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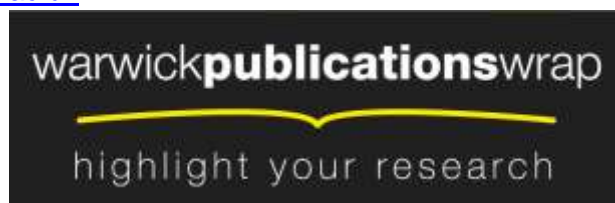
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Systematic versus opportunistic risk assessment for the primary prevention of cardiovascular disease (Protocol)

Dyakova M, Drew C, Wright N, Clarke A, Rees K



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[Intervention Protocol]

Systematic versus opportunistic risk assessment for the primary prevention of cardiovascular disease

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ABSTRACT

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

The primary objective of this review is to assess the effectiveness, costs and adverse effects of systematic risk assessment compared to opportunistic risk assessment for the primary prevention of CVD.

BACKGROUND

Description of the condition

Cardiovascular disease (CVD) includes coronary heart disease (CHD), stroke and peripheral arterial disease. It is related to conditions such as heart failure, chronic kidney disease, diabetes and dementia, and together with these forms the group of *vascular disease* (DH 2008a). The underlying pathology is atherosclerosis, which develops over many years and is usually advanced by the time symptoms occur (BHF 2012a). Acute coronary and cerebrovascular events happen suddenly, usually in middle age, and are often fatal before medical care can be given.

CVD is the number one cause of premature death and disability worldwide, contributing largely to the escalating costs of health care (WHO 2011a). It accounted for 30% of an estimated 58 million deaths globally from all causes in 2005. A substantial pro-

portion of these deaths (46%) were of people under 70 years of age, in their most productive period of life (WHO 2007). It is estimated that by 2030 CVD will account for almost 23.6 million deaths (WHO 2011a). In the UK, heart and circulatory diseases cause more than one in three of all deaths, a fifth of all hospital admissions, and account for more than 191,000 deaths each year at an estimated cost of GBP 30 billion. There are nearly 2.7 million people living with heart disease in the UK (BHF 2012b). In the United States 35% of the total deaths in 2010 were accounted for by CVD compared to 45% in Germany, 31% in Denmark, 48% in Greece, 32% in Japan, 26% in Mexico and 38% in China (WHO 2011b).

Many risk factors contribute to the development of CVD, most of which are related to lifestyle, such as physical inactivity, smoking, alcohol use and unhealthy diet (WHO 2011a). In more than 90% of cases, the risk of a first heart attack is related to nine potentially modifiable risk factors (Yusuf 2004): smoking/tobacco

use; poor diet; high blood cholesterol; high blood pressure; insufficient physical activity; overweight/obesity; diabetes; psychosocial stress and excess alcohol consumption. The combined effect of different coexisting cardiovascular risk factors determines the *total* or *global* or *absolute* risk of developing CVD. An individual with several mildly raised risk factors may be at a higher total risk of CVD than someone with just one elevated risk factor. Many people are unaware of their risk status and total risk assessment is potentially useful for finding high-risk individuals and guiding clinical decisions (Tunstall-Pedoe 2003). Such a risk stratification approach is particularly suitable to settings with limited resources (WHO 2002). Much research has been undertaken to validate different CVD risk scoring methods, so that individual CVD risk is correctly identified (Beswick 2008). Regardless of which scoring mechanism is used, assessing someone's level does not actually change their CVD risk. Short emphasises that there is no advantage in assessment, without the ability to intervene and to make changes to lower that risk (Short 2009).

A significant proportion of CVD morbidity and mortality can be prevented through population strategies for primary prevention. Efficient and effective means of identifying high-risk individuals and then providing the support to enable them to modify their lifestyles requires a delivery system which gives priority to preventive services rather than focusing on treatment (Bernard 2009). Despite various public health and clinical efforts for primary prevention of CVD, a large number of the population, considered at increased risk of vascular disease, remains unidentified, untreated and not reached by lifestyle advice or intervention. This has prompted the initiation of screening/systematic risk assessment programmes for vascular disease in healthy populations. These exist in contrast and in addition to the more ad hoc opportunistic risk assessment initiatives undertaken worldwide.

Description of the intervention

A health risk assessment is one of the most widely used screening tools in the field of health promotion. The main objectives of a risk assessment are to assess health status, to estimate health risk, and to inform and provide feedback to participants in order to reduce health risks (NPSA 2007).

This review will focus on comparing systematic (intervention) with opportunistic risk assessment (control) for primary prevention of CVD. Considering the variability of risk assessment methods and practices, definitions of systematic and opportunistic risk assessment are provided below.

Systematic risk assessment for primary prevention of CVD is defined here as a screening-like programme, involving a pre-determined process for selection of people, who are systematically invited to attend a CVD health check in a primary care or similar setting.

Systematic here means that selection, invitation and follow-up processes are determined in advance, for example specific inclusion/exclusion criteria are set; a unified method of invitation is used,

such as letter/birthday card/phone call; and there is a system for providing feedback or referral. Such a programme is repeated at pre-defined intervals, for example every five or 10 years.

The *assessment process* includes finding out and measuring CVD risk factors (for example blood pressure, serum cholesterol or physical activity) as well as estimating the total (global/absolute) CVD risk, using a specific risk scoring tool (chart/programme).

Primary prevention here means that the target population for such systematic risk assessment includes healthy individuals - in this case, those who have not been previously diagnosed with CVD. This population group consists of individuals at different levels of risk, ranging from very low (minimal) through moderate up to high risk for developing CVD in the future. Many of these people may already have been diagnosed with one or more CVD risk factors (including hypertension, dyslipidaemia, diabetes among others).

Similarly to other screening programmes, systematic risk assessment can be realised in two ways: *population (universal/mass)* systematic risk assessment - targeted to the general population in a certain age group with no regard to any underlying risk factors; *high-risk* systematic risk assessment - targeted to a specific group of individuals, considered potentially to be at increased risk of CVD due to some pre-existing risk factors, for example the population of a deprived area or from a minority ethnic group.

A recent example of such an approach is the NHS Health (Vascular) Check programme (NHS 2012). Designed as a population-based screening initiative, it is aimed at all those aged 40 to 74, ensuring that everyone in this age range is invited to determine his/her vascular risk. The Health Check is undertaken in primary care (general practices in the UK) and consists of a review of: height, weight and body mass index (BMI); demographics; smoking and lifestyle status; blood pressure; lipid profile; and, where appropriate, diabetes review and serum creatinine levels. Risk analysis and risk stratification are performed, followed by an advice and management plan for high-risk individuals. This is repeated every five years. A potential strength of the NHS Health Checks is the opportunity it provides for primary care to re-engage with their population who are relatively hard to reach, allowing support not only for vascular risk assessment but also for other concerns (Short 2009). Such a population approach may inadvertently widen health inequalities, due to low response and attendance of groups already at increased risk (for example those from deprived areas). To prevent this, primary care practitioners have been encouraged to monitor uptake and where it is low and risk/need is considered potentially high they are exhorted to use other approaches to improve uptake. *Opportunistic risk assessment for primary prevention of CVD* is defined here as CVD risk assessment occurring sporadically in a primary setting, including primary care, pharmacy chains, supermarket chains, food companies, occupational health departments or small businesses. These activities do not involve systematic planning or invitation systems and are not part of any organised CVD prevention programme. The range of such activities varies from

no CVD risk assessment at all (no risk factors are measured/no total risk is scored in healthy individuals); through random (opportunistic) risk assessment in patients attending primary care for another reason; to incentivised case-finding, for example through the Quality and Outcomes Framework for UK general practitioners (NICE 2012). Every routine physical examination provides an opportunity to obtain information about health behaviours related to CVD risk, such as smoking, eating habits, physical activity and others (Every contact counts 2012). Opportunistic screening can be facilitated by computer prompts on records of eligible patients who may attend the surgery for another complaint. Such initiatives, though not organised, can allow for follow-up to ensure feedback is given to patients and an appropriate disease management plan is offered (UKNSC 2008).

How the intervention might work

CVD risk assessment strategies have attracted considerable interest both in the clinical and public health communities and the focus on primary prevention has become stronger in recent years. According to the NHS Health Checks programme (DH 2008a), a standard assessment, based on simple questions and measurements to identify the risk of coronary heart disease (CHD), stroke, diabetes and kidney disease, would be effective. After assessing the levels of the main risk factors and the total CVD risk, a follow-up is organised with an individually tailored assessment, setting out the person's level of vascular risk and what steps they could take to reduce it. For those at low risk, this might be no more than general advice on how to stay healthy. Others at moderate risk may be recommended a weight management programme, stop smoking service, or a brief intervention to increase levels of physical activity. Those at the highest risk might also require medication or an intensive lifestyle management programme. A few may need further assessment that would require referral to a hospital consultant. People who already have a vascular disease, which has remained undiagnosed, particularly diabetes and chronic kidney disease, may be detected. In such cases, patients may benefit from an immediate start on a treatment or disease management programme to manage their condition and prevent adverse complications. Modelling work around the Health Checks approach has predicted that it would deliver significant benefits for the UK population: preventing at least 9500 heart attacks and strokes a year (2000 of which would be fatal); preventing at least 4000 people a year from developing diabetes; and detecting diabetes or kidney disease at least a year earlier for 25,000 people. It has predicted high levels of both clinical and cost-effectiveness against a range of assumptions when this approach is applied to all those aged 40 to 74 years (DH 2008b).

Recent research, published since the introduction of the NHS Health Checks, suggests that targeting high-risk individuals (high-risk based systematic risk assessment) rather than mass population screening (population passed systematic risk assessment) is a pre-

ferred route (Chamnan 2010; Lawson 2010). Lawson identified that 16 people were needed to be screened, following the population approach, to identify one individual at high risk of CVD, costing GBP 370 per high-risk person. The alternative, e.g. targeted screening of deprived communities, estimated that only six people would need to be assessed for the identification of one high-risk individual, reducing the costs to GBP 141 per positive identification. Jackson et al identify that a screening programme targeted at individuals with likely or known CVD risk factors would be preferable from a cost-effectiveness point of view (Jackson 2008). Previous research (Wood 1994) suggests that when a population screening programme is undertaken, there is a persistent level of non-attendance and that whilst cardiac risk score for non-attenders is similar to those who attended, non-attenders have significantly more risk behaviours such as smoking. Population-based (universal) risk assessment every five years was found to be cost-effective when compared with no screening; however a cost-analysis was not conducted on whether universal risk assessment would remain cost-effective when compared to targeted high-risk screening. On the other hand, following international and national recommendations, opportunistic CVD risk assessment has become a routine practice in many developed countries. Many primary care practices already run preventive risk assessment programmes particularly in relation to CHD, as well as looking at overall vascular risk. Most industrialised countries already detect a drop in CVD morbidity and mortality even without population-wide screening programmes. Before the introduction of the NHS Health Checks in the UK the National Service Framework (DH 2000) has already contributed to a significant improvement - a 40% reduction in cardiovascular deaths in people under 75 since 1996 (UKNSC 2008). The effectiveness and cost-effectiveness of the systematic risk assessment approach has not been compared to the opportunistic risk assessment approach to prevent CVD in healthy individuals.

Why it is important to do this review

There is not yet a systematic review comparing the effectiveness of systematic with opportunistic risk assessment for primary prevention of CVD. There is currently not enough indisputable evidence either showing clear clinical or economic benefits of systematic screening-like programmes over the widely practised opportunistic risk assessment of CVD in primary care. Therefore, a comprehensive systematic review is needed which examines the most up to date evidence to find out if systematic programmes are proven more effective in preventing CVD mortality and morbidity in healthy populations than opportunistic risk assessment.

OBJECTIVES

The primary objective of this review is to assess the effectiveness, costs and adverse effects of systematic risk assessment compared to opportunistic risk assessment for the primary prevention of CVD.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs).

Types of participants

Healthy adults (18 years old or over) from the general population, including those at moderate to high risk of CVD. The review will focus on the primary prevention of CVD, so we will look for RCTs including participants without known CVD (i.e. without myocardial infarction (MI), stroke, revascularisation procedure (coronary artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA)), angina or angiographically defined coronary heart disease (CHD)).

We are interested only in primary prevention of CVD, i.e. effects of CVD risk assessment on healthy individuals or those at increased risk of CVD, because if an individual is already diagnosed with CHD, they are already considered at high risk and cared for by the healthcare system (e.g. put on medication, given active lifestyle change advice etc.) Previous research has shown that there is a considerable number of individuals who are at high risk of, or already have CVD, who are not recognised/diagnosed - hence the introduction of screening programmes in the UK such as the Health Checks (DH 2008a).

Types of interventions

Intervention: systematic risk assessment for primary prevention of CVD, defined as a screening-like programme, involving a pre-determined selection process of people, who are systematically invited to attend a CVD health check in a primary care or similar setting, assessing at least two of the following risk factors:

1. blood pressure (systolic and/or diastolic) or lipid profile (total cholesterol, LDL, LDL/HDL); and
2. any other modifiable risk factor (smoking, weight, diet, exercise, alcohol, stress).

Control: opportunistic risk assessment for primary prevention of CVD, defined as a range of activities, occurring sporadically in any primary setting - from *no risk assessment at all* to *incentivised case finding*.

Types of outcome measures

Primary outcomes

1. All-cause mortality
2. Cardiovascular mortality
3. Non-fatal endpoints, including CHD, MI, CABG, PTCA, stroke, transitory ischaemic attack (TIA) and peripheral artery disease

Secondary outcomes

1. CVD major risk factors: blood pressure, lipid levels, type 2 diabetes
2. Intermediate (programme) outcomes (if reported): attendance rates (number of individuals who came for examination); case finding rates (number of high-risk individuals, identified by the health check); acceptability and participants' satisfaction; and follow-up rates (number of cases who were followed with some intervention in primary and secondary care)
3. Costs
4. Adverse effects

Search methods for identification of studies

Electronic searches

We will search the following electronic databases:

- *The Cochrane Library* (including the Cochrane Central Register of Controlled Trials (CENTRAL) and NHS Centre for Reviews and Dissemination (CRD) databases: Health Technology Assessment (HTA), Database of Abstracts of Reviews of Effects (DARE) and NHS Economic Evaluation Database (NEED))
- MEDLINE (OVID)
- EMBASE (OVID)
- Science Citation Index Expanded (SCI-EXPANDED), Social Sciences Citation Index (SSCI), Conference Proceedings Citation Index - Science (CPCI-S) on Web of Science
- AMED - Allied and Complementary Medicine Database.

We will use medical subject headings (MeSH) or equivalent and text word terms. We will design searches in accordance with the Cochrane Heart Group methods and guidance.

We will tailor searches to individual databases. The search strategy for MEDLINE is shown in [Appendix 1](#).

We will impose no language restrictions.

Searching other resources

We will also check reference lists of reviews and retrieved articles for additional studies. We will search OpenGrey for grey literature. We will search the metaRegister of controlled trials (mRCT) (www.controlled-trials.com/mrct), Clinicaltrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry platform (ICTRP) (<http://apps.who.int/trialsearch/>) for ongoing trials. We will perform citation searches on key articles and use Google Scholar to search for further studies. We will also contact experts in the field for unpublished and ongoing trials and the authors of papers where necessary for any additional information.

Data collection and analysis

Selection of studies

Two of the authors (MD, CD) will screen the title and abstract of each paper from the searches and retrieve potentially relevant references. We will then obtain the full text of potentially relevant studies and two authors (MD, CD) will independently select studies to be included in the review by using predetermined inclusion criteria. In all cases we will resolve any disagreements about study inclusion by consensus and consult a third author (KR/AC) if disagreements persist.

Data extraction and management

Two authors will extract data independently (MD, KR) using a proforma. We will contact primary investigators to provide additional relevant information if necessary. We will extract details of the study design, participant characteristics, study setting, interventions and outcome data, including details of outcome assessment, adverse effects and methodological quality (randomisation, blinding and attrition) from each included study. Disagreements about extracted data will be resolved by consensus with a third author (AC) being consulted if disagreements persist.

Assessment of risk of bias in included studies

We will assess risk of bias by examining the random sequence generation and allocation concealment, description of drop-outs and withdrawals (including analysis by intention-to-treat), blinding (participants, personnel and outcome assessment) and selective outcome reporting (Higgins 2011) in each trial. Two authors (MD, KR) will assess the risk of bias of included studies independently.

Measures of treatment effect

We will process data according to the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will express dichotomous outcomes as odds ratios or risk ratios, with 95% confidence intervals (CI) calculated for each study. We will compare net changes for continuous outcomes (i.e. intervention group minus control group differences) and a mean difference (MD) or standardised mean difference (SMD) with 95% CIs calculated for each study.

Assessment of heterogeneity

We will conduct tests of heterogeneity for each outcome, using the Chi² test of heterogeneity and the I² statistic. Where there is no heterogeneity we will perform a fixed-effect meta-analysis. The authors will look for possible explanations if substantial heterogeneity is detected (for example participants and intervention). If the heterogeneity cannot be explained, the authors will consider the following options: provide a narrative overview and not aggregate the studies at all, or use a random-effects model with appropriate cautious interpretation.

Subgroup analysis and investigation of heterogeneity

We will stratify by the types of risk assessment approaches, if sufficient studies are found. They will be as follows.

1. Systematic risk assessment will be stratified into: *population/universal/mass* risk assessment (targeting the whole population in a certain age group) and *high-risk* risk assessment (targeting specific population groups, perceived to be at increased risk).

2. Opportunistic risk assessment will be stratified into: *not/minimal* risk assessment, *sporadic/opportunistic* risk assessment and *incentivised case finding*.

We will also examine the effects of the intervention design (setting, personnel involved, invitation and follow-up system).

We will assess heterogeneity as mentioned above and consider the effects of the setting of the intervention and personnel, if possible.

Sensitivity analysis

We will carry out sensitivity analyses excluding studies with a high risk of bias. If there are sufficient trials, we will undertake assessment of funnel plots and tests of asymmetry (Egger 1997) to assess possible publication bias.

ACKNOWLEDGEMENTS

None at the protocol stage.

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* Indicates the major publication for the study

APPENDICES

Appendix I. MEDLINE search strategy

MEDLINE OVID

1. exp Cardiovascular Diseases/
2. cardio*.tw.
3. cardia*.tw.
4. heart*.tw.
5. coronary*.tw.
6. angina*.tw.
7. ventric*.tw.
8. myocard*.tw.
9. pericard*.tw.
10. isch?em*.tw.
11. emboli*.tw.
12. arrhythmi*.tw.
13. thrombo*.tw.
14. atrial fibrillat*.tw.
15. tachycardi*.tw.
16. endocardi*.tw.
17. (sick adj sinus).tw.
18. exp Stroke/
19. (stroke or stokes).tw.
20. cerebrovasc*.tw.
21. cerebral vascular.tw.
22. apoplexy.tw.
23. (brain adj2 accident*).tw.
24. ((brain* or cerebral or lacunar) adj2 infarct*).tw.
25. exp Hypertension/
26. hypertensi*.tw.
27. peripheral arter* disease*.tw.
28. ((high or increased or elevated) adj2 blood pressure).tw.
29. exp Hyperlipidemias/
30. hyperlipid*.tw.
31. hyperlip?emia*.tw.
32. hypercholesterol*.tw.
33. hypercholester?emia*.tw.
34. hyperlipoprotein?emia*.tw.
35. hypertriglycerid?emia*.tw.
36. exp Arteriosclerosis/
37. exp Cholesterol/

38. cholesterol.tw.
39. "coronary risk factor* ".tw.
40. or/1-39
41. Mass Screening/
42. Systematic risk assessment*.tw.
43. Case finding.tw.
44. ((screen* or assess* or test* or diagnos* or surveill* or identifi* or prevalence or incidence*) adj10 (structured or systematic or organised or organized or opportunistic or random)).tw.
45. Risk Assessment/
46. (risk* adj3 assess*).tw.
47. or/41-46
48. Primary Prevention/
49. (prophylaxis or prevent*).tw.
50. 48 or 49
51. 40 and 47 and 50
52. randomized controlled trial.pt.
53. controlled clinical trial.pt.
54. randomized.ab.
55. placebo.ab.
56. drug therapy.fs.
57. randomly.ab.
58. trial.ab.
59. groups.ab.
60. 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59
61. exp animals/ not humans.sh.
62. 60 not 61
63. 51 and 62

CONTRIBUTIONS OF AUTHORS

All authors contributed to the protocol development.

DECLARATIONS OF INTEREST

None known.

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