommended lifestyle changes or preventive therapies (Goff 2014).

Why it is important to do this review

Although considerable research has focused on the derivation and validation of multivariable CVD risk prediction tools in different populations, the effects of CVD risk scores to direct clinical prac-

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tice is poorly understood, and few studies have examined their utility in clinical practice (Damen 2016). In 2006 and 2008, two related systematic reviews performed with Cochrane methodology identified only four RCTs testing the clinical effects of CVD risk scores and found no clear evidence that CVD risk assessment improved health outcomes (Beswick 2008; Brindle 2006). In 2008, a systematic review examining the clinical benefits or harms of providing CVD risk scores identified six trials showing that physicians presented with risk information tended to appropriately prescribe preventive therapies (Sheridan 2008). Another systematic review examining the effect of giving CVD risk information to adults in clinical practice identified 18 studies (14 RCTs) demonstrating that global CVD risk information improved accuracy of risk perception and increased patients' intent to start pharmacotherapy (Sheridan 2010). However, in both reviews the effect of CVD risk scores on health outcomes, risk factors, and health behaviours was unclear.

In spite of widespread recommendations for the use of multivariable CVD risk scores in clinical practice guidelines (Anderson 2013; NCEP 2002; NICE 2014; Piepoli 2016; Stone 2014; WHO 2007), uncertainty remains about their effects on health-related outcomes. Given the publication of new trials and the continued prominence of multivariable CVD risk scores in primary CVD prevention guidelines, a systematic review of the literature is warranted.

OBJECTIVES

To assess the effects of evaluating and providing CVD risk scores in adults without prevalent CVD on cardiovascular outcomes, risk factor levels, preventive medication prescribing, and health behaviours.

METHODS

Criteria for considering studies for this review

Types of studies

We included RCTs and quasi-RCTs (systematic allocation) with individual or cluster allocation. We included studies reported as full text and abstracts as well as unpublished data.

Types of participants

We included studies that reported results for adults (18 years of age and older) in outpatient settings free of clinical CVD (defined as prior heart attack, stroke, heart failure, symptomatic peripheral vascular disease, or atrial fibrillation). Participants with diabetes mellitus or elevated risk factors as well as those already on background preventive medications were eligible for inclusion. For studies that included a combination of participants with and without prevalent CVD, we included studies that reported results for primary prevention participants. When studies included both primary and secondary prevention populations, we included only those studies with < 30% of the study population having prevalent CVD.

Types of interventions

We included trials that compared the systematic provision of a multivariable CVD risk score by a clinician, healthcare professional, or healthcare system versus usual care (i.e. no systematic provision of a CVD risk score) in primary CVD prevention. We excluded health risk appraisals not based on a risk score and studies testing risk of hypothetical patients.

Types of outcome measures

Primary outcomes

1. CVD events (a composite of fatal and non-fatal myocardial infarction and stroke)
2. Change in risk factor levels
   i) Cholesterol: total cholesterol, low-density lipoprotein (LDL) cholesterol
   ii) Blood pressure: systolic blood pressure, diastolic blood pressure
   iii) Change in multivariable CVD risk: a summary score or risk estimate that incorporates multiple and simultaneous changes in different CVD risk factor levels
3. Investigator-defined adverse events, including but not limited to physical or psychosocial events, including anxiety or depression

Secondary outcomes

1. Preventive medication prescribing in higher risk people
   i) Lipid-lowering medications
   ii) Antihypertensive medications
   iii) Aspirin
2. Medication adherence
3. Health-related behaviours
   i) Smoking cessation
   ii) Exercise
   iii) Diet
4. Decisional conflict, measured according to the decisional conflict scale
5. Health-related quality of life, measured according to any validated scale concerning quality of life
6. Costs

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Search methods for identification of studies

Key inclusion criteria were studies that were relevant to CVD primary prevention, employed a prospective design, and provided or incorporated a CVD risk score to guide treatment decisions in CVD prevention.

Exclusion criteria were studies that were unrelated to CVD risk scores; those addressing health risk appraisals not based on a quantitative risk score; those relying only on self-reported risk factors and lifestyle; and those involving clinical vignettes or hypothetical patients rather than real patients.

Electronic searches

We identified trials through systematic searches of the following bibliographic databases on 15 March 2016.

- Cochrane Central Register of Controlled Trials (CENTRAL; 2016 Issue 2) in the Cochrane Library (Wiley).
- Ovid MEDLINE(R) (1946 to March Week 1 2016).
- Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations (14 March 2016).
- Embase, including Embase Classic, via embase.com (1947 to 15 March 2016).
- Conference Proceedings Citation Index-Science (CPCI-S) via Web of Science (1990 to 15 March 2016).

Two authors (KNK, MAB) designed the database searches based on the MEDLINE search strategy used in a previous systematic review published with Cochrane methodology (Beswick 2008). The search strategies for each database are available in Appendix 1. For the MEDLINE search, we applied the Cochrane sensitivity and precision maximizing RCT filter (Lefebvre 2011). For Embase, we translated from Ovid to embase.com syntax, the multiterm Embase filter with the best balance of sensitivity and specificity (Wong 2006), and we limited the search to records indexed in Embase. For Conference Proceedings Citation Index-Science we used a combination of terms for identifying trials described in section 6.3.2.2 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Lefebvre 2011). We applied no filters to the CENTRAL search.

We searched all databases from their inception to March 2016, and we imposed no restriction on language of publication.

Searching other resources

We tried to identify other potentially eligible trials or ancillary publications by searching the reference lists of retrieved included studies and relevant review articles for additional references. We also searched ClinicalTrials.gov (www.ClinicalTrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) Search Portal (apps.who.int/trialsearch/) on 16 March 2016. Lastly, we contacted study authors of included or registered trials to identify further studies or unpublished data that could contribute to our review.

Data collection and analysis

Selection of studies

Three authors (KNK and SDP or MDH) independently screened titles and abstracts of every record retrieved to determine which studies to assess further, resolving disagreements by consensus. We then retrieved full-text study reports/publications of all eligible or potentially eligible reports. Three authors (KNK and SDP or MDH) independently screened full-text articles, identified studies for inclusion, and recorded reasons for exclusion of the ineligible studies. We resolved any disagreements through discussion or, if required, recourse to the third author (SDP or MDH). We identified and excluded duplicate reports and collated multiple reports of the same study so that each study, rather than each report, was the unit of analysis. We recorded the selection process in sufficient detail to complete a PRISMA flow diagram and Characteristics of excluded studies table.

Data extraction and management

For studies that fulfilled the inclusion criteria, we used standardised data extraction forms to record study characteristics and outcome data. We extracted the following study characteristics.

1. Methods: study design, total duration of study, details of any run-in period, number of study centres and location, study country and setting, withdrawals, and date of study.
2. Participants: N, mean age, age range, sex, severity of condition, diagnostic criteria, baseline CVD risk, smoking history, inclusion criteria, and exclusion criteria.
3. Interventions: CVD risk score used, comparator group.
4. Outcomes: primary and secondary outcomes specified and collected, and time points reported.
5. Notes: funding for trial, and notable conflicts of interest of trial authors.

Three authors (KNK and SDP or MDH) independently extracted outcome data from included studies in duplicate. We resolved disagreements by consensus or by involving the third author. One author (KNK) transferred data into Review Manager 5 (RevMan 2014), and another author (SDP) spot-checked to ensure that study characteristics and study data were entered correctly.

Assessment of risk of bias in included studies

Three authors (KNK and SDP or MDH) independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We resolved disagreements by consensus or by involving the third author. We assessed risk of bias according to the following domains.

1. Random sequence generation.
2. Allocation concealment.
3. Blinding of participants and personnel.

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4. Blinding of outcome assessment.
5. Incomplete outcome data.
6. Selective outcome reporting.
7. Other bias (e.g. industry funding).

We judged risk of bias criteria as low risk, unclear risk, or high risk and evaluated individual bias items as described in Higgins 2011. When considering treatment effects, we took into account the risk of bias for the studies that contributed to that outcome. For cluster-RCTs, we followed Cochrane recommendations for assessing risk of bias, with particular attention across the domains of recruitment, baseline imbalances, loss of cluster, incorrect analyses, and comparability with individually RCTs (Higgins 2011). Two of the review authors (SDP and DLJ) performed two studies included in this review (Persell 2013; Persell 2015). For these two studies, data extraction and risk of bias assessment were performed by review authors who were not involved with the conduct of either study (KNK and MDH).

Assessment of bias in conducting the systematic review

We conducted the review according to a published protocol and reported any deviations from it in the Differences between protocol and review section.

Measures of treatment effect

We analysed dichotomous data as risk ratios (RRs) with 95% confidence intervals (CIs). We used inverse variance methods to facilitate meta-analysis of outcomes from individual RCTs and appropriately analysed cluster-RCTs (Chapter 16.3.3 of Higgins 2011). We used RevMan 2014 to convert the reported effect estimates to a common risk ratio format. We analysed continuous data as mean difference (MD) or standardised mean difference (SMD) with 95% CIs. We entered data presented as a scale with a consistent direction of effect. For meta-analyses of mean differences, we pooled results of studies that reported final values with those reporting changes from baseline (Chapter 9.4.5.2 of Higgins 2011). For meta-analyses of SMDs, we pooled results of studies that reported change from baseline (change scores).

Unit of analysis issues

We included RCTs with parallel design and cluster-RCTs. For cluster-RCTs, we recorded whether investigators accounted for clustering in their analyses (e.g. multilevel model, generalised estimating equations). If analyses adjusted for clustering, then we meta-analysed individual RCTs with cluster-RCTs. For continuous outcomes, we used the inverse-variance method to calculate MDs and SMDs. For dichotomous outcomes, we used the generic inverse-variance method to meta-analyse the reported effect estimate (and corresponding standard error or confidence interval) from the appropriately-analysed cluster-RCT and the reported or calculated effect estimate from the individual RCT (Chapter 16.3.3 of Higgins 2011).

Dealing with missing data

We contacted investigators or study sponsors to verify key study characteristics and obtain missing numerical outcome data where possible (e.g. when a study is identified as abstract only). We investigated attrition rates, losses to follow-up, withdrawals, and critically appraised methods for handling missing data and imputation methods. If standard deviations for outcomes were not available, we imputed these values from data within the trial using methods outlined in Chapter 16.1.3 of Higgins 2011 and through RevMan 2014

Assessment of heterogeneity

We used the I^2 statistic to measure heterogeneity among the trials in each analysis. If we identified substantial ($I^2 > 50\%$) heterogeneity, we reported it and explored possible causes by subgroup analyses.

Assessment of reporting biases

We created and examined a funnel plot to explore possible publication and small study bias for the primary outcomes.

Data synthesis

We undertook meta-analyses only if the treatments, participants, and the underlying clinical questions in the studies were similar enough for pooling to be appropriate. If there was no or moderate heterogeneity ($I^2 \leq 50\%$), we performed fixed-effect model meta-analyses. If there was substantial heterogeneity ($I^2 > 50\%$), we performed a random-effects model meta-analyses with cautious interpretation.

Subgroup analysis and investigation of heterogeneity

We had planned on performing the following pre-specified subgroup analyses on our primary outcomes.

1. Sex (patient).
2. RCTs versus quasi-RCTs.
3. Trials providing CVD risk scores to clinicians versus trials providing CVD risk scores to patients.
4. Trials that incorporated a multivariable CVD risk score within a clinical decision support tool (either clinician-facing or patient-facing).

Among these prespecified subgroups, we were only able to perform a subgroup analysis among trials that used or did not use a clinical decision support tool. We did not have sufficient data from each trial to perform subgroup analysis by sex. We identified only one quasi-RCT. Lastly, many studies and protocols were unclear as to

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whether CVD risk scores were exclusively directed to a clinician or patient. Frequently, such risk scores were provided to both clinicians and patients during a clinical encounter.

Based on the substantial heterogeneity identified in our meta-analysis, we also performed two post hoc subgroup analyses on:

1. Trials that utilised health information technology (IT) for risk assessment or risk communication.
2. Trials that exclusively enrolled participants with higher risk (defined as 10-year CVD risk $\geq$ 10% or a high-risk condition such as diabetes mellitus).

We used the formal test for subgroup interactions in RevMan 2014.

Sensitivity analysis

We had planned to carry out sensitivity analyses excluding studies assessed as being at unclear or high risk of bias in any domain. However, we assessed nearly all studies as being at unclear or high risk of bias, so this sensitivity analysis was not performed.

Summary of findings table

We assessed the quality of the evidence for each outcome according to the GRADE approach and presented results in a 'Summary of findings' table (Guyatt 2008). We rated the quality of evidence as: high, moderate, low, or very low after consideration of within-study risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates, and risk of publication bias.

RESULTS

Description of studies

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

Results of the search

We identified 8723 records through database searching and an additional 13 records from prior systematic reviews of this topic (Brindle 2006; Beswick 2008; Sheridan 2008; Sheridan 2010; Willis 2012; Usher-Smith 2015). The article selection process is depicted in the PRISMA flowchart in Figure 1. After removing duplicates, we screened 6422 records and excluded 6238 based on title and abstract. We removed an additional 5 duplicate records and assessed 179 full-text records and 4 trial registry records for eligibility. We excluded 94 records of 77 studies and 2 trial registry records with reasons, identified 11 records of 10 ongoing studies, and listed 3 studies as awaiting classification. In total, we included 73 records of 41 studies (N = 194,035) in this systematic review.

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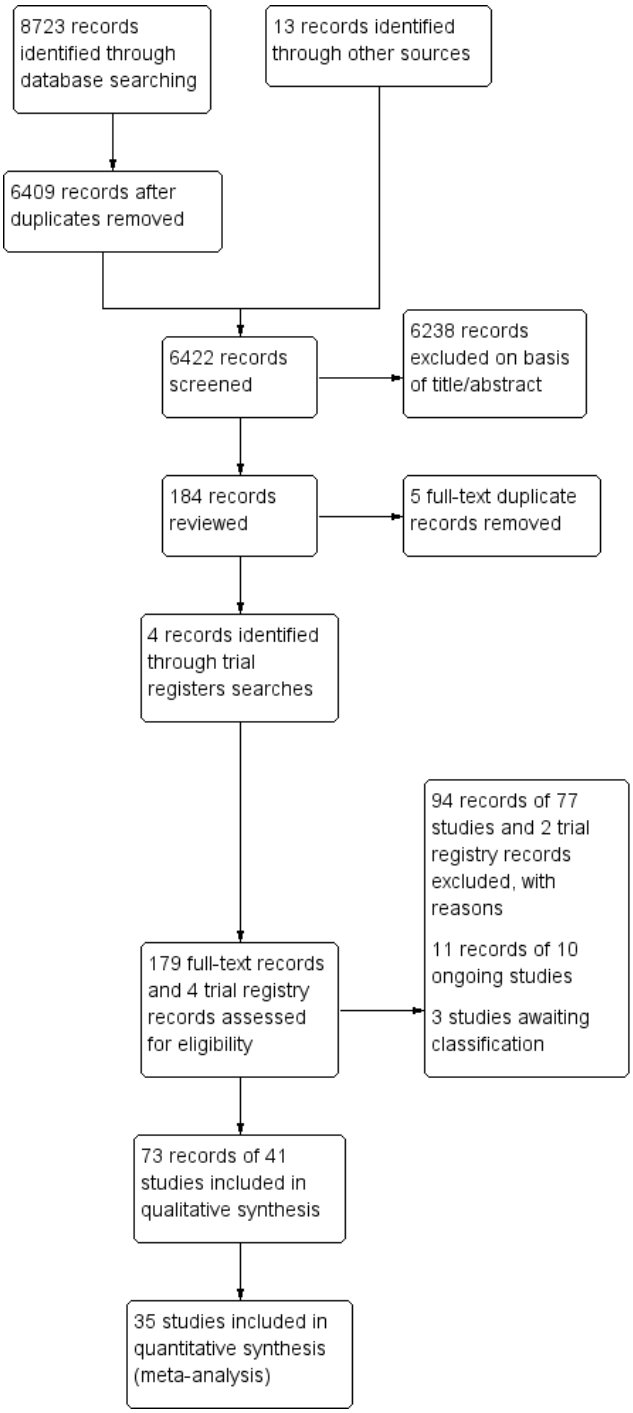
Figure 1. Study flow diagram.



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Included studies

Study design and location

Details of the methods, participants, intervention, comparison group, and outcome measures for each of the studies in this review are shown in the Characteristics of included studies table. We identified 23 individual-level RCTs (N = 117,040), 17 cluster-RCTs (N = 76,672), and 1 quasi-RCT (N = 323). The earliest trial was reported in 1994 (British Family Heart 1994), and the most recent was reported in 2016 (Perestelo-Perez 2016). Fifteen trials took place in European countries outside the UK (Benner 2008; Bucher 2010; Christensen 2004; Cobos 2005; Denig 2014; Engberg 2002; Hanon 2000; Hetlevik 1999; Jorgensen 2014; Koelewijn-van Loon 2010; Krones 2008; Lopez-Gonzalez 2015; Perestelo-Perez 2016; Van Steenkiste 2007; Welschen 2012); 12 trials in the USA (Bertoni 2009; Eaton 2011; Edelman 2006; Jacobson 2006; Mann 2010; Persell 2013; Persell 2015; Sheridan 2006; Sheridan 2011; Turner 2012; Williams 2006; Zullig 2014); 7 trials in the UK (British Family Heart 1994; Hall 2003; Hanlon 1995; Holt 2010; Montgomery 2000; Montgomery 2003; Price 2011); 3 trials in Canada (Grover 2007; Lowensteyn 1998; Wister 2007); 3 trials in Australia or New Zealand (Peiris 2015; Vagholkar 2014; Webster 2010); and 1 Internet-based trial that did not report a specific country (Soureti 2011). All studies were conducted in the outpatient setting. Participant follow-up ranged from no follow-up in Hall 2003, Jacobson 2006, and Sheridan 2006 to 10 years of extended follow-up in Jorgensen 2014. In total, 21 out of 41 trials reported a follow-up of one year or more.

Participants

Mean age reported in the trials ranged from 40 years in Engberg 2002 to 71 years in Montgomery 2000, and the proportion of female participants ranged from 8% in Hanlon 1995 to 80% in Edelman 2006. In the 20 trials that reported participants' ethnicity, most (16 out of 20) included a majority of white or European participants; the remaining 4 trials included a majority of African American participants (Jacobson 2006; Mann 2010; Persell 2015; Turner 2012). Participants in the included trials had varying past medical histories. Ten trials included only participants with higher CVD risk (defined as diabetes mellitus or 10-year CVD risk $\geq$ 10%) (Benner 2008; Denig 2014; Grover 2007; Hall 2003; Mann 2010; Perestelo-Perez 2016; Persell 2013; Persell 2015; Price 2011; Welschen 2012), and 5 of these trials included only participants with diabetes mellitus (Denig 2014; Mann 2010; Perestelo-Perez 2016; Price 2011; Welschen 2012). The other 31 trials included participants with all risk levels. There were 13 trials that included participants with prevalent CVD, but based on our selection criteria we included only those trials where these participants made up < 30% of the total sample (Bertoni 2009; British Family Heart 1994; Cobos 2005; Eaton 2011; Grover 2007; Holt 2010; Krones 2008; Montgomery 2000; Peiris 2015; Perestelo-Perez 2016; Turner 2012; Webster 2010; Zullig 2014). One trial included participants with human immunodeficiency virus (HIV) who were part of the Swiss HIV Cohort Study (Bucher 2010).

Interventions and comparison groups

Interventions varied across trials, which featured different CVD risk scores, risk presentations, and co-interventions (Figure 2). The two most common CVD risk scores used were the Framingham Coronary Heart Disease Risk Score (24 trials) and the UK Prospective Diabetes Study (UKPDS) risk engine (6 trials). In these trials, baseline CVD risk was presented as a 5- or 10-year absolute risk of a CVD event. Six trials used risk-adjusted cardiovascular age (called by various names such as heart age, cardiovascular age, or vascular age) in addition to or in lieu of the absolute CVD risk information (Eaton 2011; Grover 2007; Lopez-Gonzalez 2015; Lowensteyn 1998; Peiris 2015; Soureti 2011). In addition to the risk message, interventions also included: patient education material (31 trials); clinician- or patient-facing decision-support tools (27 trials); nurse counselling (11 trials); academic detailing/continuing medical education (9 trials); electronic health record integration (10 trials); electronic or paper-based reminders (7 trials); and audit and feedback (4 trials). A few trials implemented only one of these components (Hall 2003; Hanon 2000; Lopez-Gonzalez 2015; Welschen 2012), while on the opposite side of the spectrum, there were five or more of these components (Bertoni 2009; Denig 2014; ; Koelewijn-van Loon 2010; Peiris 2015; Sheridan 2011; Turner 2012; Vagholkar 2014; Wister 2007). In total, among the 41 studies, 28 studies incorporated health IT for some aspect of the risk score intervention. The range of co-interventions is summarised in Figure 2.

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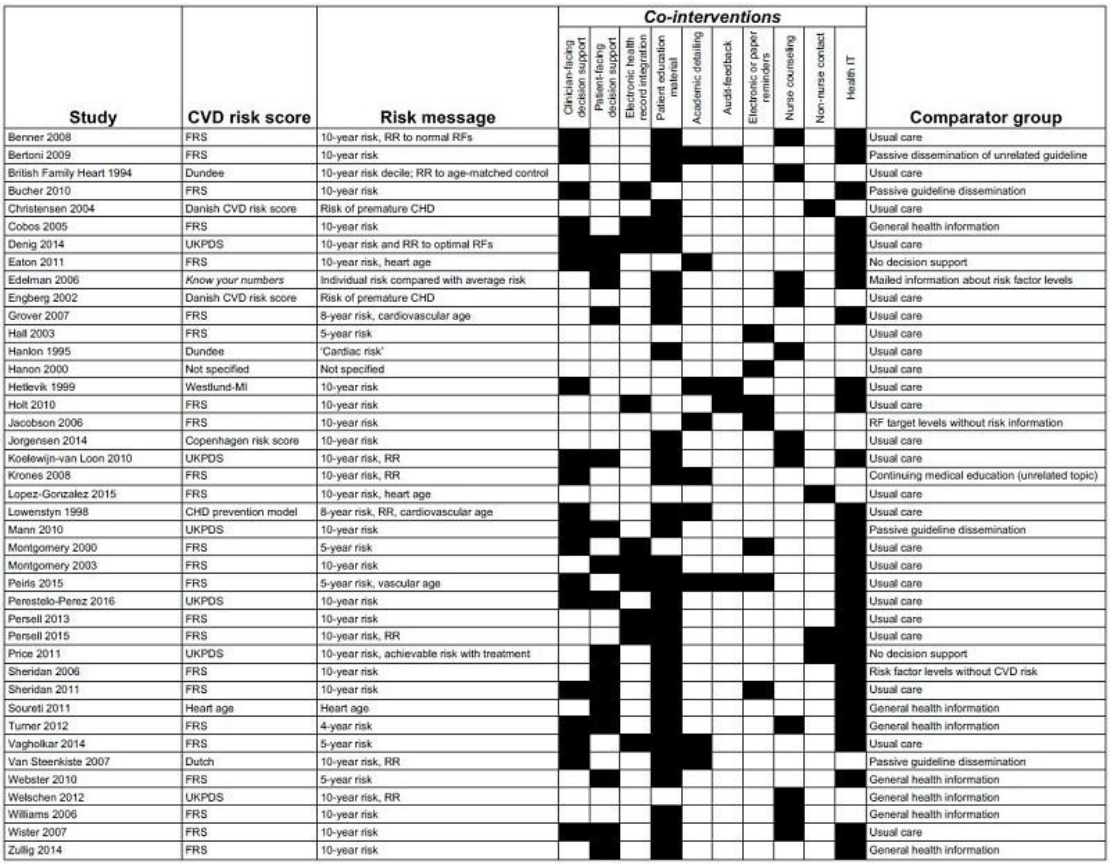
Figure 2. Summary of CVD risk score interventions by included study.Abbreviations: CHD: coronary heart disease; CVD: cardiovascular disease; FRS: Framingham risk score; MI: myocardial infarction; RF: risk factors, RR: risk ratio; UKPDS: United Kingdom Prospective Diabetes Study



Comparison groups were generally characterised as 'usual care' by study authors and did not include the systematic provision of CVD risk scores. Some studies described the addition of: passive guideline dissemination (Bucher 2010; Mann 2010; Van Steenkiste 2007), provision of risk factor levels alone (Edelman 2006; Jacobson 2006; Sheridan 2006), continuing medical education for an unrelated topic (Bertoni 2009; Krones 2008), and general health and risk factor information (Cobos 2005; Soureti 2011; Turner 2012; Webster 2010; Welschen 2012; Zullig 2014). Comparison group descriptions are summarised in Figure 2.

Outcomes

Among the included trials, the most common primary outcome in 10 trials addressed a clinical care process measure such as risk factor screening, preventive treatment discussions, guideline adherence, or achievement of risk factor targets (Bertoni 2009; Cobos 2005; Eaton 2011; Grover 2007; Jacobson 2006; Lowensteyn 1998; Montgomery 2000; Peiris 2015; Persell 2015; Sheridan 2006). Other primary outcomes reported in the included studies were multivariable CVD risk in eight trials (Benner 2008; British Family Heart 1994; Edelman 2006; Hanlon 1995; Krones 2008; Turner 2012; Wister 2007; Zullig 2014), patient-reported outcomes in seven trials (Christensen 2004; Denig 2014; Koelewijn-van Loon 2010; Mann 2010; Montgomery 2003; Perestelo-Perez 2016; Welschen 2012), CVD risk factor levels in six trials (Bucher 2010; Grover 2007; Hanon 2000; Lopez-Gonzalez 2015; Persell 2013; Persell 2015), medication prescribing rates in four trials (Hall 2003; Vagholkar 2014; Van Steenkiste 2007; Webster 2010), and health behaviours in three trials (Price 2011; Soureti 2011; Williams 2006). Only two trials reported CVD events as a primary outcome, but both reported being underpowered for this endpoint after completion of the study (Holt 2010; Jorgensen 2014).

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Study funding sources

We present detailed information on study funding sources in the Characteristics of included studies table. Five trials reported receiving study funding exclusively from pharmaceutical companies (Benner 2008; Cobos 2005; Grover 2007; Lowensteyn 1998; Soureti 2011). There were 19 trials that reported funding from public and/or federal government sources (Bertoni 2009; Denig 2014; Edelman 2006; Hanlon 1995; Hetlevik 1999; Koelewijn-van Loon 2010; Krones 2008; Montgomery 2000; Montgomery 2003; Peiris 2015; Perestelo-Perez 2016; Persell 2013; Persell 2015; Sheridan 2011; Vagholkar 2014; Van Steenkiste 2007; Welschen 2012; Williams 2006; Wister 2007), 7 trials that reported study funding from a combination of public and private sources (British Family Heart 1994; Bucher 2010; Christensen 2004; Engberg 2002; Jorgensen 2014; Turner 2012; Webster 2010), and 3 trials with study funding from internal (usually hospital) sources (Holt 2010; Jacobson 2006; Sheridan 2006). Five trials did not report sources of study funding (Eaton 2011; Hall 2003; Hanon 2000; Lopez-Gonzalez 2015; Mann 2010).

Excluded studies

We excluded 94 records of 77 studies after full-text review and 2 trial registry records. The most common reason for exclusion was that a risk score was not part of the intervention (41 trials). We excluded other studies because they provided CVD risk scores in all treatment groups without a usual care comparator group (16 trials), were not an RCT or quasi-RCT (10 trials), did not study a primary prevention population (11 trials), or used clinical vignettes and hypothetical patients (1 trial).

A complete list of excluded studies, along with the reason for exclusion of each study, is presented in the Characteristics of excluded studies table.

Studies awaiting classification

We identified three studies awaiting classification (Adamson 2013; Gryn 2012; Roach 2012). Two of these studies included participants with diabetes mellitus (Adamson 2013; Roach 2012), and one included participants with hypertension (Gryn 2012). All three studies reported having an intervention group that received a personalised CVD risk estimate, but the identified records were abstracts and did not provide sufficient details to determine eligibility for this systematic review. Authors of two of these studies reported preparing manuscripts (Gryn 2012; Roach 2012). We present additional details of these studies in the Characteristics of studies awaiting classification table.

Ongoing studies

We identified 11 reports of 10 ongoing studies. Three of these studies are taking place in Europe (Badenbroek 2014; Ijkema 2014; Maindal 2014), one in the USA (Sanghavi 2015), one in Canada (NCT00694239), one in the UK (Silarova 2015), one in Australia (Redfern 2014), and three in low- and middle-income countries (NCT02096887; Ogedegbe 2014; Praveen 2013). Two studies will supplement CVD risk scores with novel sources of CVD risk information: Ijkema 2014 with coronary artery calcium scores and Silarova 2015 with genetic risk information. Three ongoing studies will test innovative implementation models to provide CVD risk scores. These include: direct-to-patient health portals within an electronic health record (Redfern 2014), non-physician healthcare workers in resource-poor settings (Praveen 2013), and financial incentives linked to CVD risk assessment and absolute risk reduction (Sanghavi 2015). The Characteristics of ongoing studies table presents details of these studies.

Risk of bias in included studies

Overall and trial-specific assessment of risk of bias are shown in Figure 3 and Figure 4. In general, there was high risk of bias across the included studies. Due to the nature of the intervention, few trials were able to blind participants, study personnel, or both. Thus, in our overall risk of bias assessment, we put greater weight on blinding of outcome assessment (detection bias) compared to blinding of participants or study personnel (performance bias). We concluded that only three trials had an overall low risk of bias across most domains (Peiris 2015; Persell 2013; Persell 2015). We summarise risk of bias assessment across each domain below, but detailed documentation supporting risk of bias assessment for each trial is included in the Characteristics of included studies table.

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Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

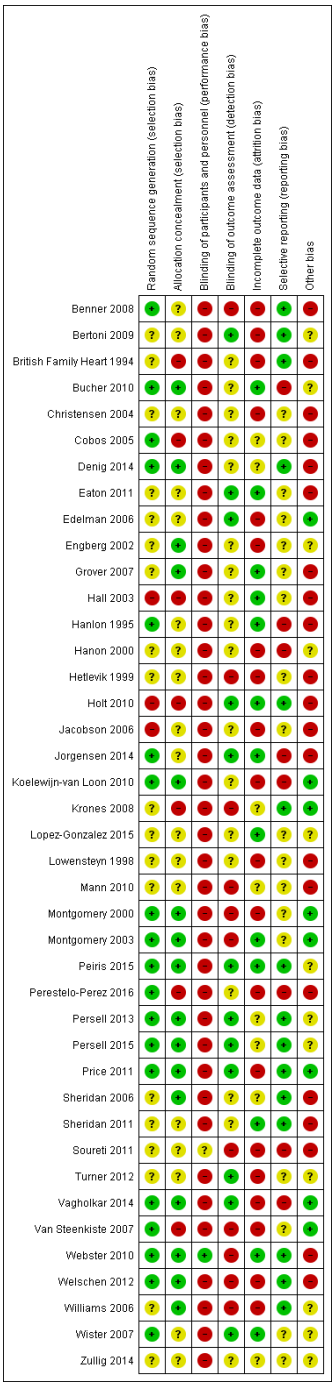

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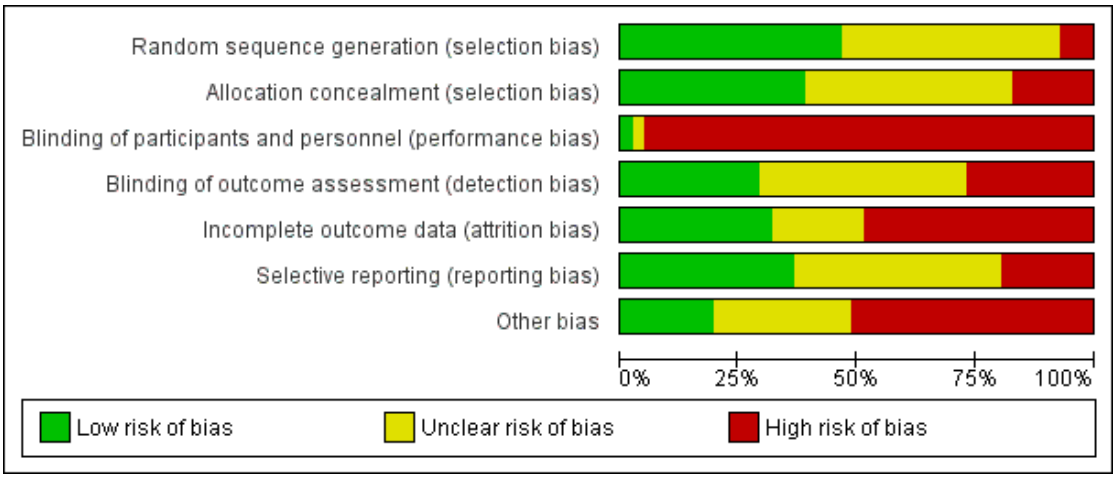
Figure 4. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

There were 19 trials that adequately reported the methods used for random sequence generation, and we assessed them as being at low risk of bias (Benner 2008; Bucher 2010; Cobos 2005; Denig 2014; Hanlon 1995; Jorgensen 2014; Koelewijn-van Loon 2010; Montgomery 2000; Montgomery 2003; Peiris 2015; Perestelo-Perez 2016; Persell 2013; Persell 2015; Price 2011; Vagholkar 2014; Van Steenkiste 2007; Webster 2010; Welschen 2012; Wister 2007). We assessed 19 trials as being at unclear risk of bias and 3 trials as having an inadequate method of random sequence generation.

Sixteen trials reported adequate allocation concealment (Bucher 2010; Denig 2014; Engberg 2002; Grover 2007; Koelewijn-van Loon 2010; Montgomery 2000; Montgomery 2003; Peiris 2015; Persell 2013; Persell 2015; Price 2011; Sheridan 2006; Vagholkar 2014; Webster 2010; Welschen 2012; Williams 2006). Among the remaining trials, there were 18 at unclear risk of bias and 7 trials at high risk of bias for allocation concealment.

In total, 12 trials were assessed as being at low risk of selection bias, that is, for both random sequence generation and allocation concealment (Bucher 2010; Denig 2014; Koelewijn-van Loon 2010; Montgomery 2000; Montgomery 2003; Peiris 2015; Persell 2013; Persell 2015; Price 2011; Vagholkar 2014; Webster 2010; Welschen 2012).

Blinding

Due to the nature of the intervention, we assessed 38 out of 41 trials as being at high risk of bias due to an unblinded study design. The trials with low or unclear risk of bias were Internet-based studies where research personnel had no direct contact with participants (Soureti 2011; Webster 2010). Therefore, we used blinding of outcome assessors to determine overall risk of bias. Among the 41 trials, 12 trials reported adequate blinding of outcome assessors (Bertoni 2009; Eaton 2011; Edelman 2006; Holt 2010; Jorgensen 2014; Peiris 2015; Persell 2013; Persell 2015; Price 2011; Turner 2012; Vagholkar 2014; Wister 2007). The remaining 18 trials were at unclear risk of bias, and 11 trials were at high risk of bias due to unblinded outcome assessors.

Incomplete outcome data

Many studies suffered from high losses to follow-up and missing data, particularly data used for calculating follow-up cholesterol levels or risk scores. Moreover, few studies performed intention-to-treat analyses. Only 13 trials adequately addressed incomplete data (Bucher 2010; Eaton 2011; Grover 2007; Hall 2003; Hanlon 1995; Holt 2010; Jorgensen 2014; Lopez-Gonzalez 2015; Montgomery 2003; Peiris 2015; Sheridan 2011; Webster 2010; Wister 2007). We assessed 8 trials as being at unclear risk of bias and 20 trials as being at high risk of bias due to incomplete outcome data.

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Selective reporting

Several of the included studies either had protocols available for review or were prospectively registered. The risk of bias associated with selective reporting was low in 15 trials (Benner 2008; Bertoni 2009; British Family Heart 1994; Denig 2014; Holt 2010; Krones 2008; Peiris 2015; Persell 2013; Persell 2015; Price 2011; Sheridan 2006; Sheridan 2011; Webster 2010; Welschen 2012; Williams 2006), unclear in 18 trials, and high in 8 trials.

Other potential sources of bias

Other potential sources of bias are reviewed in detail in the Characteristics of included studies table. Common sources of potential bias included: pharmaceutical funding or potential financial conflicts of interest among study authors (Benner 2008; Cobos 2005; Engberg 2002; Grover 2007; Holt 2010; Lowensteyn 1998; Soureti 2011; Williams 2006); contamination bias (Denig 2014; Grover 2007; Hanlon 1995; Holt 2010; Jacobson 2006; Jorgensen 2014; Persell 2015; Sheridan 2006; Sheridan 2011; Welschen 2012; Wister 2007); and poor fidelity to the intervention protocol (Bertoni 2009; British Family Heart 1994; Denig 2014; Eaton 2011; Mann 2010).

Effects of interventions

See: **Summary of findings for the main comparison** CVD risk scoring for the primary prevention of cardiovascular disease

See: Summary of findings for the main outcomes (Summary of findings for the main comparison).

Primary outcomes

Cardiovascular disease events

We identified only three RCTs (N = 99,070) that reported the effects of providing CVD risk scores on CVD events (Bucher 2010; Holt 2010; Jorgensen 2014). Among participants in the CVD risk score group, there was low-quality evidence suggesting little or no effect on CVD events compared with usual care (5.4% versus 5.3%; RR 1.01, 95% CI 0.95 to 1.08; I^2 = 25%; Analysis 1.1). Notably, study authors from two of these trials reported being underpowered for this endpoint because of limited recruitment of participants over the age of 50 and low CVD event rates (Holt 2010; Jorgensen 2014). The third trial was in a cohort of people with HIV in Switzerland (Bucher 2010). Due to the unique characteristics and limited generalisability of this cohort, we reanalysed data excluding this study; results were unchanged in direction and magnitude (Analysis 1.2).

Cholesterol level

Effects of providing CVD risk scores on cholesterol levels were reported for total cholesterol and LDL cholesterol. We identified 12 RCTs (N = 20,437) that reported the effects of providing CVD risk scores on total cholesterol and were included in the meta-analysis. There was low-quality evidence suggesting that providing CVD risk scores may slightly reduce total cholesterol levels compared with usual care (MD −0.10 mmol/L, 95% CI −0.20 to 0.00; I^2 = 94%; Analysis 1.3). We also identified 10 RCTs (N = 22,122) that reported on the effects of providing CVD risk scores on LDL cholesterol levels. There was uncertainty about the effect of providing CVD risk scores compared with usual care on LDL cholesterol levels (MD −0.03 mmol/L, 95% CI −0.10 to 0.04; I^2 = 84%; low-quality evidence; Analysis 1.4); the results were imprecise but similar in direction and magnitude to those for total cholesterol. There was substantial heterogeneity for both outcomes that was not explained by a single trial, so these effect estimates should be interpreted with caution. There was no evidence of publication bias by funnel plot for total cholesterol level (Figure 5). Many of the trials identified in this review reported on achievement of guideline-recommended cholesterol goals after provision of a CVD risk score. However, this outcome was deemed to be unsuitable for meta-analysis due to the marked variation in cholesterol goals from different countries, guidelines, and time periods. One pragmatic clinical trial (N = 435) did not use systematic follow-up procedures after providing CVD risk scores but reported that participants in the CVD risk score group had a greater proportion of repeat LDL cholesterol levels > 30 mg/dL lower than baseline compared with those in the usual care group (22.5% vs. 16.1%, OR 1.59, 95% CI 1.05 to 2.41, P = 0.029; Persell 2013).

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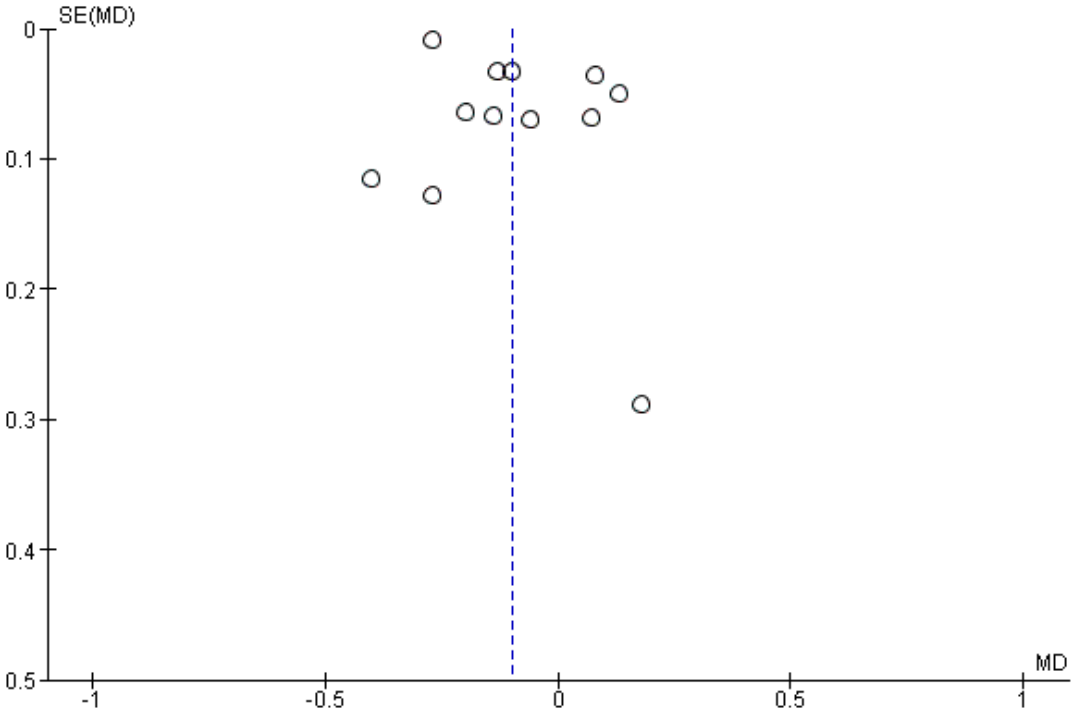
Figure 5. Funnel plot of comparison: 1 CVD risk score versus no CVD risk score/usual care, outcome: 1.3 Total cholesterol (mmol/L).



Blood pressure level

Trials reported the effects of providing CVD risk scores on blood pressure levels for systolic blood pressure, diastolic blood pressure, or both. We identified low-quality evidence suggesting that providing CVD risk scores may slightly reduce systolic blood pressure compared with usual care (MD −2.77 mmHg, 95% CI −4.16 to −1.38; I^2 = 93%; 16 trials, N = 32,954; Analysis 1.5). Similarly, we found low-quality evidence suggesting that providing CVD risk scores may slightly reduce diastolic blood pressure compared with usual care (MD −1.12 mmHg, 95% CI −2.11 to −0.13; I^2 = 94%; 14 trials, N = 22,378; Analysis 1.6). There was substantial heterogeneity for both outcomes that was not explained by a single trial, so readers should interpret these estimates with caution. There was no evidence of publication bias by funnel plot for systolic blood pressure (Figure 6). Of note, there were two RCTs that reported the effects of providing CVD risk scores on systolic and diastolic blood pressures, but we did not pool them because of insufficient data (Bucher 2010; Hanon 2000). Neither trial found a difference in blood pressure level between the CVD risk score versus usual care groups.

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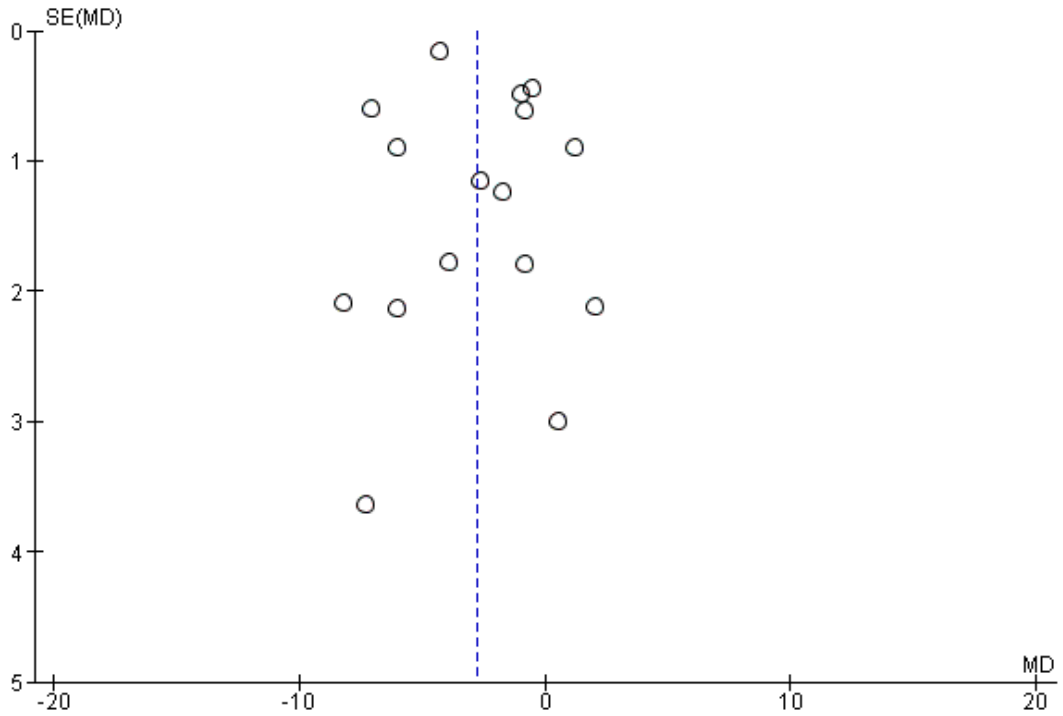
Figure 6. Funnel plot of comparison: 1 CVD risk score versus no CVD risk score/usual care, outcome: 1.5 Systolic blood pressure (mmHg).



Multivariable CVD risk

In total, 17 RCTs (N = 29,119) reported on the effects of providing CVD risk scores on multivariable CVD risk (a summary measure that incorporated changes in multiple different CVD risk factor levels simultaneously). The scale of this measure varied among studies. Moreover, some studies compared final values between the two treatment groups while others compared change from baseline values. We elected to calculate standardised mean differences (SMDs) for change from baseline values for the CVD risk score group and the usual care comparator for our main outcomes. We identified low-quality evidence suggesting that providing CVD risk scores may slightly reduce multivariable CVD risk compared with usual care (SMD −0.21, 95% CI −0.39 to −0.02; I^2 = 94%; 9 trials, N = 9549; Analysis 1.7). There was substantial heterogeneity that was not explained by a single trial, so readers should interpret these estimates with caution. There was no evidence of publication bias by funnel plot (Figure 7). We also meta-analysed studies that compared final values for multivariable CVD risk estimates between the intervention and comparison groups and observed similar findings (SMD −0.15, 95% CI −0.25 to −0.06; Analysis 5.1).

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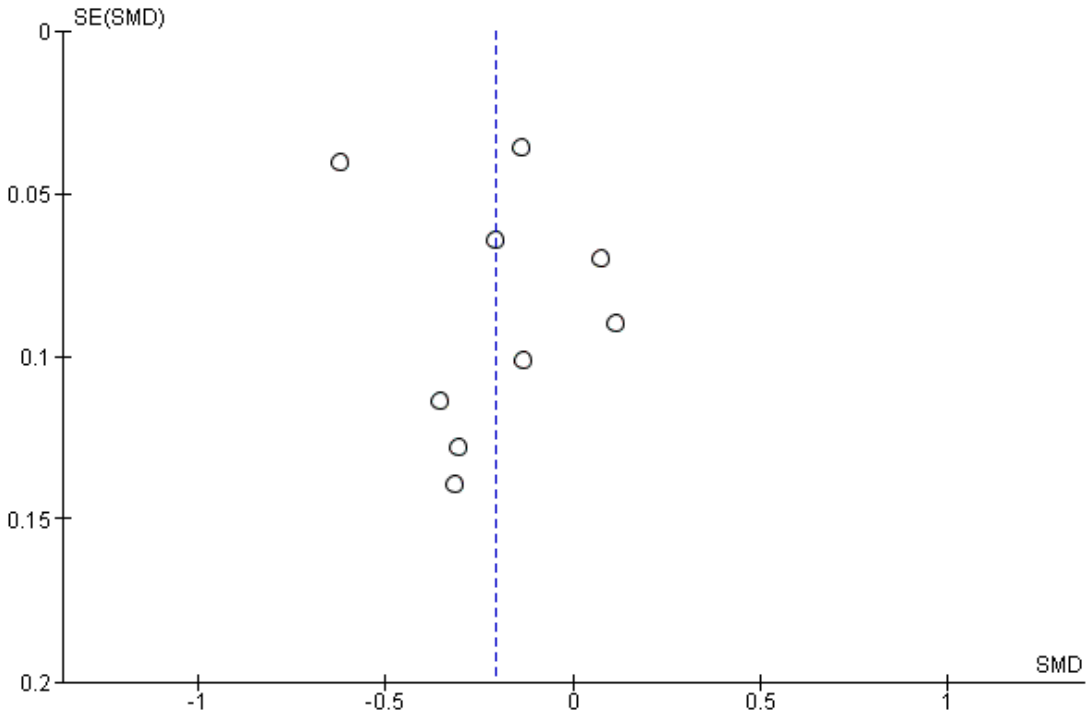
Figure 7. Funnel plot of comparison: 1 CVD risk score versus no CVD risk score/usual care, outcome: 1.7 Change in multivariable CVD risk.



Five trials reported the effects of the intervention on multivariable CVD risk, but we did not pool these in the meta-analyses because of how they reported data (British Family Heart 1994, Bucher 2010; Hetlevik 1999; Price 2011; Zullig 2014). One of these trials demonstrated a reduction in multivariable CVD risk with the provision of a CVD risk score (British Family Heart 1994). This cluster-RCT randomised 12,472 men and women in 13 towns in Britain to a nurse-led screening and counselling programme based on Dundee score (a measure of coronary heart disease risk) or usual care. After one year, the intervention reduced the Dundee risk score by 16.1% (95% CI 10.9% to 21.1%) in men and 15.7% (95% CI 7.4% to 23.3%) in women compared with usual care. The other four studies (N = 6626), however, did not find that provision of a CVD risk score changed multivariable CVD risk (Bucher 2010; Hetlevik 1999; Price 2011; Zullig 2014).

Adverse events

There were four RCTs (N = 4630) that reported on adverse events after providing a CVD risk score (Benner 2008; Grover 2007; Price 2011; Turner 2012). Definition of adverse events varied between studies and included back pain, headache, cough, upper respiratory infection, musculoskeletal pain, and anxiety. There was low-quality evidence suggesting that providing a CVD risk score may reduce adverse events compared with usual care, but the results were imprecise (1.9% versus 2.7%; RR 0.72, 95% CI 0.49 to 1.04; I^2 = 0%; Analysis 1.8). There were three RCTs (N = 968) that specifically reported on the effect of the CVD risk scores on anxiety (Montgomery 2000; Van Steenkiste 2007; Welschen 2012). Two measured anxiety as a continuous variable and observed that providing CVD risk scores may have little to no effect on anxiety compared with usual care (SMD −0.07, 95% CI −0.27 to 0.13; I^2 = 0%; 2 studies, N = 388; low-quality evidence; Analysis 1.9). We did not include Van Steenkiste 2007 in meta-analysis due to insufficient reporting of data but observed no difference in the proportion of anxious participants who received a CVD score versus usual care (16% vs 16%, P value not provided). Lastly, one trial measured psychological distress in middle-aged participants who received a CVD risk assessment (with or without primary care physician follow-up) compared with usual care (Christensen 2004). This trial found no difference in psychological distress at one and five years between participants in the two treatment groups that received a CVD risk assessment compared with those in the usual care group (P = 0.466 at one year and P = 0.579 at five years).

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Secondary outcomes

Medication prescriptions in higher risk individuals

New or intensified lipid-lowering medications

We identified low-quality evidence suggesting that providing CVD risk scores may increase prescriptions for new or intensified lipid-lowering medications in higher risk people compared with usual care (15.7% versus 10.7%; RR 1.47, 95% CI 1.15 to 1.87; I^2 = 40%; 11 trials, N = 14,175; Analysis 1.10). There was substantial heterogeneity among studies that was not explained by a single trial, so readers should interpret these estimates with caution.

Four additional studies reported the effects of providing a CVD risk score on lipid-lowering medication prescribing compared with usual care, but we did not include them in the meta-analysis because they did not report sufficient data to determine which higher-risk participants received a lipid-lowering medication (Bertoni 2009; Cobos 2005; Krones 2008; Webster 2010). None of these studies reported a change in lipid-lowering medication prescribing. In Bertoni 2009, use of a CVD risk score-based decision support tool increased "guideline-concordant lipid-lowering therapy" compared with passive dissemination of an unrelated guideline (9.7%, 95% CI 2.8% to 16.6%), but this was primarily driven by a reduction in inappropriate prescribing in lower risk individuals. Authors reported no difference in appropriate lipid-lowering medication prescribing rates (P = 0.37) (Bertoni 2009). Similarly, in Cobos 2005, a computerised decision-support tool that provided a personalised CVD risk score decreased inappropriate statin prescribing (primarily in lower risk individuals) but did not increase guideline-recommended statin prescribing compared with usual care. In Krones 2008, the authors reported no difference in the proportion of participants with CVD risk >15% who were treated with preventive medications between the CVD risk score group and the usual care comparator but formal statistical testing was not presented. Lastly, in Webster 2010, there was no difference in new or increased lipid-lowering medication prescribing in a group of Australian adults randomised to a web-based decision support tool (percent difference −1.6%, 95% CI −3.57 to 0.57, P = 0.15), but insufficient data were available to determine risk status of participants who received therapy.

New or intensified antihypertensive medications

We identified low-quality evidence that providing CVD risk scores may increase new or intensified antihypertensive medications compared with usual care (17.2% versus 11.4%; RR 1.51, 95% CI 1.08 to 2.11, I^2 = 53%; 8 studies, N = 13,255; Analysis 1.11). There was substantial heterogeneity among studies that was not explained by a single trial, so readers should interpret these estimates with caution. We did not pool three studies reporting the effects of providing CVD risk scores on antihypertensive medication prescribing in the meta-analysis because they did not provide sufficient information to determine which high-risk participants were prescribed antihypertensive medications. None of these studies reported a difference in antihypertensive medication prescribing between the two groups (Jacobson 2006; Krones 2008; Montgomery 2003).

New aspirin prescriptions

Providing CVD risk scores may increase new aspirin prescribing compared with usual care (RR 2.71, 95% CI 1.24 to 5.91, I^2 = 0%; 3 studies, N = 1614; Analysis 1.12). We did not pool three additional studies reporting the effect of providing CVD risk scores on aspirin prescribing in the meta-analysis because it was unclear which participants were at higher risk (Jacobson 2006; Krones 2008), and the trials did not provide data on primary prevention (Peiris 2015). Two of these studies reported no difference in aspirin prescribing in the overall study population (Jacobson 2006; Krones 2008). The other study reported an increase in aspirin prescribing among participants with prevalent CVD (17.8% vs 2.7%; RR 4.79, 95% CI 2.47 to 9.29), but this did not meet the primary prevention focus of this review (Peiris 2015).

Medication adherence

There was uncertainty whether providing CVD risk scores had an effect on medication adherence compared with usual care (RR 1.14, 95% CI 0.92 to 1.41, I^2 = 58%; 4 studies, N = 621; Analysis 1.13). One additional study (N = 150) reported "no difference" in medication adherence rates between participants randomised to a statin decision support tool but did not provide specific estimates or statistical testing (Mann 2010).

Health behaviours

Smoking

Providing a CVD risk score may increase smoking cessation compared with usual care (RR 1.38, 95% CI 1.13 to 1.69, I^2 = 0%; 7 studies, N = 5346; Analysis 1.14). There were nine additional studies that reported on the effects of providing CVD risk scores on the prevalence of smoking rates, and results were mixed. Five of these studies reported reductions in smoking prevalence in the CVD risk score group compared with the usual care group (British Family Heart 1994; Jorgensen 2014; Koelewijn-van Loon 2010; Lopez-Gonzalez 2015; Van Steenkiste 2007), whereas four studies reported no change in smoking prevalence in the CVD risk score group compared with usual care (Denig 2014; Hetlevik 1999; Price 2011; Zullig 2014). In the only study to biochemically verify

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smoking status, there was no difference in urine cotinine for participants who received a CVD risk score compared with usual care (SMD −0.53, 95% CI −1.23 to 0.17, P = 0.136; Price 2011).

Exercise

There were eight RCTs (N = 8391) that reported the effects of providing CVD risk scores on physical activity (Edelman 2006; Hanlon 1995; Koelewijn-van Loon 2010; Lopez-Gonzalez 2015; Price 2011; Van Steenkiste 2007; Webster 2010; Wister 2007). Physical activity outcomes varied by studies and included: self-reported increase in physical activity, number of days exercising > 30 minutes, and proportion meeting physical activity guidelines. Two studies (N = 2595) measured self-reported increase in physical activity, and demonstrated no evidence that providing a CVD risk score had an effect on this outcome compared with usual care (RR 0.98, 95% CI 0.90 to 1.06, I^2 = 0%; Analysis 1.15). The remaining 6 RCTs reported mixed results on physical activity. One RCT of 154 participants reported an increase in the number of days with physical activity > 30 minutes (3.7 days in intervention versus 2.4 days in control; P = 0.002; Edelman 2006). Similarly, Lopez-Gonzalez 2015 reported an increase in self-reported exercise sessions per week in participants receiving a Framingham risk message compared with usual care: 3.48 sessions (95% CI 3.35 to 3.62) in the Framingham risk message group versus 3.60 sessions (95% CI 3.47 to 3.73) in the usual care group. In Van Steenkiste 2007, authors reported an increase in within-group physical activity among participants receiving a CVD risk score compared with usual care, but there were marked baseline imbalances between the two treatment groups and follow-up data were missing from >50% of participants. In contrast, there was no change in physical activity in the CVD risk score group compared with usual care in two RCTs involving 930 participants (Koelewijn-van Loon 2010; Wister 2007). Only one RCT (N = 198) used an objective measure of physical activity with an accelerometer and showed no difference in total accelerometer counts between those in the CVD risk score group and those in the usual care group (SMD 0.086, 95% CI −0.202 to 0.374, P = 0.559; Price 2011).

Diet

There were six RCTs (N = 5375) that reported information on the effects of providing CVD risk scores on diet (Hanlon 1995; Koelewijn-van Loon 2010; Price 2011; Soureti 2011; Webster 2010; Wister 2007). Measures of diet were highly variable with little overlap, so we did not perform quantitative meta-analysis. Results varied among studies. Two studies reported improvements in heart-healthy diets after providing a CVD risk score (Hanlon 1995; Wister 2007). In Hanlon 1995, self-reported increase in fruit and vegetable consumption (24.3% versus 11.6%, P < 0.001) and self-reported reduction in fat consumption (30.0% versus 9.4%, P < 0.001) was greater in the CVD risk score group compared with usual care (Hanlon 1995). Similarly, in Wister 2007 nutritional level (as measured by a 5-point ordinal scale based on the number of recommended food groups met per day)was higher in the CVD risk score group compared with the usual care group (0.30, 95% CI 0.13 to 0.47 versus −0.05, 95% CI −0.22 to 0.12; p <0.01; units not provided). In contrast, four studies reported no difference in healthy dietary patterns between the two groups (Koelewijn-van Loon 2010; Price 2011; Soureti 2011; Webster 2010).

Decisional conflict

We identified evidence suggesting that providing a CVD risk score may reduce decisional conflict compared with usual care (SMD −0.29, 95% CI −0.57 to −0.01, I^2 = 79%; 4 studies, N = 1261; Analysis 1.16). The effect estimate had substantial heterogeneity that was explained by Montgomery 2003, the study with the largest magnitude reduction in decisional conflict. The direction of the effect was similar, but the magnitude was attenuated when excluding this trial from the analysis (SMD −0.16, 95% CI −0.28 to −0.04, I^2 = 0%; 3 studies, N = 1049 participants).

Health-related quality of life

One trial (N = 308) reported on the effect of providing CVD risk scores on health-related quality of life, measured by the Dutch Euro quality of life (EQ5D-NL) scale. There was no evidence to suggest that providing CVD risk scores compared with usual care had an effect on quality of life in this one study (effect size −0.006, 95% CI −0.035 to 0.023, I^2 = 0%; Denig 2014).

Costs

One trial conducted in Spain reported the effects of providing CVD risk scores on direct costs (Cobos 2005). Providing a CVD risk score to a clinician decreased overall lipid-lowering medication prescribing rates by decreasing prescriptions in low-risk individuals. The adjusted mean treatment cost per patient was EUR 237 in the usual care group versus EUR 178 in the intervention group, for a difference of EUR 59 (95% CI 34, 83; P < 0.001), a savings of 25% in treatment costs. Similarly, the adjusted means of the total costs per patient were EUR 283 in the usual care group versus EUR 223 in the intervention group, for a difference of EUR 60 (95% CI 33, 86; P = 0.001), a total savings of 21%. A reduction in lipid-lowering medication prescribing rates among low-risk participants was also seen in a quality improvement trial employing a personal digital assistant (PDA) that calculated 10-year coronary heart disease risk (Bertoni 2009); however, investigators performed no formal cost-effectiveness analysis. Likewise, British Family Heart 1994 did not perform a formal cost-effectiveness analysis, but based on the observed risk factor changes and the projected reduction in coronary events, the authors suggested that the modest improvements did not support broader implementation of the intervention.

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Subgroup and sensitivity analyses

We performed a subgroup analysis evaluating the effects of providing CVD risk scores on CVD risk factor levels (total cholesterol, LDL-cholesterol, systolic blood pressure, diastolic blood pressure, and multivariable CVD risk) by use of clinical decision-support tools to provide CVD risk scores. Results were similar in magnitude and direction, but substantial heterogeneity remained for all analyses (Analysis 2.1; Analysis 2.2; Analysis 2.3; Analysis 2.4; Analysis 2.5).

Due to the substantial heterogeneity observed for CVD risk factor levels, we also performed post hoc subgroup analyses evaluating the effects of providing CVD risk scores by use of health IT and by trials that exclusively enrolled participants with higher risk (defined as 10-year CVD risk $\geq$ 10% or a high-risk condition such as diabetes mellitus). For subgroup analyses by use of health IT, results were similar in magnitude and direction, but substantial heterogeneity remained for all analyses (Analysis 3.1; Analysis 3.2; Analysis 3.3; Analysis 3.4; Analysis 3.5). In contrast, heterogeneity for the effects of providing CVD risk scores on total cholesterol and LDL cholesterol was attenuated when including trials that exclusively enrolled higher-risk participants (MD −0.13 mmol/L, 95% CI −0.22 to −0.03, I^2 = 34%; 3 studies, N = 4105 for total cholesterol, Analysis 4.1; and MD −0.07 mmol/L, 95% CI −0.11 to −0.03, I^2 = 0%; 3 studies, N = 14,219 for LDL cholesterol, Analysis 4.2). This attenuation of heterogeneity was not seen for systolic blood pressure (Analysis 4.3), diastolic blood pressure (Analysis 4.4), or multivariable CVD risk (Analysis 4.5), which may reflect the greater emphasis on risk-based treatment in cholesterol guidelines compared with blood pressure guidelines.

We did not identify sufficient data to perform subgroup analyses by sex or trial design (RCT versus quasi-RCT). Additionally, after reading study protocols, it was often unclear whether CVD risk scores were provided directly to patients or to clinicians because frequently CVD risk scores were provided to both within the context of a clinical encounter. We did not perform sensitivity analyses because we assessed all studies as being at unclear or high risk of bias.

DISCUSSION

Summary of main results

The trials identified in this systematic review provide low-quality evidence that current strategies for providing CVD risk scores in primary prevention may have little to no effect on CVD events compared with usual care. However, only three studies reported this outcome, and all had limitations. Compared with usual care, providing CVD risk scores may reduce CVD risk factors like cholesterol, blood pressure and multivariable CVD risk by a small amount and may reduce adverse events, but results were imprecise. There was substantial heterogeneity for many analyses, particularly when analysing change in risk factor levels. This was likely a result of: diverse risk levels of the participants recruited for the studies; the multifaceted and varying nature of the interventions tested; different baseline medication treatment rates; and the different outcomes collected. Given this heterogeneity, readers should interpret results with caution.

Providing CVD risk scores may increase prescriptions for new or intensified lipid-lowering medications, new or intensified antihypertensive medications, and new aspirin therapy in higher-risk people. Further, providing CVD risk scores may increase smoking cessation and may reduce decisional conflict compared with usual care. However, providing CVD risk scores may have little to no effect on medication adherence or health-related quality of life. Measurement of exercise and diet was highly variable among the included studies, and the effects of providing CVD risk scores on these outcomes were mixed. Data on costs were also limited but suggest a reduction in healthcare costs after providing CVD risks scores. Full reporting of effect sizes and quality of evidence ratings for main outcomes are listed in Summary of findings for the main comparison.

Overall completeness and applicability of evidence

This review provides the most contemporary appraisal of the evidence to date. We identified 73 records of 41 studies (N = 193,614), 8 ongoing studies, and 3 studies awaiting classification. This compares with only four trials (N = 4648) identified in two previous systematic reviews addressing a similar objective and using Cochrane methodology (Brindle 2006; Beswick 2008). We employed broad selection criteria that led to the inclusion of a wide range of trials with different designs, risk levels among participants, and choices of outcomes. CVD risk score interventions also ranged from simple CVD risk score presentations to multifaceted interventions that incorporated different risk messages, clinical decision support tools, electronic reminders, patient activation material, audit and feedback, and nurse-led counselling sessions. These inclusive selection criteria led to substantial heterogeneity in many of our pooled estimates. However, they also enhance the external validity of our findings due to the varied settings, populations, and interventions studied in the trials. Although many CVD prevention guidelines recommend the use of multivariable CVD risk scores to guide primary prevention treatment strategies (Anderson 2013; NCEP 2002; NICE 2014; Piepoli 2016; Stone 2014; WHO 2007), we identified multiple evidence gaps to guide the application of CVD risk scores in clinical practice. Trials generally had a short-term focus, had methodological limitations particularly in the domains of attrition bias and detection bias, and were underpowered for clinical endpoints. Given the multifactorial nature of many of the CVD risk score interventions, it is also

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unclear which component of the intervention was most effective at improving CVD prevention. Thus, there is uncertainty about optimal implementation of CVD risk scores in practice to improve cardiovascular health outcomes.

Quality of the evidence

Using the GRADE framework, we rated the quality of evidence guiding the clinical application of CVD risk scores in primary CVD prevention as low overall. Quality assessments were generally downgraded due to: study limitations across multiple risk of bias domains; inconsistency of results due to the substantial unexplained heterogeneity in pooled estimates; and imprecision. Specifically, we rated the quality of evidence for the effects of providing CVD risk scores on CVD events as low, downgrading due to study limitations and imprecision. We rated the quality of evidence for the effects of providing CVD risk scores on CVD risk factor levels (total cholesterol, systolic blood pressure, and multivariable CVD risk) as low, downgrading due to study limitations and inconsistency. We rated the quality of evidence for the effects of providing CVD risk scores on adverse events as low, downgrading due to study limitations and imprecision. We rated the quality of evidence for the effects of providing CVD risk scores on new or intensified lipid-lowering medications and antihypertensive medications as low, downgrading due to study limitations and inconsistency.

Potential biases in the review process

Our review has several strengths. First, we followed a pre-specified, published protocol to guide our systematic review and noted any deviations from this protocol. Second, we conducted a comprehensive, transparent search strategy that was guided by an information specialist (MAB) and that identified published reports, conference abstracts, and clinical trial registers. Third, we included only RCTs or quasi-RCTs that used a systematic method of allocation to the CVD risk score intervention. Fourth, we performed all title screening, data extraction, and risk of bias assessments in duplicate to minimise bias. Fifth, we used the GRADE framework to rate the quality of evidence and factored this quality assessment to guide our conclusions regarding the effects of providing CVD risk scores.

The principal limitation of this review is the quality of the available data. Nearly all trials (38 out of 41) had high or unclear risk of bias across multiple domains. Moreover, most trials were powered for process outcomes rather than clinical outcomes, were designed for short duration, did not use systematic follow-up procedures, and delivered CVD risk messages at a single time point only. Trials also varied in terms of design, risk levels of participants, complexity of CVD risk score interventions, content of risk messages, and choice of outcomes. This heterogeneity is demonstrated in the results of our meta-analysis and should temper confidence in our reported effect estimates. This inconsistency is also reflected in our GRADE quality assessments. Our selection criteria of trials with all or ≥70% primary prevention participants and where only the intervention group received a multivariable CVD risk score led to the exclusion of several well-known trials that included a majority of participants with established CVD (Cleveringa 2008; Ketola 2001; Weymiller 2007). Other prominent but excluded trials provided a CVD risk score to both treatment groups (Keyserling 2014; Kullo 2016). Nevertheless, we feel that our inclusive definition of a CVD risk score intervention and the methods we used to select and evaluate the evidence outweigh these limitations.

Agreements and disagreements with other studies or reviews

Our results are consistent with prior systematic reviews performed on this topic. Two previous systematic reviews performed with Cochrane methodology identified no strong evidence that CVD risk scores improved health outcomes (Beswick 2008; Brindle 2006). However, both reviews searched literature through 2004 and only included interventions that provided a CVD risk score to clinicians. Therefore, they identified only four studies (N = 4648). In contrast, our search was performed through March 2016 and included CVD risk score assessment provided directly to patients or performed at the health system level. Consequently, we identified a greater number of trials and were able to provide greater detail about the effects of CVD risk scores on a variety of intermediate outcomes and health behaviours. Other systematic reviews have also highlighted that CVD risk scores can increase patients' intent to start therapy and physicians' prescribing of cardiovascular medications with no evidence of harm (Sheridan 2008; Sheridan 2010). However, these reviews did not systematically collect or report effects of CVD risk scores on individual risk factor levels or cardiovascular outcomes.

Our results complement the findings of a recently published non-Cochrane systematic review that evaluated the effect of providing a CVD risk score on clinical outcomes (Usher-Smith 2015). This review identified 17 trials (N = 19,036) and reported a small reduction in modelled CVD risk (−0.39%, 95% CI −0.71 to −0.07); a trend toward lower mean total or LDL cholesterol (−0.11 mmol/L, 95% CI −0.23 to 0.01); an increase in lipid-lowering and antihypertensive medication prescribing in high-risk participants (RR 2.11, 95% CI 1.27 to 3.49 and RR 2.38, 95% CI 1.11 to 5.10, respectively); and mixed effects on smoking cessation, physical activity, and alcohol consumption. Notably, this review did not identify evidence that providing CVD risk scores had an effect on blood pressure level (systolic blood pressure: −0.82 mmHg, 95% CI −2.70 to 1.05; diastolic blood pressure: −0.48 mmHg, 95% CI −1.41 to 0.44). This review, however, has notable limitations. For example, it included non-randomised, before-after studies at high risk of selection bias. Additionally, the authors did not use a

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systematic framework, such as GRADE, to assess the quality of evidence or guide recommendations. Lastly, the authors used restrictive inclusion criteria that led to the exclusion of many contemporary trials that incorporated CVD risk score interventions within complex, multifaceted interventions. Our review addresses many of these limitations by including only RCTs or quasi-RCTs, using GRADE to assess the quality of evidence, and including trials with multifaceted interventions such as Peiris 2015, where provision of a CVD risk score was just one component of a larger implementation model. Thus, our review may provide a more comprehensive and generalisable assessment of the current state of the science.

AUTHORS' CONCLUSIONS

Implications for practice

Due to the low-quality evidence available, we are unable to draw firm conclusions about the clinical effectiveness of providing CVD risk scores in primary CVD prevention. Providing CVD risk scores may increase lipid-lowering and blood pressure-lowering medication prescribing in higher risk people and may have a small effect on reducing cardiovascular risk factor levels; however, there is insufficient high-quality evidence to determine whether this translates into improved CVD outcomes. For clinical outcomes, not only was there low-quality evidence, but only three studies reported this endpoint. Much uncertainty remains about the optimal implementation of CVD risk scores in clinical practice to improve cardiovascular health outcomes.

Implications for research

In spite of the widespread promulgation of CVD risk scores in prevention guidelines, there is low-quality evidence and several gaps in evidence for guiding implementation in practice. Given the low event rates in primary prevention, it may not be feasible or practical to conduct a study with a large enough size and duration to determine the effects of providing CVD risk scores on CVD outcomes. Future studies should clearly identify how well the intended CVD risk score application was implemented in practice and evaluate its effectiveness in studies powered to identify reductions in causal risk factor levels. Moreover, studies should identify the optimal content and format of CVD risk messages that motivate behaviour change in physicians and patients, assess the impact of providing CVD risk information longitudinally over time, and look beyond initiation of evidence-based risk-reducing therapies to address uptake and long-term adherence to these therapies to achieve risk factor changes and eventual improvements in health outcomes.

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* *Indicates the major publication for the study*

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CHARACTERISTICS OF STUDIES

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

Benner 2008

Methods	Cluster-randomised trial, parallel group (1:1)
Participants	Patients from outpatient clinics in 9 European countries Unit of randomisation: primary care clinic Inclusion criteria: 45-64 years of age with a history of hypertension, systolic blood pressure ≥ 140 mmHg (or ≥ 130 mmHg if renal disease), and a 10-year risk of coronary heart disease (CHD) ≥ 10% Exclusion criteria: individuals with a history of CHD, diabetes mellitus, fasting plasma glucose > 6.9 mmol/L, or practices that routinely used risk calculators 101 clinics randomised: n = 51 intervention, n = 50 usual care; 1 clinic excluded prior to participant recruitment 1103 participants randomised: n = 565 intervention, n = 538 usual care Mean (SD) age: 56.8 (5.1) years, 14% women, 96% white; no diabetes mellitus
Interventions	Intervention group: • Physicians calculated participants 10-year predicted CHD risk using a hand-held electronic device and advised participants according to a risk communication programme; • participants were provided with a 'Heart Health' report including absolute and relative risk information and bar charts • nurse-led education sessions by phone to discuss behaviour modifications every 4 weeks (weeks 6, 12, 18). Comparison group: usual care (risk factor assessment but 10-year CHD risk not provided)
Outcomes	Primary outcome: Framingham 10-year CHD risk at 6 months Secondary outcomes: changes in blood pressure and cholesterol levels; attainment of blood pressure and ATP-III LDL-C goals; knowledge; attitude; behaviour; adverse effects Number of clinics analysed: n = 50 intervention, n = 50 usual care Number of participants analysed for safety: n = 563 intervention, n = 533 usual care Number of participants analysed for efficacy: n = 524 intervention, n = 461 usual care Follow-up: 6 months
Study funding sources	"This study was sponsored by Pfizer Inc, who were involved in the study design, data collection, data analysis, manuscript preparation and publication decisions."
Notes	Endpoints analysed using mixed effects models to account for clustering Did not meet recruitment target. 91 participants (n = 30 intervention, n = 61 usual care) were excluded from efficacy analyses due to failure of hand-held electronic devices

Risk of bias		*Risk of bias*
Bias	**Authors' judgement**	**Support for judgement**

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Benner 2008 (*Continued*)

Random sequence generation (selection bias)	Low risk	Computer based algorithm to assign study sites to allocation
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Physicians unblinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Risk factors in follow-up were measured by the unblinded physicians
Incomplete outcome data (attrition bias) All outcomes	High risk	> 10% excluded due to device failure or loss to follow-up. Disproportionate loss to follow-up in usual care and these individuals were excluded from analyses. ITT analysis not performed
Selective reporting (reporting bias)	Low risk	All outcomes from protocol were reported
Other bias	High risk	Pharmaceutical funding and several investigators had ties to industry

Bertoni 2009

Methods	Cluster-randomised trial, parallel group (1:1)
Participants	66 primary care practices in North Carolina randomised (n = 32 intervention, n = 34 comparison). 5 practices withdrew before intervention started (3 intervention, 2 comparison) Medical records abstracted from 5057 participants at baseline (n = 2841 intervention, n = 2216 comparison) Inclusion criteria: self-described primary care practices, staffed by internal medicine or family medicine providers, 3 h driving radius of research site in North Carolina Exclusion criteria: direct affiliation to medical school or residency programme, practices providing subspecialty care, sites outside of North Carolina Mean age of participants: 46 years, 57% women, 62% non-Hispanic white, 9% African American; 7% established CVD, 9% diabetes mellitus
Interventions	Both groups received guideline dissemination, patient education materials, continuing medical education, feedback based on baseline chart audit, and 4 visits for intervention-specific academic detailing Intervention group: • Hand-held computerised decision support tool (personal digital assistant) with ATP-III treatment recommendations • Personalised risk information printed for participants

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Bertoni 2009 (*Continued*)

	Comparison group: no decision support, dissemination of JNC-7 guidelines, blood pressure measurement devices provided to participants
Outcomes	Primary outcome: proportion of participants treated appropriately to lipid-lowering treatment 4 months after intervention Secondary outcomes: proportion of participants with appropriate lipid-lowering treatment, inappropriate lipid-lowering treatment, and lipid screening 61 practices analysed (n = 29 intervention; n = 32 comparison) Medical records abstracted from 3821 participants at follow-up (n = 2010 intervention, n = 1811 comparison) Follow-up: 1 year
Study funding sources	Funded by that National Heart, Lung, and Blood Institute, USA
Notes	Endpoints analysed using generalised estimating equations to account for clustering Analyses compared overall prescribing rates in randomly selected participants before and after the intervention but did not follow individual participants Analyses Trial reported a net improvement in appropriate management but this was due to a reduction in inappropriate lipid-lowering treatment compared with the comparison group

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported by authors "Randomization was stratified by practice type and size and blocked"
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported by authors
Blinding of participants and personnel (performance bias) All outcomes	High risk	"The intervention was not blinded."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Abstractors were not informed regarding the practice's intervention arm."
Incomplete outcome data (attrition bias) All outcomes	High risk	2 practices withdrew after randomisation and data were not collected
Selective reporting (reporting bias)	Low risk	All outcomes reported in clinical trial registration were reported

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Other bias	Unclear risk	46% of practices stopped using the clinical decision support tool

British Family Heart 1994

Methods	Cluster-randomised trial with internal and external comparators
Participants	Men and women from 14 towns in the UK with 2 matched-practices within each town Unit of randomisation: general medical practice Inclusion criteria: all men aged 40-59 years and their partners regardless of age Exclusion criteria: not specified The trial consisted of 2 comparison groups, an internal comparison and an external comparison. Regions were first randomised to the study or usual care (defined as the external comparison group). Within the study region, general medical practices were then randomised to the nurse-led screening and the CVD risk score intervention or usual care (defined as the internal comparison) Total randomised: 28 practices (n = 14 intervention, n = 14 comparison). Authors did not specify how many practices were in the internal comparison group and how many were in the external comparison group Total participants (n = 12,924): intervention, 2011 men and 1425 women; internal comparison, 2174 men and 1402 women; external comparison, 3519 men and 2393 women Mean (SD) age: 51.5 (5.7) years for men and 49.1 (6.8) years for women; 42% women; 5.1% of men and 1.6% of women reported prior coronary heart disease; 1.8% of men and 0.5% of women reported diabetes mellitus
Interventions	Intervention group: nurse-led cardiovascular risk screening and lifestyle intervention: • Communication of risk decile by Dundee risk score • Counselling on diet, weight, smoking, exercise, and alcohol • Frequency of follow-up determined by Dundee risk score Comparison group: usual care without nurse-screening, lifestyle counselling, or communication of Dundee risk score (Note: for analyses, we used comparisons between the intervention group and the internal control group as this was the authors' primary outcome)
Outcomes	Primary outcome: change in Dundee risk score Secondary outcome: distribution and means of cardiovascular risk factors (systolic blood pressure, diastolic blood pressure, total cholesterol, smoking prevalence); proportion of participants with risk factor levels above prespecified cut-points Number analysed in follow-up: 26 practices (13 intervention, 13 comparison) Participants analysed at 1-year follow-up: total, n = 12,472; intervention, 1767 men and 1217 women; internal comparison, 2174 men and 1402 women; external comparison, 3519 men and 2393 women Follow-up: 1 year
Study funding sources	Public and private sources. "The study was funded by the Family Heart Association with an educational grant from Merck Sharp and Dohme, the family health service authorities and Fife Health Board, Boehringer Mannheim UK, Wessex Regional Health Authority,

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	the Health Education Authority, the Scottish Home and Health Department, and the Department of Health."
Notes	Endpoints analysed using random effects models to account for clustering Data reported separately for men and women by the authors but combined for meta-analyses in this review Protocol deviation identified by 1 nurse in an intervention practice. An executive committee decided (without sight of data) to discard all data from this intervention practice and therefore to disregard all data from the comparison practice Authors did not perform a formal cost-effectiveness analysis but the overall predicted risk reduction of 12% from the intervention was not felt to be cost-effective

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"All men aged 40-59 years in each intervention and comparison practice were randomly ordered at the same time within five year age groups . . . [and] randomly divided into two groups: intervention and an internal comparison group"
Allocation concealment (selection bias)	High risk	"[W]ithin each age group their households were approached in order" Participants were also recruited after individual practices were randomised
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel unblinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	14% lost to follow-up in intervention group; those who did not return were more likely to be smokers and have higher risk factor levels
Selective reporting (reporting bias)	Low risk	All outcomes from protocol reported
Other bias	High risk	Protocol deviations by 1 nurse in intervention group. Executive committee decided to discard data from the entire practice and the comparator practice. No baseline measurements in comparison groups

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Bucher 2010

Methods	Cluster-randomised trial, parallel group (1:1)
Participants	Physicians in the Swiss HIV Cohort Study (SHCS) in Switzerland caring for HIV-infected participants Unit of randomisation: physician Inclusion criteria: all physicians who were part of the SCHS were eligible. Eligible patients were those registered with the SHCS, not pregnant, aged ≥ 18 years, continuous ART for 90 days prior to baseline and with complete data on CHD risk factors at baseline Exclusion criteria: no additional criteria from above 165 physicians randomised at baseline (n = 80 intervention, n = 85 comparison) 117 physicians included (n = 57 intervention, n = 60 comparison) - 45 physicians were excluded because they did not have any participants with risk factor assessment and 3 physicians did not have any eligible participants 4097 participants eligible at baseline (n = 2097 intervention, n = 2000 comparison) Mean age (IQR): 44 (39-51) , 30% women, 5% diabetes mellitus, 26% with Framingham risk score (FRS) ≥ 10%
Interventions	Intervention group: risk profile generated by the data centre for each participant randomised to the intervention group; profile consisted of 10-year CHD risk as calculated by FRS. Study nurses added the FRS risk profile to the patient chart. Each risk profile also included individualised targets for LDL cholesterol, systolic/diastolic blood pressure Comparison group: booklet of evidence-based guidelines for management of CHD risk factors. Guidelines also gave directions on how to approach and motivate lifestyle modifications and how to calculate CHD risk from a website
Outcomes	Primary outcome: total cholesterol Secondary outcomes: systolic and diastolic blood pressure, Framingham risk score Follow-up: 12-18 months 3362 participants analysed at follow-up (n = 1680 intervention, n = 1682 comparison)
Study funding sources	Public and private sources. "This trial was funded by a grant from the Swiss National Science Foundation for nested cohort projects . . . and an unrestricted educational grant from Bristol-Myers Squibb, Baar, Switzerland."
Notes	Primary and secondary outcomes analysed using generalised estimating equations to account for clustering Analyses reporting the effect of the intervention on medication prescribing and CVD events (not mentioned in methods, or in trial registration)

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Randomized groups were assigned according to a computerized list for each strata generated by a biostatistician not otherwise involved in the trial."
Allocation concealment (selection bias)	Low risk	See above

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Bucher 2010 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	"This was an open intervention trial, that is, physicians knew whether they received the intervention or not but were not told what outcomes would be measured."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method used for outcome assessment not provided
Incomplete outcome data (attrition bias) All outcomes	Low risk	80% of participants had a final assessment with data recorded for the primary outcome; ITT analysis performed
Selective reporting (reporting bias)	High risk	Trial prospectively registered (NCT00264394). Primary and secondary outcomes reported but medication prescribing outcome not prespecified
Other bias	Unclear risk	Analyses for primary and secondary outcomes accounted for clustering but unclear if medication prescribing outcome accounted for clustering

Christensen 2004

Methods	Randomised controlled, parallel group (1:1:1) trial
Participants	1507 middle-aged (30-49 years) participants registered in general practice clinics in the district of Ebeltoft, Denmark Inclusion criteria: aged 30-49 years (by 1 January 1991); registered with a local general practitioner (GP) in Ebeltoft, Denmark Exclusion criteria: none reported Baseline characteristics not provided, 11% were high CVD risk
Interventions	Participants were randomised into a control group and 2 intervention groups Intervention group 1: health screening + written feedback from GP + optional discussions with GP (n = 502) Intervention group 2: health screening + written feedback from GP + scheduled 45-min discussion with GP annually (n = 504) Control group: usual care (n = 501) Among those randomised to intervention group 1, 89% (449/502) received a health screening. Among those randomised to intervention group 2, 90% (456/504) received health screening and 88% (443/504) received GP visit. In total, 90% of those in the 2 intervention groups received a cardiovascular risk score Health screening was performed by laboratory assistants and consisted of cardiovascular risk calculation and categorisation into low, moderate, elevated, or high. Intervention groups were combined for analyses by the authors because there were no differences between the 2 groups. Results were compared to usual care participants who did not

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Christensen 2004 (*Continued*)

	receive a CVD risk score
Outcomes	Psychological distress, measured by GHQ-12 - measured anxiety/insomnia, depression, social impairment/hypochondria, and social dysfunction Measured at baseline, 1 year, and 5 years Authors report 84.1% follow-up at 1 year and 79.2% follow-up at 5 years but few other details on the number of participants analysed in follow-up
Study funding sources	Study funded by a combination of Danish public organisations and private industry (i. e. Novo Nordisk, Bayer Denmark, Roche)
Notes	Few trial details provided. No details on baseline characteristics. Psychological distress measured 1 and 5 years after participants received their CVD risk score

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	20% missing data for GHQ-12 at 1 year; 25% missing data for GHQ-12 at 5 year; ITT analysis reported but not performed
Selective reporting (reporting bias)	Unclear risk	Protocol document not available
Other bias	High risk	Unlikely that measurement of psychological distress at 1 and 5 years after a CVD risk score intervention is meaningful

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Cobos 2005

Methods	Cluster-randomised trial, parallel group (1:1)
Participants	People with hypercholesterolemia recruited from primary care health practices in Catalonia region, Spain Unit of randomisation: primary care health practices Inclusion criteria: total cholesterol level > 200 mg/dL Exclusion criteria: triglycerides > 400 mg/dL or participating in another study within the medical centre 44 primary care health practices randomised (n = 22 intervention, n = 22 comparison). 2 practices withdrew before participants recruited 2191 participants recruited after selection criteria (n = 1046 intervention, n = 1145 comparison) Mean age: 60 years, 57% women, 16% with diabetes mellitus, and 12% with CHD; ~ 50% of participants were previously treated with lipid-lowering drugs
Interventions	Intervention group: • Practices provided patient education material promoting a health cardiovascular lifestyle • Physicians were asked to use a clinical decision support software module that calculated 10-year CHD risk and provided treatment recommendations from within the electronic health record Control group: usual care with health promotion pamphlets but no calculation of CHD risk
Outcomes	ITT analysis performed on the 2191 participants recruited (described above). Per-protocol analyses also presented in the manuscript Primary outcomes: proportion of participants meeting LDL goals (for CHD, 10-year CHD risk ≥ 20%, and 10-year CHD risk < 20%); total direct costs Secondary outcomes: final lipid profile; healthcare resource consumption incurred during the study Mean follow-up: 12 months
Study funding sources	"Study supported by the Department of Outcomes Research & Disease Management, Novartis Farmaceutica SA, Spain"
Notes	Endpoints analysed using generalised estimating equations to account for clustering Only 71% of physicians in the intervention group used the decision support tool

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"The randomization table was prepared by the statistician, using blocks of four practices."
Allocation concealment (selection bias)	High risk	Randomisation performed using blocks of 4 practices

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Cobos 2005 (*Continued*)

Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of personnel or participants
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method for outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	> 20% missing lipid levels in follow-up; ITT analysis used but no imputation of missing values
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Other bias	High risk	Study supported by Novartis and 1 author had industry ties. Approximately 71% of physicians in the intervention group did not use the decision support tool

Denig 2014

Methods	Randomised controlled trial, 2 × 2 factorial
Participants	Participants with type 2 diabetes mellitus aged < 65 years managed in primary care setting Inclusion criteria: no additional criteria reported Exclusion criteria: people with myocardial infarction (MI) in preceding year, stroke, heart failure, angina, or terminal illness 344 participants randomised at baseline (n = 225 intervention, n = 119 for usual care group) Mean (SD) age: 61.7 (8.5), 44% women, > 90% white, 100% diabetes mellitus; high-rate of baseline treatment (76% treated with statin)
Interventions	Intervention group: decision aid for people with diabetes mellitus that provided individually-tailored risk information and treatment options for multiple cardiovascular risk factors; the decision-aid was offered to participants before a regular diabetes mellitus check-up and to healthcare provider during the consultation Comparison group: usual care For this systematic review, groups randomised to the decision aid, which provided a CVD risk score, were compared to those in the usual care group (who did not receive a decision aid)
Outcomes	Primary outcome: diabetes empowerment scale Secondary outcome: changes in drug prescription in those with high HbA1c, systolic blood pressure, or LDL; self-efficacy; satisfaction; negative emotions; and general health status (EQ-5D); smoking status 306 participants analysed for the study's primary outcome (n = 199 intervention, n = 107 comparison). Not explicitly stated how many were analysed for secondary outcomes obtained from the electronic health record

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Denig 2014 (*Continued*)

	Follow-up: 6 months before and after intervention
Study funding sources	Funded by Netherlands Organization for Health Research and Development
Notes	4 different formats of the decision aid were tested in exploratory analyses but outcomes for participants allocated to any decision aid were combined by the study authors in this manuscript and was similarly done for this systematic review

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"A stratified computer generated allocation sequence was used."
Allocation concealment (selection bias)	Low risk	"We used a predefined computer algorithm with a blockwise scheme to conceal the allocation process from the healthcare provider."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	High-risk for patient-reported outcomes Low-risk for clinical outcomes (automatic data extraction from database)
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	31 participants excluded (22 intervention vs 9 control); excluded from analysis
Selective reporting (reporting bias)	Low risk	All outcomes from protocol reported
Other bias	High risk	Randomisation occurred within a practice, increasing the risk for contamination. Decision aid was accessed for 88% (198/225) of intervention participants but only 46% (103/225) of intervention participants received all basic elements of the intervention

Eaton 2011

Methods	Cluster-randomised trial, parallel group (1:1)
Participants	Patients from 30 primary care practices in southeastern New England, USA Inclusion criteria: no additional criteria reported Exclusion criteria: no additional criteria reported in text but PRISMA flow diagram in the paper notes that participants were excluded if they were pregnant, died, or left the

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Eaton 2011 (*Continued*)

	practice during the 1 year follow-up 30 practices randomised (n = 15 intervention, n = 15 comparison) 4105 participants after exclusion criteria (n = 2100 intervention, n = 2000 comparison) Mean (SD) age: 54.0 years (1.1) in intervention group and 52.3 (1.1) in control group; 29% women; 96% white; 20% CHD; 10% diabetes mellitus
Interventions	Both groups received a 1-h academic detailing session where ATP-III guidelines were discussed and pocket guidelines were given Intervention group: • Patient education toolkit • Computer kiosk with patient activation software • Personal digital assistant-based decision support tool for clinician • 4 booster academic detailing sessions Comparison group: personal digital assistant without decision support
Outcomes	Primary outcome: proportion of participants screened and treated per 2001 guidelines Follow-up: 1 year 30 practices analysed (n = 15 intervention, n = 15 comparison) 4105 participants analysed (n = 2100 intervention, n = 2000 comparison)
Study funding sources	Not reported
Notes	Endpoints analysed using generalised linear mixed models to account for clustering Only 39% had a Heart Age calculated by clinicians. In post hoc analyses, physicians with above-median use of the decision support tool were more likely to have their participants meet LDL goals (OR 1.23, 95% CI 1.04 to 1.06)

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Chart outcome abstractors blinded to physician and practice
Incomplete outcome data (attrition bias) All outcomes	Low risk	No practices lost to follow-up and ITT analysis performed for primary outcome
Selective reporting (reporting bias)	Unclear risk	Protocol document unavailable

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Eaton 2011 (*Continued*)

Other bias	High risk	Low uptake of both patient activation tool among patients and decision support tool among physicians

Edelman 2006

Methods	Randomised controlled trial, parallel group (1:1)
Participants	Adults ≥ 45 years without prevalent CVD Inclusion criteria: ≥ 1 cardiovascular risk factors (diabetes mellitus, HTN, dyslipidaemia, smoking, or elevated BMI) Exclusion criteria: history of MI, stroke, heart failure, terminal illness, pregnant women 154 adults enrolled and randomised (n = 77 intervention, n = 77 comparison) Mean (SD) age: 52.2 years (5.2) in intervention group, 53.4 years (4.8) in control group; 81% women, 76% white, 20% African American, 16% diabetes mellitus
Interventions	Intervention group: • Personalised risk education • Personalised health plan delivered by health coach • Individual coaching sessions biweekly by phone • Group sessions weekly for the first 4 months, bi-weekly for months 5-9, and then at conclusion Comparison group: usual care, mailed health assessment (blood test values but CVD risk score not provided)
Outcomes	Primary outcome: Framingham risk score Secondary outcome: BMI, waist circumference, blood pressure, fasting lipid profile, smoking status, exercise frequency, readiness to increase exercise Follow-up: baseline, 5 months, and 10 months
Study funding sources	Center for Medicare and Medicaid Services, Veterans Affairs Health Services Research & Development career development award
Notes	Resource intensive intervention from health coaches with multiple follow-up meetings

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias)	High risk	Participants and personnel not blinded

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Edelman 2006 (*Continued*)

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"A research assistant blinded to treatment arm assignment measured the data required to calculate FRS at baseline, 5 months, and 10 months."
Incomplete outcome data (attrition bias) All outcomes	High risk	> 20% loss to follow-up
Selective reporting (reporting bias)	Unclear risk	Protocol document not available for review
Other bias	Low risk	Other sources of bias not identified

Engberg 2002

Methods	Randomised controlled trial, parallel group (1:1:1)
Participants	Men and women aged 30-49 years from primary care clinics in Ebeltoft, Denmark Inclusion criteria: additional criteria not reported Exclusion criteria: none reported 1507 participants randomised (n = 504 health screening + physician discussion, n = 502 health screening only, n = 501 comparison/usual care) Mean age: 40.5 years, 51% women, 100% Danish
Interventions	Intervention groups: 2 health screenings or 2 health screenings + 45 min follow-up consultation with general practitioner to discuss health-related lifestyle goals Comparison group: usual care For the analyses in this review, the "health screening + physician discussion" and "health screening only" groups were combined since both groups received a personalised CVD risk score
Outcomes	Primary outcome not specified; Danish CVD risk score, BMI, cholesterol level, systolic blood pressure, and diastolic blood pressure reported 1093 participants analysed at 5 years (n = 346 health screening + physician discussion, n = 378 health screening only, n = 369 usual care) Follow-up: 1 year and 5 years
Study funding sources	Funded by County Health Insurance office and other private/public sponsors, including Novo Nordisk, ASTRA-Denmark, Bayer, and Roche
Notes	-

Risk of bias			***Risk of bias***
Bias	**Authors' judgement**	**Support for judgement**	

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Engberg 2002 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	Low risk	"An employee of Aarhus County who was not otherwise involved in the study carried out the randomization."
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Participants were informed by their general practitioner about which intervention they would be offered."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear risk of bias for cardiovascular risk factors. High-risk of bias for patient-reported outcomes
Incomplete outcome data (attrition bias) All outcomes	High risk	25-30% loss to follow-up in all 3 treatment groups by 5 years. No imputation of missing values
Selective reporting (reporting bias)	Unclear risk	Primary and secondary outcomes unclear in protocol document
Other bias	Unclear risk	Partial funding from pharmaceutical industry. Authors speculate on potential risk of contamination between participants in different treatment groups but attempted to mitigate this risk by allocating cohabitating couples into the same intervention group

Grover 2007

Methods	Randomised controlled trial, parallel group (1:1)
Participants	Patients in primary care clinics across 10 provinces in Canada Inclusion criteria: • CVD, DM, or 10-year CHD risk > 30% and TC:HDL ratio > 4 • 10-year CHD risk 20-30% and TC:HDL ratio > 5 • 10-year CHD risk 10-20% and TC:HDL ratio > 6 Exclusion criteria: hypersensitivity to statins, risk of pregnancy, breastfeeding, active liver disease or liver enzyme abnormalities, elevated creatine kinase, elevated triglycerides (> 939 mg/dL), history of pancreatitis, significant renal insufficiency 3053 participants enrolled and randomised (n = 1510 intervention, n = 1543 comparison) Mean age: 56 years, 32% women, 50% diabetes mellitus, 23% CVD
Interventions	Intervention group: physicians and participants provided with coronary risk profile consisting of a 8-year CHD risk estimate, cardiovascular age, and age gap; repeat profile provided at 3 months to demonstrate response to therapy and amount of risk reduction

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Grover 2007 (*Continued*)

	Comparison group: usual care
Outcomes	Primary outcomes: change in LDL-C level, change in TC/HDL ratio, percentage of participants reaching national lipid targets Secondary outcomes: change in nonlipid risk factors, global 10-year risk 3053 participants analysed for efficacy outcomes (n = 1510 intervention, n = 1543 comparison) Follow-up: 1 year
Study funding sources	Funded by Pfizer Canada and multiple investigators with pharmaceutical industry ties
Notes	Protocol violation noted for 121 participants (n = 56 intervention, n = 65 comparison)

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	Low risk	"Randomization was completed at a central coordinating centre"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method for outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	12% loss to follow-up which was similar in the 2 groups; ITT analysis performed
Selective reporting (reporting bias)	Unclear risk	Protocol document not available for review
Other bias	High risk	Pharmaceutical funding Potential for contamination bias since randomisation occurred within physician practice (investigators attempted to evaluate for this with sensitivity analyses) Protocol violation noted for 4% of participants (n = 121)

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Hall 2003

Methods	Quasi-randomised controlled trial, parallel group (1:1)
Participants	Participants aged 35-75 years, with type 2 diabetes mellitus and no history of CVD or renal disease attending a specialised diabetes mellitus clinic in the UK Inclusion criteria: not reported Exclusion criteria: not reported 323 participants recruited (n = 162 intervention, n = 161 comparison) Mean age of participants not reported; 48% women; 100% diabetes mellitus
Interventions	The New Zealand cardiovascular risk score was calculated for all participants Intervention group: CVD risk score was documented on the front of the participant's chart before visit Comparison group: no risk score documentation
Outcomes	Primary outcome: not specified Outcomes reported: changes in diabetes mellitus treatment, changes in antihypertensive treatment, referral to dietician, risk score mentioned in letter to GP Follow-up: none
Study funding sources	Funding source not reported by authors
Notes	-

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	"We allocated patients alternately to experimental and control groups."
Allocation concealment (selection bias)	High risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method for outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants included in study were analysed
Selective reporting (reporting bias)	Unclear risk	No protocol available for review
Other bias	High risk	Small study bias

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Hanlon 1995

Methods	Randomised controlled trial, parallel group (1:1:1:1:1)
Participants	1371 employees from 2 Glasgow factories randomised to 5 groups (n = 293 group 1, n = 297 group 2, n = 285 group 3, n = 263 group 4, n = 233 group 5) Inclusion criteria: additional criteria not reported Exclusion criteria: night-shift workers and workers participating in another cholesterol treatment study 58% of sample were 40-59 years of age, 9% women
Interventions	4 intervention groups: • Group 1: health education • Group 2: health education and feedback on cholesterol concentration • Group 3: health education and feedback on risk score • Group 4: health education with feedback on cholesterol concentration and risk score 1 comparison group (internal control): group 5 no health intervention This review reports results for the comparison of group 4 and group 5
Outcomes	Outcomes reported: change in Dundee score; plasma cholesterol concentration; diastolic blood pressure, BMI; self-reported behaviours 1157 employees analysed at 5 months (n = 247 group 1, n = 250 group 2, n = 241 group 3, n = 219 group 4, n = 200 group 5) 1107 employees analysed at 12 months (n = 240 group 1, n = 237 group 2, n = 226 group 3, n = 211 group 4, n = 193 group 5) Follow-up: baseline, 5 months, and 12 months
Study funding sources	Scottish Chief Scientist Office
Notes	Authors also compared the effects of the intervention to an external control site that was not randomised. These comparisons were reported in the manuscript but are not presented in this review Outcomes for changes in risk factors and health behaviours only reported at 5 months

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"[S]ubjects were allocated, by means of computer generated randomisation, to one of five groups."
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded

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Hanlon 1995 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis performed
Selective reporting (reporting bias)	High risk	Protocol not available and no trial registration. 12 month outcomes not reported
Other bias	High risk	Potential for contamination bias. "We recognised that subjects in group 5 (internal control) were open to influences from colleagues because the messages given to other participants were being freely discussed in the workplace."

Hanon 2000

Methods	Randomised controlled trial, parallel group (1:1)
Participants	1526 hypertensive participants (aged 18-75 years) with uncontrolled treated hypertension (systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg). Number randomised per group not reported Inclusion criteria: same criteria as above Exclusion criteria: pregnancy, diabetes mellitus, severe hypertension, renal or pulmonary disease, psychiatric disease, secondary hypertension Baseline age (SD): 60 years (10); 46% women
Interventions	All groups were treated with a therapeutic strategy that consisted of fosinopril 20 mg/day for 8 weeks with the possible increase to fosinopril + hydrochlorothiazide at 4 weeks. Participants randomised to the intervention group had their 10-year Framingham risk information provided to their treating physician
Outcomes	Primary and secondary outcomes not specified. Outcomes reported include: agreement between calculated risk and estimated risk by general practitioner, blood pressure at week 8 1273 participants analysed but number per group not reported Follow-up: 8 weeks
Study funding sources	Not reported. 1 author affiliated with a pharmaceutical company
Notes	Study published in French

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**

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Hanon 2000 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Randomisation stated but method for random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Blinding of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	1527 randomised but only 1273 analysed; no reasons provided for loss to follow-up; no imputation
Selective reporting (reporting bias)	High risk	Outcomes not prespecified and study not registered
Other bias	Unclear risk	Few study details provided in text

Hetlevik 1999

Methods	Cluster-randomised controlled trial, parallel group (1:1)
Participants	People with hypertension from 29 primary care health centres in Sor and Nord-Trondelag counties in Norway Unit of randomisation: health centre Number recruited: 29 health centres and 2239 participants total (n = 17 health centres with 984 participants in the intervention group; n = 12 health centres with 1255 participants in the comparison group) Mean age: 64 years, 58% women, 100% Norwegian
Interventions	Intervention group: • Computerised clinical decision support software with risk scores and guideline-based treatment recommendations • Educational seminars • Audit and feedback Comparison group: usual care
Outcomes	Outcomes measured: last registered cholesterol, blood pressure, weight (or BMI), number of cigarettes Risk score calculated only if enough information available during the search period Number analysed at 18 month follow-up: n = 887 intervention, n = 1127 comparison Number analysed after 3 month extension (21 month follow-up): n = 879 intervention, n = 1119 comparison

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Hetlevik 1999 (*Continued*)

	Follow-up: 18 months initially, trial extended 3 months due to missing data
Study funding sources	Norwegian Medical Association with contribution from the foundation promoting general practice in Sor-Trondelag
Notes	Issues with intervention fidelity: "After 18 months the CDSS had been used, partly or totally, in the treatment of 104 patient in the intervention group." Trial extended by 3 months because of inadequate collection of data at 18 months

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Personnel not blinded, and not clear that participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcomes abstracted by primary investigator who was not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	> 90% of participants in both groups were missing data to calculate 10-year CHD risk at 18 months. The trial was extended by 3 months which decreased this amount to ~ 50%
Selective reporting (reporting bias)	Unclear risk	No protocol available for review
Other bias	High risk	Trial extended by 3 months due to missing data. Clinicians provided lists of missing participant information and were asked to resolve this. Poor intervention fidelity (CDSS was used partially or totally in the treatment of only 104 participants in the intervention group)

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Holt 2010

Methods	Randomised controlled trial, parallel group (1:1)
Participants	People aged 50 years and older from primary care practices in West Midlands, UK running the EMIS (Egton Medical Information Systems) LV software Total number randomised: 38,417 (n = 18,912 intervention, n = 19,235 comparison)
Interventions	Intervention group: receives electronic alert messages identifying participants at high-risk for CVD, those whose risk factor data is incomplete, and those who may have undiagnosed diabetes mellitus. Health record searched and updated every 24 h. Treatment recommendations not provided. Alerts can be ignored by clinicians Comparison group: usual care. Computer software acquires data from the electronic health record but does not generate an electronic alert for the clinician
Outcomes	Primary outcome: difference in annual incidence rate of CVD events (composite of CHD, stroke/TIA, myocardial infarction, sudden cardiac death) Secondary outcomes include differences in the proportion of: high-risk participants identified, participants with missing data, participants with undefined diabetes mellitus status Number analysed at follow-up: 36,092 (n = 18,021 intervention, n = 18,071 comparison) Follow-up: 2 years
Study funding sources	Department of Health PhD Studentship from Warwick Medical School
Notes	User was not obliged to respond to the alert "Recruitment into the study had to be closed before the required number of patients over 50 years could be achieved, due to resource constraints."

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	"The e-Nudge software automatically randomised registered patients within each practice to intervention and control arms, depending on whether the last digit of the 10-digit NHS number was odd or even."
Allocation concealment (selection bias)	High risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	Physicians were kept unaware of odd/even rule for allocation but an alert would appear each time a patient record was opened Personnel not blinded; unclear if participants were blind
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes assessed by electronic abstraction from medical record

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Holt 2010 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	Low risk	1 practice withdrew from study at 6 months but overall < 10% missing data
Selective reporting (reporting bias)	Low risk	Authors clearly report changes to the protocol and outcomes reported match the protocol and trial registration
Other bias	High risk	Risk of contamination bias because randomisation was at the individual level, and the same physician may have taken care of participants randomised to intervention and control groups Senior author is the medical director of the software company that provided the e-Nudge software Underpowered for primary outcome

Jacobson 2006

Methods	Randomised controlled trial, parallel group (1:1)
Participants	People with LDL-C > 100 mg/dL , no history of CHD or vascular disease, and not currently receiving lipid-lowering therapy Inclusion criteria: additional criteria not reported Exclusion criteria: people older than 74 years, LDL-C < 100 mg/dL, charts missing risk factor information used to calculate 10-year CHD risk Total number of participants randomised: 368 (n = 186 intervention, n = 182 comparison) Mean (SD) age: 58 (9), 72% women, 92% African American, 6% white, 23% diabetes mellitus
Interventions	Intervention group: charts appended to include 10-year absolute CHD risk, ATP-II risk category, and potential treatment options Comparison group: charts appended with ATP-II LDL-C targets and consensus targets for blood pressure, BMI, and haemoglobin A1c. No risk information included Both groups received a 1-h academic detailing session to review the importance of risk assessment in cholesterol management
Outcomes	Primary outcome: proportion of high-risk participants who were recommended a statin Secondary outcomes: proportion of moderate-risk participants who were recommended a statin; proportion of entire cohort receiving lifestyle counselling, intensified blood pressure management, or documentation of risk in chart Total number of participants analysed: 351 (n = 182 intervention, n = 169 comparison)
Study funding sources	Emory University Medical Care Foundation
Notes	Authors report possible protocol violations and randomisation errors

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Jacobson 2006 (*Continued*)

Risk of bias		*Risk of bias*
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Method of random sequence generation not reported. "Randomization errors" reported by authors
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of personnel; unclear if participants were blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	High risk	Differential loss to follow-up (greater in control group); ITT analysis not performed
Selective reporting (reporting bias)	Unclear risk	No protocol available for review
Other bias	High risk	Risk of contamination bias as same physician may have taken care of participants randomised to intervention and control groups

Jorgensen 2014

Methods	Randomised controlled trial, parallel group (1:1)
Participants	Danish residents aged 30-60 years from 11 municipalities in suburban Copenhagen, Denmark 61,301 people originally randomised within the study but 59,993 people met the inclusion criteria at baseline for this analysis Total randomised: 59,993 (n = 11,708 intervention, n = 48,285 comparison) Mean age: not reported, 50% women, 88% Danish
Interventions	Intervention group: invited for screening, risk assessment, and lifestyle counselling up to 4 times over a 5-year period; high-risk individuals were offered additional lifestyle counselling on smoking cessation, diet, and physical activity Comparison group: not invited for screening; formal risk assessment not provided
Outcomes	Primary outcome: incident ischaemic heart disease Secondary outcome: incident stroke, incident combined ischaemic heart disease and

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	stroke, mortality, and attendance rates Total analysed in follow-up: 59,616 (n = 11,629 intervention, n = 47,987 comparison) Follow-up: 10 years
Study funding sources	Public, private, and industry sources: Danish Research Councils, Health Foundation, Danish Centre for Evaluation and Health Technology Assessment, Copenhagen County, Danish Heart Foundation, Ministry of Health and Prevention, Association of Danish Pharmacies, Augustinus Foundation, Novo Nordisk, Velux Foundation, Becket Foundation, and Ib Henriksens Foundation
Notes	Trial powered for 70% participation rate in the intervention group but only 52% of people in the intervention group accepted the invitation and were examined at baseline Data for risk factor levels not available given the pragmatic study design

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"The 61 301 people were randomised by computer generated random numbers with different randomisation ratios in the different age and sex groups …" *Note for this analysis, 59,313 people met the baseline inclusion criteria
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Personnel and participants not blinded to intervention but "neither the control group nor their doctor knew that they formed a control group."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Use of data from central registers further blinded the assessment of endpoints in relation to randomisation group."
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 1% loss to follow-up of event data
Selective reporting (reporting bias)	High risk	Cardiovascular outcomes were not prespecified in the original trial protocol
Other bias	High risk	Potential for contamination bias because randomisation was at the participant level

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Koelewijn-van Loon 2010

Methods	Cluster-randomised controlled trial, parallel group (1:1)
Participants	Adults from 25 practices with blood pressure ≥ 140 mmHg or already being treated for high blood pressure, total cholesterol ≥ 6.5 mmol/L or already being treated for high cholesterol, smoking (men ≥ 50 years, women ≥ 55 years), diabetes mellitus, family history of CVD and visible obesity Unit of randomisation: primary care practice Exclusion criteria: existing CVD, familial hypercholesterolaemia Total randomised: 25 practices with 615 participants (13 practices with 322 participants in the intervention group, 12 practices with 293 participants in the comparison group) Mean age: 57 years, 55% women, 14% diabetes mellitus
Interventions	Intervention group: received individual 10-year CVD risk assessment, risk communication via decision aid, motivational interviewing by nurses regarding lifestyle modifications Comparison group: usual care consistent with Dutch guidelines
Outcomes	Primary outcome: questionnaires to assess fruits and vegetables intake, fat intake, physical exercise, smoking, alcohol consumption; self-reported adherence to medical treatment; cardiovascular risk factor levels Secondary outcomes: perception of own health behaviour, attitude towards behaviour change, self-efficacy, risk perception, anxiety, satisfaction Total analysed at follow-up: 24 practices with 526 participants (13 practices with 264 participants in the intervention group, 11 practices with 258 participants in the comparison group) Follow-up: baseline, 12 weeks, and 52 weeks
Study funding sources	The Netherlands Organization for Health Research and Development
Notes	Study includes patient-reported outcomes only

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"An independent statistician performed a central block randomization"
Allocation concealment (selection bias)	Low risk	Treatment allocation performed centrally by an independent statistician
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Because of the training, nurses could not be blinded. To minimize potential bias, patients were informed about the aim of the study, but not about being part of an intervention or control group."

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Koelewijn-van Loon 2010 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of outcome assessment was not reported for all outcomes, but several outcomes were self-report questionnaires
Incomplete outcome data (attrition bias) All outcomes	High risk	Participants with missing data were excluded; ITT analysis not performed
Selective reporting (reporting bias)	High risk	Protocol and trial registration reports risk factor levels (cholesterol, blood pressure, and 10-year CVD risk) as outcomes that would be collected. Protocol also discusses economic analysis but these data are not provided in the published report
Other bias	Low risk	Other sources of bias not identified

Krones 2008

Methods	Cluster-randomised controlled trial, parallel group (1:1)
Participants	Adults with measured cholesterol level from 162 primary care practices in Hessen, Germany; recruited from 14 continuing medical education (CME) groups Unit of randomisation: CME group Inclusion criteria: additional criteria not reported Exclusion criteria: CME groups excluded if they participated in previous quality improvement projects Total randomised at baseline: 14 CME groups (N = 1132) Intervention group: 7 CME groups with 44 practices (n = 550) Comparison group: 7 CME groups with 47 practices (n = 582) Mean age: 59 years, 56% women, 97% German nationality, 18% diabetes mellitus, 20% CVD
Interventions	Intervention group: 2 CME sessions to learn shared decision-making communication strategies, guideline booklet, paper-based risk calculator, and individual risk summary sheet for each participant Comparison group: CME unrelated to CVD prevention
Outcomes	Primary outcomes: relative change in global risk at 6 months, patient participant scale Secondary outcomes: GP prescription behaviour, CV risk status after 6 months Total analysed at follow-up: Intervention group: 7 CME groups with 40 practices (n = 460) Comparison group: 7 CME groups with 41 practices (n = 466) Follow-up: baseline, after consultation, at 6 months
Study funding sources	The study was funded by the German Federal Ministry of Education and Research, grant No. 01GK0401

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Notes	Baseline imbalances with more diabetics and more participants with prior CVD events in the comparison group

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	High risk	Physicians recruited participants after cluster-randomisation "physicians were asked to approach all consecutive patients who had their cholesterol levels measured during a period of 4 weeks" Baseline imbalances between the 2 groups for diabetes mellitus, secondary prevention, and desire to participate in decision-making
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Participating family doctors could not be blinded because of the intervention. Patients were informed that different kinds of risk communication and decision support would be assessed; they were unaware of their physicians' group allocation, however. "
Blinding of outcome assessment (detection bias) All outcomes	High risk	"Family doctors provided data on risk factors to calculate a CVD risk score for each patient at baseline and at follow-up."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	18% loss to follow-up. Imputed missing values for individuals missing a single value to calculate 10-year CVD risk. Large amount of missing data for shared decision-making questionnaire (but this outcome was not included in this systematic review)
Selective reporting (reporting bias)	Low risk	All outcomes reported in trial registration were reported
Other bias	Low risk	Other sources of bias not identified

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Lopez-Gonzalez 2015

Methods	Randomised controlled trial, parallel group (1:1:1)
Participants	Public sector workers from Spain recruited from an annual work health assessment Inclusion criteria: additional criteria not reported Exclusion criteria: unable to understand medical advice, lacking permanent work contract, failed to attend the 2 scheduled visits - separated by 1 year Total randomised 3153 participants: (n = 1051 intervention group receiving 10-year Framingham risk score, n = 1045 intervention group receiving heart age, n = 1057 comparison group with conventional medical advice) Mean age: 46 (7.1) years, 52% women
Interventions	Intervention groups: • Group 1: Framingham 10-year risk score re-calibrated to Spanish population + conventional medical advice • Group 2: heart age + conventional medical advice. Groups 1 and 2 were combined for these analyses since both of these groups received a CVD risk score. Risk estimates were provided by research assistants trained in risk communication Comparison group: conventional medical advice without provision of a CVD risk score
Outcomes	Outcomes reported: BMI, fasting lipids (total cholesterol, triglycerides, HDL, glucose) , blood pressure, self-reported smoking, self-reported physical activity. Results for intervention groups 1 and 2 were combined for the analyses reported in this systematic review Number analysed at follow-up 2844 participants: (n = 955 in group 1, n = 914 in group 2, n = 975 in comparison group) Follow-up: 1 year
Study funding sources	Not reported by authors
Notes	Few details provided within the study about the means used for calculating and providing the CVD risk score

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"Using a computerized random number generator, the 3153 participants were randomly allocated to one of the three study groups" However, marked differences in baseline characteristics raises questions about the adequacy of randomisation
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	"[S]ingle blind design"

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Lopez-Gonzalez 2015 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of outcome assessment unclear
Incomplete outcome data (attrition bias) All outcomes	Low risk	10% loss to follow-up
Selective reporting (reporting bias)	Unclear risk	No protocol available for review
Other bias	Unclear risk	Risk calculator developed by Unilever. Unclear if this model was validated

Lowensteyn 1998

Methods	Cluster-randomised controlled trial, parallel group (2:1)
Participants	Adults age 30-74 years without CVD, recruited from 253 physician practices in Quebec, Canada Unit of randomisation: continuing medical education (CME) meeting Inclusion and exclusion criteria: additional criteria not reported Total randomised at baseline: 24 CME meetings with 253 physicians and 958 enrolled participants Intervention group: 16 CME meetings with 170 physicians and 782 enrolled participants Comparison group: 8 CME meetings with 83 comparison group physicians and 176 enrolled participants Mean age 51 years, 35% women
Interventions	Intervention group: physicians received coronary risk profile (8-year CHD risk and cardiovascular age) for their participants within 10 working days after the baseline participant assessment Comparison group: usual care, received coronary risk profile at completion of study (after outcomes collected)
Outcomes	Primary outcome: likelihood of high-risk vs low-risk participants being seen at 3-month follow-up Secondary outcome: CVD risk factor levels, 8-year CHD risk Total analysed at follow-up: 291 participants (n = 202 intervention and n = 89 comparison) Follow-up: 3 months
Study funding sources	Grant-in-aid from Merck Frosst Canada, Inc
Notes	Authors of the study had a financial stake in the computer risk model used for risk prediction

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**

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Lowensteyn 1998 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Method of sequence generation not reported by authors, but participants "selected" by physicians after randomisation
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of outcome assessment unclear but likely clinicians who were not blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	High loss to follow-up rate. Approximately 70% of participants (667/958) were not reassessed at follow-up and not included in analyses. Differential loss to follow-up in intervention group
Selective reporting (reporting bias)	Unclear risk	No protocol available for review
Other bias	High risk	Study funded by Merck. 4 authors had financial stake in the prediction tool that was developed

Mann 2010

Methods	Randomised controlled trial, parallel group (1:1)
Participants	Adult primary care patients with a diagnosis of diabetes mellitus; English- or Spanish-speaking from urban New York Exclusion criteria: additional criteria not reported Total randomised at baseline 150 participants (n = 80 intervention, n = 70 comparison) Mean age: 58 years (SD 11.5), women 73%, 89% Black or Latino, 100% diabetes mellitus
Interventions	The intervention consisted of a provider-led discussion of the participant's risk using the Statin Choice tool which provided a 10-year underlying risk category (average ≤ 15%, elevated = 15%-30%, or high > 30%), a revised risk with statin therapy, and risks of statin treatment Comparison group: printed material from the American Diabetes Association on how to reduce cholesterol through dietary modifications
Outcomes	Primary outcomes not specified Outcomes assessed from surveys: statin knowledge, decision Total analysed at follow-up - not specified by authors

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Mann 2010 (*Continued*)

Study funding sources	Not reported by authors
Notes	There was limited use of the Statin Choice decision support tool by the 46 providers (mean use 1.7 times) Adherence outcome poorly reported: "At 3 and 6 months, 70% and 80% of the participants reported good adherence to statins with no difference between groups." No further details provided

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded to intervention group
Blinding of outcome assessment (detection bias) All outcomes	High risk	Self-reported outcomes
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not reported
Selective reporting (reporting bias)	Unclear risk	Protocol not available
Other bias	High risk	Limited use of decision support tool in trial

Montgomery 2000

Methods	Cluster-randomised controlled trial, parallel group (1:1:1)
Participants	Adults aged 60-79 years with high blood pressure from 27 general practices from UK Unit of randomisation: general practice Exclusion criteria: non-ambulatory patients, life-threatening illness, recent major surgery Total randomised at baseline: 27 general practices with 715 participants (n = 269 computerised decision support + risk chart, n = 264 risk chart, n = 182 usual care) Mean age: 71 years, 54% women, 11% diabetes mellitus, 11% history of MI or stroke
Interventions	Intervention groups: • Group 1: computer-based clinical decision support + CVD risk chart • Group 2: CVD risk chart.

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Montgomery 2000 (*Continued*)

	In the "CVD risk chart" group, CVD risk information was manually extracted by nurses and included in the medical record Comparison group: usual care
Outcomes	Primary outcome: percentage of participants in each group with 5-year CVD risk ≥ 10% Secondary outcomes: systolic and diastolic blood pressure, CVD drug prescription Total analysed at 12 months follow-up 531 participants (n = 202 computerised decision support + risk chart, n = 199 risk chart, n = 1 usual care) Follow-up: 12 months
Study funding sources	NHS Wales Office of Research and Development, grant number RC016, NHS Research and Development Primary Care Career Scientist Award
Notes	For the analyses in this systematic review, participants randomised to both intervention groups were combined (both these groups received CVD risk scores) and were compared with usual care (did not receive systematic provision of a CVD risk score)

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Randomisation was performed with a table of random numbers by a researcher not involved in the study and who was blind to the identity of the practices."
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Because of the nature of the study, neither the doctors and nurses nor the patients were blind to their study group."
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcome assessors were unblinded clinic staff
Incomplete outcome data (attrition bias) All outcomes	High risk	41% of participants had missing cholesterol data
Selective reporting (reporting bias)	Unclear risk	Protocol not available for review
Other bias	Low risk	Other sources of bias not identified

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Montgomery 2003

Methods	Randomised controlled trial, factorial design (2 × 2)
Participants	Adults aged 32-80 years with newly diagnosed hypertension from South Western UK Exclusion criteria: severe hypertension requiring immediate treatment, secondary hypertension, hypertension associated with pregnancy, dementia Total randomised: n = 217 participants (n = 51 to decision aid + video/leaflet, n = 52 decision aid only, n = 55 video/leaflet only, n = 59 usual care) Mean age: 59 years, 49% women
Interventions	Intervention group: factorial design with decision support tool ± instructional video and leaflet about cardiovascular risk factors Comparison group: usual care Participants randomised to the decision support tool received a CVD risk score
Outcomes	Primary outcome: decisional conflict scale Secondary outcomes: subscales of decision conflict scale related to uncertainty and decision quality; intention to start treatment; anxiety; knowledge; treatment decision Total analysed at follow-up for primary outcome: n = 212 (n = 50 decision aid + video/leaflet, n = 50 decision aid only, n = 54 video/leaflet only, n = 58 usual care) Total analysed at 3-month follow-up for secondary outcomes: n = 199 (n = 48 decision aid + video/leaflet, n = 48 decision aid only, n = 51 video/leaflet only, n = 52 usual care) Follow-up: 3 months for initial study 3-year extended follow-up reported in a subsequent study published by Emmert et al. 2005 Total analysed at 3 years follow-up: n = 188 (n = 87 decision aid, n = 101 no decision aid)
Study funding sources	Medical Research Council, National Health Service Primary Care Career Scientist Award
Notes	For the analyses in this systematic review, all participants randomised to the decision support tool, which provided a CVD risk score, were combined and compared with participants not randomised to the decision support tool

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"The allocation schedule was computer-generated by an individual not involved in the study and executed by one of the authors (AM), to whom the allocation was concealed in advance by the nature of the minimisation procedure."
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Given the nature of the interventions, there was no masking of participants or the researcher administering the interventions

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Montgomery 2003 (*Continued*)

		(AM)."
Blinding of outcome assessment (detection bias) All outcomes	High risk	"Likewise, blinding was not possible for outcome assessment, as this was conducted principally through self-completion questionnaires."
Incomplete outcome data (attrition bias) All outcomes	Low risk	< 10% loss to follow-up; ITT analysis performed
Selective reporting (reporting bias)	Unclear risk	Protocol document not available
Other bias	Low risk	Other sources of bias not identified

Peiris 2015

Methods	Cluster-randomised controlled trial, parallel group (1:1)
Participants	Patients from primary care practices in Sydney, Australia and New Zealand who had attended the service 3 or more times in a 24 month period and at least once in a 6 month period Unit of randomisation: primary care practice Specific inclusion and exclusion criteria not reported Total randomised at baseline: 61 primary care practices with 38,725 participants (n = 31 practices with 19,385 participants in intervention group; n = 30 practices with 19,340 participants in comparison group) Total "high-risk" participants randomised at baseline: 10,308 participants (n = 5392 intervention group, n = 4916 comparison group) Mean age: 61 years, 58% women, 17% diabetes mellitus, 13% CVD
Interventions	Intervention group: clinical decision support software, audit and feedback tools, guideline dissemination and staff training. Clinical decision support software presented 5-year CVD risk information and heart age Comparison group: usual care
Outcomes	Primary outcome: proportion of participants who received "appropriate" screening of CVD risk factors by end of study; proportion of high-risk participants receiving recommended medication prescription Secondary outcomes: CV risk factor levels, incident CVD events, escalation of drug prescriptions in high-risk people Total analysed at follow-up: 60 primary care practices (n = 30 intervention group, n = 30 comparison group). 1 practice withdrew from the intervention group shortly after randomisation, but this did not affect number of total participants Total 'high-risk' participants analysed at follow-up: 10,181 participants (n = 5335 intervention group, n = 4846 comparison group) Median follow-up: 17 months

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Peiris 2015 (*Continued*)

Study funding sources	The National Health and Medical Research Council of Australia and the New South Wales Department of Health
Notes	Authors report higher than anticipated intracluster coefficients in their analyses

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Permuted block randomisation was centrally performed using a web-based form."
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Participating services did not make any special provisions to advertise the trial and their allocation status to patients; however, it would be reasonable to assume that when the tools were used during a consultation, patients may have been aware of the intervention."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"[O]utcome analyses were conducted blinded to randomised allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis used
Selective reporting (reporting bias)	Low risk	All outcomes from protocol and trial registration were reported
Other bias	Unclear risk	Marked baseline imbalances between the groups that were not statistically significant due to larger than expected intracluster coefficients (ICC)

Perestelo-Perez 2016

Methods	Cluster-randomised trial, parallel group (1:1)
Participants	Patients from primary care centres in Tenerife, Spain Unit of randomisation: clinician Study aim: to assess the efficacy of the statin choice decision aid compared to usual primary care in Spanish participants with type 2 diabetes mellitus Inclusion criteria: 18 years of age or older, type 2 diabetes mellitus, Spanish language-speaking, and no cognitive or sensorial impairments Exclusion criteria: no additional criteria listed

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Perestelo-Perez 2016 (*Continued*)

	Total randomised at baseline: 29 physicians with 168 participants (n = 15 physicians with 86 participants in intervention group, n = 14 physicians with 82 participants in the comparison group) Mean age (SD): intervention 63.9 years (9.7) and control 59.6 years (12.3); sex: intervention 41% women, control 34% women; 100% diabetes mellitus; 10-year risk category: intervention 37.6% high risk, control 25.3% high risk; ischaemic heart disease: intervention 24%, control 18%
Interventions	Intervention group: statin choice decision aid about the use of statins. The decision aid consisted of a 3-page pamphlet listing: CVD risk factors, 10-year CVD risk based on the UKPDS risk engine presented in pictographs with and without statins, list of adverse effects of statins and their incidence Comparison group: usual care
Outcomes	Primary and secondary outcomes not specified Outcomes reported: statin knowledge, risk perception, decisional conflict scale (DCS) , satisfaction with decision-making, problem areas in diabetes questionnaire, self-report of statin taking, self-report of adherence at 3 months (Morisky), consultation time by physician Follow-up: immediately after encounter and at 3 months Total analysed at 3 months follow-up: 131 participants (n = 67 intervention, n = 64 comparison)
Study funding sources	Spanish Ministry of Health, Social Services and Equality (grant number: EC10-005)
Notes	Analyses of outcomes accounted for clustering, but no power calculations performed. Significant baseline differences between intervention and control groups. At 3 months, 20% of participants were lost to follow-up (but 42% missing data for adherence outcome) . ITT analysis not performed Study funded by Spanish Ministry of Health, Social Services and Equality (grant number: EC10-005) No conflicts of interest reported

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Physicians who consented to participate were randomised to intervention or usual care by means of a computer-generated list. "
Allocation concealment (selection bias)	High risk	Participants were recruited to the trial by clinicians and this occurred after clinicians were randomised Significant baseline difference between the 2 treatment groups suggests high risk of selection bias. Participants in the intervention group were significantly older, had

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Perestelo-Perez 2016 (*Continued*)

		more hypertension, and were more likely to be prescribed statins at baseline than participants in the control group
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and clinicians not blinded to intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported by authors but all outcomes were measured by participant self-report
Incomplete outcome data (attrition bias) All outcomes	High risk	34/168 (20%) participants were lost to follow-up. Adherence data were missing for 71/168 (42%) participants. ITT analysis not performed
Selective reporting (reporting bias)	High risk	Per clinical trial registration, the primary outcome was adherence at 3 months as measured by Morisky scale, chart abstraction, and pharmacy records. This was not reported as a primary outcome by the authors and the latter 2 methods were not used to measure adherence Several secondary outcomes not reported: haemoglobin A1c, lipid profile, health-related quality of life, consultation time
Other bias	High risk	Small study bias

Persell 2013

Methods	Cluster-randomised controlled trial, parallel group (1:1)
Participants	Participants aged 40-79 years from 29 physician panels with a Framingham risk score of at least 5%, LDL cholesterol level above guideline threshold for drug treatment, and not prescribed a lipid-lowering medication Exclusion criteria: coronary heart disease, heart failure, stroke, diabetes mellitus, peripheral vascular disease Total randomised at baseline: 29 physicians with 435 participants (n = 14 physicians and 218 participants in the intervention group, n = 15 physicians and 217 participants in the comparison group) Mean age 60.7 years, 23% women, mean Framingham Risk score (SD): 14.2 (6.7) in intervention group and 13.8 (6.3) in comparison group
Interventions	Intervention group: patients of physicians randomised to the intervention group were mailed individualised CVD risk messages that described benefits of using a statin (and controlling hypertension or quitting smoking when relevant)

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Persell 2013 (*Continued*)

	Comparison group: usual care
Outcomes	Primary outcome: occurrence of a LDL-cholesterol level that was at least 30 mg/dL lower than prior Secondary outcome: lipid-lowering drug prescription, aspirin prescription, change in systolic and diastolic blood pressure, difference in number of antihypertensive medications prescribed, documentation of quitting smoking Follow-up: 9 months; but extended to 18 months post hoc Total analysed in follow-up: same as above
Study funding sources	Agency for Healthcare Research and Quality, USA
Notes	Primary endpoint at 9 months not met in the original protocol but analyses included a 18-month post hoc analysis that did achieve the primary endpoint

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Randomization was performed using a random number generator (SAS 9.2, SAS Institute Inc., Cary, NC) by a researcher who was not aware of the physicians' order in the blocks. Allocation to intervention or control groups was not revealed until after randomization was completed."
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"All outcomes were assessed by applying the outcome criteria to patient data automatically collected from EHRs using automated searches. No human judgment was involved in outcome assessments."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	ITT analysis performed All included participants analysed but only 38% of intervention and 34% of control had LDL testing which biases result to null
Selective reporting (reporting bias)	Low risk	All outcomes from trial registration were reported

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Persell 2013 (*Continued*)

Other bias	Unclear risk	Initial trial follow-up planned for 9 months; extended to 18 months post hoc

Persell 2015

Methods	Randomised controlled trial, parallel group (1:1)
Participants	646 men 35 years or older and women 45 years or older, without CVD or diabetes mellitus, and with a 10-year risk of CHD > 10% in 11 federally qualified health centres in the USA Exclusion criteria: diagnosed vascular disease, diabetes mellitus, primary language other than English or Spanish, primary care clinician discretion Mean age 60 years, 11% women, 50% African American, 33% non-Hispanic white, 13% Hispanic
Interventions	Intervention group: the intervention group received telephone and mailed outreach with individualised CVD risk information and uncontrolled risk factors provided by lay health workers Comparison group: usual care
Outcomes	Primary outcome: discussion about drug treatment for cholesterol at 6 months, follow-up LDL-cholesterol level > 30 mg/dL lower than baseline value Secondary outcome: statin prescription at 6 months, repeat LDL-cholesterol test at 1 year Follow-up: 1 year
Study funding sources	Agency for Healthcare Research and Quality, USA
Notes	-

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"A Northwestern investigator (SP) who was not aware of patients' identities, stratified eligible patients by CHC network then randomly assigned patients in a 1:1 ratio within each stratum using a random number generator in SAS 9.3 statistical software. "
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to intervention

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Persell 2015 (*Continued*)

Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Northwestern investigators reviewed these charts and were blinded to study group assignments."
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Pragmatic trial design. Outcomes obtained as a part of routine care. Only 36% of participants had a repeat LDL cholesterol test after 1 year
Selective reporting (reporting bias)	Low risk	All outcomes from clinical trial registration reported. Post hoc outcomes and analyses delineated in manuscript
Other bias	Unclear risk	Potential for contamination bias since randomisation occurred at the level of participant

Price 2011

Methods	Randomised controlled trial, 2 × 2 factorial design
Participants	Adults at increased CVD risk (10-year Framingham risk ≥ 20%) recruited from 4 general practices in Oxfordshire, UK Exclusion criteria: prevalent cardiovascular disease (MI, stroke, TIA, prior revascularisation), physical disability or condition reducing the ability to walk Total randomised at baseline 194 (n = 99 to personalised 10-year CVD risk estimate, n = 95 to risk factor levels only) Mean age: 62 years, 33% women, 98% white, 19% diabetes mellitus
Interventions	Participants were randomised in a 2 × 2 factorial design to receive: either a personalised 10-year cardiovascular disease risk estimate from a decision support tool or were told their blood pressure, total cholesterol, and fasting glucose values and if they were elevated per guidelines. Participants were simultaneously randomised to receive or not receive a brief lifestyle intervention by slideshow targeting physical activity, diet, and smoking Results presented for decision support tool compared with no decision support
Outcomes	Primary outcome: physical activity at 1 month, cardiovascular risk factor levels at 1 month Secondary outcomes: BMI, cholesterol levels, fasting glucose, anxiety, quality of life, self-regulation, worry about heart attack risk, intention to increase physical activity, recall of risk information Total analysed at follow-up 185 (n = 94 in personalised 10-year CVD risk group, n = 91 in risk factor levels only group) Follow-up: 1 month
Study funding sources	Diabetes Trials Unit Fellowship, Insulin Dependent Diabetes Trust

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Price 2011 (*Continued*)

Notes	-

Risk of bias		***Risk of bias***
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Computerized randomization was used to allocate participants and was performed internally."
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded. "One research fellow remained unblinded in order to deliver the intervention."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Research nurses who inputted data were blind to intervention allocation."
Incomplete outcome data (attrition bias) All outcomes	High risk	ITT analysis but "valid baseline and follow-up accelerometer data were only available for 125 participants (64%)"
Selective reporting (reporting bias)	Low risk	Outcomes reported as outlined in the protocol document
Other bias	Low risk	Other sources of bias not identified

Sheridan 2006

Methods	Randomised controlled trial, parallel group (1:1)
Participants	Men and women aged 35-75 years without CVD in North Carolina, USA Exclusion criteria: prior history of CVD, serious chronic medical condition that would limit their candidacy for screening (i.e. chronic renal failure, cirrhosis of the liver, HIV, current non-skin cancer), people who had participated in a previous quality improvement initiative Total randomised 87 adults (n = 49 to intervention group, n = 38 to comparison group) Mean age 53 years, 59% women, 73% white, 23% African American, 8% diabetes mellitus
Interventions	Intervention group: participants provided with most-recent risk factor information and instructed to review a computerised decision support tool prior to clinic visit. The decision support tool provided individualised CHD risk, the pros and cons of pertinent risk-reducing therapies, and the amount of risk reduction achievable after 1 or more therapeutic interventions Comparison group: provided a list of their cardiovascular risk factors

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Sheridan 2006 (*Continued*)

Outcomes	Primary outcome: discussion with provider about CHD risk reduction, plans for CHD risk reduction Secondary outcomes: knowledge about CHD prevention, perception of CHD risk, interest in participating in decision-making, accuracy of risk perception, self-perceived barriers to risk reduction Total analysed 75 adults (n = 41 in intervention group, n = 34 in comparison group)
Study funding sources	Internal funding from Department of Medicine at University of North Carolina
Notes	2 authors received consulting and licensing fees from Bayer, Inc. 1 author received honoraria and consulting fees from Merck, Pfizer, and Glaxo Smith Kline Small pilot study

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"We used a computerized random number generator to randomize patients to receive either the Heart to Heart decision aid or a list of their CHD risk factors that they could present to their doctor." Baseline imbalances in key parameters such as CHD risk factors, baseline CHD risk, and interest in prevention strategies
Allocation concealment (selection bias)	Low risk	"Intervention assignments were sealed in security envelopes until after subjects agreed to participate in the study. The research assistant then broke the seal to determine intervention assignment."
Blinding of participants and personnel (performance bias) All outcomes	High risk	"We blinded patients to the purpose of our study by telling them only that they were participating in a study about "prevention of CHD." Doctors were not blinded and saw patients in both the decision aid and control group
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	12 participants excluded postrandomisation (8 because they did not meet eligibility criteria); ITT analysis not performed

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Sheridan 2006 (*Continued*)

Selective reporting (reporting bias)	Low risk	All outcomes from trial registration were reported
Other bias	High risk	Small study bias with key baseline imbalances in spite of randomisation Possible contamination bias as same doctors saw participants who were in intervention and control groups

Sheridan 2011

Methods	Randomised controlled trial, parallel group (1:1)
Participants	Men and women aged 40-79 years with no history of CVD or diabetes mellitus, at moderate or high-risk based on Framingham risk score Exclusion criteria: serious medical condition that limited life expectancy to less than 5 years, first clinic visit, no cholesterol level checked in 18 months, extreme risk factor levels (systolic blood pressure > 180 mmHg or total cholesterol > 300 mg/dL) Total randomised at baseline: 160 participants (n = 81 to intervention group, n = 79 to comparison group) Mean age: 63 years, 28% women, 86% white, 10% African American
Interventions	Intervention group: • web-based, computerised decision support tool to promote initiation of effective CHD prevention strategies prior to clinic visit that included provision of personalised CVD risk estimate • series of automated mailed tailored messages to promote adherence to medications at 2, 4, and 6 weeks Comparison group: usual care
Outcomes	Primary outcome: feasibility of subject recruitment, intervention delivery, and measurement of study outcomes Secondary outcomes: self-reported adherence, global CHD risk, blood pressure, serum total and HDL cholesterol levels, smoking status, aspirin use, intent to start CHD reducing medication, self-efficacy for CHD risk reduction Total analysed: 154 participants (n = 77 intervention group, n = 77 comparison group) Follow-up: 3 months
Study funding sources	National Heart, Lung, and Blood Institute, USA; National Cancer Institute, USA; American Heart Association
Notes	Feasibility study, no power calculation

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**

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Sheridan 2011 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Method for sequence generation not reported. Baseline imbalances between intervention and control noted
Allocation concealment (selection bias)	Unclear risk	"Patients were randomised by study staff who accessed an online randomised schedule."
Blinding of participants and personnel (performance bias) All outcomes	High risk	"Physicians were not blinded and saw patients in both the intervention and control group."
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Method of outcome assessment not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	"The study lost 6 patient participants during follow-up, resulting in a 96% follow up rate."
Selective reporting (reporting bias)	Low risk	All outcomes reported in trial registration reported
Other bias	High risk	"[P]hysicians saw patients in both the intervention and control groups, which may have resulted in contamination between study groups."

Soureti 2011

Methods	Randomised controlled trial, parallel group (1:1:1:1)
Participants	Men and women age 30-60 years with obesity (BMI $\geq$ 29 kg/m^2) Exclusion criteria: diagnosis of a heart condition or cancer, being pregnant Total randomised at baseline 781 participants (n = 197 to CVD risk message, n = 194 to CVD risk message + automated health planning tool, n = 195 to health planning tool alone, n = 195 to educational information (control) Mean age: 47 years. Few baseline characteristics presented
Interventions	Participants randomised to 1 of 3 intervention groups: a CVD risk message, CVD risk message + automated health planning tool, health planning tool alone Comparison group: educational information about diet low in saturated fats without CVD risk message or planning tool For this systematic review, data for participants in the 2 CVD risk message groups were combined and compared with participants in the 2 groups that did not receive a CVD risk message (n = 392 intervention group, n = 389 comparison group)

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Soureti 2011 (*Continued*)

Outcomes	Primary outcome: saturated fat intake as measured by self-reported food-frequency questionnaire, 2-item scale to evaluate consumption of low-fat foods Secondary outcomes: CVD risk perception, intention to reduce saturated fat intake, self-efficacy, planning and outcome expectancies Total analysed in follow-up 581 participants (n = 141 in CVD risk message group, n = 137 in CVD risk message + automated health planning tool, n = 141 in automated health planning tool alone, n = 141 in educational information (control) For this systematic review, n = 278 in CVD risk groups, n = 282 in comparison groups Follow-up: 5 weeks
Study funding sources	Unilever funded and created the Heart Age score tested in the study
Notes	Internet-based trial with a large amount of missing data

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Method of blinding not reported
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcomes were patient-reported
Incomplete outcome data (attrition bias) All outcomes	High risk	> 20% loss to follow-up; ITT analysis not performed
Selective reporting (reporting bias)	High risk	Trial registered retrospectively
Other bias	High risk	Trial funded by Unilever and multiple authors were employees of Unilever. Heart Age Calculator software was also proprietary of Unilever

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Turner 2012

Methods	Randomised controlled trial, parallel group (1:1)
Participants	African American adults aged 40-75 years with uncontrolled hypertension Exclusion criteria: individuals with > 40% missed or cancelled clinic appointments during the past 3 years Total randomised: 280 participants (n = 136 intervention group, n = 144 comparison group) Mean age: 62 years, 65% women, 100% African Americans, 54% diabetes mellitus, 18% with CAD or equivalent
Interventions	Intervention group: • 3 monthly calls from trained peer coach with well-controlled hypertension • 2 visits on alternate months with health educator to review a personalised 4-year heart disease calculator and slide shows about heart disease risks Comparison group: received written material, brochures, and cookbook from American Heart Association addressing healthy lifestyle
Outcomes	Primary outcome: change in 4-year CHD risk at 6 months Secondary outcomes: 5 mmHg or greater reduction in SBP at 6 months; absolute change in blood pressure Total analysed for primary outcome: 212 participants (n = 96 intervention group, n = 118 comparison group) Follow-up: 6 months
Study funding sources	Robert Wood Johnson Foundation and the staff of the Finding Answers, Disparities Research for Change Program; unrestricted
Notes	Intervention targeted to individuals with uncontrolled hypertension but mean blood pressure was 140.5/81.2 mmHg

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	"[R]andomised at a 1:1 ratio using random computer-generated assignments"
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	"[S]ingle-blinded study;" "All providers were blinded to the study arm."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"The 6-month endpoint blood pressure was performed by blinded office medical assistants"

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Turner 2012 (*Continued*)

Incomplete outcome data (attrition bias) All outcomes	High risk	Greater missing data in the intervention group "After 6 months, 94 (69%) intervention subjects and 118 (82%) control subjects had 4-year CHD risk assessed"
Selective reporting (reporting bias)	Unclear risk	Trial registration retrospectively; all outcomes from trial registration reported
Other bias	Unclear risk	Unrestricted supplementary funding from Pfizer, Inc

Vagholkar 2014

Methods	Cluster-randomised trial, parallel group (1:1)
Participants	People aged 45-69 years without CVD, recruited from 34 general practices in urban Sydney, Australia Unit of randomisation: practice Exclusion criteria: insufficient English skills, cognitively impaired, Aboriginal or Torres Strait Islander, diagnosed or treated CVD Total randomised: 34 clusters of 1074 participants (n = 18 practices with 567 participants in the intervention group, n = 16 practice with 507 participants in the comparison group) Mean age: 56 years, 58% women, 56% Anglo-Celtic, 12% diabetes mellitus
Interventions	Intervention group: physicians received training on the importance of absolute risk assessment and use of a CVD risk calculator; participants received a 20-30 min consultation that involved calculating cardiovascular risk and providing appropriate management based on risk level and current guidelines Comparison group: general health check
Outcomes	Primary outcome: antihypertensive medication prescription, lipid-lowering medication prescription at 12 months Secondary outcomes: changes in blood pressure and blood lipids; self-reported smoking; self-reported physical activity levels; diet consumption Total analysed: 34 clusters of 906 participants (n = 18 practices with 475 participants in the intervention group; n = 15 practices with 431 participants in the comparison group) Follow-up: 12 months
Study funding sources	National Health and Medical Research Council of Australia
Notes	Only 685/1074 (64%) had values available for risk assessment

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**

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Vagholkar 2014 (*Continued*)

Random sequence generation (selection bias)	Low risk	"A person (U.J.) independent of the intervention and data collection conducted the allocation using a computer randomization program."
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias) All outcomes	High risk	Personnel not blinded to intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"Research staff collecting practice data were blinded to group allocation, as were patients."
Incomplete outcome data (attrition bias) All outcomes	High risk	Large amount of missing data. Only 64% of participants had values available for risk assessment
Selective reporting (reporting bias)	High risk	Several outcomes (such as health-related quality of life) mentioned in trial registry and protocol were not reported in this report
Other bias	Low risk	Other sources of bias not identified

Van Steenkiste 2007

Methods	Cluster-randomised controlled trial, parallel group (1:1)
Participants	People aged 40-75 years without CVD recruited from 45 primary care clinicians Unit of randomisation: primary care clinician Additional inclusion and exclusion criteria not reported Total randomised: 45 primary care clinicians with 623 participants (n = 19 primary care clinicians with 332 participants in intervention group, n = 26 primary care clinicians with 291 participants in the comparison group Mean age: 54 years, 55% women, 100% Dutch, 20% diabetes mellitus
Interventions	Intervention group: primary care clinicians trained to use cardiovascular risk in guidelines and in the use of a clinical decision support tool (paper booklet) provided to participants prior to clinic visit (2 clinic visits separated by 2 weeks) Comparison group: educational materials about the guidelines on paper
Outcomes	Primary outcome not specified. Outcomes reported: appropriate risk classification, appropriate assessment, appropriate smoking advice, appropriate dietary advice Secondary outcomes: anxiety, appropriateness of perceived risk, self-reported lifestyle changes (smoking in past 7 d, phys activity > 2 h, EtOH use, BMI > 30), self-efficacy regarding lifestyle changes

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Van Steenkiste 2007 (*Continued*)

	Total analysed at 0 weeks: 490 participants (n = 276 intervention group, n = 200 comparison group) Total analysed at 26 weeks: 427 participants (n = 227 intervention group, n = 200 comparison group) Follow-up: 26 weeks
Study funding sources	The Netherlands Organization for Health Research and Development
Notes	-

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"A computer was used for the stratified randomization, which was at practice level to prevent contamination of the intervention within group practices."
Allocation concealment (selection bias)	High risk	Participant recruitment occurred after cluster-randomisation which increases the risk of selection bias
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcomes assessed by physicians who were not blinded to intervention
Incomplete outcome data (attrition bias) All outcomes	High risk	> 20% loss to follow-up; ITT analysis not performed
Selective reporting (reporting bias)	Unclear risk	Protocol not available for review
Other bias	Low risk	Other sources of bias not identified

Webster 2010

Methods	Randomised controlled trial, parallel group (1:1)
Participants	Adult Australian residents with access to the Internet, trial recruitment strategies geared toward individuals with self-reported hypercholesterolemia Total randomised: 2099 participants (n = 1062 participants intervention group, n = 1037 participants comparison group) Mean age: 56 years, 55% women, 12% diabetes mellitus, 9% CHD

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Webster 2010 (*Continued*)

Interventions	Intervention group: individuals assigned to intervention received immediate, fully automated, personally tailored cholesterol treatment advice based on current Australian guidelines regarding the need for starting or increasing statin therapy or non-drug intervention strategies Comparison group: provided with general information about cholesterol management
Outcomes	Primary outcome: number of participants reporting starting or increasing lipid-lowering medication Secondary outcomes: number of participants who self-reported: a cholesterol level, doctor visit, start of a healthy diet, start of an exercise programme, weight-loss, smoking cessation, blood pressure check-up Total analysed: same as above (ITT) Follow-up: 8 weeks
Study funding sources	MBF Australia, Pfizer, National Health and Medical Research Council of Australia Program Grant (Grant ID: 571281)
Notes	Internet-based study, no human contact

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"Randomization was done automatically in real time by a central computerized service run by the investigators at The George Institute for International Health."
Allocation concealment (selection bias)	Low risk	See above
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"Participants were not informed of the precise randomised comparison being made and were simply told that they were participating in a trial that sought to 'find out if advice about cholesterol provided on the Internet can improve your cholesterol management."' "Investigators were blinded to the allocation of all individuals throughout the trial. "
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcomes self-reported by participants
Incomplete outcome data (attrition bias) All outcomes	Low risk	93% follow-up, ITT analysis performed

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Webster 2010 (*Continued*)

Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Other bias	High risk	Outcomes subject to recall bias

Welschen 2012

Methods	Randomised controlled trial, parallel group (1:1)
Participants	Type-2 diabetics under the age of 75 years newly referred to the Diabetes Care System West-Friesland, a managed care system in the Netherlands Exclusion criteria: unable to read/write Dutch, history of stroke/TIA Total randomised: 262 participants (n = 132 intervention group, n = 130 comparison group) Mean age 59 years, 44% women, 100% diabetes mellitus
Interventions	Intervention group: received: risk communication intervention from trained diabetes nurses and dieticians in addition to usual care. Risk communication consisted of: general explanation about risks of diabetes mellitus, presentation of 10-year absolute CVD risk, visual/graphical presentation of absolute and relative risk, and explanation of treatment benefits using a 'positive' frame Comparison group: received usual care provided by the diabetes nurses and dieticians of the Diabetes Care System which consisted of general information about having diabetes mellitus and education about treatment options and lifestyle modifications
Outcomes	Primary outcome: appropriateness of risk perception. Secondary outcomes: anxiety, generalised worry, illness perception, attitude, intention to change behaviour, satisfaction with communication Total analysed: 204 participants (n = 102 intervention group, n = 102 comparison group) Follow-up: 12 weeks
Study funding sources	Dutch Diabetes Research Foundation Grant 2007.13.004
Notes	-

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"All participating patients gave written informed consent and were randomised into an intervention and a control group by means of a list drawn up by a computerized randomisation program (version 1.0.0; Random Allocation Software)."
Allocation concealment (selection bias)	Low risk	"The manager of the DCS [Diabetes Care System], who is not involved in the pa-

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Welschen 2012 (*Continued*)

		tients' care, allocates the patient to one of the two groups on the basis of the randomisation list."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded to intervention
Blinding of outcome assessment (detection bias) All outcomes	High risk	Outcomes derived from self-report questionnaires
Incomplete outcome data (attrition bias) All outcomes	High risk	> 20% loss to follow-up; ITT analysis not performed
Selective reporting (reporting bias)	Low risk	All pre-specified outcomes from protocol were reported
Other bias	High risk	Potential for contamination because the same diabetes nurses and dieticians delivered the risk communication intervention and usual care

Williams 2006

Methods	Randomised controlled trial, parallel group (7:3)
Participants	Inclusion criteria: adult smokers who smoked > 5 cigarettes/day Exclusion criteria: history of psychotic illness, unable to read/speak English, minimum life expectancy of 18 months Total randomised: 1006 participants (n = 714 intervention group, n = 292 comparison group) Mean age: 46 years, 64% women, 82% white
Interventions	Intervention group: multifaceted intervention • Encouraged to meet at least 4 times with a counsellor (in-person or by phone) • Encouraged to meet twice with a dietician if LDL cholesterol was elevated • Provided with a choice of a study physician or 1 of their own to prescribe medications Counselors were trained to support participants in making clear and autonomous choices and goal-setting Comparison group: received booklets on smoking cessation and healthy diet; also encouraged to enrol in a smoking cessation programme and to meet with their physician
Outcomes	Primary outcome: 12-month prolonged tobacco abstinence Secondary outcomes: change in percent calories from fat, LDL-C from baseline to 18 months Total analysed: same as above (ITT analysis) Follow-up: 18 months

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Williams 2006 (*Continued*)

Study funding sources	National Institute of Mental Health, USA; National Cancer Institute, USA
Notes	-

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported
Allocation concealment (selection bias)	Low risk	"The results of a stratified permutated blocked randomization were placed in numbered double-sealed security envelopes."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel not blinded to treatment assignment
Blinding of outcome assessment (detection bias) All outcomes	High risk	Self-reported outcomes
Incomplete outcome data (attrition bias) All outcomes	High risk	28% loss to follow-up at 18 months; ITT analysis reported by authors but analyses appear to be completers analysis for LDL
Selective reporting (reporting bias)	Low risk	Prespecified outcomes all reported
Other bias	Unclear risk	Received funding from pharmaceutical industry

Wister 2007

Methods	Randomised controlled trial, parallel group (1:1)
Participants	Participants age 45-64 years from the Fraser Health region in British Columbia, Canada Exclusion criteria: no additional criteria specified Number of primary prevention participants randomised: 315 participants (n = 157 intervention group, n = 158 comparison group) Mean age: 56 years, 58% women
Interventions	Intervention group: participants and their primary care doctor received a 'report card' showing the person's CVD risk profile; also participants received Telehealth lifestyle counselling by 2 kinesiologists trained in motivational interviewing every 6 months for approximately 30 min per session Comparison group: usual care

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Wister 2007 (*Continued*)

Outcomes	Primary outcome: Framingham risk score Total analysed: same as above (ITT analysis) Follow-up: 1 year
Study funding sources	Canadian Institutes of Health Research, Community Alliance for Health Research Program, project 43267
Notes	This study included participants eligible for either primary or secondary prevention but randomised and analysed these 2 groups separately. For this systematic review, we report on the 315 participants in the primary prevention group

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	"The study statistician then randomly assigned the participants to the intervention or control study arm according to computer-generated random numbers."
Allocation concealment (selection bias)	Unclear risk	"The research coordinator received the assignment codes in envelopes, which were concealed from all members of the research team and were not opened by the coordinator until the point of randomization." Not reported if sealed or opaque
Blinding of participants and personnel (performance bias) All outcomes	High risk	Personnel not blinded to intervention but "all data were collected without patients' knowledge of group allocation."
Blinding of outcome assessment (detection bias) All outcomes	Low risk	"The outcome assessors were blinded to group allocation …"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No major loss to follow-up. ITT analysis with multiple imputation of missing data performed
Selective reporting (reporting bias)	Unclear risk	No protocol document available for review
Other bias	Unclear risk	Potential for contamination bias but sensitivity analysis removing analysis of all participants who shared a physician did not result in change in point estimates

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Zullig 2014

Methods	Randomised controlled trial, parallel group (1:1)
Participants	Adults with CVD or a CVD-risk equivalent condition, at least 1 modifiable risk factor (e.g. hypertension or active smoking) Exclusion criteria: patients with metastatic cancer, dementia, psychosis, or end-stage renal disease; no Internet access; nursing care; unable to read English; heart transplant; hospitalised for a cardiac-related illness in the previous 3 months Total randomised: 96 participants (n = 47 intervention group. n = 49 comparison group) Mean age: 63 years, 68% women, 62% white, 32% African American, 29% diabetes mellitus
Interventions	Intervention group: participants were presented a web-based decision support tool that calculated their CVD risk based on the Framingham risk score and in subsequent on-line encounters could select modules with evidence-based recommendations regarding healthy lifestyle behaviours (medication adherence, diet, risk factor knowledge, smoking cessation) Comparison group: usual care, received general printed educational CVD information
Outcomes	Outcomes reported: mean differences in 10-year Framingham risk score, BMI, smoking status, systolic blood pressure, and self-reported medication adherence Total analysed: not reported Follow-up: 3 months
Study funding sources	Informed Medical Decisions Foundation, grant number 0170-1
Notes	-

Risk of bias ***Risk of bias***

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of random sequence generation not reported but authors report baseline differences between participants, so this may be high risk of bias
Allocation concealment (selection bias)	Unclear risk	"Randomization assignments were placed in sealed, consecutively numbered envelopes." Not reported if envelopes were opaque
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to the intervention
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Unclear who assessed 3 month follow-up visit outcomes. Medication use was self-reported

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Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Outcome data were not clearly reported including number of participants contributing to data
Selective reporting (reporting bias)	Unclear risk	Protocol document not available
Other bias	Unclear risk	Small study bias

ATP: Adult Treatment Panel, of the National Cholesterol Education Program; **BMI**: body mass index; **CAD**: coronary artery disease; **CDSS**: computerised clinical decision support; **CHD**: coronary heart disease; **CME**: continuing medical education; **CVD**: cardiovascular disease; **FRS**: Framingham risk score; **GHQ**: general health questionnaire; **HTN**: hypertension; **ITT**: intention-to-treat; **LDL**: low-density lipoprotein; **MI**: myocardial infarction; **SBP**: systolic blood pressure; **TIA**: transient ischaemic attack.

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

Study	Reason for exclusion
Ajay 2014	Risk score not part of the intervention
Allen 2011	Risk score not part of the intervention
Avis 1989	Risk score not part of the intervention (health risk appraisal)
Baruth 2011	Risk score not part of the intervention
Berra 2007	Risk score not part of the intervention
Bjarnason-Wehrens 2013	Risk score not part of the intervention
Black 2014	Risk score not part of the intervention
Botija-Yague 2007	Risk score not part of the intervention
Branda 2013	Risk intervention used in both groups
Brett 2012	Risk score used in both groups
Bruckert 2008	Risk score not part of the intervention
Carrington 2012	Risk score not part of the intervention
CARRS 2012	Risk score not part of the intervention

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(*Continued*)

Carter 2009	Risk score not part of the intervention
Carter 2015	Not primary prevention
Chow 2009	Risk score not part of the intervention
Claes 2007	Risk score used in both groups
Cleveringa 2008	Not primary prevention
Cochrane 2012	Risk score not part of the intervention
Colwell 2011	Risk score not part of the intervention
Daniels 2012	Risk score not part of the intervention
Deales 2014	Risk score not part of the intervention
Dresser 2009	Risk score not part of the intervention
Edwards 2006	Clinical vignettes/hypothetical patients
El Fakiri 2008	Risk score not part of the intervention
Evans 2010	Risk score used in both groups
Fabregas 2014	Risk score not part of the intervention
Fretheim 2006	Risk score not part of the intervention
Freund 2015	Not RCT or quasi-RCT
Gill 2009	Risk score not part of the intervention
Gomez-Marcos 2006	Risk score not part of the intervention
Green 2014	Risk score used in both groups
Harmsen 2014	Risk score used in both groups
Holbrook 2011	Risk score not part of the intervention
Hormigo-Pozo 2009	Risk score not part of the intervention
Huntink 2013	Risk score not part of the intervention

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(*Continued*)

Ishani 2011	Risk score not part of the intervention
Jacobs 2011	Risk score used in both groups
Jennings 2006	Risk score not part of the intervention
Jones 2009	Not primary prevention
Kaczorowski 2011	Risk score not part of the intervention
Ketola 2001	Not primary prevention
Keyserling 2014	Risk score used in both groups
Kullo 2016	Risk score used in both groups
Laan 2012	Not RCT or quasi-RCT
Lalonde 2004	Not RCT or quasi-RCT
Lalonde 2006	Risk score used in both groups
Lauritzen 2008	Risk score not part of the intervention
Liddy 2015	Risk score not part of the intervention
Lindholm 1995	Risk score not part of the intervention
Ma 2009	Risk score not part of the intervention
Mendis 2010	Risk score not part of the intervention
Mills 2010	Risk score not part of the intervention
Mortsiefer 2015	Risk score not part of the intervention
NCT01134458	Not primary prevention
NCT01979471	Not primary prevention
Nebieridze 2011	Risk score used in both groups
Paterson 2002	Not RCT or quasi-RCT
Pignone 2004	Not RCT or quasi-RCT

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(*Continued*)

Powers 2011	Not primary prevention
Qureshi 2012	Risk score used in both groups
Reid 1995	Risk score not part of the intervention
Rodriguez-Salceda 2010	Risk score used in both groups
Selvaraj 2012	Risk score not part of the intervention
Sheridan 2012	Risk score used in both groups
Skinner 2011	Risk score not part of the intervention
Smith 2008	Risk score not part of the intervention
Soureti 2010	Risk score used in both groups
Stewart 2012	Risk score not part of the intervention
Thomsen 2001	Not RCT or quasi-RCT
Vaidya 2012	Not RCT or quasi-RCT
Van Breukelen-van der Stoep 2014	Not RCT or quasi-RCT
Van den Brekel-Dijkstra 2016	Not RCT or quasi-RCT
Van Limpt 2011	Not primary prevention
Waldron 2010	Risk score used in both groups
Weymiller 2007	Not primary prevention
Zamora 2013	Not primary prevention
Zamora 2015	Not primary prevention
Zhu 2013	Not RCT or quasi-RCT

RCT: randomised controlled trial.

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Characteristics of studies awaiting assessment *[ordered by study ID]*

Adamson 2013

Methods	Randomised controlled trial, parallel group (1:1)
Participants	31 participants attending a specialist diabetes clinic appointment at the Oxford Centre for Diabetes Mean age: 51 years, 55% women, 100% diabetes mellitus
Interventions	Intervention group: received a facilitated discussion based on 10-year coronary heart disease and stroke risk estimate generated by the UKPDS Risk engine Control group: received routine discussion of CVD risk factors
Outcomes	Participant satisfaction, measured by questionnaire and semi-structured interviews
Notes	Abstract only, full report not published

Gryn 2012

Methods	Randomised controlled trial, parallel group (1:1)
Participants	78 individuals with hypertension aged 30-84 years Exclusion criteria: no prior MI, stroke, heart failure, or pregnancy Mean age 62 years, 55% women, 17% diabetes mellitus
Interventions	Intervention group: received information on their personalised estimated risk of heart disease and stroke and education about the utility of effective blood pressure management in decreasing their risk estimate Control group: usual care
Outcomes	Primary outcome: adherence at baseline, 3, 6, and 12 months measured by pill counting and electronic pill bottles Secondary outcomes: blood pressure, self-perception of cardiovascular and stroke risk, perceived benefit of treatment
Notes	Published abstract and scientific poster reviewed. Manuscript still in preparation

Roach 2012

Methods	Randomised controlled trial, parallel group (1:1)
Participants	144 type-2 diabetics from 4 urban primary care clinics
Interventions	Intervention group: randomised to a Spanish-language, tablet computer-based CVD risk communication intervention incorporating the individual's unique 10-year CVD risk information Comparison group: usual care
Outcomes	CVD risk discussion during clinic visit, medication change
Notes	Published abstract reviewed. Manuscript in preparation

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CVD: cardiovascular disease; **MI**: myocardial infarction; **UKPDS**: United Kingdom Prospective Diabetes Study.

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

Badenbroek 2014

Trial name or title	The INTEGRATE study
Methods	Stepped-wedge randomised controlled trial
Participants	All eligible patients 45-70 years of age from 40 general practices in the Netherlands with electronic medical records
Interventions	The intervention is the Personalized Prevention Approach for CardioMetabolic Risk (PPA CMR). An online risk estimation tool based on the FINDRISK score is used to screen for participants with increased CVD risk. Participants with a FINDRISK score above risk threshold are offered additional measurements by their GP. In clinic, a GP uses SCORE to assess 10-year CVD risk and then provides participants with increased risk with tailored lifestyle advice and/or medication Control group: wailting list control; do not receive risk score nor lifestyle advice; recieve intervention at 1 year
Outcomes	Primary outcomes: number of newly detected participants with CVD; change in individual risk factors (smoking, physical inactivity, obesity, unhealthy diet, blood pressure, cholesterol levels); expected new participants with CVD and mortality at 5, 10, 20 years; cost-effectiveness; non-participation and compliance Secondary outcomes: difference in primary outcome at 5 years; willingness to change lifestyle; change in health status
Starting date	1 April 2014
Contact information	Professor N. J. de Wit Julius Health Centre UMC Utrecht Huispost Str. 6.131 PO Box 85500 3508 GA Utrecht Netherlands N.J.deWit@umcutrecht.nl
Notes	www.integrateproject.nl NTR4277, the Netherlands National Trial Register

Ijkema 2014

Trial name or title	Risk Or Benefit IN Screening for CArdiovascular disease (ROBINSCA) study
Methods	Population-based randomised screening trial, parallel group (1:1:1)
Participants	39,000 participants at increased risk for CVD
Interventions	Comparison of 3 cardiovascular screening strategies: classic risk screening based on the Systematic COronary Risk Evaluation (SCORE) model; screening for coronary artery calcium using computed tomography; usual care All groups will receive written general lifestyle advice. Individuals at increased risk for CVD based on classic risk assessment or coronary calcium will be referred to general practitioner for lifestyle advice or medical therapy

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Ijkema 2014 (*Continued*)

Outcomes	Primary outcome: cumulative 5-year fatal and non-fatal coronary heart disease Secondary outcomes: sensitivity of the screening tests, favorable and unfavorable effects of screening, cost-effectiveness
Starting date	First quarter 2014
Contact information	H.J. de Koning, Department of Public Health, Erasmus MC, University Medical Center Rotterdam, PO Box 2040, 3000 CA Rotterdam, The Netherlands h.dekoning@erasmusmc.nl.
Notes	www.robinsca.nl

Maindal 2014

Trial name or title	The CORE-trial: a pragmatic randomized controlled trial in primary care investigating effectiveness and cost-effectiveness of the Check Your Health Preventive Programme offered population-wide to 30-49 years
Methods	Pragmatic household-cluster-randomised trial
Participants	10,505 participants aged 30-49 years from 35 practices within central Denmark
Interventions	The intervention consists of a preventive health check that consists of a health examination and individual risk profile (Heart-SCORE model) during a single office visit. Follow-up visits are stratified by risk profile to a health promoting consultation, behavioural programme, or no follow-up Comparison group: standard prevention and treatment strategy
Outcomes	Primary outcomes: 10-year risk of fatal CVD, physical activity (self-report and cardiorespiratory fitness), health-related quality of life, functional capacity (affiliation to the labour market and sick leave > 3 weeks) Secondary outcomes: cost-effectiveness as measured by life-years gained, direct costs, and total health cost
Starting date	May 2013; anticipated completion April 2017
Contact information	Annelli Sandbæk, PhD Professor, Department of Public Health, University of Aarhus; annelli.sandbaek@alm.au.dk Helle T Maindal, PhD, Associate Professor, Department of Public Health, University of Aarhus; htm@ph.au.dk
Notes	ClinicalTrials.gov ID: NCT02028195

NCT00694239

Trial name or title	Risk Assessment and Treat Compliance in Hypertension Education Trial (RATCHET)
Methods	Randomised controlled trial, parallel group (1:1)

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NCT00694239 (*Continued*)

Participants	Adults aged 30-84 years Inclusion criteria: essential hypertension (new diagnosis or established diagnosis) meeting criteria for pharmacologic therapy as defined by current guidelines Exclusion criteria: lack of written informed consent, previous myocardial infarction, previous stroke, congestive heart failure, stage 3 or greater chronic kidney disease, pregnancy, use of medication bubble/blister package
Interventions	Intervention group: knowledge of cardiovascular risk assessment plus standard care Control group: standard/usual care
Outcomes	Primary outcome: medication compliance Secondary outcomes: patient perception of cardiovascular risk, pilot feasibility study, blood pressure, cholesterol level, Framingham risk score Follow-up: 1 year
Starting date	May 2007
Contact information	George Dresser University of Western Ontario, Canada LHSC Victoria Hospital, Rm E6-302 519.685.8500 ext.33342 George.Dresser@lhsc.on.ca
Notes	Anticipated completion date March 2011 but no results posted yet

NCT02096887

Trial name or title	Effect of Patient Education on Compliance and Cardiovascular Risk Parameters (FAILAKA)
Methods	Cluster-randomised controlled trial, parallel group (1:1)
Participants	Adults aged 30-70 years Inclusion criteria: 1. Participants with 1 or more CVD risk factors will be consecutively enrolled, smokers and obese participants should have an additional risk factors 2. The risk factors are based on Framingham risk score calculator and include smoking, high blood pressure, high blood cholesterol, diabetes mellitus and being overweight or obese 3. All participants must be adults (30-70 years of age) who give informed consent 4. All participants should be of Kuwaity nationality, literate and fluent in either Arabic or English 5. Participants are likely to be available for a 1 year follow-up Exclusion criteria: 1. People with mental disability or severe psychiatric disorder who are unable to provide informed consent or participate in educational activities 2. People with severe visual or hearing disability that will prevent participation in the educational activity 3. People < 30 years or > 70 years of age 4. Illiterate people 5. Non-Kuwaiti nationals

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NCT02096887 (*Continued*)

	6. People who are not permanently resident in Kuwait 7. People who refuse to provide the informed consent
Interventions	Intervention group: participants attending clinics randomised to structured patient education will receive education targeting their risk factors and receive information about evidence-based targets. Physician in education clinics will also calculate Framingham risk score and provide a booklet entitled, 'Know your numbers' Control group: usual care
Outcomes	Primary outcome: cardiovascular risk factor control (HbA1c, blood pressure, LDL-cholesterol, body mass index, and smoking cessation) Medication compliance: assessed by Morisky scale
Starting date	June 2014
Contact information	Dr. Samia Almusallam Director of the Family Medicine residency programme Kuwait Institute for Medical Specialization
Notes	Anticipated completion date January 2016 but no results posted

Ogedegbe 2014

Trial name or title	Task shifting and blood pressure control in Ghana: a cluster-randomized trial
Methods	Cluster-randomised trial, parallel group (1:1) assignment
Participants	640 participants with uncomplicated hypertension (BP 140-179/90-99 mmHg and absence of target organ damage) from 32 community health centres and district hospitals in Ghana
Interventions	The intervention consists of WHO Package CV risk assessment, patient education, initiation and titration of antihypertensive medications, behavioural counselling, and assessment of barriers to adherence Comparison group: usual care
Outcomes	Primary outcome: mean change in systolic blood pressure from baseline to 12 months Secondary outcomes: proportion of participants with adequate systolic blood pressure control at 12 months; levels of physical activity; percent change in weight; and dietary intake of fruits and vegetables at 12 months
Starting date	May 2013; completion date March 2017
Contact information	Gbenga Ogedegbe, MD, MS, MPH, Center for Healthful Behavior Change, Division of Health & Behavior, Department of Population Health, New York University School of Medicine, 550 1st Avenue, New York, NY 10016 Olugbenga.ogedegbe@nyumc.org
Notes	ClinicalTrials.gov ID: NCT01802372

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Praveen 2013

Trial name or title	Systematic Appraisal Referral and Treatment of CVD risk in rural India (SMARTHealth India)
Methods	Stepped wedge cluster-randomised trial
Participants	15,000 adults age 40 years and older at high cardiovascular disease risk from 18 primary health centres and 54 villages in rural Andhra Pradesh
Interventions	Intervention group: a mobile device-based clinical decision support system for non-physician healthcare workers and primary care doctors to assess and manage CVD risk, provide lifestyle advice, and manage risk factors according to Indian national guidelines Comparison group: usual care
Outcomes	The primary study outcome is the difference in the proportion of people meeting guideline-recommended blood pressure targets in the intervention period vs the control period Secondary outcomes include mean reduction in blood pressure levels; change in cardiovascular disease risk factors (BMI, smoking, healthy eating habits, physical activity, self-reported use of BP and other cardiovascular medicines, quality of life), and CVD event rates (hospitalisation data)
Starting date	Fourth quarter of 2013; randomisation planned to continue until first quarter of 2016
Contact information	Devarsetty Praveen, the George Institute for Global Health, Hyderabad, India, dpraveen@georgeinstitute.org.in
Notes	-

Redfern 2014

Trial name or title	Consumer Navigation of Electronic Cardiovascular Tools (CONNECT) study
Methods	Randomised controlled trial, parallel group (1:1)
Participants	2000 regular adult health service attendees at Australian general practice or Aboriginal Community Controlled Health Services
Interventions	Intervention group: will be able to securely access a consumer portal to view participant data uploaded from the clinic record, use interactive tools to view their personal CVD risk and explore relative risk reductions from various CVD management strategies, access healthy lifestyle reminders and motivational message prompts, and connect with peers to set healthy lifestyle goals Comparison group: usual care
Outcomes	Primary outcome: proportion of participants meeting the Australian guideline BP and lipid targets. Secondary outcomes: proportion meeting guideline-recommended BP and LDL-cholesterol targets separately, difference in mean systolic and diastolic blood pressure, difference in mean cholesterol levels, difference in mean BMI, difference in health literacy scores, difference in cardiovascular and renal events, physical activity levels, smoking, fruits/vegetable intake, adherence to cardioprotective medications, health-related quality of life
Starting date	October 2014; still recruiting

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Redfern 2014 (*Continued*)

Contact information	Professor Julie Redfern, the George Institute for Global Health, Level 10, King George V Building, Missenden Road, Camperdown NSW 2050, Australia jredfern@georgeinstitute.org.au
Notes	Australian New Zealand Clinical Trials Registry number: ACTRN12613000715774

Sanghavi 2015

Trial name or title	Million hearts: cardiovascular disease risk reduction model
Methods	Cluster-randomised trial (1:1) parallel group
Participants	720 general medical practices, Medicare fee-for-service beneficiaries aged 18-79 years of age without history of myocardial infarction or stroke
Interventions	Intervention group: practices will be asked to screen all eligible Medicare beneficiaries for their 10-year risk of a heart attack or stroke using the American College of Cardiology/American Heart Association (ACC/AHA) 10-year Atherosclerotic Cardiovascular Disease (ASCVD) pooled cohort risk calculator. For participants at the highest risk (10-year ASCVD risk > 30%), providers will receive a monthly per beneficiary Cardiovascular Care Management payment to reduce their practice-wide absolute risk Control group: practices will be asked to report only clinical data (such as age, cholesterol level, and other information) on their attributed Medicare Beneficiaries at years 1, 2, 3, and 5 of the model. Control group practices will be paid a USD 20 per-beneficiary payment (based on the estimated costs of preparing and transmitting the required data) for each reporting cycle
Outcomes	Population-wide reduction in 10-year composite risk and population-wide reduction in composite incidence of myocardial infarction and stroke. Trial is powered for latter outcome based on Medicare fee-for-service claims data
Starting date	January 2016 reported. Trial has not started yet.
Contact information	Darshak M Sanghavi, MD, Centers for Medicare and Medicaid Services, Prevention and Population Health Models Group, 7500 Security Blvd, Baltimore, MD 21244 darshak.sanghavi@cms.hhs.gov
Notes	Trial conducted by Center for Medicare and Medicaid Innovation

Silarova 2015

Trial name or title	Information and Risk Modification Trial (INFORM)
Methods	Randomised controlled trial, parallel group (1:1:1:1)
Participants	932 men and women blood donors with no previous history of CVD aged 40-94 years in England

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Silarova 2015 (*Continued*)

Interventions	4 groups: • Group 1: lifestyle advice only • Group 2: lifestyle advice + 10-year CHD risk based on phenotypic characteristics • Group 3: lifestyle advice + 10-year CHD risk based on phenotypic and genetic characteristics • Group 4: no intervention/usual care
Outcomes	Primary outcome: change in objectively measured physical activity Secondary outcomes: objectively measured dietary behaviours, CVD risk factors, medication and healthcare usage, perceived risk, cognitive evaluation of provision of CHD risk scores, psychological outcomes
Starting date	January 2015
Contact information	Professor Simon Griffin, Cambridge Institute of Public Health, University of Cambridge School of Clinical Medicine Forvie Site, Cambridge Biomedical Campus, Cambridge CB2 0SR, United Kingdom sjg49@medschl.cam.ac.uk
Notes	Participants who took part in the INTERVAL study (www.intervalstudy.org.uk, ISRCTN24760606) and completed their 2-year questionnaire participate in the INFORM study

CVD: cardiovascular disease.

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DATA AND ANALYSES

Comparison 1. CVD risk score versus no CVD risk score/usual care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 CVD events	3	99070	Risk Ratio (IV, Fixed, 95% CI)	1.01 [0.95, 1.08]
2 CVD events, excluding Bucher 2010	2	95708	Risk Ratio (IV, Fixed, 95% CI)	1.01 [0.94, 1.08]
3 Total cholesterol	12	20437	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.20, 0.00]
4 Low-density lipoprotein cholesterol	10	22122	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.10, 0.04]
5 Systolic blood pressure	16	32954	Mean Difference (IV, Random, 95% CI)	-2.77 [-4.16, -1.38]
6 Diastolic blood pressure	14	22378	Mean Difference (IV, Random, 95% CI)	-1.12 [-2.11, -0.13]
7 Change in multivariable CVD risk	9	9549	Std. Mean Difference (IV, Random, 95% CI)	-0.21 [-0.39, -0.02]
8 Adverse events (investigator defined)	4	4630	Risk Ratio (IV, Fixed, 95% CI)	0.72 [0.49, 1.04]
9 Anxiety	2	388	Std. Mean Difference (IV, Fixed, 95% CI)	-0.07 [-0.27, 0.13]
10 New/intensified lipid-lowering medication	11	14175	Risk Ratio (Random, 95% CI)	1.47 [1.15, 1.87]
11 New/intensified antihypertensive medication	8	13255	Risk Ratio (Random, 95% CI)	1.51 [1.08, 2.11]
12 New aspirin	3	1614	Risk Ratio (Fixed, 95% CI)	2.71 [1.24, 5.91]
13 Medication adherence	4	621	Risk Ratio (IV, Random, 95% CI)	1.14 [0.92, 1.40]
14 Smoking cessation	7	5346	Risk Ratio (Fixed, 95% CI)	1.38 [1.13, 1.69]
15 Exercise	2	2595	Risk Ratio (IV, Fixed, 95% CI)	0.98 [0.90, 1.06]
16 Decisional conflict	4	1261	Std. Mean Difference (IV, Random, 95% CI)	-0.29 [-0.57, -0.01]

Comparison 2. CVD risk score versus no CVD risk score/usual care by decision support use

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total cholesterol by decision support use	12	20437	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.20, 0.00]
1.1 Decision support use	8	9444	Mean Difference (IV, Random, 95% CI)	-0.09 [-0.20, 0.01]
1.2 No decision support use	4	10993	Mean Difference (IV, Random, 95% CI)	-0.11 [-0.27, 0.06]
2 Low-density lipoprotein cholesterol by decision support	10	22122	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.10, 0.04]
2.1 Decision support use	9	21739	Mean Difference (IV, Random, 95% CI)	-0.02 [-0.10, 0.06]
2.2 No decision support use	1	383	Mean Difference (IV, Random, 95% CI)	-0.11 [-0.25, 0.03]
3 Systolic blood pressure by decision support use	16	32954	Mean Difference (IV, Random, 95% CI)	-2.77 [-4.16, -1.38]
3.1 Decision support use	13	22457	Mean Difference (IV, Random, 95% CI)	-2.17 [-3.52, -0.82]
3.2 No decision support use	3	10497	Mean Difference (IV, Random, 95% CI)	-4.57 [-6.89, -2.25]

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4 Diastolic blood pressure by decision support use	14	22378	Mean Difference (IV, Random, 95% CI)	-1.12 [-2.11, -0.13]
4.1 Decision support use	10	11385	Mean Difference (IV, Random, 95% CI)	-0.76 [-1.29, -0.23]
4.2 No decision support use	4	10993	Mean Difference (IV, Random, 95% CI)	-2.09 [-3.33, -0.85]
5 Change in multivariable CVD risk by decision support	9	9549	Std. Mean Difference (IV, Random, 95% CI)	-0.21 [-0.39, -0.02]
5.1 Decision support use	7	6209	Std. Mean Difference (IV, Random, 95% CI)	-0.17 [-0.27, -0.07]
5.2 No decision support use	2	3340	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-0.98, 0.46]

Comparison 3. CVD risk score versus no CVD risk score/usual care by health IT use

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total cholesterol by health IT use	12	20437	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.20, 0.00]
1.1 Health IT use	8	9444	Mean Difference (IV, Random, 95% CI)	-0.09 [-0.20, 0.01]
1.2 No health IT use	4	10993	Mean Difference (IV, Random, 95% CI)	-0.11 [-0.27, 0.06]
2 Low-density lipoprotein cholesterol by health IT use	10	22122	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.10, 0.04]
2.1 Health IT use	9	21739	Mean Difference (IV, Random, 95% CI)	-0.02 [-0.10, 0.06]
2.2 No health IT use	1	383	Mean Difference (IV, Random, 95% CI)	-0.11 [-0.25, 0.03]
3 Systolic blood pressure by health IT use	16	32954	Mean Difference (IV, Random, 95% CI)	-2.77 [-4.16, -1.38]
3.1 Health IT use	13	22457	Mean Difference (IV, Random, 95% CI)	-2.17 [-3.52, -0.82]
3.2 No health IT use	3	10497	Mean Difference (IV, Random, 95% CI)	-4.57 [-6.89, -2.25]
4 Diastolic blood pressure by health IT use	14	22378	Mean Difference (IV, Random, 95% CI)	-1.12 [-2.11, -0.13]
4.1 Health IT use	10	11385	Mean Difference (IV, Random, 95% CI)	-0.76 [-1.29, -0.23]
4.2 No health IT use	4	10993	Mean Difference (IV, Random, 95% CI)	-2.09 [-3.33, -0.85]
5 Change in multivariable CVD risk by health IT use	9	9549	Std. Mean Difference (IV, Random, 95% CI)	-0.21 [-0.39, -0.02]
5.1 Health IT use	6	5387	Std. Mean Difference (IV, Random, 95% CI)	-0.19 [-0.26, -0.12]
5.2 No health IT use	3	4162	Std. Mean Difference (IV, Random, 95% CI)	-0.15 [-0.69, 0.39]

Comparison 4. CVD risk score versus no CVD risk score/usual care by risk status of participants

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total cholesterol by risk status	12	20437	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.20, 0.00]
1.1 High-risk participants only	3	4105	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.22, -0.03]
1.2 Participants of all risk levels	9	16332	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.23, 0.03]
2 Low-density lipoprotein cholesterol by risk status	10	22122	Mean Difference (IV, Random, 95% CI)	-0.03 [-0.10, 0.04]

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2.1 High-risk participants only	3	14219	Mean Difference (IV, Random, 95% CI)	-0.07 [-0.11, -0.03]
2.2 Participants of all risk levels	7	7903	Mean Difference (IV, Random, 95% CI)	-0.01 [-0.11, 0.09]
3 Systolic blood pressure by risk status	16	32954	Mean Difference (IV, Random, 95% CI)	-2.77 [-4.16, -1.38]
3.1 High-risk participants only	5	18375	Mean Difference (IV, Random, 95% CI)	-2.22 [-4.04, -0.40]
3.2 Participants of all risk levels	11	14579	Mean Difference (IV, Random, 95% CI)	-2.96 [-4.68, -1.24]
4 Diastolic blood pressure by risk status	14	22378	Mean Difference (IV, Random, 95% CI)	-1.12 [-2.11, -0.13]
4.1 High-risk participants only	3	4091	Mean Difference (IV, Random, 95% CI)	-0.90 [-2.42, 0.63]
4.2 Participants of all risk levels	11	18287	Mean Difference (IV, Random, 95% CI)	-1.20 [-2.26, -0.14]
5 Change in multivariable CVD risk by risk status	9	9549	Std. Mean Difference (IV, Random, 95% CI)	-0.21 [-0.39, -0.02]
5.1 High-risk participants only	2	4038	Std. Mean Difference (IV, Random, 95% CI)	-0.15 [-0.21, -0.09]
5.2 Participants of all risk levels	7	5511	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.49, 0.05]

Comparison 5. Multivariable CVD risk

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Multivariable CVD risk	5	1921	Std. Mean Difference (IV, Fixed, 95% CI)	-0.15 [-0.25, -0.06]

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Analysis 1.1. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 1 CVD events.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

Outcome: 1 CVD events

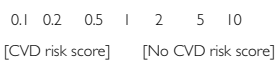
Study or subgroup	[CVD risk score] n/N	No CVD risk score n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Bucher 2010 (1)	9/1680	4/1682		0.3 %	2.25 [0.70, 7.30]
Holt 2010	454/18021	476/18071		26.1 %	0.96 [0.84, 1.09]
Jorgensen 2014	782/11629	3143/47987		73.6 %	1.03 [0.95, 1.11]
Total (95% CI)	**31330**	**67740**		**100.0 %**	**1.01 [0.95, 1.08]**

Total events: 1245 ([CVD risk score]), 3623 (No CVD risk score)

Heterogeneity: $Chi^2 = 2.68$, df = 2 (P = 0.26); $I^2 = 25\%$

Test for overall effect: Z = 0.31 (P = 0.76)

Test for subgroup differences: Not applicable



(1) This study included patients with HIV, so findings may not be generalizable to the general population.

Analysis 1.2. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 2 CVD events, excluding Bucher 2010.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

Outcome: 2 CVD events, excluding Bucher 2010

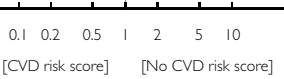
Study or subgroup	CVD risk score n/N	No CVD risk score n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Holt 2010	454/18021	476/18071		26.2 %	0.96 [0.84, 1.09]
Jorgensen 2014	782/11629	3143/47987		73.8 %	1.03 [0.95, 1.11]
Total (95% CI)	**29650**	**66058**		**100.0 %**	**1.01 [0.94, 1.08]**

Total events: 1236 (CVD risk score), 3619 (No CVD risk score)

Heterogeneity: $Chi^2 = 0.88$, df = 1 (P = 0.35); $I^2 = 0.0\%$

Test for overall effect: Z = 0.23 (P = 0.81)

Test for subgroup differences: Not applicable



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Analysis 1.3. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 3 Total cholesterol.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

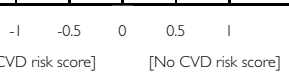
Outcome: 3 Total cholesterol

Study or subgroup	CVD risk score N	Mean(SD)[mmol/L]	No CVD risk score N	Mean(SD)[mmol/L]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Benner 2008	524	5.4 (1)	461	5.6 (1)		8.9 %	-0.20 [-0.33, -0.07]
British Family Heart 1994	2984	5.54 (1.35)	3576	5.67 (1.33)		9.9 %	-0.13 [-0.20, -0.06]
Cobos 2005	1046	6.05 (0.86)	1145	5.97 (0.86)		9.8 %	0.08 [0.01, 0.15]
Engberg 2002	724	5.54 (1.03)	369	5.68 (1.06)		8.8 %	-0.14 [-0.27, -0.01]
Grover 2007 (1)	1510	-1.51 (0.88)	1543	-1.41 (0.92)		9.9 %	-0.10 [-0.16, -0.04]
Hanlon 1995 (2)	263	0.16 (0.57)	233	0.03 (0.55)		9.4 %	0.13 [0.03, 0.23]
Hetlevik 1999	581	6.64 (1.2)	768	6.57 (1.3)		8.7 %	0.07 [-0.06, 0.20]
Lopez-Gonzalez 2015 (3)	1869	-0.13 (0.23)	975	0.14 (0.24)		10.2 %	-0.27 [-0.29, -0.25]
Lowensteyn 1998 (4)	202	-0.49 (0.99)	89	-0.09 (0.87)		6.9 %	-0.40 [-0.63, -0.17]
Sheridan 2011	33	5.25 (1.18)	34	5.07 (1.18)		2.5 %	0.18 [-0.39, 0.75]
Webster 2010	600	5.45 (1.21)	593	5.51 (1.23)		8.7 %	-0.06 [-0.20, 0.08]
Wister 2007 (5)	157	-0.41 (1.14)	158	-0.14 (1.14)		6.4 %	-0.27 [-0.52, -0.02]
Total (95% CI)	**10493**		**9944**			**100.0 %**	**-0.10 [-0.20, 0.00]**

Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 193.00$, df = 11 (P<0.00001); $I^2 = 94\%$

Test for overall effect: Z = 1.90 (P = 0.057)

Test for subgroup differences: Not applicable



(1) Change from baseline.

(2) Change from baseline.

(3) Change from baseline.

(4) Change from baseline.

(5) Change from baseline.

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Analysis 1.4. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 4 Low-density lipoprotein cholesterol.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

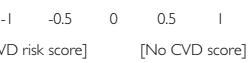
Outcome: 4 Low-density lipoprotein cholesterol

Study or subgroup	CVD risk score		No CVD risk score		Mean Difference	Weight	Mean Difference
	N	Mean(SD)[mmol/L]	N	Mean(SD)[mmol/L]	IV,Random,95% CI		IV,Random,95% CI
Benner 2008	524	3.4 (0.9)	461	3.5 (1)		10.4 %	-0.10 [-0.22, 0.02]
Cobos 2005	1046	3.86 (0.83)	1145	3.79 (0.83)		12.8 %	0.07 [0.00, 0.14]
Eaton 2011	1780	2.96 (0.82)	1683	2.92 (0.8)		13.4 %	0.04 [-0.01, 0.09]
Edelman 2006	56	3.13 (1.22)	66	3.44 (1.22)		2.4 %	-0.31 [-0.74, 0.12]
Grover 2007 (1)	1510	-1.32 (0.76)	1543	-1.24 (0.77)		13.4 %	-0.08 [-0.13, -0.03]
Lowensteyn 1998 (2)	202	-0.4 (0.87)	89	-0.01 (0.8)		6.8 %	-0.39 [-0.59, -0.19]
Peiris 2015 (3)	5335	-0.14 (1.8)	4846	-0.09 (1.8)		12.7 %	-0.05 [-0.12, 0.02]
Vagholkar 2014	413	3.2 (0.8)	417	3 (0.8)		10.9 %	0.20 [0.09, 0.31]
Webster 2010	317	3.38 (1.13)	306	3.31 (1.06)		8.0 %	0.07 [-0.10, 0.24]
Williams 2006	174	3.74 (0.71)	209	3.85 (0.71)		9.3 %	-0.11 [-0.25, 0.03]
Total (95% CI)	**11357**		**10765**			**100.0 %**	**-0.03 [-0.10, 0.04]**

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 50.25$, df = 9 ($P<0.00001$); $I^2 = 82\%$

Test for overall effect: Z = 0.79 (P = 0.43)

Test for subgroup differences: Not applicable



(1) Change from baseline.

(2) Change from baseline.

(3) Low-density lipoprotein cholesterol data only reported for the "high-risk" subgroup. Change from baseline.

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Analysis 1.5. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 5 Systolic blood pressure.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

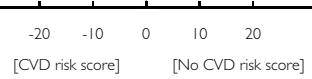
Outcome: 5 Systolic blood pressure

Study or subgroup	CVD risk score		No CVD risk score		Mean Difference	Weight	Mean Difference
	N	Mean(SD)[mmHg]	N	Mean(SD)[mmHg]	IV,Random,95% CI		IV,Random,95% CI
Benner 2008	524	138 (14)	461	144 (14)		7.4 %	-6.00 [-7.75, -4.25]
British Family Heart 1994	2984	128.2 (24.5)	3576	135.3 (24.6)		7.9 %	-7.10 [-8.29, -5.91]
Eaton 2011	2104	123.6 (14.4)	1999	124.1 (13.8)		8.1 %	-0.50 [-1.36, 0.36]
Engberg 2002	724	130.9 (18.2)	369	132.6 (19.9)		6.7 %	-1.70 [-4.12, 0.72]
Grover 2007 (1)	1510	-6.3 (13.5)	1543	-5.3 (13.2)		8.1 %	-1.00 [-1.95, -0.05]
Hetlevik 1999	816	156.8 (19.4)	1023	155.6 (19)		7.4 %	1.20 [-0.57, 2.97]
Lopez-Gonzalez 2015 (2)	1869	-3.3 (5.1)	975	1 (3.6)		8.4 %	-4.30 [-4.62, -3.98]
Lowensteyn 1998 (3)	202	-2 (14.2)	89	-1.2 (14.1)		5.4 %	-0.80 [-4.32, 2.72]
Montgomery 2000	401	153 (18)	130	159 (22)		4.8 %	-6.00 [-10.17, -1.83]
Montgomery 2003	87	149 (14)	101	147 (15)		4.8 %	2.00 [-2.15, 6.15]
Peiris 2015 (4)	5335	-2.3 (30.9)	4846	-1.5 (30.9)		7.9 %	-0.80 [-2.00, 0.40]
Sheridan 2011	26	139.3 (13.2)	27	146.6 (13.2)		2.6 %	-7.30 [-14.41, -0.19]
Turner 2012	116	131.8 (14.7)	131	140 (18.1)		4.9 %	-8.20 [-12.29, -4.11]
Vagholkar 2014	313	126.4 (14.5)	262	129 (13.3)		6.8 %	-2.60 [-4.87, -0.33]
Wister 2007 (5)	157	-7.5 (15.7)	158	-3.6 (15.9)		5.5 %	-3.90 [-7.39, -0.41]
Zullig 2014	47	125.1 (14.7)	49	124.6 (14.7)		3.4 %	0.50 [-5.38, 6.38]
Total (95% CI)	**17215**		**15739**			**100.0 %**	**-2.77 [-4.16, -1.38]**

Heterogeneity: Tau² = 5.99; Chi² = 207.12, df = 15 (P<0.00001); I² =93%

Test for overall effect: Z = 3.91 (P = 0.000092)

Test for subgroup differences: Not applicable



(1) Change from baseline.

(2) Change from baseline.

(3) Change from baseline.

(4) Systolic blood pressure data only reported for the "high-risk" subgroup within this study. Change from baseline.

(5) Change from baseline.

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Analysis 1.6. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 6 Diastolic blood pressure.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

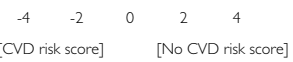
Outcome: 6 Diastolic blood pressure

Study or subgroup	CVD risk score		No CVD risk score		Mean Difference	Weight	Mean Difference
	N	Mean(SD)[mmHg]	N	Mean(SD)[mmHg]	IV,Random,95% CI		IV,Random,95% CI
Benner 2008	524	85 (8.4)	461	87 (9.7)		8.2 %	-2.00 [-3.14, -0.86]
British Family Heart 1994	2984	81.4 (10.8)	3576	84.5 (10.8)		9.0 %	-3.10 [-3.62, -2.58]
Eaton 2011	2103	75.8 (9)	1999	76.7 (8.2)		9.0 %	-0.90 [-1.43, -0.37]
Engberg 2002	724	79.8 (10.5)	369	81 (11.7)		7.8 %	-1.20 [-2.62, 0.22]
Grover 2007 (1)	1510	-3.8 (7.9)	1543	-3.6 (7.7)		9.0 %	-0.20 [-0.75, 0.35]
Hanlon 1995 (2)	263	1.2 (7.6)	233	0.9 (7.3)		8.0 %	0.30 [-1.01, 1.61]
Hetlevik 1999	816	88.8 (9.7)	1023	89.8 (8.9)		8.6 %	-1.00 [-1.86, -0.14]
Lopez-Gonzalez 2015 (3)	1869	-2.3 (4)	975	1.3 (2.9)		9.2 %	-3.60 [-3.86, -3.34]
Lowensteyn 1998 (4)	202	-0.9 (8.1)	89	0.1 (9.8)		6.1 %	-1.00 [-3.32, 1.32]
Montgomery 2000	401	85.5 (9.5)	130	84 (11)		6.5 %	1.50 [-0.61, 3.61]
Montgomery 2003	87	85 (8)	101	85 (10)		5.7 %	0.0 [-2.57, 2.57]
Sheridan 2011	26	80.4 (8.2)	27	80.2 (8.2)		3.3 %	0.20 [-4.22, 4.62]
Turner 2012	116	76.4 (9.4)	131	78.6 (10.4)		5.9 %	-2.20 [-4.67, 0.27]
Zullig 2014	47	73.4 (10)	49	73.5 (10)		3.7 %	-0.10 [-4.10, 3.90]
Total (95% CI)	**11672**		**10706**			**100.0 %**	**-1.12 [-2.11, -0.13]**

Heterogeneity: $Tau^2 = 2.77$; $Chi^2 = 232.17$, df = 13 (P<0.00001); $I^2 = 94\%$

Test for overall effect: Z = 2.21 (P = 0.027)

Test for subgroup differences: Not applicable



(1) Change from baseline.

(2) Change from baseline.

(3) Change from baseline.

(4) Change from baseline.

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Analysis 1.7. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 7 Change in multivariable CVD risk.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

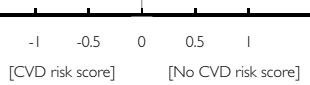
Outcome: 7 Change in multivariable CVD risk

Study or subgroup	CVD risk score N	Mean(SD)	No CVD risk score N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Benner 2008	524	-6.3 (7)	461	-4.9 (6.6)		11.7 %	-0.21 [-0.33, -0.08]
Grover 2007	1510	-5.9 (4.5)	1543	-5.3 (4.3)		12.2 %	-0.14 [-0.21, -0.07]
Hanlon 1995	263	0.53 (1.59)	233	0.34 (1.81)		11.1 %	0.11 [-0.06, 0.29]
Krones 2008	415	-3 (4.61)	407	-3.33 (4.61)		11.6 %	0.07 [-0.07, 0.21]
Lopez-Gonzalez 2015	1869	-0.27 (0.84)	975	0.24 (0.78)		12.1 %	-0.62 [-0.70, -0.54]
Lowensteyn 1998	202	-1.8 (4.7)	89	-0.3 (5.3)		10.1 %	-0.31 [-0.56, -0.06]
Montgomery 2000	401	0.09 (5.27)	130	0.77 (4.22)		10.9 %	-0.13 [-0.33, 0.06]
Turner 2012	94	-0.51 (2)	118	0.31 (3)		9.8 %	-0.31 [-0.59, -0.04]
Wister 2007	157	-3.07 (5.52)	158	-1.1 (5.54)		10.5 %	-0.36 [-0.58, -0.13]
Total (95% CI)	**5435**		**4114**			**100.0 %**	**-0.21 [-0.39, -0.02]**

Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 134.90$, df = 8 ($P<0.00001$); $I^2 = 94\%$

Test for overall effect: Z = 2.20 (P = 0.028)

Test for subgroup differences: Not applicable



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Analysis 1.8. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 8 Adverse events (investigator defined).

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

Outcome: 8 Adverse events (investigator defined)

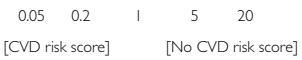
Study or subgroup	CVD risk score n/N	No CVD risk score n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Benner 2008	11/565	15/538		23.4 %	0.70 [0.32, 1.51]
Grover 2007	20/1510	28/1543		42.6 %	0.73 [0.41, 1.29]
Price 2011	13/99	18/95		32.2 %	0.69 [0.36, 1.33]
Turner 2012	1/136	1/144		1.8 %	1.06 [0.07, 16.76]
Total (95% CI)	**2310**	**2320**		**100.0 %**	**0.72 [0.49, 1.04]**

Total events: 45 (CVD risk score), 62 (No CVD risk score)

Heterogeneity: $Chi^2 = 0.10$, df = 3 (P = 0.99); $I^2 = 0.0\%$

Test for overall effect: Z = 1.77 (P = 0.077)

Test for subgroup differences: Not applicable



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Analysis 1.9. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 9 Anxiety.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

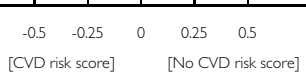
Outcome: 9 Anxiety

Study or subgroup	CVD risk score N	Mean(SD)	No CVD risk score N	Mean(SD)	Std. Mean Difference IV,Fixed,95% CI	Weight	Std. Mean Difference IV,Fixed,95% CI
Montgomery 2003	87	34.8 (10.3)	97	36.8 (13.8)		47.3 %	-0.16 [-0.45, 0.13]
Welschen 2012	102	34.1 (11.2)	102	33.9 (11.7)		52.7 %	0.02 [-0.26, 0.29]
Total (95% CI)	**189**		**199**			**100.0 %**	**-0.07 [-0.27, 0.13]**

Heterogeneity: Chi^2 = 0.78, df = 1 (P = 0.38); I^2 =0.0%

Test for overall effect: Z = 0.66 (P = 0.51)

Test for subgroup differences: Not applicable



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Analysis 1.10. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 10 New/intensified lipid-lowering medication.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

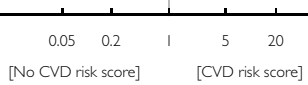
Outcome: 10 New/intensified lipid-lowering medication

Study or subgroup	CVD risk score N	No CVD risk score N	log [Risk Ratio] (SE)	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Benner 2008	524	461	0.0072 (0.1519)		18.6 %	1.01 [0.75, 1.36]
Bucher 2010	436	425	0.137 (0.3228)		9.4 %	1.15 [0.61, 2.16]
Denig 2014	88	44	0.7885 (0.4597)		5.7 %	2.20 [0.89, 5.42]
Hall 2003	162	161	0.3505 (0.3302)		9.1 %	1.42 [0.74, 2.71]
Jacobson 2006	93	92	0.312 (0.2459)		12.8 %	1.37 [0.84, 2.21]
Mann 2010	80	70	0.9651 (0.6463)		3.2 %	2.63 [0.74, 9.32]
Peiris 2015	5335	4846	1.1694 (0.3053)		10.1 %	3.22 [1.77, 5.86]
Persell 2013	218	217	0.6905 (0.3255)		9.3 %	1.99 [1.05, 3.78]
Persell 2015	328	318	0.2241 (0.2144)		14.6 %	1.25 [0.82, 1.90]
Price 2011	99	95	-0.2772 (0.6868)		2.9 %	0.76 [0.20, 2.91]
Vagholkar 2014	38	45	0.3514 (0.564)		4.1 %	1.42 [0.47, 4.29]
Total (95% CI)	**7401**	**6774**			**100.0 %**	**1.47 [1.15, 1.87]**

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 16.57$, df = 10 (P = 0.08); $I^2 = 40\%$

Test for overall effect: Z = 3.09 (P = 0.0020)

Test for subgroup differences: Not applicable



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Analysis 1.11. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 11 New/intensified antihypertensive medication.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

Outcome: 11 New/intensified antihypertensive medication

Study or subgroup	CVD risk score N	No CVD risk score N	log [Risk Ratio] (SE)	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Bucher 2010	436	425	0.039 (0.3529)		12.9 %	1.04 [0.52, 2.08]
Denig 2014	107	48	-0.0479 (0.392)		11.4 %	0.95 [0.44, 2.06]
Grover 2007	629	668	0.235 (0.0851)		26.9 %	1.26 [1.07, 1.49]
Hall 2003	162	161	0.4187 (0.2914)		15.7 %	1.52 [0.86, 2.69]
Peiris 2015	5335	4846	1.1694 (0.3053)		15.0 %	3.22 [1.77, 5.86]
Persell 2013	76	85	0.9761 (0.5748)		6.7 %	2.65 [0.86, 8.19]
Price 2011	99	95	2.7924 (1.4482)		1.3 %	16.32 [0.96, 278.89]
Vagholkar 2014	38	45	0.0513 (0.4331)		10.1 %	1.05 [0.45, 2.46]
Total (95% CI)	**6882**	**6373**			**100.0 %**	**1.51 [1.08, 2.11]**

Heterogeneity: $Tau^2 = 0.10$; $Chi^2 = 14.87$, df = 7 (P = 0.04); $I^2 = 53\%$

Test for overall effect: Z = 2.41 (P = 0.016)

Test for subgroup differences: Not applicable

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Analysis 1.12. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 12 New aspirin.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

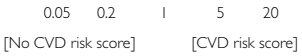
Outcome: 12 New aspirin

Study or subgroup	CVD risk score N	No CVD risk score N	log [Risk Ratio] (SE)	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Benner 2008	524	461	1.1247 (0.5633)		50.1 %	3.08 [1.02, 9.29]
Persell 2013	218	217	0.7583 (0.6051)		43.4 %	2.13 [0.65, 6.99]
Price 2011	99	95	1.5887 (1.5559)		6.6 %	4.90 [0.23, 103.36]
Total (95% CI)	**841**	**773**			**100.0 %**	**2.71 [1.24, 5.91]**

Heterogeneity: Chi² = 0.35, df = 2 (P = 0.84); I² =0.0%

Test for overall effect: Z = 2.50 (P = 0.012)

Test for subgroup differences: Not applicable



Analysis 1.13. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 13 Medication adherence.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

Outcome: 13 Medication adherence

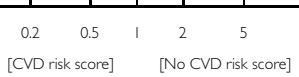
Study or subgroup	CVD risk score n/N	No CVD risk score n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Perestelo-Perez 2016	51/55	36/42		37.4 %	1.08 [0.94, 1.25]
Sheridan 2011	45/76	25/73		18.7 %	1.73 [1.20, 2.50]
Turner 2012	70/136	69/144		28.7 %	1.07 [0.85, 1.36]
Zullig 2014	20/47	24/48		15.1 %	0.85 [0.55, 1.32]
Total (95% CI)	**314**	**307**		**100.0 %**	**1.14 [0.92, 1.40]**

Total events: 186 (CVD risk score), 154 (No CVD risk score)

Heterogeneity: Tau² = 0.02; Chi² = 7.17, df = 3 (P = 0.07); I² =58%

Test for overall effect: Z = 1.21 (P = 0.23)

Test for subgroup differences: Not applicable



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Analysis 1.14. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 14 Smoking cessation.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

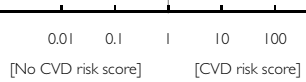
Outcome: 14 Smoking cessation

Study or subgroup	CVD risk score N	No CVD risk score N	log [Risk Ratio] (SE)	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Benner 2008	524	461	0.3137 (0.1119)		85.0 %	1.37 [1.10, 1.70]
Hanlon 1995	263	233	-0.1226 (0.8215)		1.6 %	0.88 [0.18, 4.43]
Lowensteyn 1998	202	89	-0.4219 (0.9219)		1.3 %	0.66 [0.11, 3.99]
Sheridan 2011	77	77	1.1116 (1.6409)		0.4 %	3.04 [0.12, 75.77]
Webster 2010	1062	1037	-0.024 (0.4734)		4.7 %	0.98 [0.39, 2.47]
Williams 2006	714	292	0.9442 (0.4009)		6.6 %	2.57 [1.17, 5.64]
Wister 2007	157	158	-1.0986 (1.6369)		0.4 %	0.33 [0.01, 8.25]
Total (95% CI)	**2999**	**2347**			**100.0 %**	**1.38 [1.13, 1.69]**

Heterogeneity: Chi^2 = 4.88, df = 6 (P = 0.56); I^2 =0.0%

Test for overall effect: Z = 3.11 (P = 0.0019)

Test for subgroup differences: Not applicable



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Analysis 1.15. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 15 Exercise.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

Outcome: 15 Exercise

Study or subgroup	CVD risk score n/N	No CVD risk score n/N	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
Hanlon 1995	208/263	191/233		89.7 %	0.96 [0.88, 1.05]
Webster 2010	112/1062	100/1037		10.3 %	1.09 [0.85, 1.41]
Total (95% CI)	**1325**	**1270**		**100.0 %**	**0.98 [0.90, 1.06]**

Total events: 320 (CVD risk score), 291 (No CVD risk score)

Heterogeneity: Chi^2 = 0.83, df = 1 (P = 0.36); I^2 =0.0%

Test for overall effect: Z = 0.55 (P = 0.58)

Test for subgroup differences: Not applicable

Analysis 1.16. Comparison 1 CVD risk score versus no CVD risk score/usual care, Outcome 16 Decisional conflict.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 1 CVD risk score versus no CVD risk score/usual care

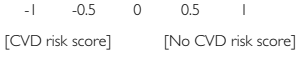
Outcome: 16 Decisional conflict

Study or subgroup	CVD risk score N	Mean(SD)	No CVD risk score N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
Krones 2008	372	14.7 (20)	372	18.1 (20)		29.8 %	-0.17 [-0.31, -0.03]
Mann 2010	80	25.5 (11.1)	70	28.5 (11.1)		22.7 %	-0.27 [-0.59, 0.05]
Montgomery 2003	100	27.6 (12.1)	112	38.9 (18.3)		24.5 %	-0.72 [-1.00, -0.44]
Perestelo-Perez 2016	78	23.9 (16.8)	77	23.8 (14.8)		23.0 %	0.01 [-0.31, 0.32]
Total (95% CI)	**630**		**631**			**100.0 %**	**-0.29 [-0.57, -0.01]**

Heterogeneity: Tau^2 = 0.06; Chi^2 = 14.60, df = 3 (P = 0.002); I^2 =79%

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

Test for subgroup differences: Not applicable



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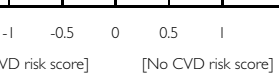
Analysis 2.1. Comparison 2 CVD risk score versus no CVD risk score/usual care by decision support use, Outcome 1 Total cholesterol by decision support use.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 2 CVD risk score versus no CVD risk score/usual care by decision support use

Outcome: 1 Total cholesterol by decision support use

Study or subgroup	CVD risk score N	CVD risk score Mean(SD)[mmol/L]	No CVD risk score N	No CVD risk score Mean(SD)[mmol/L]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Decision support use							
Benner 2008	524	5.4 (1)	461	5.6 (1)		8.9 %	-0.20 [-0.33, -0.07]
Cobos 2005	1046	6.05 (0.86)	1145	5.97 (0.86)		9.8 %	0.08 [0.01, 0.15]
Grover 2007 (1)	1510	-1.51 (0.88)	1543	-1.41 (0.92)		9.9 %	-0.10 [-0.16, -0.04]
Hetlevik 1999	581	6.64 (1.2)	768	6.57 (1.3)		8.7 %	0.07 [-0.06, 0.20]
Lowensteyn 1998 (2)	202	-0.49 (0.99)	89	-0.09 (0.87)		6.9 %	-0.40 [-0.63, -0.17]
Sheridan 2011	33	5.25 (1.18)	34	5.07 (1.18)		2.5 %	0.18 [-0.39, 0.75]
Webster 2010	600	5.45 (1.21)	593	5.51 (1.23)		8.7 %	-0.06 [-0.20, 0.08]
Wister 2007 (3)	157	-0.41 (1.14)	158	-0.14 (1.14)		6.4 %	-0.27 [-0.52, -0.02]
Subtotal (95% CI)	**4653**		**4791**			**61.7 %**	**-0.09 [-0.20, 0.01]**
Heterogeneity: Tau^2 = 0.02; Chi^2 = 36.20, df = 7 (P<0.00001); I^2 =81%							
Test for overall effect: Z = 1.68 (P = 0.092)							
2 No decision support use							
British Family Heart 1994	2984	5.54 (1.35)	3576	5.67 (1.33)		9.9 %	-0.13 [-0.20, -0.06]
Engberg 2002	724	5.54 (1.03)	369	5.68 (1.06)		8.8 %	-0.14 [-0.27, -0.01]
Hanlon 1995 (4)	263	0.16 (0.57)	233	0.03 (0.55)		9.4 %	0.13 [0.03, 0.23]
Lopez-Gonzalez 2015 (5)	1869	-0.13 (0.23)	975	0.14 (0.24)		10.2 %	-0.27 [-0.29, -0.25]
Subtotal (95% CI)	**5840**		**5153**			**38.3 %**	**-0.11 [-0.27, 0.06]**
Heterogeneity: Tau^2 = 0.03; Chi^2 = 77.05, df = 3 (P<0.00001); I^2 =96%							
Test for overall effect: Z = 1.25 (P = 0.21)							
Total (95% CI)	**10493**		**9944**			**100.0 %**	**-0.10 [-0.20, 0.00]**
Heterogeneity: Tau^2 = 0.03; Chi^2 = 193.00, df = 11 (P<0.00001); I^2 =94%							
Test for overall effect: Z = 1.90 (P = 0.057)							
Test for subgroup differences: Chi^2 = 0.02, df = 1 (P = 0.88), I^2 =0.0%							



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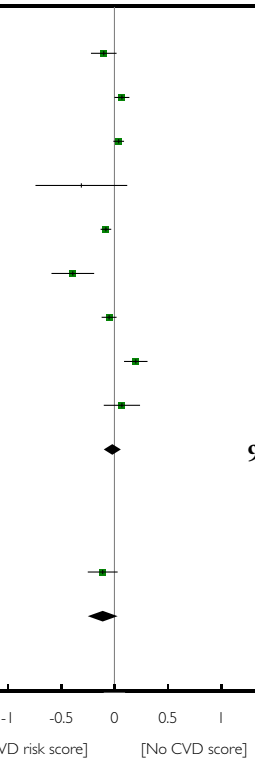
Analysis 2.2. Comparison 2 CVD risk score versus no CVD risk score/usual care by decision support use, Outcome 2 Low-density lipoprotein cholesterol by decision support.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 2 CVD risk score versus no CVD risk score/usual care by decision support use

Outcome: 2 Low-density lipoprotein cholesterol by decision support

Study or subgroup	CVD risk score N	CVD risk score Mean(SD)[mmol/L]	No CVD risk score N	No CVD risk score Mean(SD)[mmol/L]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Decision support use							
Benner 2008	524	3.4 (0.9)	461	3.5 (1)		10.4 %	-0.10 [-0.22, 0.02]
Cobos 2005	1046	3.86 (0.83)	1145	3.79 (0.83)		12.8 %	0.07 [0.00, 0.14]
Eaton 2011	1780	2.96 (0.82)	1683	2.92 (0.8)		13.4 %	0.04 [-0.01, 0.09]
Edelman 2006	56	3.13 (1.22)	66	3.44 (1.22)		2.4 %	-0.31 [-0.74, 0.12]
Grover 2007 (1)	1510	-1.32 (0.76)	1543	-1.24 (0.77)		13.4 %	-0.08 [-0.13, -0.03]
Lowensteyn 1998 (2)	202	-0.4 (0.87)	89	-0.01 (0.8)		6.8 %	-0.39 [-0.59, -0.19]
Peiris 2015 (3)	5335	-0.14 (1.8)	4846	-0.09 (1.8)		12.7 %	-0.05 [-0.12, 0.02]
Vagholkar 2014	413	3.2 (0.8)	417	3 (0.8)		10.9 %	0.20 [0.09, 0.31]
Webster 2010	317	3.38 (1.13)	306	3.31 (1.06)		8.0 %	0.07 [-0.10, 0.24]
Subtotal (95% CI)	**11183**		**10556**			**90.7 %**	**-0.02 [-0.10, 0.06]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 48.28$, df = 8 (P<0.00001); $I^2 = 83\%$							
Test for overall effect: Z = 0.55 (P = 0.58)							
2 No decision support use							
Williams 2006	174	3.74 (0.71)	209	3.85 (0.71)		9.3 %	-0.11 [-0.25, 0.03]
Subtotal (95% CI)	**174**		**209**			**9.3 %**	**-0.11 [-0.25, 0.03]**
Heterogeneity: not applicable							



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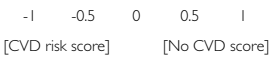
Study or subgroup	CVD risk score N	Mean(SD)[mmol/L]	No CVD risk score N	Mean(SD)[mmol/L]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Test for overall effect: Z = 1.51 (P = 0.13)							
Total (95% CI)	**11357**		**10765**			**100.0 %**	**-0.03 [-0.10, 0.04]**
Heterogeneity: Tau² = 0.01; Chi² = 50.25, df = 9 (P<0.00001); I² =82%							
Test for overall effect: Z = 0.79 (P = 0.43)							
Test for subgroup differences: Chi² = 1.13, df = 1 (P = 0.29), I² =12%							



(1) Change from baseline.

(2) Change from baseline.

(3) Low-density lipoprotein cholesterol data only reported for the "high-risk" subgroup within this study. Change from baseline.

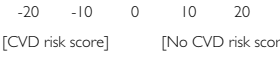
Analysis 2.3. Comparison 2 CVD risk score versus no CVD risk score/usual care by decision support use, Outcome 3 Systolic blood pressure by decision support use.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 2 CVD risk score versus no CVD risk score/usual care by decision support use

Outcome: 3 Systolic blood pressure by decision support use

Study or subgroup	CVD risk score N	Mean(SD)[mmHg]	No CVD risk score N	Mean(SD)[mmHg]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Decision support use							
Benner 2008	524	138 (14)	461	144 (14)		7.4 %	-6.00 [-7.75, -4.25]
Eaton 2011	2104	123.6 (14.4)	1999	124.1 (13.8)		8.1 %	-0.50 [-1.36, 0.36]
Grover 2007 (1)	1510	-6.3 (13.5)	1543	-5.3 (13.2)		8.1 %	-1.00 [-1.95, -0.05]
Hetlevik 1999	816	156.8 (19.4)	1023	155.6 (19)		7.4 %	1.20 [-0.57, 2.97]
Lowensteyn 1998 (2)	202	-2 (14.2)	89	-1.2 (14.1)		5.4 %	-0.80 [-4.32, 2.72]
Montgomery 2000	401	153 (18)	130	159 (22)		4.8 %	-6.00 [-10.17, -1.83]
Montgomery 2003	87	149 (14)	101	147 (15)		4.8 %	2.00 [-2.15, 6.15]
Peiris 2015 (3)	5335	-2.3 (30.9)	4846	-1.5 (30.9)		7.9 %	-0.80 [-2.00, 0.40]



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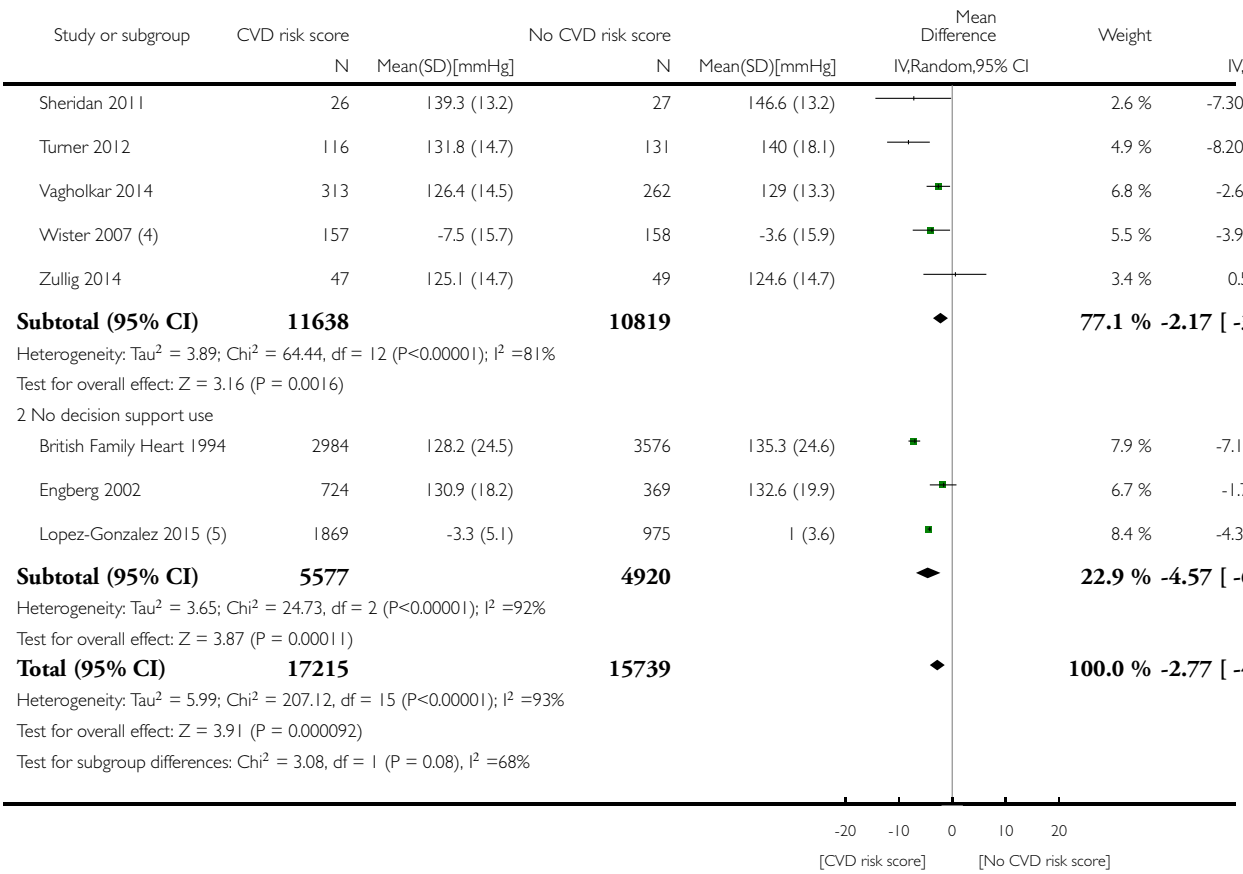

(1) Change from baseline.

(2) Change from baseline.

(3) Systolic blood pressure data only reported for the "high-risk" subgroup within this study. Change from baseline.

(4) Change from baseline.

(5) Change from baseline.

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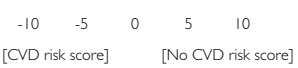
Analysis 2.4. Comparison 2 CVD risk score versus no CVD risk score/usual care by decision support use, Outcome 4 Diastolic blood pressure by decision support use.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 2 CVD risk score versus no CVD risk score/usual care by decision support use

Outcome: 4 Diastolic blood pressure by decision support use

Study or subgroup	CVD risk score N	CVD risk score Mean(SD)[mmHg]	No CVD risk score N	No CVD risk score Mean(SD)[mmHg]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Decision support use							
Benner 2008	524	85 (8.4)	461	87 (9.7)		8.2 %	-2.00 [-3.14, -0.86]
Eaton 2011	2103	75.8 (9)	1999	76.7 (8.2)		9.0 %	-0.90 [-1.43, -0.37]
Grover 2007 (1)	1510	-3.8 (7.9)	1543	-3.6 (7.7)		9.0 %	-0.20 [-0.75, 0.35]
Hetlevik 1999	816	88.8 (9.7)	1023	89.8 (8.9)		8.6 %	-1.00 [-1.86, -0.14]
Lowensteyn 1998 (2)	202	-0.9 (8.1)	89	0.1 (9.8)		6.1 %	-1.00 [-3.32, 1.32]
Montgomery 2000	401	85.5 (9.5)	130	84 (11)		6.5 %	1.50 [-0.61, 3.61]
Montgomery 2003	87	85 (8)	101	85 (10)		5.7 %	0.0 [-2.57, 2.57]
Sheridan 2011	26	80.4 (8.2)	27	80.2 (8.2)		3.3 %	0.20 [-4.22, 4.62]
Turner 2012	116	76.4 (9.4)	131	78.6 (10.4)		5.9 %	-2.20 [-4.67, 0.27]
Zullig 2014	47	73.4 (10)	49	73.5 (10)		3.7 %	-0.10 [-4.10, 3.90]
Subtotal (95% CI)	**5832**		**5553**			**66.1 %**	**-0.76 [-1.29, -0.23]**
Heterogeneity: Tau^2 = 0.23; Chi^2 = 15.34, df = 9 (P = 0.08); I^2 =41%							
Test for overall effect: Z = 2.79 (P = 0.0053)							
2 No decision support use							
British Family Heart 1994	2984	81.4 (10.8)	3576	84.5 (10.8)		9.0 %	-3.10 [-3.62, -2.58]
Engberg 2002	724	79.8 (10.5)	369	81 (11.7)		7.8 %	-1.20 [-2.62, 0.22]
Hanlon 1995 (3)	263	1.2 (7.6)	233	0.9 (7.3)		8.0 %	0.30 [-1.01, 1.61]
Lopez-Gonzalez 2015 (4)	1869	-2.3 (4)	975	1.3 (2.9)		9.2 %	-3.60 [-3.86, -3.34]
Subtotal (95% CI)	**5840**		**5153**			**33.9 %**	**-2.09 [-3.33, -0.85]**
Heterogeneity: Tau^2 = 1.37; Chi^2 = 43.04, df = 3 (P<0.00001); I^2 =93%							
Test for overall effect: Z = 3.30 (P = 0.00096)							
Total (95% CI)	**11672**		**10706**			**100.0 %**	**-1.12 [-2.11, -0.13]**
Heterogeneity: Tau^2 = 2.77; Chi^2 = 232.17, df = 13 (P<0.00001); I^2 =94%							
Test for overall effect: Z = 2.21 (P = 0.027)							
Test for subgroup differences: Chi^2 = 3.73, df = 1 (P = 0.05), I^2 =73%							



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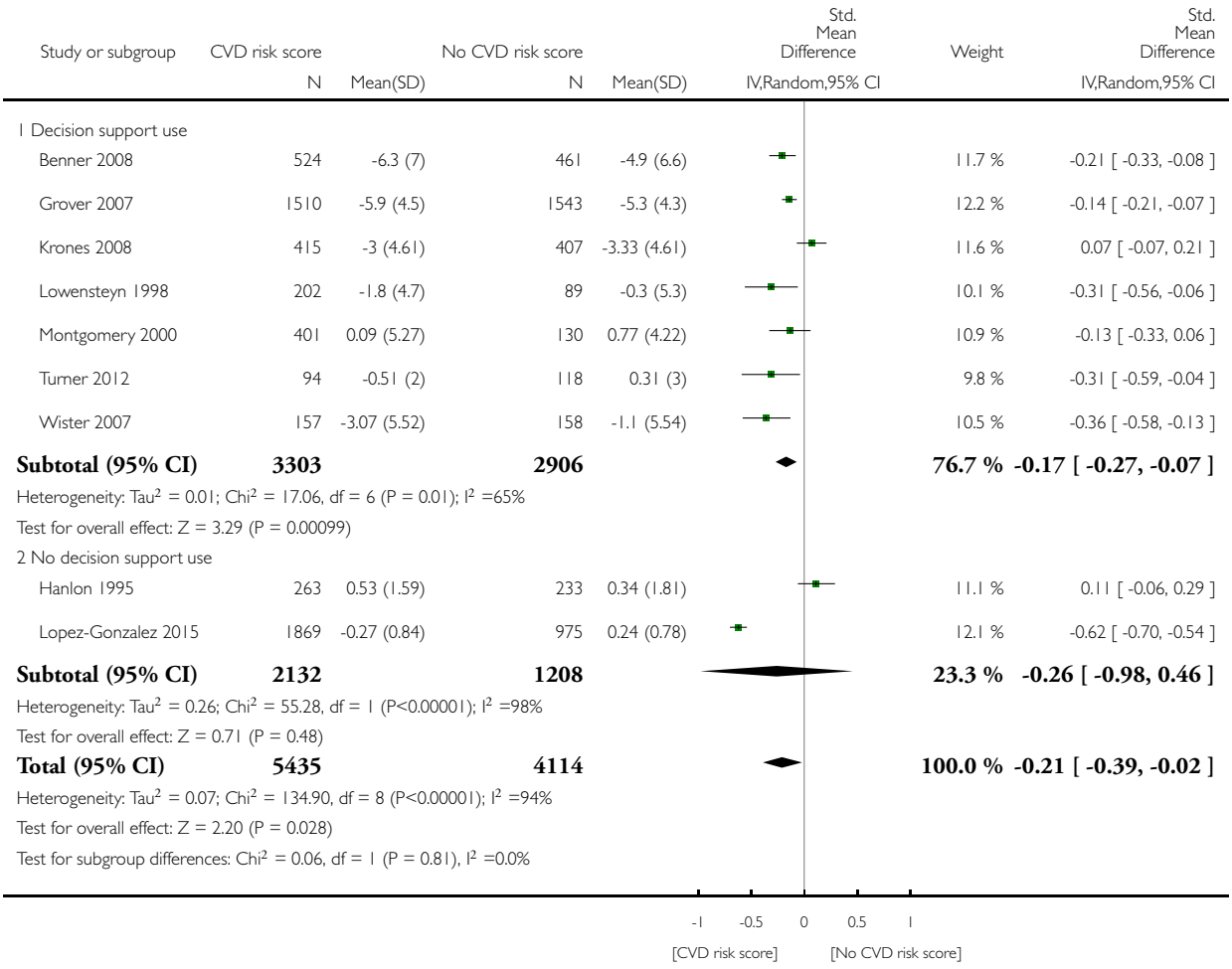
Analysis 2.5. Comparison 2 CVD risk score versus no CVD risk score/usual care by decision support use, Outcome 5 Change in multivariable CVD risk by decision support.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 2 CVD risk score versus no CVD risk score/usual care by decision support use

Outcome: 5 Change in multivariable CVD risk by decision support



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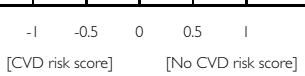
Analysis 3.1. Comparison 3 CVD risk score versus no CVD risk score/usual care by health IT use, Outcome 1 Total cholesterol by health IT use.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 3 CVD risk score versus no CVD risk score/usual care by health IT use

Outcome: 1 Total cholesterol by health IT use

Study or subgroup	CVD risk score N	Mean(SD)[mmol/L]	No CVD risk score N	Mean(SD)[mmol/L]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Health IT use							
Benner 2008	524	5.4 (1)	461	5.6 (1)		8.9 %	-0.20 [-0.33, -0.07]
Cobos 2005	1046	6.05 (0.86)	1145	5.97 (0.86)		9.8 %	0.08 [0.01, 0.15]
Grover 2007 (1)	1510	-1.51 (0.88)	1543	-1.41 (0.92)		9.9 %	-0.10 [-0.16, -0.04]
Hetlevik 1999	581	6.64 (1.2)	768	6.57 (1.3)		8.7 %	0.07 [-0.06, 0.20]
Lowensteyn 1998 (2)	202	-0.49 (0.99)	89	-0.09 (0.87)		6.9 %	-0.40 [-0.63, -0.17]
Sheridan 2011	33	5.25 (1.18)	34	5.07 (1.18)		2.5 %	0.18 [-0.39, 0.75]
Webster 2010	600	5.45 (1.21)	593	5.51 (1.23)		8.7 %	-0.06 [-0.20, 0.08]
Wister 2007 (3)	157	-0.41 (1.14)	158	-0.14 (1.14)		6.4 %	-0.27 [-0.52, -0.02]
Subtotal (95% CI)	**4653**		**4791**			**61.7 %**	**-0.09 [-0.20, 0.01]**
Heterogeneity: Tau^2 = 0.02; Chi^2 = 36.20, df = 7 (P<0.00001); I^2 =81%							
Test for overall effect: Z = 1.68 (P = 0.092)							
2 No health IT use							
British Family Heart 1994	2984	5.54 (1.35)	3576	5.67 (1.33)		9.9 %	-0.13 [-0.20, -0.06]
Engberg 2002	724	5.54 (1.03)	369	5.68 (1.06)		8.8 %	-0.14 [-0.27, -0.01]
Hanlon 1995 (4)	263	0.16 (0.57)	233	0.03 (0.55)		9.4 %	0.13 [0.03, 0.23]
Lopez-Gonzalez 2015 (5)	1869	-0.13 (0.23)	975	0.14 (0.24)		10.2 %	-0.27 [-0.29, -0.25]
Subtotal (95% CI)	**5840**		**5153**			**38.3 %**	**-0.11 [-0.27, 0.06]**
Heterogeneity: Tau^2 = 0.03; Chi^2 = 77.05, df = 3 (P<0.00001); I^2 =96%							
Test for overall effect: Z = 1.25 (P = 0.21)							
Total (95% CI)	**10493**		**9944**			**100.0 %**	**-0.10 [-0.20, 0.00]**
Heterogeneity: Tau^2 = 0.03; Chi^2 = 193.00, df = 11 (P<0.00001); I^2 =94%							
Test for overall effect: Z = 1.90 (P = 0.057)							
Test for subgroup differences: Chi^2 = 0.02, df = 1 (P = 0.88), I^2 =0.0%							



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(4) Change from baseline.

(5) Change from baseline.

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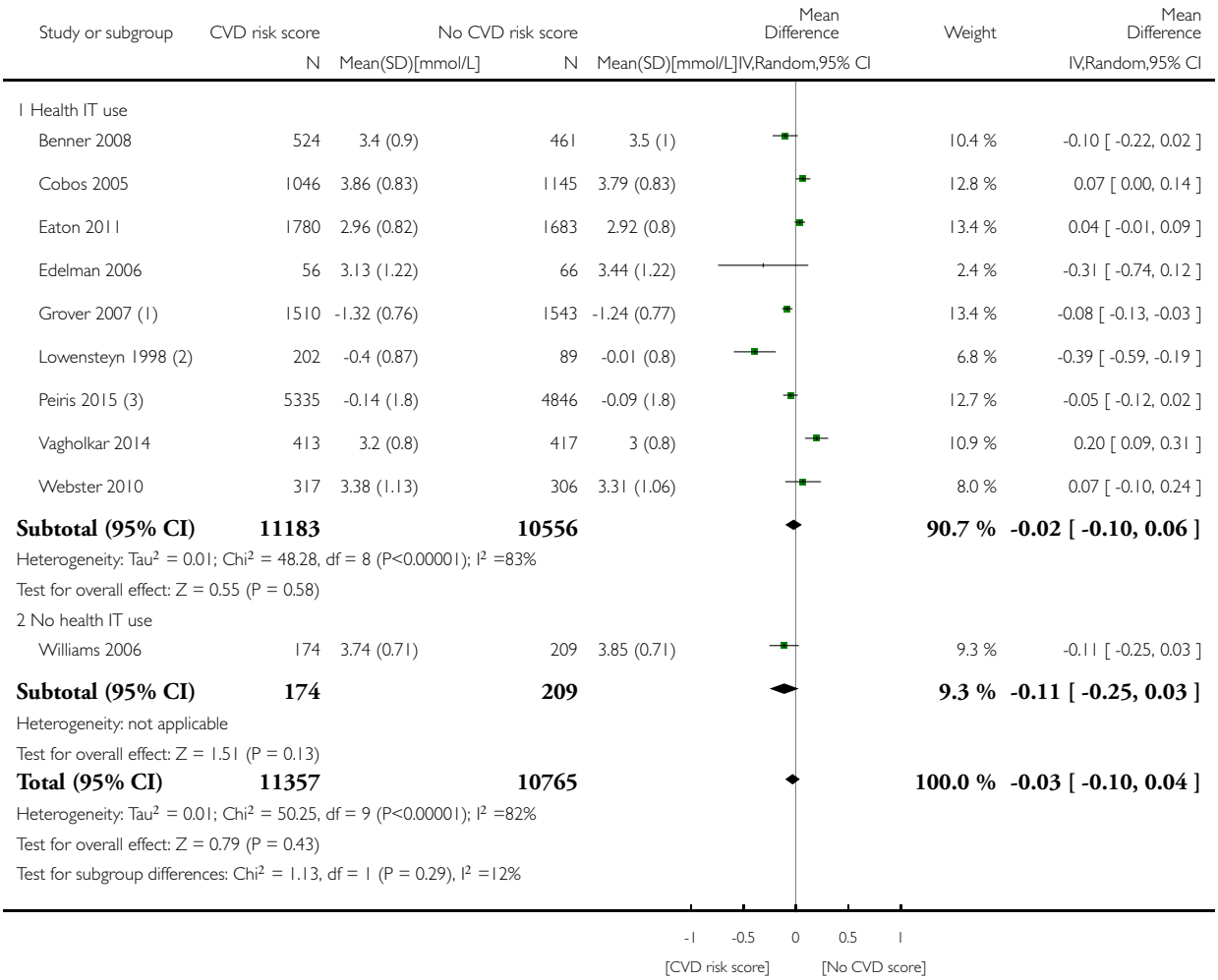
Analysis 3.2. Comparison 3 CVD risk score versus no CVD risk score/usual care by health IT use, Outcome 2 Low-density lipoprotein cholesterol by health IT use.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 3 CVD risk score versus no CVD risk score/usual care by health IT use

Outcome: 2 Low-density lipoprotein cholesterol by health IT use

Study or subgroup	CVD risk score N	CVD risk score Mean(SD)[mmol/L]	No CVD risk score N	No CVD risk score Mean(SD)[mmol/L]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Health IT use							
Benner 2008	524	3.4 (0.9)	461	3.5 (1)		10.4 %	-0.10 [-0.22, 0.02]
Cobos 2005	1046	3.86 (0.83)	1145	3.79 (0.83)		12.8 %	0.07 [0.00, 0.14]
Eaton 2011	1780	2.96 (0.82)	1683	2.92 (0.8)		13.4 %	0.04 [-0.01, 0.09]
Edelman 2006	56	3.13 (1.22)	66	3.44 (1.22)		2.4 %	-0.31 [-0.74, 0.12]
Grover 2007 (1)	1510	-1.32 (0.76)	1543	-1.24 (0.77)		13.4 %	-0.08 [-0.13, -0.03]
Lowensteyn 1998 (2)	202	-0.4 (0.87)	89	-0.01 (0.8)		6.8 %	-0.39 [-0.59, -0.19]
Peiris 2015 (3)	5335	-0.14 (1.8)	4846	-0.09 (1.8)		12.7 %	-0.05 [-0.12, 0.02]
Vagholkar 2014	413	3.2 (0.8)	417	3 (0.8)		10.9 %	0.20 [0.09, 0.31]
Webster 2010	317	3.38 (1.13)	306	3.31 (1.06)		8.0 %	0.07 [-0.10, 0.24]
Subtotal (95% CI)	**11183**		**10556**			**90.7 %**	**-0.02 [-0.10, 0.06]**
Heterogeneity: Tau^2 = 0.01; Chi^2 = 48.28, df = 8 (P<0.00001); I^2 =83%							
Test for overall effect: Z = 0.55 (P = 0.58)							
2 No health IT use							
Williams 2006	174	3.74 (0.71)	209	3.85 (0.71)		9.3 %	-0.11 [-0.25, 0.03]
Subtotal (95% CI)	**174**		**209**			**9.3 %**	**-0.11 [-0.25, 0.03]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.51 (P = 0.13)							
Total (95% CI)	**11357**		**10765**			**100.0 %**	**-0.03 [-0.10, 0.04]**
Heterogeneity: Tau^2 = 0.01; Chi^2 = 50.25, df = 9 (P<0.00001); I^2 =82%							
Test for overall effect: Z = 0.79 (P = 0.43)							
Test for subgroup differences: Chi^2 = 1.13, df = 1 (P = 0.29), I^2 =12%							



(1) Change from baseline.

(2) Change from baseline.

(3) Low-density lipoprotein cholesterol data only reported for the "high-risk" subgroup within this study. Change from baseline.

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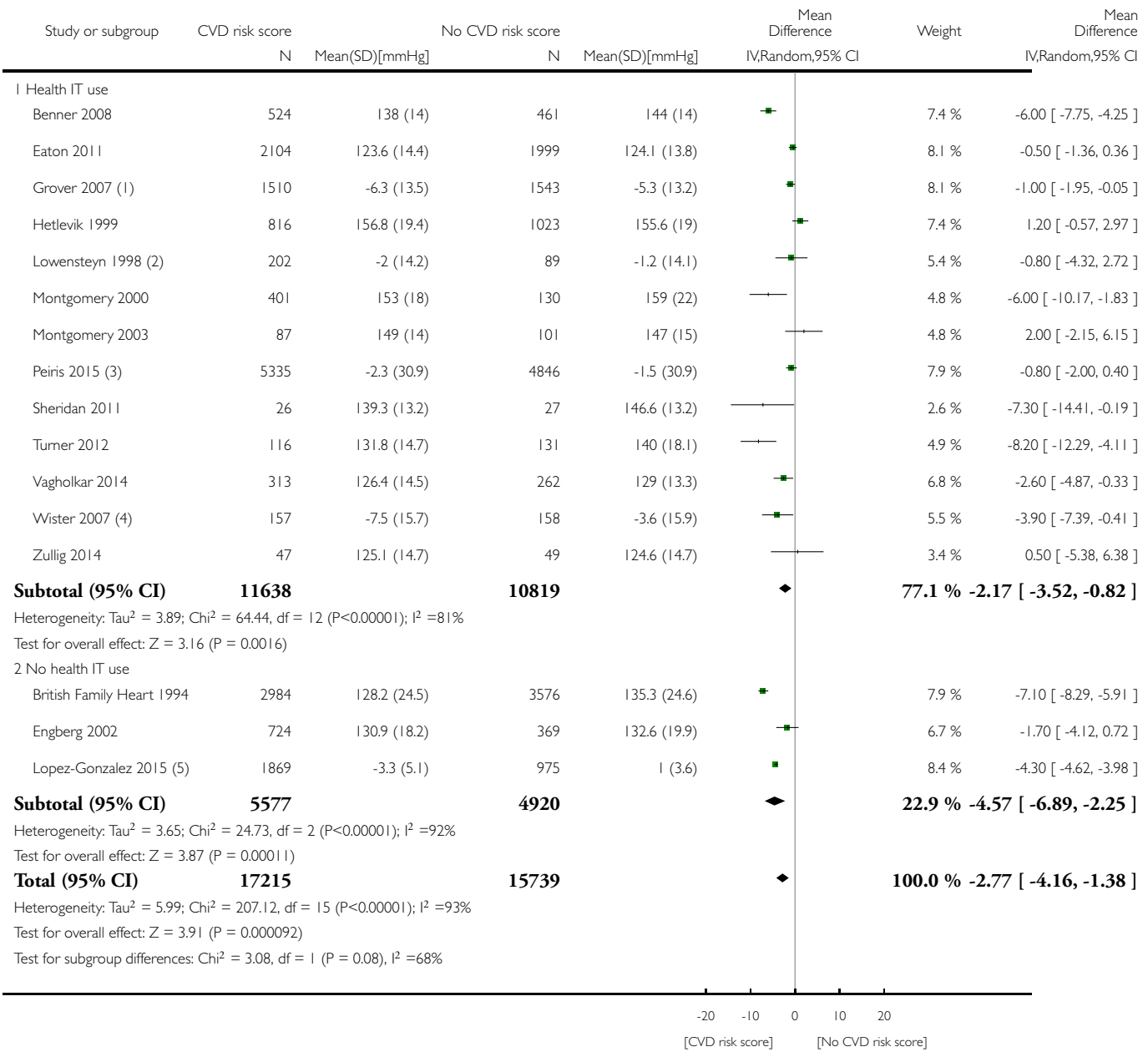
Analysis 3.3. Comparison 3 CVD risk score versus no CVD risk score/usual care by health IT use, Outcome 3 Systolic blood pressure by health IT use.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 3 CVD risk score versus no CVD risk score/usual care by health IT use

Outcome: 3 Systolic blood pressure by health IT use



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(1) Change from baseline.

(2) Change from baseline.

(3) Systolic blood pressure data only reported for the "high-risk" subgroup within this study. Change from baseline.

(4) Change from baseline.

(5) Change from baseline.

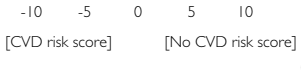
Analysis 3.4. Comparison 3 CVD risk score versus no CVD risk score/usual care by health IT use, Outcome 4 Diastolic blood pressure by health IT use.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 3 CVD risk score versus no CVD risk score/usual care by health IT use

Outcome: 4 Diastolic blood pressure by health IT use

Study or subgroup	CVD risk score N	Mean(SD)[mmHg]	No CVD risk score N	Mean(SD)[mmHg]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 Health IT use							
Benner 2008	524	85 (8.4)	461	87 (9.7)		8.2 %	-2.00 [-3.14, -0.86]
Eaton 2011	2103	75.8 (9)	1999	76.7 (8.2)		9.0 %	-0.90 [-1.43, -0.37]
Grover 2007 (1)	1510	-3.8 (7.9)	1543	-3.6 (7.7)		9.0 %	-0.20 [-0.75, 0.35]
Hetlevik 1999	816	88.8 (9.7)	1023	89.8 (8.9)		8.6 %	-1.00 [-1.86, -0.14]
Lowensteyn 1998 (2)	202	-0.9 (8.1)	89	0.1 (9.8)		6.1 %	-1.00 [-3.32, 1.32]
Montgomery 2000	401	85.5 (9.5)	130	84 (11)		6.5 %	1.50 [-0.61, 3.61]
Montgomery 2003	87	85 (8)	101	85 (10)		5.7 %	0.0 [-2.57, 2.57]
Sheridan 2011	26	80.4 (8.2)	27	80.2 (8.2)		3.3 %	0.20 [-4.22, 4.62]
Turner 2012	116	76.4 (9.4)	131	78.6 (10.4)		5.9 %	-2.20 [-4.67, 0.27]
Zullig 2014	47	73.4 (10)	49	73.5 (10)		3.7 %	-0.10 [-4.10, 3.90]
Subtotal (95% CI)	**5832**		**5553**			**66.1 %**	**-0.76 [-1.29, -0.23]**
Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 15.34$, df = 9 (P = 0.08); $I^2 = 41\%$							
Test for overall effect: Z = 2.79 (P = 0.0053)							
2 No health IT use							
British Family Heart 1994	2984	81.4 (10.8)	3576	84.5 (10.8)		9.0 %	-3.10 [-3.62, -2.58]



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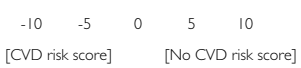
Study or subgroup	CVD risk score N	Mean(SD)[mmHg]	No CVD risk score N	Mean(SD)[mmHg]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Engberg 2002	724	79.8 (10.5)	369	81 (11.7)		7.8 %	-1.20 [-2.62, 0.22]
Hanlon 1995 (3)	263	1.2 (7.6)	233	0.9 (7.3)		8.0 %	0.30 [-1.01, 1.61]
Lopez-Gonzalez 2015 (4)	1869	-2.3 (4)	975	1.3 (2.9)		9.2 %	-3.60 [-3.86, -3.34]
Subtotal (95% CI)	**5840**		**5153**			**33.9 %**	**-2.09 [-3.33, -0.85]**
Heterogeneity: Tau^2 = 1.37; Chi^2 = 43.04, df = 3 (P<0.00001); I^2 =93%							
Test for overall effect: Z = 3.30 (P = 0.00096)							
Total (95% CI)	**11672**		**10706**			**100.0 %**	**-1.12 [-2.11, -0.13]**
Heterogeneity: Tau^2 = 2.77; Chi^2 = 232.17, df = 13 (P<0.00001); I^2 =94%							
Test for overall effect: Z = 2.21 (P = 0.027)							
Test for subgroup differences: Chi^2 = 3.73, df = 1 (P = 0.05), I^2 =73%							



(1) Change from baseline.

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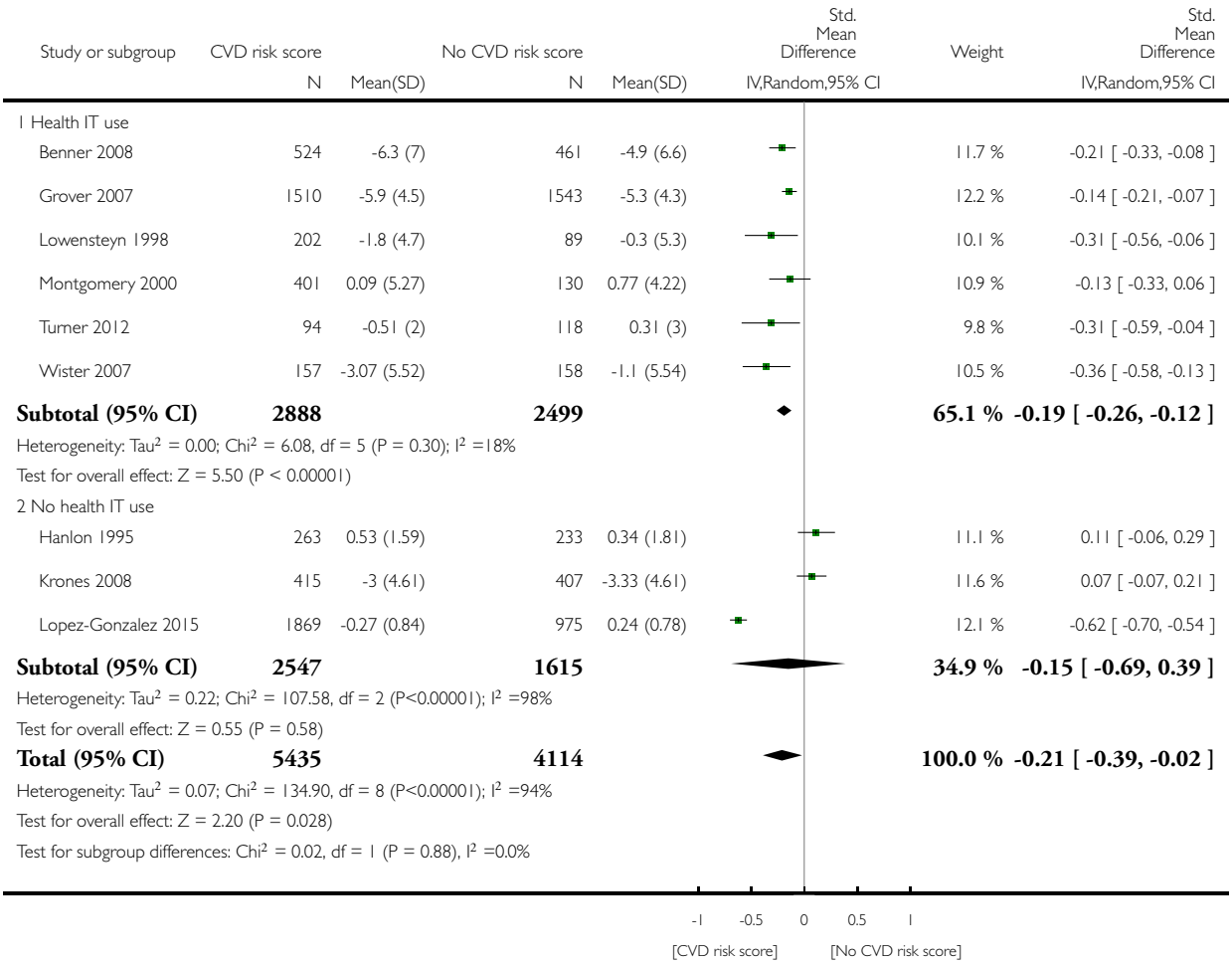
Analysis 3.5. Comparison 3 CVD risk score versus no CVD risk score/usual care by health IT use, Outcome 5 Change in multivariable CVD risk by health IT use.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 3 CVD risk score versus no CVD risk score/usual care by health IT use

Outcome: 5 Change in multivariable CVD risk by health IT use



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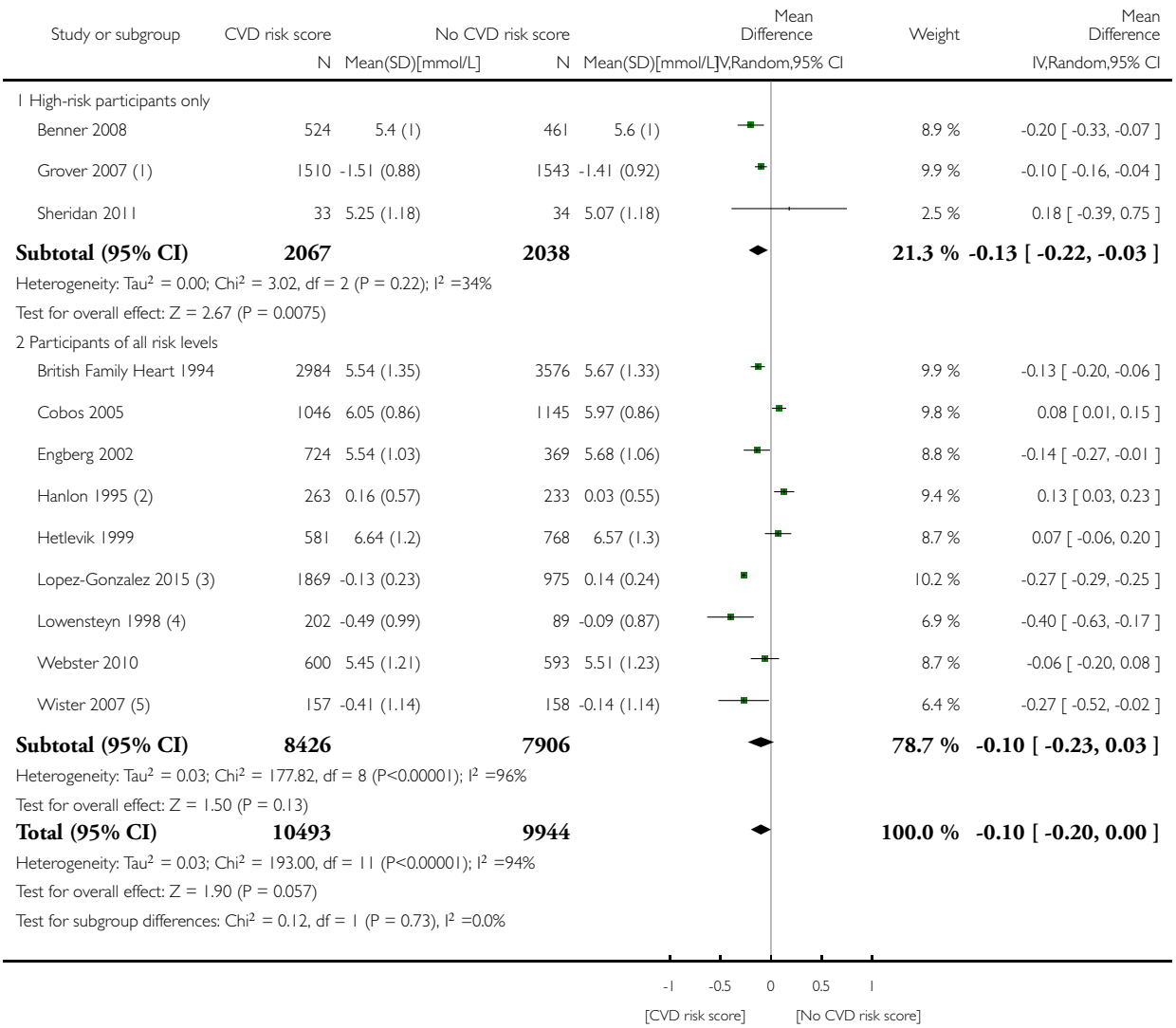
Analysis 4.1. Comparison 4 CVD risk score versus no CVD risk score/usual care by risk status of participants, Outcome 1 Total cholesterol by risk status.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 4 CVD risk score versus no CVD risk score/usual care by risk status of participants

Outcome: 1 Total cholesterol by risk status

Study or subgroup	CVD risk score N	CVD risk score Mean(SD)[mmol/L]	No CVD risk score N	No CVD risk score Mean(SD)[mmol/L]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 High-risk participants only							
Benner 2008	524	5.4 (1)	461	5.6 (1)		8.9 %	-0.20 [-0.33, -0.07]
Grover 2007 (1)	1510	-1.51 (0.88)	1543	-1.41 (0.92)		9.9 %	-0.10 [-0.16, -0.04]
Sheridan 2011	33	5.25 (1.18)	34	5.07 (1.18)		2.5 %	0.18 [-0.39, 0.75]
Subtotal (95% CI)	**2067**		**2038**			**21.3 %**	**-0.13 [-0.22, -0.03]**
Heterogeneity: Tau^2 = 0.00; Chi^2 = 3.02, df = 2 (P = 0.22); I^2 =34%							
Test for overall effect: Z = 2.67 (P = 0.0075)							
2 Participants of all risk levels							
British Family Heart 1994	2984	5.54 (1.35)	3576	5.67 (1.33)		9.9 %	-0.13 [-0.20, -0.06]
Cobos 2005	1046	6.05 (0.86)	1145	5.97 (0.86)		9.8 %	0.08 [0.01, 0.15]
Engberg 2002	724	5.54 (1.03)	369	5.68 (1.06)		8.8 %	-0.14 [-0.27, -0.01]
Hanlon 1995 (2)	263	0.16 (0.57)	233	0.03 (0.55)		9.4 %	0.13 [0.03, 0.23]
Hetlevik 1999	581	6.64 (1.2)	768	6.57 (1.3)		8.7 %	0.07 [-0.06, 0.20]
Lopez-Gonzalez 2015 (3)	1869	-0.13 (0.23)	975	0.14 (0.24)		10.2 %	-0.27 [-0.29, -0.25]
Lowensteyn 1998 (4)	202	-0.49 (0.99)	89	-0.09 (0.87)		6.9 %	-0.40 [-0.63, -0.17]
Webster 2010	600	5.45 (1.21)	593	5.51 (1.23)		8.7 %	-0.06 [-0.20, 0.08]
Wister 2007 (5)	157	-0.41 (1.14)	158	-0.14 (1.14)		6.4 %	-0.27 [-0.52, -0.02]
Subtotal (95% CI)	**8426**		**7906**			**78.7 %**	**-0.10 [-0.23, 0.03]**
Heterogeneity: Tau^2 = 0.03; Chi^2 = 177.82, df = 8 (P<0.00001); I^2 =96%							
Test for overall effect: Z = 1.50 (P = 0.13)							
Total (95% CI)	**10493**		**9944**			**100.0 %**	**-0.10 [-0.20, 0.00]**
Heterogeneity: Tau^2 = 0.03; Chi^2 = 193.00, df = 11 (P<0.00001); I^2 =94%							
Test for overall effect: Z = 1.90 (P = 0.057)							
Test for subgroup differences: Chi^2 = 0.12, df = 1 (P = 0.73), I^2 =0.0%							



(1) Change from baseline.

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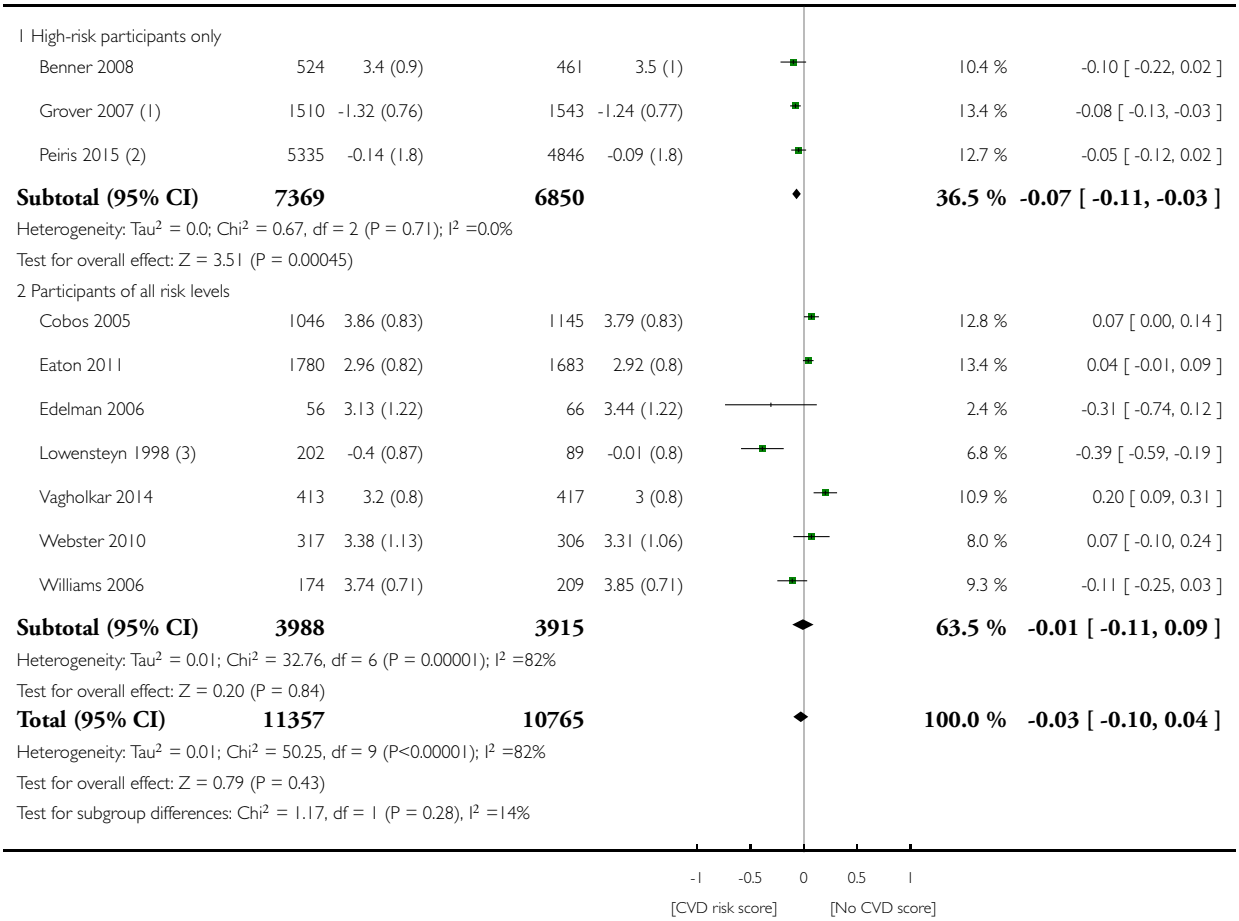
Analysis 4.2. Comparison 4 CVD risk score versus no CVD risk score/usual care by risk status of participants, Outcome 2 Low-density lipoprotein cholesterol by risk status.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 4 CVD risk score versus no CVD risk score/usual care by risk status of participants

Outcome: 2 Low-density lipoprotein cholesterol by risk status

Study or subgroup	CVD risk score N	CVD risk score Mean(SD)[mmol/L]	No CVD risk score N	No CVD risk score Mean(SD)[mmol/L]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 High-risk participants only							
Benner 2008	524	3.4 (0.9)	461	3.5 (1)		10.4 %	-0.10 [-0.22, 0.02]
Grover 2007 (1)	1510	-1.32 (0.76)	1543	-1.24 (0.77)		13.4 %	-0.08 [-0.13, -0.03]
Peiris 2015 (2)	5335	-0.14 (1.8)	4846	-0.09 (1.8)		12.7 %	-0.05 [-0.12, 0.02]
Subtotal (95% CI)	**7369**		**6850**			**36.5 %**	**-0.07 [-0.11, -0.03]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.67$, df = 2 (P = 0.71); $I^2 = 0.0\%$							
Test for overall effect: Z = 3.51 (P = 0.00045)							
2 Participants of all risk levels							
Cobos 2005	1046	3.86 (0.83)	1145	3.79 (0.83)		12.8 %	0.07 [0.00, 0.14]
Eaton 2011	1780	2.96 (0.82)	1683	2.92 (0.8)		13.4 %	0.04 [-0.01, 0.09]
Edelman 2006	56	3.13 (1.22)	66	3.44 (1.22)		2.4 %	-0.31 [-0.74, 0.12]
Lowensteyn 1998 (3)	202	-0.4 (0.87)	89	-0.01 (0.8)		6.8 %	-0.39 [-0.59, -0.19]
Vagholkar 2014	413	3.2 (0.8)	417	3 (0.8)		10.9 %	0.20 [0.09, 0.31]
Webster 2010	317	3.38 (1.13)	306	3.31 (1.06)		8.0 %	0.07 [-0.10, 0.24]
Williams 2006	174	3.74 (0.71)	209	3.85 (0.71)		9.3 %	-0.11 [-0.25, 0.03]
Subtotal (95% CI)	**3988**		**3915**			**63.5 %**	**-0.01 [-0.11, 0.09]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 32.76$, df = 6 (P = 0.00001); $I^2 = 82\%$							
Test for overall effect: Z = 0.20 (P = 0.84)							
Total (95% CI)	**11357**		**10765**			**100.0 %**	**-0.03 [-0.10, 0.04]**
Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 50.25$, df = 9 (P<0.00001); $I^2 = 82\%$							
Test for overall effect: Z = 0.79 (P = 0.43)							
Test for subgroup differences: $Chi^2 = 1.17$, df = 1 (P = 0.28), $I^2 = 14\%$							



(1) Change from baseline.

(2) Low-density lipoprotein cholesterol data only reported for the "high-risk" subgroup within this study. Change from baseline.

(3) Change from baseline.

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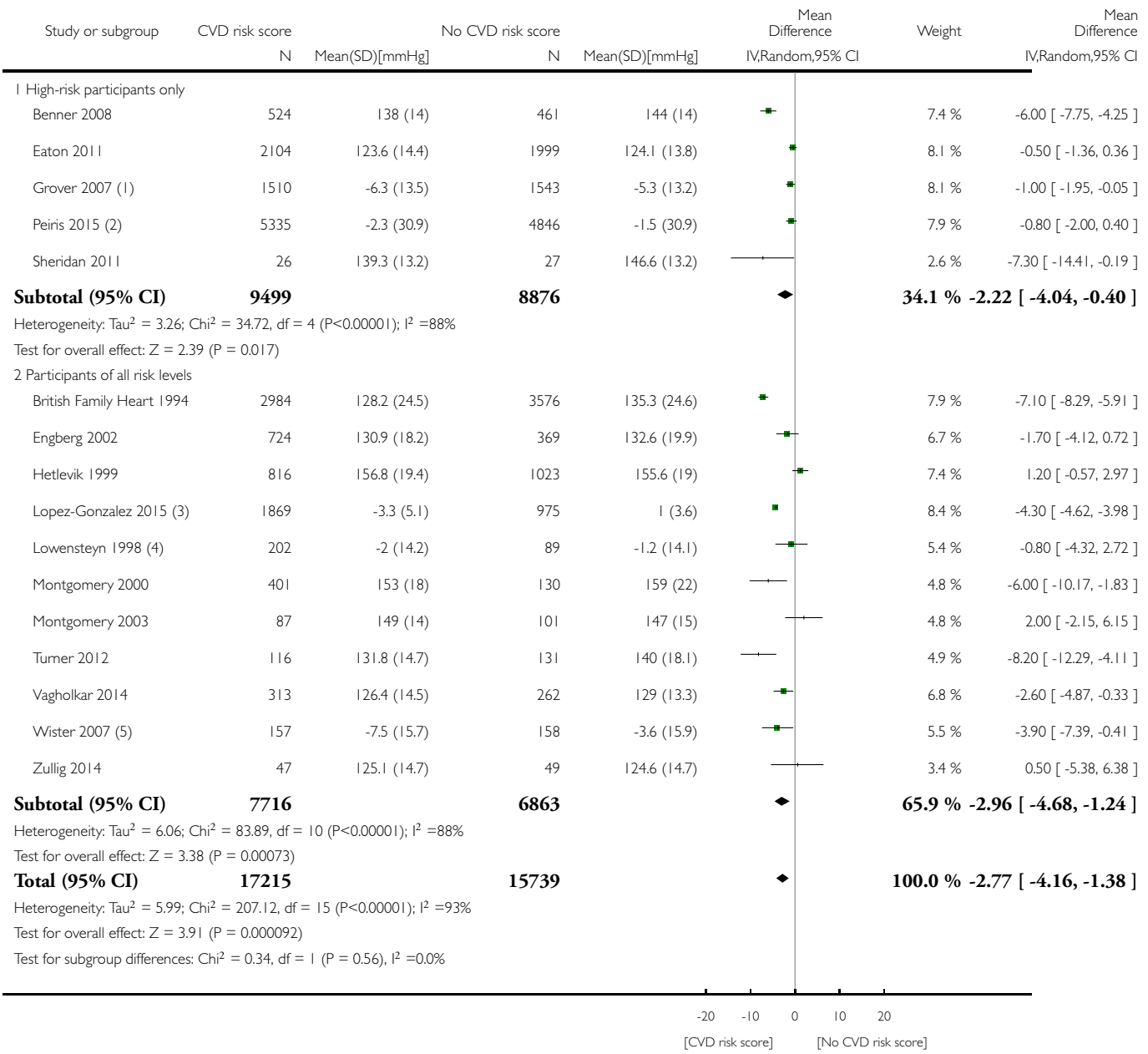
Analysis 4.3. Comparison 4 CVD risk score versus no CVD risk score/usual care by risk status of participants, Outcome 3 Systolic blood pressure by risk status.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 4 CVD risk score versus no CVD risk score/usual care by risk status of participants

Outcome: 3 Systolic blood pressure by risk status



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(1) Change from baseline.

(2) Systolic blood pressure data only reported for the "high-risk" subgroup within this study. Change from baseline.

(3) Change from baseline.

(4) Change from baseline.

(5) Change from baseline.

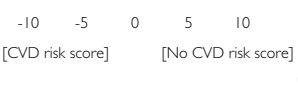
Analysis 4.4. Comparison 4 CVD risk score versus no CVD risk score/usual care by risk status of participants, Outcome 4 Diastolic blood pressure by risk status.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 4 CVD risk score versus no CVD risk score/usual care by risk status of participants

Outcome: 4 Diastolic blood pressure by risk status

Study or subgroup	CVD risk score N	Mean(SD)[mmHg]	No CVD risk score N	Mean(SD)[mmHg]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
1 High-risk participants only							
Benner 2008	524	85 (8.4)	461	87 (9.7)		8.2 %	-2.00 [-3.14, -0.86]
Grover 2007 (1)	1510	-3.8 (7.9)	1543	-3.6 (7.7)		9.0 %	-0.20 [-0.75, 0.35]
Sheridan 2011	26	80.4 (8.2)	27	80.2 (8.2)		3.3 %	0.20 [-4.22, 4.62]
Subtotal (95% CI)	**2060**		**2031**			**20.5 %**	**-0.90 [-2.42, 0.63]**
Heterogeneity: Tau^2 = 1.15; Chi^2 = 7.85, df = 2 (P = 0.02); I^2 =75%							
Test for overall effect: Z = 1.15 (P = 0.25)							
2 Participants of all risk levels							
British Family Heart 1994	2984	81.4 (10.8)	3576	84.5 (10.8)		9.0 %	-3.10 [-3.62, -2.58]
Eaton 2011	2103	75.8 (9)	1999	76.7 (8.2)		9.0 %	-0.90 [-1.43, -0.37]
Engberg 2002	724	79.8 (10.5)	369	81 (11.7)		7.8 %	-1.20 [-2.62, 0.22]
Hanlon 1995 (2)	263	1.2 (7.6)	233	0.9 (7.3)		8.0 %	0.30 [-1.01, 1.61]
Hetlevik 1999	816	88.8 (9.7)	1023	89.8 (8.9)		8.6 %	-1.00 [-1.86, -0.14]
Lopez-Gonzalez 2015 (3)	1869	-2.3 (4)	975	1.3 (2.9)		9.2 %	-3.60 [-3.86, -3.34]
Lowensteyn 1998 (4)	202	-0.9 (8.1)	89	0.1 (9.8)		6.1 %	-1.00 [-3.32, 1.32]
Montgomery 2000	401	85.5 (9.5)	130	84 (11)		6.5 %	1.50 [-0.61, 3.61]



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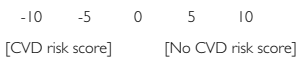
Study or subgroup	CVD risk score N	Mean(SD)[mmHg]	No CVD risk score N	Mean(SD)[mmHg]	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Montgomery 2003	87	85 (8)	101	85 (10)		5.7 %	0.0 [-2.57, 2.57]
Turner 2012	116	76.4 (9.4)	131	78.6 (10.4)		5.9 %	-2.20 [-4.67, 0.27]
Zullig 2014	47	73.4 (10)	49	73.5 (10)		3.7 %	-0.10 [-4.10, 3.90]
Subtotal (95% CI)	**9612**		**8675**			**79.5 %**	**-1.20 [-2.26, -0.14]**
Heterogeneity: Tau^2 = 2.46; Chi^2 = 156.42, df = 10 (P<0.00001); I^2 =94%							
Test for overall effect: Z = 2.22 (P = 0.026)							
Total (95% CI)	**11672**		**10706**			**100.0 %**	**-1.12 [-2.11, -0.13]**
Heterogeneity: Tau^2 = 2.77; Chi^2 = 232.17, df = 13 (P<0.00001); I^2 =94%							
Test for overall effect: Z = 2.21 (P = 0.027)							
Test for subgroup differences: Chi^2 = 0.10, df = 1 (P = 0.75), I^2 =0.0%							



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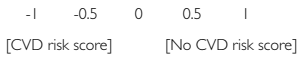
Analysis 4.5. Comparison 4 CVD risk score versus no CVD risk score/usual care by risk status of participants, Outcome 5 Change in multivariable CVD risk by risk status.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 4 CVD risk score versus no CVD risk score/usual care by risk status of participants

Outcome: 5 Change in multivariable CVD risk by risk status

Study or subgroup	CVD risk score N	Mean(SD)	No CVD risk score N	Mean(SD)	Std. Mean Difference IV,Random,95% CI	Weight	Std. Mean Difference IV,Random,95% CI
1 High-risk participants only							
Benner 2008	524	-6.3 (7)	461	-4.9 (6.6)		11.7 %	-0.21 [-0.33, -0.08]
Grover 2007	1510	-5.9 (4.5)	1543	-5.3 (4.3)		12.2 %	-0.14 [-0.21, -0.07]
Subtotal (95% CI)	**2034**		**2004**			**23.9 %**	**-0.15 [-0.21, -0.09]**
Heterogeneity: $Tau^2 = 0.0$; $Chi^2 = 0.88$, df = 1 (P = 0.35); $I^2 = 0.0\%$							
Test for overall effect: Z = 4.85 (P < 0.00001)							
2 Participants of all risk levels							
Hanlon 1995	263	0.53 (1.59)	233	0.34 (1.81)		11.1 %	0.11 [-0.06, 0.29]
Krones 2008	415	-3 (4.61)	407	-3.33 (4.61)		11.6 %	0.07 [-0.07, 0.21]
Lopez-Gonzalez 2015	1869	-0.27 (0.84)	975	0.24 (0.78)		12.1 %	-0.62 [-0.70, -0.54]
Lowensteyn 1998	202	-1.8 (4.7)	89	-0.3 (5.3)		10.1 %	-0.31 [-0.56, -0.06]
Montgomery 2000	401	0.09 (5.27)	130	0.77 (4.22)		10.9 %	-0.13 [-0.33, 0.06]
Turner 2012	94	-0.51 (2)	118	0.31 (3)		9.8 %	-0.31 [-0.59, -0.04]
Wister 2007	157	-3.07 (5.52)	158	-1.1 (5.54)		10.5 %	-0.36 [-0.58, -0.13]
Subtotal (95% CI)	**3401**		**2110**			**76.1 %**	**-0.22 [-0.49, 0.05]**
Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 112.88$, df = 6 (P<0.00001); $I^2 = 95\%$							
Test for overall effect: Z = 1.59 (P = 0.11)							
Total (95% CI)	**5435**		**4114**			**100.0 %**	**-0.21 [-0.39, -0.02]**
Heterogeneity: $Tau^2 = 0.07$; $Chi^2 = 134.90$, df = 8 (P<0.00001); $I^2 = 94\%$							
Test for overall effect: Z = 2.20 (P = 0.028)							
Test for subgroup differences: $Chi^2 = 0.23$, df = 1 (P = 0.63), $I^2 = 0.0\%$							



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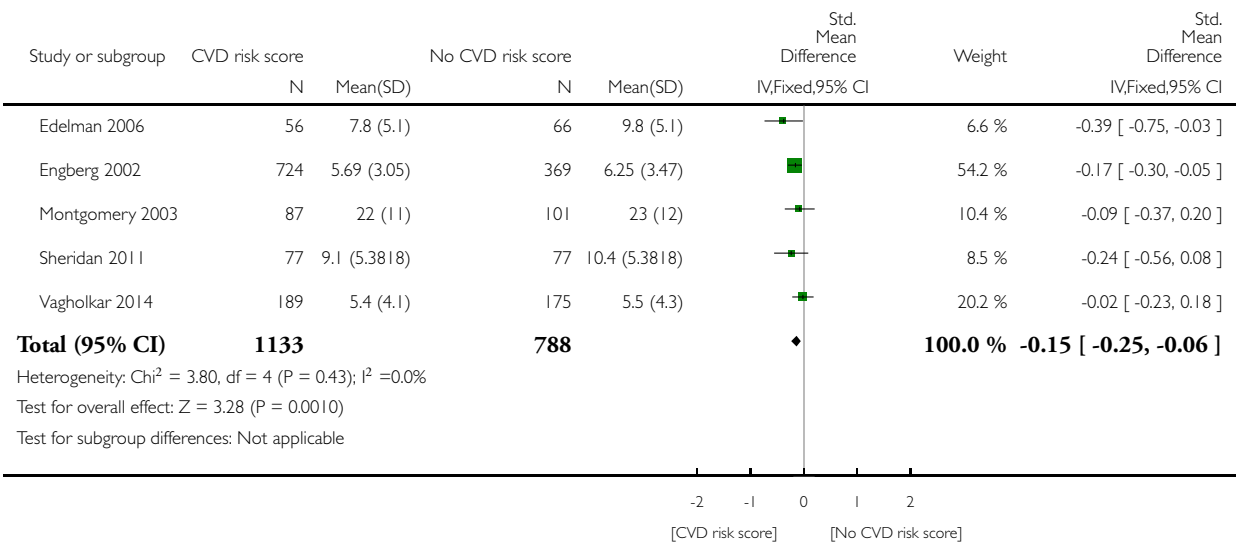
Analysis 5.1. Comparison 5 Multivariable CVD risk, Outcome 1 Multivariable CVD risk.

Review: Risk scoring for the primary prevention of cardiovascular disease

Comparison: 5 Multivariable CVD risk

Outcome: 1 Multivariable CVD risk



APPENDICES

Appendix 1. Database search strategies

Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 2) in the Cochrane Library-Wiley

#1 ((cardiovascular or cv or cvd or coronary or chd or "heart disease") near/3 risk):ti,ab,kw and (risk next (estimat* or assessment* or scor* or equation* or calculat*)):ti,ab,kw
#2 MeSH descriptor: [Cardiovascular Diseases] this term only
#3 (cardiovascular next disease*):ti,ab,kw
#4 MeSH descriptor: [Coronary Disease] this term only
#5 (heart next disease*):ti,ab,kw
#6 (coronary near/2 disease*):ti,ab,kw
#7 (coronary next risk*):ti,ab,kw
#8 (cardiovascular next risk*):ti,ab,kw
#9 MeSH descriptor: [Hypertension] this term only
#10 MeSH descriptor: [Hyperlipidemias] explode all trees
#11 cholesterol:ti,ab,kw
#12 MeSH descriptor: [Arteriosclerosis] explode all trees

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#13 (arteriosclerosis or atherosclerosis):ti,ab,kw
#14 {or #2-#13}
#15 (risk next function*):ti,ab,kw
#16 (risk next equation*):ti,ab,kw
#17 (risk next chart*):ti,ab,kw
#18 (risk near/3 tool*):ti,ab,kw
#19 ("risk assessment" next function*):ti,ab,kw
#20 "risk assessor":ti,ab,kw
#21 (risk next appraisal*):ti,ab,kw
#22 (risk next calculation*):ti,ab,kw
#23 (risk next calculator*):ti,ab,kw
#24 (("risk factor" or "risk factors") next calculator*):ti,ab,kw
#25 (("risk factor" or "risk factors") next calculation*):ti,ab,kw
#26 (risk next engine*):ti,ab,kw
#27 (risk next estimate*):ti,ab,kw
#28 (risk next table*):ti,ab,kw
#29 (risk next threshold*):ti,ab,kw
#30 (risk next disc*):ti,ab,kw
#31 (risk next disk*):ti,ab,kw
#32 ("risk scoring" next (method* or system*)):ti,ab,kw
#33 (scoring next scheme*):ti,ab,kw
#34 (risk next prediction*):ti,ab,kw
#35 ((predictive or prediction or prognostic) next (instrument* or model*)):ti,ab,kw
#36 (project* near/1 risk*):ti,ab,kw
#37 {or #15-#36}
#38 #14 and #37
#39 #1 or #38
#40 ("new zealand" near/3 (equation* or table* or chart*)):ti,ab,kw
#41 (sheffield next table*):ti,ab,kw
#42 procam:ti,ab,kw
#43 "general rule to enable atheroma treatment":ti,ab,kw
#44 (dundee near/3 (guideline* or risk* or score*)):ti,ab,kw
#45 ("British Family Heart" or "British Regional Heart" or brhs):ti,ab,kw
#46 precard:ti,ab,kw
#47 (framingham near/3 (guideline* or function* or risk or equation or model* or algorithm* or score*)):ti,ab,kw
#48 busselton:ti,ab,kw and (risk*:ti,ab,kw or score*:ti,ab,kw)
#49 (who near/3 erica):ti,ab,kw
#50 (("National Cholesterol Education Program" or NCEP) near/6 guideline*):ti,ab,kw
#51 (("Standing Medical Advisory Committee" or SMAC) near/6 guideline*):ti,ab,kw
#52 (copenhagen near/3 risk*):ti,ab,kw
#53 (aboriginal and (cardio* or coronary) and (risk* or score*)):ti,ab,kw
#54 (("american heart association" or aha) near/3 (risk* or score*)):ti,ab,kw
#55 (("american college of cardiology" or acc) near/3 (risk* or score*)):ti,ab,kw
#56 (aric near/3 (risk or score*)):ti,ab,kw
#57 assign:ti,ab,kw and score*:ti,ab,kw and (cardio*:ti,ab,kw or coronary:ti,ab,kw)
#58 (("adult treatment panel" or atp) near/3 (risk* or score*)):ti,ab,kw
#59 cardiff:ti,ab,kw and (risk:ti,ab,kw or score*:ti,ab,kw) and (cardio*:ti,ab,kw or coronary:ti,ab,kw or vasc*:ti,ab,kw)
#60 "carta del rischio":ti,ab,kw
#61 "cardiovascular event reduction tool":ti,ab,kw
#62 (cha and (cardio* or coronary or vasc*) and (risk or score*)):ti,ab,kw
#63 morgam:ti,ab,kw
#64 "chinese multi-provincial cohort":ti,ab,kw
#65 ("cardiorisk manager" or "cardio risk manager"):ti,ab,kw

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#66 (("diabetes audit" or darts or godarts) and tayside):ti,ab,kw
#67 ("diabetes epidemiology" and "collaborative analysis of diagnostic criteria"):ti,ab,kw
#68 (dubbo and (cardio* or coronary or vasc*)):ti,ab,kw
#69 ((esc or "european society of cardiology") near/3 (risk or score*)):ti,ab,kw
#70 ("family heart study" near/3 (risk or score*)):ti,ab,kw
#71 (finrisk and (cardio* or coronary or vasc*)):ti,ab,kw
#72 (global near/3 ("risk score" or "risk scores")):ti,ab,kw
#73 ("hong kong diabetes" near/3 (risk or score* or equation*)):ti,ab,kw
#74 "progetto cuore":ti,ab,kw
#75 indana:ti,ab,kw
#76 ((jbs2 or jbs3 or jbsrc or jhss) and (risk or score*)):ti,ab,kw
#77 ("johns hopkins" and ("multiple risk" or (risk near/3 (score* or equation*)))):ti,ab,kw
#78 "metabolic syndrome model":ti,ab,kw
#79 (mrfit or "chd prevention model"):ti,ab,kw
#80 "paris prospective study":ti,ab,kw
#81 "personal heart":ti,ab,kw
#82 ((predict next cvd*) or "heart forecast"):ti,ab,kw
#83 (((heart or cardio* or coronary) near/3 (risk or score*)) and predict and "new zealand"):ti,ab,kw
#84 qrisk*:ti,ab,kw
#85 (cvr next pc):ti,ab,kw
#86 regicor:ti,ab,kw
#87 (reynolds and ((risk next assessment*) or (risk next score*))):ti,ab,kw
#88 ("scottish heart health extended cohort" or shhec or stulong or "assign score"):ti,ab,kw
#89 ((ukpds or ulsam) near/3 (risk or score*)):ti,ab,kw
#90 ("world health organization" near/3 (risk or score*)):ti,ab,kw
#91 ((women* next "health study"):ti,ab,kw or whs:ti,ab,kw or (women* next "health intiative"):ti,ab,kw or whi:ti,ab,kw) and (risk:ti,ab,kw or scor*:ti,ab,kw)
#92 cardiovascular:ti,ab,kw and ("check up study":ti,ab,kw or "uninformed patients":ti,ab,kw)
#93 ("systematic coronary risk evaluation" or (euro next score)):ti,ab,kw
#94 ("pooled cohort" near/3 (risk or scor* or equation*)):ti,ab,kw
#95 {or #40-#94}
#96 MeSH descriptor: [Decision Support Techniques] explode all trees
#97 MeSH descriptor: [Diagnosis, Computer-Assisted] explode all trees
#98 MeSH descriptor: [Decision Making, Computer-Assisted] this term only
#99 MeSH descriptor: [Decision Support Systems, Clinical] this term only
#100 MeSH descriptor: [Algorithms] this term only
#101 (algorithm or algorithms or algorythm or algorythms):ti,ab,kw
#102 (decision next (support or aid)):ti,ab,kw
#103 ((predictive or prediction or prognostic) next model*):ti,ab,kw
#104 (treatment next decision*):ti,ab,kw
#105 (scoring next method*):ti,ab,kw
#106 (prediction* near/3 method*):ti,ab,kw
#107 cdss:ti,ab,kw
#108 {or #96-#107}
#109 MeSH descriptor: [Risk Factors] this term only
#110 MeSH descriptor: [Risk Assessment] explode all trees
#111 ((risk* near/1 assess*) or risk):ti,ab,kw
#112 (risk next factor*):ti,ab,kw
#113 {or #109-#112}
#114 #14 and #108 and #113
#115 #14 and #95
#116 #39 or #114 or #115

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Ovid MEDLINE(R) 1946 to March Week 1 2016 and Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations March 14, 2016

1. ((cardiovascular or cv or cvd or coronary or chd or heart disease) adj3 risk adj (estimat* or assessment* or scor* or equation* or calculat*)).tw.
2. Cardiovascular Diseases/
3. cardiovascular disease*.tw.
4. coronary disease/
5. heart disease*.tw.
6. (coronary adj2 disease*).tw.
7. coronary risk?.tw.
8. cardiovascular risk?.tw.
9. hypertension/
10. exp Hyperlipidemias/
11. cholesterol.tw.
12. exp Arteriosclerosis/
13. (arteriosclerosis or atherosclerosis).tw.
14. or/2-13
15. risk function.tw.
16. Risk Assessment/mt [Methods]
17. risk functions.tw.
18. risk equation*.tw.
19. risk chart?.tw.
20. (risk adj3 tool*).tw.
21. risk assessment function?.tw.
22. risk assessor.tw.
23. risk appraisal*.tw.
24. risk calculation*.tw.
25. risk calculator*.tw.
26. risk factor* calculator*.tw.
27. risk factor* calculation*.tw.
28. risk engine*.tw.
29. risk estimate*.tw.
30. risk table*.tw.
31. risk threshold*.tw.
32. risk disc?.tw.
33. risk disk?.tw.
34. risk scoring method?.tw.
35. scoring scheme?.tw.
36. risk scoring system?.tw.
37. risk prediction?.tw.
38. predictive instrument?.tw.
39. ((predictive or prediction or prognostic) adj model*).tw.
40. project* risk?.tw.
41. or/15-40
42. 14 and 41
43. 1 or 42
44. (new zealand adj3 (equation* or table* or chart*)).tw.
45. sheffield table*.tw.
46. procam.tw.
47. General Rule to Enable Atheroma Treatment.tw.
48. (dundee adj3 (guideline* or risk* or score*)).tw.
49. (British Family Heart or British Regional Heart or brhs).tw.

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50. precard.tw.
51. (framingham adj3 (guideline* or function* or risk or equation or model* or algorithm* or score*)).tw.
52. busselton.tw. and (risk* or score*).mp.
53. (WHO adj3 ERICA).tw.
54. ((National Cholesterol Education Program or NCEP) adj guideline?).tw.
55. ((Standing Medical Advisory Committee or SMAC) adj guideline?).tw.
56. (copenhagen adj3 risk?).tw.
57. ((aboriginal and (cardio* or coronary)) adj3 (risk* or score*)).tw.
58. ((American Heart Association or AHA) adj3 (risk* or score*)).tw.
59. (("American College of Cardiology" or ACC) adj3 (risk* or score*)).tw.
60. (ARIC adj3 (risk or score*)).tw.
61. (assign and score* and (cardio* or coronary)).tw.
62. ((Adult Treatment Panel or ATP) adj3 (risk* or score*)).tw.
63. (Cardiff and (risk or score*) and (cardio* or coronary or vasc*)).tw.
64. (Carta del Rischio adj3 (risk or score*)).tw.
65. cardiovascular event reduction tool.tw.
66. (CHA and (cardio* or coronary or vasc*) and (risk or score*)).tw.
67. morgam.tw.
68. chinese multi-provincial cohort.tw.
69. CardioRisk Manager.tw.
70. ((diabetes audit or DARTS or goDARTs) and tayside).tw.
71. "DECODE Study Group".au.
72. (Diabetes Epidemiology and "Collaborative analysis of Diagnostic criteria").tw.
73. (dubbo and (cardio* or coronary or vasc*)).tw.
74. ((ESC or European Society of Cardiology) adj3 (risk or score*)).tw.
75. (Family heart study adj3 (risk or score*)).tw.
76. (finrisk and (cardio* or coronary or vasc*)).tw.
77. (global adj3 risk score*).tw.
78. (hong kong diabetes adj3 (risk or score* or equation*)).tw.
79. progetto cuore.tw.
80. INDANA.tw.
81. ((JBS2 or JBS3 or JBSRC or JHSS) and (risk or score*)).tw.
82. (Johns Hopkins and (multiple risk or (risk adj3 (score* or equation*)))).tw.
83. Metabolic Syndrome Model.tw.
84. (mrfit or chd prevention model).tw.
85. Paris Prospective Study.tw.
86. personal heart.tw.
87. (PREDICT-CVD* or heart forecast).tw.
88. (((heart or cardio* or coronary) adj3 (risk or score*)) and PREDICT).tw. and new zealand.mp.
89. QRISK?.tw.
90. cvr-pc.tw.
91. REGICOR.tw.
92. (reynolds and (risk assessment* or risk score*)).tw.
93. (Scottish Heart Health Extended Cohort or SHHEC or STULONG or ASSIGN score).tw.
94. ((UKPDS or ULSAM) adj3 (risk or score*)).tw.
95. (World Health Organization adj3 (risk or score*)).tw.
96. ((Women's Health Study or WHS or Women's Health Intiative or WHI) and (risk or scor*)).tw.
97. (cardiovascular and (check up study or uninformed patients)).tw.
98. ("Systematic Coronary Risk Evaluation" or euro-score).tw.
99. (pooled cohort adj3 (risk or scor* or equation*)).tw.
100. or/44-99
101. exp decision support techniques/
102. Diagnosis, Computer-Assisted/

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103. Decision Making, Computer-Assisted/
104. Decision Support Systems, Clinical/
105. algorithms/
106. algorithm?.tw.
107. algorythm?.tw.
108. decision support?.mp.
109. decision aid.tw.
110. ((predictive or prediction or prognostic) adj model*).tw.
111. treatment decision?.tw.
112. scoring method*.tw.
113. (prediction* adj3 method*).tw.
114. cdss.tw.
115. or/101-114
116. Risk Factors/
117. exp Risk Assessment/
118. ((risk? adj1 assess*) or risk).tw.
119. risk factor?.tw.
120. or/116-119
121. 14 and 115 and 120
122. 14 and 100
123. 43 or 121 or 122
124. randomised controlled trial.pt.
125. controlled clinical trial.pt.
126. randomized.ab.
127. placebo.ab.
128. clinical trials as topic.sh.
129. randomly.ab.
130. trial.ti.
131. 124 or 125 or 126 or 127 or 128 or 129 or 130
132. exp animals/ not humans.sh.
133. 131 not 132
134. 123 and 133

Embase 1974 to 15 March 2016; Embase Classic 1947-1973; Medline 1966 to 15 March 2016 (embase.com)

#118 #117 NOT ('animal'/exp NOT 'human'/exp)
#117 #116 AND [embase]/lim
#116 #114 AND #115
#115 random*:ab,ti OR placebo* OR (double NEXT/1 blind*):ab,ti
#114 #39 OR #112 OR #113
#113 #14 AND #95
#112 #14 AND #106 AND #111
#111 #107 OR #108 OR #109 OR #110
#110 (risk NEXT/1 factor*):ab,ti
#109 (risk* NEAR/1 assess*):ab,ti OR risk:ab,ti
#108 'risk assessment'/de
#107 'risk factor'/de
#106 #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105
#105 cdss:ab,ti
#104 (prediction* NEAR/3 method*):ab,ti
#103 (scoring NEXT/1 method*):ab,ti
#102 (treatment NEXT/1 decision*):ab,ti
#101 ((predictive OR prediction OR prognostic) NEXT/1 model*):ab,ti

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#100 (decision NEXT/1 (support OR aid)):ab,ti
#99 algorithm:ab,ti OR algorithms:ab,ti OR algorythm:ab,ti OR algorythms:ab,ti
#98 'algorithm'/de
#97 'computer assisted diagnosis'/de
#96 'decision support system'/de
#95 #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 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94
#94 ('pooled cohort' NEAR/3 (risk OR scor* OR equation*)):ab,ti
#93 'systematic coronary risk evaluation':ab,ti OR (euro NEXT/1 score):ab,ti
#92 cardiovascular:ab,ti AND ('check up study':ab,ti OR 'uninformed patients':ab,ti)
#91 (women* NEXT/1 'health study'):ab,ti OR whs:ab,ti OR (women* NEXT/1 'health intiative'):ab,ti OR whi:ab,ti AND (risk:ab,ti OR scor*:ab,ti)
#90 ('world health organization' NEAR/3 (risk OR score*)):ab,ti
#89 ((ukpds OR ulsam) NEAR/3 (risk OR score*)):ab,ti
#88 'scottish heart health extended cohort':ab,ti OR shhec:ab,ti OR stulong:ab,ti OR 'assign score':ab,ti
#87 reynolds:ab,ti AND ((risk NEXT/1 assessment*):ab,ti OR (risk NEXT/1 score*):ab,ti)
#86 regicor:ab,ti
#85 (cvr NEXT/1 pc):ab,ti
#84 qrisk*:ab,ti
#83 ((heart OR cardio* OR coronary) NEAR/3 (risk OR score*)):ab,ti AND predict:ab,ti AND 'new zealand'
#82 (predict NEXT/1 cvd*):ab,ti OR 'heart forecast':ab,ti
#81 'personal heart':ab,ti
#80 'paris prospective study':ab,ti
#79 mrfit:ab,ti OR 'chd prevention model':ab,ti
#78 'metabolic syndrome model':ab,ti
#77 'johns hopkins':ab,ti AND ('multiple risk':ab,ti OR (risk NEAR/3 (score* OR equation*)):ab,ti)
#76 jbs2:ab,ti OR jbs3:ab,ti OR jbsrc:ab,ti OR jhss:ab,ti AND (risk:ab,ti OR score*:ab,ti)
#75 indana:ab,ti
#74 'progetto cuore':ab,ti
#73 ('hong kong diabetes' NEAR/3 (risk OR score* OR equation*)):ab,ti
#72 (global NEAR/3 ('risk score' OR 'risk scores')):ab,ti
#71 finrisk:ab,ti AND (cardio*:ab,ti OR coronary:ab,ti OR vasc*:ab,ti)
#70 ('family heart study' NEAR/3 (risk OR score*)):ab,ti
#69 ((esc OR 'european society of cardiology') NEAR/3 (risk OR score*)):ab,ti
#68 dubbo:ab,ti AND (cardio*:ab,ti OR coronary:ab,ti OR vasc*:ab,ti)
#67 'diabetes epidemiology':ab,ti AND 'collaborative analysis of diagnostic criteria':ab,ti
#66 'diabetes audit':ab,ti OR darts:ab,ti OR godarts:ab,ti AND tayside:ab,ti
#65 'cardiorisk manager':ab,ti OR 'cardio risk manager':ab,ti
#64 'chinese multi-provincial cohort':ab,ti
#63 morgam:ab,ti
#62 cha:ab,ti AND (cardio*:ab,ti OR coronary:ab,ti OR vasc*:ab,ti) AND (risk:ab,ti OR score*:ab,ti)
#61 'cardiovascular event reduction tool':ab,ti
#60 'carta del rischio':ab,ti
#59 cardiff:ab,ti AND (risk:ab,ti OR score*:ab,ti) AND (cardio*:ab,ti OR coronary:ab,ti OR vasc*:ab,ti)
#58 (('adult treatment panel' OR atp) NEAR/3 (risk* OR score*)):ab,ti
#57 assign:ab,ti AND score*:ab,ti AND (cardio*:ab,ti OR coronary:ab,ti)
#56 (aric NEAR/3 (risk OR score*)):ab,ti
#55 (('american college of cardiology' OR acc) NEAR/3 (risk* OR score*)):ab,ti
#54 (('american heart association' OR aha) NEAR/3 (risk* OR score*)):ab,ti
#53 aboriginal:ab,ti AND (cardio*:ab,ti OR coronary:ab,ti) AND (risk*:ab,ti OR score*:ab,ti)
#52 (copenhagen NEAR/3 risk*):ab,ti

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#51 (('standing medical advisory committee' OR smac) NEAR/1 guideline*):ab,ti
#50 (('national cholesterol education program' OR ncep) NEAR/1 guideline*):ab,ti
#49 (who NEAR/3 erica):ab,ti
#48 busselton:ab,ti AND (risk*:ab,ti OR score*:ab,ti)
#47 (framingham NEAR/3 (guideline* OR function* OR risk OR equation OR model* OR algorithm* OR score*)):ab,ti
#46 precard:ab,ti
#45 'british family heart':ab,ti OR 'british regional heart':ab,ti OR brhs:ab,ti
#44 (dundee NEAR/3 (guideline* OR risk* OR score*)):ab,ti
#43 'general rule to enable atheroma treatment':ab,ti
#42 procam:ab,ti
#41 (sheffield NEXT/1 table*):ab,ti
#40 ('new zealand' NEAR/3 (equation* OR table* OR chart*)):ab,ti
#39 #1 OR #38
#38 #14 AND #37
#37 #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36
#36 (project* NEAR/1 risk*):ab,ti
#35 ((predictive OR prediction OR prognostic) NEXT/1 (instrument* OR model*)):ab,ti
#34 (risk NEXT/1 prediction*):ab,ti
#33 (scoring NEXT/1 scheme*):ab,ti
#32 ('risk scoring' NEXT/1 (method* OR system*)):ab,ti
#31 (risk NEXT/1 disk*):ab,ti
#30 (risk NEXT/1 disc*):ab,ti
#29 (risk NEXT/1 threshold*):ab,ti
#28 (risk NEXT/1 table*):ab,ti
#27 (risk NEXT/1 estimate*):ab,ti
#26 (risk NEXT/1 engine*):ab,ti
#25 (('risk factor' OR 'risk factors') NEXT/1 calculation*):ab,ti
#24 (('risk factor' OR 'risk factors') NEXT/1 calculator*):ab,ti
#23 (risk NEXT/1 calculator*):ab,ti
#22 (risk NEXT/1 calculation*):ab,ti
#21 (risk NEXT/1 appraisal*):ab,ti
#20 'risk assessor':ab,ti
#19 ('risk assessment' NEXT/1 function*):ab,ti
#18 (risk NEAR/3 tool*):ab,ti
#17 (risk NEXT/1 chart*):ab,ti
#16 (risk NEXT/1 equation*):ab,ti
#15 (risk NEXT/1 function*):ab,ti
#14 #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13
#13 arteriosclerosis:ab,ti OR atherosclerosis:ab,ti
#12 'arteriosclerosis'/exp
#11 cholesterol:ab,ti
#10 'hyperlipidemia'/exp
#9 'hypertension'/de
#8 (cardiovascular NEXT/1 risk*):ab,ti
#7 (coronary NEXT/1 risk*):ab,ti
#6 (coronary NEAR/2 disease*):ab,ti
#5 (heart NEXT/1 disease*):ab,ti
#4 'coronary artery disease'/de
#3 (cardiovascular NEXT/1 disease*):ab,ti
#2 'cardiovascular disease'/de
#1 ((cardiovascular OR cv OR cvd OR coronary OR chd OR 'heart disease') NEAR/3 risk):ab,ti AND (risk NEXT/1 (estimat* OR assessment* OR scor* OR equation* OR calculat*)):ab,ti

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Conference Proceedings Citation Index- Science (CPCI-S; 1990 to 15 March 2016) via Web of Science

#13 #12 AND #11
#12 TS=(random* or blind* or allocat* or assign* or trial* or placebo* or crossover* or cross-over* or group*)
#11 #5 OR #9 OR #10
#10 #2 AND #6
#9 #2 AND #7 AND #8
#8 TS=(risk* NEAR/1 (assess* OR factor*)) OR TS=risk
#7 TS=(decision NEAR/1 (support OR aid)) OR TS=("computer assisted" NEAR/3 (diagnosis OR decision)) OR TS=(algorithm OR algorithms OR algorythm OR algorythms) OR TS=((predictive OR prediction OR prognostic) NEAR/1 model*) OR TS=(treatment NEAR/1 decision*) OR TS=(scoring NEAR/1 method*) OR TS=(prediction* NEAR/3 method*) OR TS=cdss
#6 TS=("new zealand" NEAR/3 (equation* or table* or chart*)) OR TS=(sheffield NEAR/1 table*) OR TS=procam OR TS=("general rule" AND atheroma) OR TS=(dundee NEAR/3 (guideline* or risk* or score*)) OR TS=("British Family Heart" or "British Regional Heart" or brhs) OR TS=precard OR TS=(framingham NEAR/3 (guideline* OR function* OR risk OR equation OR model* OR algorithm* OR score*)) OR TS=(busselton AND (risk* OR score*)) OR TS=(who NEAR/3 erica) OR TS=(("National Cholesterol Education Program" or NCEP) NEAR/6 guideline*) OR TS=(("Standing Medical Advisory Committee" or SMAC) NEAR/6 guideline*) OR TS=(copenhagen NEAR/3 risk*) OR TS=(aboriginal AND (cardio* OR coronary) AND (risk* OR score*)) OR TS=(("american heart association" OR aha) NEAR/3 (risk* OR score*)) OR TS=(("american college" NEAR/2 cardiology) NEAR/3 (risk* OR score*)) OR TS=(aric NEAR/3 (risk OR score*)) OR TS=(assign AND score* AND (cardio* OR coronary)) OR TS=(("adult treatment panel" OR atp) NEAR/3 (risk* OR score*)) OR TS=(cardiff AND (risk OR score*) AND (cardio* OR coronary OR vasc*)) OR TS="carta del rischio" OR TS=("cardiovascular event reduction tool") OR TS=(cha AND (cardio* OR coronary OR vasc*) AND (risk OR score*)) OR TS=morgam OR TS="chinese multi-provincial cohort" OR TS=("cardiorisk manager" OR "cardio risk manager") OR TS=(("diabetes audit" OR darts OR godarts) AND tayside) OR TS=("diabetes epidemiology" AND ("collaborative analysis" NEAR/2 "diagnostic criteria")) OR TS=(dubbo AND (cardio* OR coronary OR vasc*)) OR TS=((esc OR "european society" NEAR/2 cardiology) NEAR/3 (risk OR score*)) OR TS=("family heart study" NEAR/3 (risk OR score*)) OR TS=(finrisk AND (cardio* OR coronary OR vasc*)) OR TS=(global NEAR/3 ("risk score" OR "risk scores")) OR TS=("hong kong diabetes" NEAR/3 (risk OR score* OR equation*)) OR TS="progetto cuore" OR TS=indana OR TS=((jbs2 OR jbs3 OR jbsrc OR jhss) AND (risk OR score*)) OR TS=("johns hopkins" AND ("multiple risk" OR (risk NEAR/3 (score* OR equation*)))) OR TS="metabolic syndrome model" OR TS=(mrfit OR "chd prevention model") OR TS="paris prospective study" OR TS="personal heart" OR TS=((predict NEAR/1 cvd*) OR "heart forecast") OR TS=(((heart OR cardio* OR coronary) NEAR/3 (risk OR score*)) AND predict AND "new zealand") OR TS=(qrisk*) OR TS=(cvr NEAR/1 pc) OR TS=regicor OR TS=(reynolds AND (risk NEAR/1 (assessment* OR score*))) OR TS=("scottish heart health extended cohort" OR shhec OR stulong OR "assign score") OR TS=((ukpds OR ulsam) NEAR/3 (risk OR score*)) OR TS=("world health organization" NEAR/3 (risk OR score*)) OR TS=(((women* NEAR/1 "health study") OR whs OR (women* NEAR/1 "health intiative") OR whi) AND (risk OR scor*)) OR TS=(cardiovascular AND ("check up study" OR "uninformed patients")) OR TS=("systematic coronary risk evaluation" OR (euro NEAR/1 score)) OR TS=("pooled cohort" NEAR/3 (risk OR scor* OR equation*))
#5 #1 OR #4
#4 #2 AND #3
#3 TS=(risk NEAR/1 (function* OR equation* OR chart* OR appraisal* OR calculation* OR calculator* OR engine* OR estimate* OR table* OR threshold* OR disc* OR disk* OR prediction*)) OR TS=("risk assessment" NEAR/1 function*) OR TS=("risk assessor") OR TS=("risk factor*" NEAR/1 (calculator* OR calculation*)) OR TS=("risk scoring" NEAR/1 (method* or system*)) OR TS=(scoring NEAR/1 scheme*) OR TS=((predictive OR prediction OR prognostic) NEAR/1 (instrument* or model*)) OR TS=(project* NEAR/1 risk*)
#2 TS=("cardiovascular disease*") OR TS=((heart OR coronary) NEAR/2 disease*) OR TS=((coronary OR cardiovascular) NEAR/1 risk*) OR TS=(hypertension OR hyperlipidemia OR cholesterol OR arteriosclerosis OR atherosclerosis)
#1 TS=((cardiovascular OR cv OR cvd OR coronary OR chd OR "heart disease") NEAR/3 risk) AND TS=(risk NEAR/1 (estimat* OR assessment* OR scor* OR equation* OR calculat*))

Clinicaltrials.gov

clinicaltrials.gov/ct2/home
Advanced Search on 16 March 2016
Search Terms: risk AND (calculator OR calculation OR equation or score OR scoring)
Study Type: Interventional Studies
Conditions: cardiovascular OR atherosclerosis OR coronary

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World Health Organization International Clinical Trials Registry Platform (WHO ICTRP)

apps.who.int/trialsearch
Advanced Search on 16 March 2016
Title: risk AND calculator OR risk AND calculation OR risk AND equation or risk AND score OR risk AND scoring
Condition: cardiovascular OR atherosclerosis OR coronary
Recruitment Status: ALL

CONTRIBUTIONS OF AUTHORS

KNK - design of review, article screening, data collection, data analysis, data interpretation, manuscript writing

SDP - design of review, article screening, data collection, data interpretation, and manuscript revision for important intellectual content

PP - data interpretation and manuscript revision for important intellectual content

DML-J - data interpretation and manuscript revision for important intellectual content

MAB - development and execution of database searches, manuscript revision for important intellectual content

MDH - design of review, article screening, data collection, data interpretation, manuscript revision for important intellectual content

DECLARATIONS OF INTEREST

KNK - none known. KNK received support from the National Heart, Lung, and Blood Institute training grant in cardiovascular epidemiology and prevention during the conduct of this work (T32 HL069771).

SDP - author on 2 included studies*. SDP receives grant support from Pfizer, Inc. for research outside the submitted work.

PP - none known.

DML-J - author on 2 included studies*.

MAB - none known.

MDH - MDH receives support from the World Heart Federation to serve as the senior programme advisor for its Emerging Leaders programme, which has been supported by Boehringer Ingelheim, Novartis, Bupa, and AstraZeneca. MDH is also a Cochrane Heart Group satellite coordinating editor and associate editor for JAMA for which he receives compensation from the American Medical Association. MDH also receives travel support from the American Heart Association.

*Note that data extraction and risk of bias assessment for these two trials were performed by authors not involved in the study (KNK and MDH).

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

1. For the main outcomes presented in our Abstract, Plain language summary, and 'Summary of findings' table, we prioritised clinical outcomes (CVD events, adverse events), selected CVD risk factor levels (total cholesterol, systolic blood pressure, and multivariable CVD risk), and commonly prescribed medications for primary CVD prevention (lipid-lowering medications and antihypertensive medications). We included a mixture of these primary and secondary outcomes because we judged these to be of greatest relevance for stakeholders such as patients, clinicians, policy makers, and guideline developers.

2. We modified the secondary outcome of preventive medication prescribing to 'new or intensified medication prescribing in higher risk participants' to capture the anticipated behaviour change from providing a CVD risk score. Similarly, for the smoking outcome, we reported 'smoking cessation,' the desired behaviour change from providing a CVD risk score.

3. We edited the 'objectives' sentence to include main outcomes including risk factor levels and preventive medication prescribing.

4. We had initially planned on analysing all data at the level of the individual using the intra-cluster coefficient (ICC) to generate a cluster design effect. However, few studies reported outcome-specific ICC and estimates varied substantially between trials. After statistical consultation, we meta-analysed data from cluster-RCTs using the reported effect estimate with its 95% confidence interval as long as the authors reported using appropriate statistical analyses (e.g. multilevel model, generalised estimating equations) that accounted for clustering (Chapter 16.3.3 of Higgins 2011). All 17 cluster-RCTs included in this review reported adjusting for clustering in their analyses.

5. We imputed standard deviations for some trials that reported standard errors or 95% confidence intervals (Chapter 16.1.3 of Higgins 2011).

6. We included two post hoc subgroup analyses to identify reasons for heterogeneity. These included subgroups comparing: trials including high-risk participants only versus trials including all risk levels; and trials incorporating the CVD risk score with health IT versus trials that did not incorporate health IT.

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