Protocol for the development of

The BHF and Joint British Societies' Guideline on the Prevention of Cardiovascular Disease

Date: November 2025

Written with input from groups listed on bhf.org.uk/cvd-prevention-guideline

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1. Background

Cardiovascular disease (CVD) is the leading cause of death worldwide, responsible for approximately 19 million deaths each year.[1] An aging population and an increasing frequency of risk factors for CVD such as obesity and diabetes mellitus is projected to lead to an increase in the prevalence of CVD.[2, 3] In the United Kingdom (UK), heart and circulatory diseases account for 25% of all deaths, equivalent to approximately 160,000 deaths per year. There are over 7.6 million people in the UK currently living with CVD, a burden which disproportionately affects socioeconomically disadvantaged groups, minority ethnic groups and those living in rural or isolated settings .[4, 5]

Clinical practice guidelines

The Joint British Societies' first recommendations on prevention of coronary heart disease were developed by the British Cardiac Society, British Hypertension Society, British Atherosclerosis Society (endorsed by the British Diabetes Association) and published in Heart in 1998.[6] This followed the publication of recommendations on the prevention of coronary heart disease in clinical practice by the Task Force of the European Society of Cardiology, European Atherosclerosis Society and European Society of Hypertension in 1994.[7]

The order of priorities proposed for Coronary Heart Disease (CHD; sometimes ischaemic heart disease (IHD) or coronary artery disease (CAD), respectively) prevention in clinical practice in the UK were: (1) Patients with established CHD or other major atherosclerotic disease; (2) Patients with hypertension, dyslipidaemia, diabetes mellitus, family history of premature CHD or a combination of these risk factors which puts them at high risk of developing CHD or other atherosclerotic disease. The 'Coronary Risk Prediction Charts', based on the Framingham population study, were proposed as a new way of identifying people at high multifactorial risk of developing CHD, and these were supplemented with a 'Cardiac Risk Assessor' computer programme. An absolute risk estimate of cardiovascular events of more than 30% over 10 years was considered sufficiently high to justify therapeutic intervention.

The three founding Joint British Societies, subsequently expanded to include Diabetes UK, HEART UK, the Primary Care Cardiovascular Society, and the Stroke Association updated their recommendations in 2005.[8] Clinical priorities remained the same but patients with diabetes mellitus were specifically highlighted as a subgroup at increased CVD risk who should be considered for therapeutic intervention. The new CVD risk prediction charts now recommended therapeutic intervention for a CVD risk threshold of >20% over 10 years. Furthermore, the guidelines set treatment targets for: blood pressure (<140/85 mmHg); LDL-cholesterol (<2.0 mmol/l); and diabetic control HbA1c (<6.5%).

In 2014, the Joint British Societies consensus recommendations advocated a new approach to risk estimation and management based not only on short term (10-year) risk but also on CVD risk over a lifetime.[9] The JBS3 calculator provided novel metrics such as 'heart age' and CVD event free survival together with 10-year risk. QRISK Lifetime was the basis for the JBS3

calculator because it provided the option of a calculation of lifetime risk and is based on a UK population. The Joint British Societies advocated for national policies on prevention of CVD. The third guideline prioritised for preventive and rehabilitative care patients who had already presented with symptomatic atherosclerotic disease while it also sought to identify using cardiovascular risk estimation tools, those who were at high-risk of developing CVD and likely to benefit from primary prevention. Lifestyle and risk factor targets were set for the clinical management of these patients. However, these guidelines have not been updated for more than a decade and given the pace of new scientific discoveries and new treatments in this area, it is necessary to update guidance on a regular basis, using rigorous methodology, to create a 'living guideline' which can be kept up to date and easily used by health professionals in their daily practice.

This guideline

It was recognised that it had been more than a decade since the last iteration of the Joint British Societies' Cardiovascular Prevention Guidelines and that many new therapies and a compendium of new evidence of their effectiveness had subsequently emerged. The BHF, therefore, proposed that it would coordinate the development of a new guideline and work in partnership with the Joint British Societies, charities, and other relevant organisations in doing so. The purpose was to establish a new state of the art guideline on CVD prevention with a focus on preventing the development and/or consequences of atherosclerotic CVD.[10] A stakeholder meeting was held to introduce the guideline plan to the various stakeholder organisations and to agree the scope and target audience of the guideline. These discussions are reflected in this protocol. The costs associated with developing the guideline, including the costs associated with carrying out systematic reviews, are being funded by the BHF.

Objectives of the project

The primary objective of this project is to develop a comprehensive clinical practice guideline (CPG) for the prevention of atherosclerotic CVD. The CPG aims to serve as a resource for all healthcare professionals who are involved in the management of patients with or at increased risk of CVD, providing them with up-to-date evidence-based recommendations to improve prevention strategies and patient outcomes.

Specific considerations for this project include, but are not limited to:

1. **Synthesising existing evidence**: By conducting a hierarchical review process, beginning with reviews of systematic reviews and guidelines to establish a broad evidence base and identify gaps. Evidence will be presented using the GRADE approach in order to allow the guideline development group (GDG) to make evidence-based recommendations on relevant questions, including covering the needs of underserved and high-risk populations, ensuring equitable access to preventive care.
2. **Enabling scalability**: By developing a guideline that serves as a foundation for dynamic updates, for example, to integrate future advances in evidence and technology, such as artificial intelligence (AI)-driven updates as a "living guideline" that can be rapidly updated as new evidence emerges and to form the basis of a personalised clinical

decision support system. The well-established GRADEpro and MAGICapp platforms (see https://www.gradepro.org/ and https://app.magicapp.org, respectively) will provide a framework for future updates.

3. **Enhancing accessibility**: By including patient-centred materials such as infographics to improve public understanding and engagement with CVD prevention strategies.

By achieving these objectives, the CPG will not only address the current limitations of static guideline models but also provide a template for future innovations in dynamic guideline development as a “living guideline”.

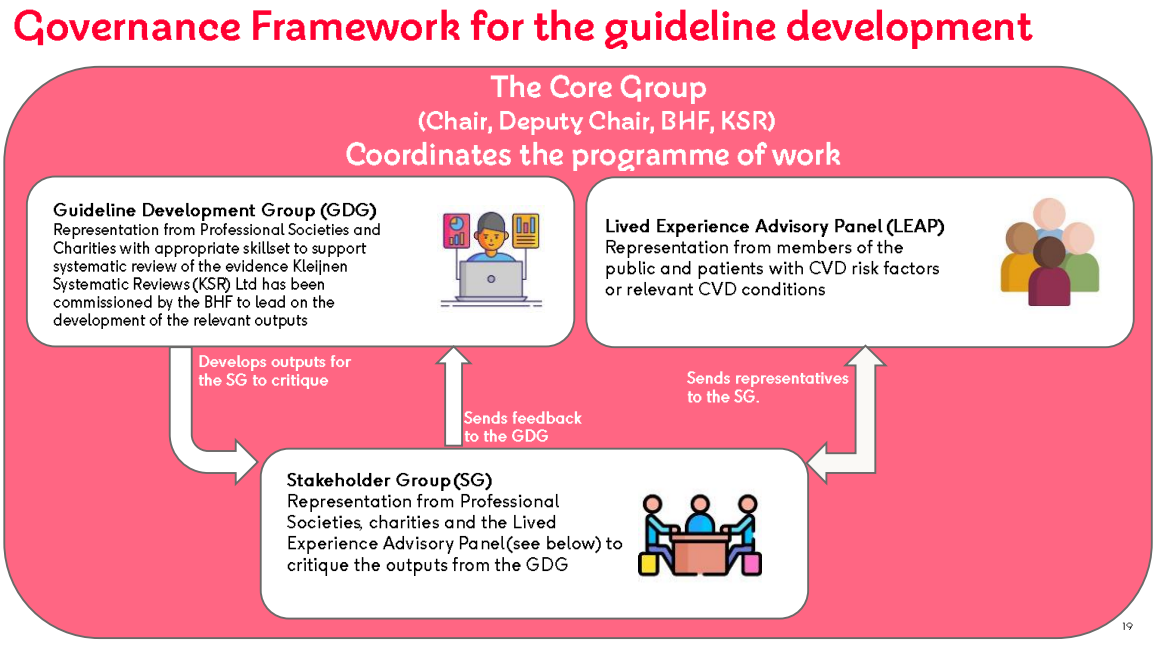
2. Processes

The BHF has set up a GDG which will be responsible for the development of the guideline text and recommendations. The GDG includes health care professionals in relevant clinical areas, with representation from the different UK professional societies and charities, the four nations of the UK, as well as international and methodological experts. Kleijnen Systematic Reviews Ltd (KSR) was commissioned to provide information specialists, systematic reviewers, writers and methodologists to support the GDG.

In addition, a Stakeholder Groug (SG) has been established to provide advice and comments about the scope and the intended audience for the guideline, the research questions, methods, recommendations, and drafts of the guideline text. The SG will meet face to face on several occasions and will also be invited to make contributions using email correspondence and critiquing electronic documents.

A Lived Experience Advisory Panel (LEAP) has also been set up to facilitate input from members of the public and patients. The intention is for the panel to meet virtually as well as face-to-face. Members will be invited to comment on electronic documents or provide feedback by email. Panel members are also represented in the SG.

All processes will be co-ordinated by a Core Team of the GDG chair, GDG Deputy chair and staff from the BHF and KSR.



Conflicts of interest

Conflicts of interest (CoI) are documented and regularly updated for all members of the different groups and submitted to the BHF. In addition, for the GDG group meetings, any CoI will be established at the start of each meeting and where relevant CoIs exist, members will be asked not to contribute to the relevant parts of the guideline.

The Guideline Development Group

The GDG includes the following members

Name	Representing	Based in UK Nation
Professor Bryan Williams (Chair)	British Heart Foundation	England
Professor David Wood (Deputy Chair)	Imperial College London	England
Professor Jos Kleijnen	Kleijnen Systematic Review	England
Professor John R Petrie	Diabetes UK	Scotland
Professor Tahseen A. Chowdhury	Association of British Clinical Diabetologists	England
Professor Alastair Webb	British and Irish Association of Stroke Physicians	England
Professor David Werring	British and Irish Association of Stroke Physicians	England
Professor Susan Dawkes	British Association of Cardiac Rehabilitation	Scotland
Professor Rod Taylor	British Association of Cardiac Rehabilitation	Scotland
Dr Carmel M McEniery	British and Irish Hypertension Society	England
Dr Philip Stuart Lewis	British and Irish Hypertension Society	England
Mr Paul Wright	Royal Pharmaceutical Society	England
Ms Joanne Bateman	Royal Pharmaceutical Society	England
Professor Patrick Mark	UK Kidney Association	Scotland
Professor Debasish Banerjee	UK Kidney Association	England
Professor Stephen B Wheatcroft	British Cardiovascular Society	England
Professor Amitava Banerjee	British Cardiovascular Society	England
Dr Jaimini Cegla	Heart UK	England
Professor Handrean Soran	Heart UK	England
Professor Tomasz Guzik	British Atherosclerosis Society	Scotland
Ms Janine O'Rourke	British Association of Nurses in Cardiovascular Care (BANCC)	England
Dr Karen Higginbotham	British Association of Nurses in Cardiovascular Care	England
Dr Kirstie Truman	Nominated by Cardiovascular Strategic Network to represent Wales	Wales
Name TBC	Representing a GP perspective	Northern Ireland
Nicola Thompson	Lived Experience Advisor Panel representative	England
Joanne Lloyd	Lived Experience Advisor Panel representative	England
Professor Jako Burgers	International Perspective Dutch College of General Practitioners	Netherlands

GRADE

The GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach is a widely used framework for evaluating quality of evidence and strength of recommendations and was used for this guideline. GRADE assesses the quality of evidence based on factors like study design, risk of bias, inconsistency, indirectness, imprecision, and

publication bias.[11-18] Using this approach, recommendations are categorised as strong or weak (also called conditional or discretionary) based on the quality of the evidence and the balance between desirable and undesirable consequences of the recommended action. The GRADE approach emphasises transparency and clarity in evaluating evidence and formulating recommendations. It provides a structured way to present evidence summaries and the rationale for recommendations, see https://www.gradeworkinggroup.org/ for details.

A priori definition of outcomes to be assessed in the GRADE process

At its first meeting, the GDG discussed the outcomes relevant to this guideline following input from the LEAP.

When it comes to defining outcomes, GRADE emphasises clarity, relevance, and patient-centeredness. The process begins by identifying all potentially relevant outcomes associated with an intervention, including both benefits and harms, as well as burdens. These outcomes are then prioritised based on their importance to clinical decision-making. Outcomes are categorised as critical, important (but not critical), or not important. Only those deemed critical or important are used to inform guideline recommendations.

A central principle of the GRADE approach is to focus on outcomes that matter most to patients. This requires incorporating patient input, alongside perspectives from clinicians and other stakeholders, to ensure the outcomes reflect real-world values and preferences. Outcomes must be clearly and consistently defined. This includes specifying the target population, the precise measure or metric used, the timeframe over which the outcome is assessed, and the units of measurement. Such clarity allows for meaningful interpretation of evidence and consistent use across studies.

Composite outcomes, which combine multiple individual outcomes into one measure, are generally discouraged unless they are clinically meaningful and reflect what patients care about. Individual outcomes are usually more transparent and interpretable. The GDG will document how outcomes were selected and prioritised, who was involved, and the rationale for decisions. This ensures the process is transparent and reproducible.

Ultimately, outcomes selected through the GRADE approach feed into evidence profiles and decision frameworks that underpin the strength and direction of recommendations. By focusing on outcomes that are clearly defined, relevant to patients, and prioritised transparently, the GRADE approach enhances the quality and trustworthiness of clinical practice guidelines.

Developing and writing recommendations

Levels of evidence will be summarised using the GRADE approach, by outcome across all relevant studies. We intend to complete the GRADE assessments once the recommendations are at an advanced stage, so that this laborious process will be as efficient as possible.

Levels of evidence are classified within GRADE as high, moderate, low or very low.

High	Further research is very unlikely to change our confidence in the estimate of effect. GRADE ++++
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. GRADE +++
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. GRADE ++
Very low	Any estimate of effect is very uncertain. GRADE +

According to these levels of evidence, recommendations will be designated as strong or weak. Some recommendations are 'strong' in that the GDG believe that the vast majority of practitioners or commissioners and people using services would choose a particular intervention if they considered the evidence in the same way as the GDG. Similarly, if the GDG believe that the vast majority of practitioners or commissioners and people using services would not choose a particular intervention, if they considered the evidence in the same way as the GDG, a negative ('Do not offer') recommendation will be made. If evidence of effectiveness for an intervention is either lacking or too weak for firm conclusions to be reached, the GDG will use expert opinion; or make no recommendation. In these cases, recommendations for further research will also be given.

Editorial independence

For all recommendations, the final wording will be the sole responsibility of the members of the GDG. Neither the BHF (the funder) nor any other stakeholders will have veto rights about the recommendations.

Consultation about the draft guideline

The draft version of the guideline will be posted on the BHF website for consultation with registered stakeholders and respondents. The BHF will inform registered stakeholders and respondents that the draft is available and invite them to comment by the deadline. Questions for stakeholders will be posted with the draft guideline.

Cost consideration for recommendations

Where the GDG considers that there may be significant costs or organisational consequences for certain recommendations, evidence for cost-effectiveness and organisational impact will be sought and presented, but the principal focus will be on what the best available evidence recommends.

The BHF will also ask stakeholders to comment on recommendations identified as likely to substantially increase costs, and their justification, and to consider whether any other draft recommendations are expected to add substantial costs.

Health equity

The BHF recognises the critical importance of embedding health equity more effectively into guideline development. When health systems come under strain, it is often the most

disadvantaged in society who bear the greatest burden. As a result, inequalities in health outcomes are widening—most notably, the growing gap in healthy life expectancy between the richest and poorest groups, much of which is driven by the burden of CVD.

Reducing these inequalities requires acknowledging and addressing the influence of social and commercial determinants of health—factors increasingly recognised as key drivers of health outcomes. However, incorporating these determinants into guideline development remains a significant challenge.

To support this effort, GRADE has proposed a seven-step approach:[19]

1. Identify disadvantaged populations.
2. Examine available data for these populations.
3. Evaluate baseline risk for primary outcomes.
4. Assess how well these populations are represented in primary studies.
5. Appraise subgroup analyses.
6. Identify barriers to implementing effective interventions.
7. Propose strategies to support implementation in disadvantaged populations.

The current CPG will apply the GRADE seven-step approach. To achieve this, members of the GDG, the SG, and the LEAP will be invited to consider and provide feedback on the following questions:

1. Which disadvantaged populations should be considered?
2. What data relevant to these populations are you aware of?
3. What are the main barriers to implementing effective interventions for these populations?
4. What supportive strategies could help facilitate implementation of the guideline recommendations?

Advice and tools for guideline implementation

Potential facilitators and barriers to implementation will be identified. As part of the guideline outputs, a summary document, educational tools, patient information sources, and infographics will be developed.

Monitoring and/or auditing criteria

The guideline will consider a range of monitoring and audit criteria which may help with the implementation of the guideline recommendations.

Updating the guideline

The guideline is intended to become a living guideline which will be constantly and rapidly updated as new evidence emerges.

3. Methods for evidence reviews

Research questions

The research questions (RQs) for this CPG are yet to be fully defined. RQs will be refined iteratively through systematic evidence mapping, stakeholder engagement, and consultation with the GDG. The following preliminary question themes guided the CPG development:

1. What evidence-based strategies are most effective in preventing CVD in those with and without established atherosclerotic disease?
2. How can prevention strategies be tailored to address health inequities and improve outcomes for those with established CVD and those at high risk of developing CVD?
3. What are the gaps in current CPGs, and how can they be addressed in this new CVD prevention guideline?

This iterative refinement process will culminate in well-defined questions that align with the objectives of the CPG. The review questions were formulated using the PICO (population, intervention, comparator and outcome) framework to assess the effectiveness of an intervention and similar frameworks for other types of questions, for example, about diagnosis. The PICO framework is a helpful structured approach for developing questions about interventions.

Scope and inclusion criteria

The inclusion criteria listed below provide a framework to operationalise the aforementioned RQs. The KSR project team will work alongside the GDG to identify and refine possible RQs. The scope of the guideline is reflected in the inclusion criteria outlined as follows:

Population

Populations to be covered include:

- Those with atherosclerosis who have been diagnosed with one or more of these clinical conditions:
    - Myocardial infarction
    - Ischaemic stroke or transient ischaemic attack
    - Peripheral arterial disease
- Those with significant atherosclerosis, diagnosed by imaging, such as CT angiography, with or without symptoms
- Adults from the general population without CVD, including high-risk populations such as those with any, some, or all of the following:
    - Elevated total CVD risk
    - Diabetes (distinguishing between type 1 and type 2 diabetes, where possible)
    - Hypertension
    - Heart failure
    - Atrial fibrillation
    - Haemorrhagic stroke

- Hyperlipidaemia/Dyslipidaemia
- Chronic kidney disease
- Obesity
- Smokers

In the development of the CPGs, relevant populations may be identified and relevant information reported. Where relevant, "flags of risk" (e.g., pre-eclampsia, erectile dysfunction) will be reported.

The CPG will provide definitions for the aforementioned conditions and identify relevant minimally important differences (MIDs).

Interventions

Lifestyle Interventions:
Lifestyle interventions can be effective at reducing the risk of CVD and form a key part of any CVD prevention strategy. These include:

- Smoking cessation
- Salt restriction
- Alcohol restriction
- Adherence to cardioprotective diet,
- Regular physical activity
- Weight loss
- Measures to improve sleep quality
- Stress management
- Measures to improve mental health

There have been many recent systematic reviews on lifestyle interventions that reduce CVD risk. We decided not to replicate this work; instead, the guideline will reference relevant existing systematic reviews and CPGs which provide guidance on lifestyle interventions in order to frame our recommendations on lifestyle interventions for CVD prevention.

Drug Interventions:
The focus of the GDG is on pharmacological interventions, including:

- Antihypertensive drugs
- Lipid-lowering drugs
- Weight-loss drugs
- Antiplatelet agents
- Anticoagulants
- Diabetes drugs
- Multi-drug combinations (polypills)

Comparisons

Comparators include the interventions listed above, placebo, or usual care.

Outcomes

A hierarchy of outcomes was agreed by the GDG, as outlined before.

Critical outcomes:

- Mortality (all-cause, CVD-specific)
- Major adverse cardiovascular events (MACE; core, extended)
- Cognition

Important outcomes:

- Quality of life
- Development of new comorbidities
- Adverse events (all, serious)
- CVD-free (inverse of the aforementioned outcomes)

Study types

A hierarchical approach will be taken when considering the evidence if insufficient evidence is available from the highest tier, evidence from the next level will be considered. The tiers of evidence, from the highest to the lowest are defined below:

- Umbrella reviews (reviews of reviews) and CPGs
- Systematic reviews (SRs)
- Randomised controlled trials (RCTs)
- Additional study designs (to be discussed within the GDG)

Literature searches

In order to manage the volume of evidence, a hierarchical approach to the literature searching will be taken. Initial searches will focus on the identification of umbrella reviews (reviews of reviews) and CPGs for the prevention of CVD, then additional searches for SRs will be conducted as required as updates to the above. Should only limited relevant or good quality secondary evidence be found in specific areas, RCT data will be sought. Additional study designs can be considered as required in specific areas. This will be decided with the GDG.

Search strategies will be developed to identify studies on CVD prevention, as recommended in the Centre for Reviews and Dissemination (CRD) guidance for undertaking reviews in health care and the Cochrane Handbook.[20, 21] Searches will be refined based on clinical input from the GDG or working group members. Where needed, it is likely that a general search will be amended with searches specific to the research question.

Candidate search terms will be identified from target references, browsing database thesauri (e.g., MEDLINE MeSH and Embase EMTREE), existing reviews and initial scoping searches. Strategy development will involve an iterative approach which tests candidate text and indexing terms across a sample of bibliographic databases, aiming to reach a satisfactory

balance of sensitivity and specificity. Search strategies (keywords and thesaurus terms) will be adapted according to the configuration of each database.

KSR works in conjunction with KSR Evidence Ltd. to produce KSR Evidence - a comprehensive database of systematic reviews, meta-analyses and health technology assessments (see https://ksrevidence.com/). The project team, therefore, has extensive experience in identifying SRs, including the development of sensitive search strategies used across a wide range of bibliographic databases. An example search strategy is provided in Appendix 1.

Initial searches to identify umbrella reviews and guidelines will include the following resources:

- MEDLINE and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily (Ovid)
- EMBASE (Ovid)
- CINAHL (EBSCO)
- PsycInfo (Ovid)
- Cochrane Database of Systematic Reviews (https://www.cochranelibrary.com/)
- Trip Database (Internet) (https://www.tripdatabase.com/)
- Guidelines International Network (GIN) (Internet) (https://g-i-n.net/international-guidelines-library/)
- National Institute for Health and Care Excellence (NICE) (Internet) (https://www.nice.org.uk/)
- NIHR Health Technology Assessment (HTA) (Internet) (https://www.nihr.ac.uk/)
- ECRI Guidelines Trust (Internet) (https://home.ecri.org/)
- International HTA Database (https://database.inahta.org/)

Searches for the identification of systematic reviews will include the following resources:

- KSR Evidence (https://ksrevidence.com/)
- Cochrane Database of Systematic Reviews (https://www.cochranelibrary.com/)
- MEDLINE and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily (Ovid)
- EMBASE (Ovid)
- CINAHL (EBSCO)
- PsycInfo (Ovid)

Searches for primary studies, where required, will be conducted using the following resources:

- MEDLINE and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations and Daily (Ovid)
- EMBASE (Ovid)
- CINAHL (EBSCO)
- Cochrane Central Register of Controlled Trials (CENTRAL) (Wiley)

- PsycInfo (Ovid)

The main strategy for each search will be independently peer reviewed by a second Information Specialist based on the CADTH Peer Review checklist.[22]

Reference checking

The bibliographies of included primary studies and systematic reviews will be checked for relevant studies.

Handling of citations

Identified references from the bibliographic database searches will be downloaded into EndNote bibliographic management software for further assessment and handling. Individual records within the EndNote libraries will be tagged with the search information, such as searcher, date searched, database host, database searched, strategy name and iteration, theme or search question. This enables the information specialist to track the origin of each individual database record, and its progress through the screening and review process.

Methods of study selection, quality assessment and data extraction

Titles and abstracts identified through electronic database and web searching will be independently screened by two reviewers. References which clearly do not meet the inclusion criteria of the review will be excluded. Full electronic article copies will be obtained for all of the remaining references. These will then be independently examined in detail by two reviewers in order to determine whether or not they meet the criteria for inclusion in the review. Details of studies assessed during full paper screening will be reported in a table, which will include reasons for exclusion from the review. With respect to both screening stages, any discrepancies between reviewers will be resolved through discussion or by the intervention of a third reviewer.

All titles and abstracts retrieved from the literature searches (from inception) will be screened to identify studies meeting the inclusion criteria.

Quality (risk of bias) assessment

The risk of bias (ROB) (methodological quality) of each included study will be assessed in order to ensure that the conclusions and findings of the reviews are based on the best available evidence. Assessment tools which will be used for this process will be chosen based on the study design. These will include:

- Umbrella reviews (reviews of reviews): JBI ROB of umbrella reviews[23]
- CPGs: AGREE II[24]
- Systematic reviews: ROBIS[25]
- Randomised controlled trials (RCTs): Cochrane RoB[26]
- Additional study designs: Tool as recommended by the LATITUDES Network (https://www.latitudes-network.org)

The risk of bias assessments will be performed independently by two reviewers. Any discrepancies will be resolved through discussion or through the intervention of a third reviewer.

Summaries of the evidence

Summaries of the evidence will be prepared following the structure of the example record in Appendix 2.

GRADE summary of findings tables

GRADE summary of findings tables will be prepared according to the format chosen by the GDG, see next page for an example of this.

Statins for prevention of clinical outcomes in heart failure patients

Patient or population: patients with heart failure
Settings:
Intervention: Statins

Outcomes	Illustrative comparative risks* (95% CI) Assumed risk* Control	Corresponding risk Statins	Relative effect (95% CI)	No of Participants (No of studies)	Quality of the evidence (GRADE)	Comments
Sudden cardiac death	**108 per 1000**	**100 per 1000** (76 to 131)	**RR 0.92** (0.7 to 1.21)	10077 (8 studies)	⊕⊕⊕⊖ **moderate**[1]	
All-cause mortality	**273 per 1000**	**240 per 1000** (205 to 278)	**RR 0.88** (0.75 to 1.02)	11024 (13 studies)	⊕⊕⊕⊖ **moderate**[1]	
Hospitalization for worsening heart failure	**380 per 1000**	**300 per 1000** (251 to 357)	**RR 0.79** (0.66 to 0.94)	10761 (12 studies)	⊕⊕⊕⊖ **moderate**[1]	

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (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; **RR:** Risk ratio;

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

* The basis of the assumed risk is the average risk of control group patients.

[1] Publication bias is likely as the funnel plot seems asymmetric.

4. References

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5. Appendix 1

Example search strategy

Example KSR Evidence search strategies for systematic reviews in cardiovascular disease and primary prevention, and one covering pharmaceutical treatment for both primary and secondary prevention are provided below. This gives suggested search terms and facets and is designed as a starting point for discussions with the GDG in order to tailor the search to the RQs, as appropriate. All searches will be adapted for use on other resources.

KSR Evidence: 2015-13.11.24
https://ksrevidence.com/
Date searched: 13.11.24
Records found: 5954

CARDIOVASCULAR DISEASE

1 (cardiovascular or "cardio vascular") adj3 (accident* or event* or disease* or disorder*) in Title or Abstract 9004 results
2 (cerebrovascular or "cerebro vascular") adj3 (accident* or event* or disease* or disorder*) in Title or Abstract 1236 results
3 ("peripheral vascular" or "peripheral arter*") adj3 (disease* or event* or disorder*) in Title or Abstract 763 results
4 (coronary or heart or cardiopulmonary or "cardio pulmonary" or cardiac) adj3 (disease* or death* or event* or disorder* or arrest* or attack* or failure) in Title or Abstract 11575 results
5 CVD or CHD or CAD or PAD or CVA in Title or Abstract 4394 results
6 angina in Title or Abstract 616 results
7 "atrial fibrillation" in Title or Abstract 3109 results
8 stroke or strokes in Title or Abstract 11344 results
9 (high adj2 cholesterol) or hypercholesterol* in Title or Abstract 1504 results
10 (high or raised or elevated) adj2 ("blood pressure" or bp) in Title or Abstract 706 results
11 "transient isch?emic attack*" in Title or Abstract 631 results
12 "deep vein thrombosis" or "venous thrombosis" or "thromboembolic disease*" in Title or Abstract 1332 results
13 "abnormal heart rhythm*" in Title or Abstract 8 results
14 "acute coronary syndrome*" in Title or Abstract 1068 results
15 "aorta disease*" or "aortic aneurysm*" or "aortic dissection" or "aortic stenosis" in Title or Abstract 1279 results
16 arrhythmia* in Title or Abstract 1477 results
17 atherosclero* or atherosclerotic or arteriosclero* or arteriosclerotic in Title or Abstract 1425 results
18 cardiac dysrhythmia* in Title or Abstract 23 results
19 cardiomyopathy in Title or Abstract 778 results
20 carditis in Title or Abstract 9 results
21 endocarditis in Title or Abstract 338 results
22 hypertension or hypertensive in Title or Abstract 7700 results

23 "Marfan syndrome" in Title or Abstract 39 results
24 "myocardial infarct*" in Title or Abstract 4753 results
25 "pericardial disease*" or "pericardial effusion" or pericarditis in Title or Abstract 262 results
26 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 in All text 39309 results

PRIMARY PREVENTION
27 primary adj3 prevent* in Title or Abstract 1287 results
28 (lifestyle or life-style or behavio?r*) adj2 (interven* or educat* or advice* or advise* or alter* or chang* or inform* or modif*) in Title or Abstract 5990 results
29 (weight or overweight or obese or obesity or diet* or smok* or exercis*) adj2 (interven* or educat* or promot* or advice* or advise* or educat*) in Title or Abstract 5804 results
30 (nonpharmacologic* or pharmacologic*) adj2 prevent* in Title or Abstract 219 results
31 asymptomatic or nonclinical or "non-clinical" in Title or Abstract 3101 results
32 reduc* adj2 risk* in Title or Abstract 11880 results
33 "risk factor*" adj2 (manage* or managing or interven* or program* or modif*) in Title or Abstract 1321 results
34 #27 or #28 or #29 or #30 or #31 or #32 or #33 in All text 26948 results

35 #26 and #34 in All text 5948 results

KSR Evidence: to 5.8.25
https://ksrevidence.com/
Date searched: 5.8.25
Records found: 5950

CARDIOVASCULAR DISEASE

1 (cardiovascular or "cardio vascular") adj3 (accident* or event* or disease* or disorder*) in Title or Abstract 10097 results
2 (cerebrovascular or "cerebro vascular") adj3 (accident* or event* or disease* or disorder*) in Title or Abstract 1347 results
3 ("peripheral vascular" or "peripheral arter*") adj3 (disease* or event* or disorder*) in Title or Abstract 831 results
4 (coronary or heart or cardiopulmonary or "cardio pulmonary" or cardiac) adj3 (disease* or death* or event* or disorder* or arrest* or attack* or failure) in Title or Abstract 12823 results
5 CVD or CHD or CAD or PAD or CVA in Title or Abstract 4912 results
6 angina in Title or Abstract 668 results
7 "atrial fibrillation" in Title or Abstract 3455 results
8 stroke or strokes in Title or Abstract 12642 results
9 "transient isch?emic attack*" in Title or Abstract 686 results

10 "deep vein thrombosis" or "venous thrombosis" or "thromboembolic disease*" in Title or Abstract 1466 results
11 "abnormal heart rhythm*" in Title or Abstract 8 results
12 "acute coronary syndrome*" in Title or Abstract 1193 results
13 "aorta disease*" or "aortic aneurysm*" or "aortic dissection" or "aortic stenosis" in Title or Abstract 1423 results
14 arrhythmia* in Title or Abstract 1676 results
15 atheroscleros* or atherosclerotic or arterioscleros* or arteriosclerotic in Title or Abstract 1621 results
16 cardiac dysrhythmia* in Title or Abstract 24 results
17 cardiomyopathy in Title or Abstract 900 results
18 carditis in Title or Abstract 10 results
19 endocarditis in Title or Abstract 386 results
20 "Marfan syndrome" in Title or Abstract 41 results
21 "myocardial infarct*" or STEMI or NSTEMI in Title or Abstract 5273 results
22 "pericardial disease*" or "pericardial effusion" or pericarditis in Title or Abstract 296 results
23 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 in Title or Abstract 37066 results

PHARMACEUTICAL TREATMENT

24 (drug* or medication*) adj3 ("blood pressure") in Title or Abstract 190 results
25 Antihypertensive* or "anti-hypertensive*" in Title or Abstract 990 results
26 "ACE inhibitor*" or ACEI* or "angiotensin-converting enzyme inhibitor*" or enalapril or lisinopril or perindopril or ramipril in Title or Abstract 779 results
27 ARB* or "angiotensin receptor blocker*" or angiotensin-II receptor blocker* or candesartan or irbesartan or losartan or valsartan or olmesartan in Title or Abstract 1294 results
28 "calcium-channel blocker*" or CCB* or amlodipine or felodipine or nifedipine in Title or Abstract 525 results
29 "thiazide diuretic*" or indapamide or bendroflumethiazide in Title or Abstract 63 results
30 "beta blocker*" or "alpha blocker*" or "central alpha antagonist*" or vasodilator* or "renin inhibitor*" or "renin-angiotensin-aldosterone system inhibitor*" in Title or Abstract 1170 results
31 (drug* or medication*) adj3 ("lipid lower*" or "high cholesterol" or hyperlipid?emia or hypercholesterol?emia or "hyper-lipid?emia" or "hyper-cholesterol?emia") in Title or Abstract 154 results
32 statin* or atorvastatin or lipitor or fluvastatin or lescol or pravastatin or lipostat or rosuvastatin or crestor or simvastatin or zocor or ezetimibe or "bempedoic acid" or alirocumab or evolocumab or inclisiran in Title or Abstract 1974 results
33 (drug* or medication*) adj3 (obesity or obese or "weight loss") in Title or Abstract 167 results
34 orlistat or liraglutide or semaglutide or tirzepatide or mounjaro or semaglutide or wegovy or liraglutide or saxenda or Ozempic or Rybelsus or Trulicity or dulaglutide or "GLP-1 agonist" in Title or Abstract 635 results
35 antiplatelet* or "anti-platelet*" or DAPT in Title or Abstract 1489 results
36 aspirin or "acetylsalicylic acid" or clopidogrel or dipyridamole or prasugrel or ticagrelor or cangrelor or ticlopidine in Title or Abstract 1622 results

37 Anticoagulant* or "anti coagulant*" or NOAC* or "blood thinner*" in Title or Abstract 2332 results
38 (drug* or medication*) adj3 "blood clot*" in Title or Abstract 24 results
39 warfarin or Coumadin or rivaroxaban or Xarelto or dabigatran or pradaxa or apixaban or Eliquis or edoxaban or lixiana in Title or Abstract 1202 results
40 (drug* or medication*) adj3 diabet* in Title or Abstract 477 results
41 "sodium-glucose co-transporter-2 inhibitor*" or "SGLT2 inhibitor*" in Title or Abstract 682 results
42 "DPP-4 inhibitor*" or gliptin* or alogliptin or linagliptin or saxagliptin or sitagliptin in Title or Abstract 436 results
43 dapagliflozin or forxiga or metformin or insulin or sulphonylurea* or "alpha glucosidase inhibitor*" or empagliflozin in Title or Abstract 5785 results
44 Polypill* in Title or Abstract 29 results
45 "cardioprotective drug*" or "cardioprotective medication*" or "cardio protective drug*" or "cardio protective medication*" in Title or Abstract 21 results
46 #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 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 in All text 16567 results

47 #46 and #23 in All text 5950 results

6. Appendix 2

Example evidence presentation and risk of bias assessment

Adobe Acrobat Document