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Recommendations for the primary prevention of atherosclerotic cardiovascular disease in primary care: study protocol for a systematic guideline review

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ABSTRACT

Introduction Atherosclerotic cardiovascular disease (ASCVD) was the main cause of death in Germany in 2021, with major risk factors (ie, hypertension, diabetes, dyslipidaemia, obesity and certain lifestyle factors) being highly prevalent. Preventing ASCVD by assessment and modification of these risk factors is an important challenge for general practitioners. This study aims to systematically review and synthesise recent recommendations of national and international guidelines regarding the primary prevention of ASCVD in adults in primary care.

Methods and analysis We will conduct a systematic review of clinical practice guidelines (CPGs) to evaluate primary prevention strategies for ASCVD. CPGs will be retrieved from MEDLINE and the Turning Research Into Practice database, guideline-specific databases and websites of guidelines-producing societies, with searches limited to publications from 2016 onwards. We will include CPGs in English, Spanish, German or Dutch languages that provide evidence-based recommendations for ASCVD prevention. The study population will include adults without diagnosed ASCVD. Two independent reviewers will assess guideline eligibility and quality by means of the mini-checklist MiChe, and extract study characteristics and relevant recommendations for further consistency analysis. A third reviewer will resolve disagreements. Findings will be presented as a narrative synthesis and in tabular form.

Ethics and dissemination This review does not require ethical approval. Our systematic review will inform the CPG of the German College of General Practitioners and Family Physicians on the primary prevention of ASCVD. The review results will also be disseminated through publications in peer-reviewed journals and presentations at local, national and international conferences.

PROSPERO registration number CRD42023394605.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ We will conduct a systematic search in the most relevant literature databases, applying a highly sensitive search strategy, which will be complemented by a manual search in guideline-specific databases and websites.
⇒ The two-step approach to guideline assessment developed by Muth *et al* will be applied by rating the quality of included guidelines using the mini-checklist (MiChe), and by performing a consistency analysis of the recommendations within these guidelines.
⇒ To meet the expected challenge of great heterogeneity among the clinical practice guidelines included, we will use qualitative data analysis software.
⇒ While the review will include a broad spectrum of clinically relevant questions and population subgroups, paediatric populations and secondary prevention of cardiovascular disease will not be covered.

INTRODUCTION

Similar to other developed countries, cardiovascular disease (CVD) is the main cause of death in Germany, with 33% of all deaths being attributable to it in 2021.[1] Atherosclerotic CVD (ASCVD) involves the build-up of cholesterol plaque in the coronary, cerebral, iliac and femoral arteries and the aorta, and includes mainly coronary heart disease, stroke and transient ischaemic attacks, peripheral artery disease and aortic disease.[2] The most important modifiable ASCVD risk factors include hypertension, diabetes, dyslipidaemia, obesity and certain lifestyles, such as smoking, physical inactivity and unhealthy diet.[3 4] Almost every third adult in Germany (31% of women and 33% of men) has been diagnosed with high blood pressure.[5] Diabetes (excluding gestational diabetes) affects 8% of adults,[6] and 65% of men and 66% of women suffer from dyslipidaemia.[7] Furthermore, 47% of women and 61% of men in Germany have excess weight, and both women and men suffer from obesity in 19% of the

cases.[8 9] Only 45% of the German population maintains 2.5 hours of moderate-intensity aerobic physical activity per week, as recommended by the WHO,[10 11] and 29% of adults in Germany smoke at least occasionally.[12] These risk factors are also highly prevalent in other industrialised societies,[13–16] making cardiovascular prevention an important issue not only for Germany but for other European countries as well.

Modification of these risk factors by either lifestyle changes or/and pharmacological treatment can reduce the risk of cardiovascular events.[17–22] In Germany, most interventions on primary prevention are designated to be implemented through general practitioners (GPs).[23] Due to the continuity of care, GPs are well positioned to weigh individual risks and benefits for their patients, help them make informed decisions, and follow them up to help maintain behavioural and pharmacological changes.[24–26]

Clinical practice guidelines (CPGs) are evidence-informed recommendations intended to optimise patient care. Currently, the German College of General Practitioners and Family Physicians (Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin e. V.,) is updating its CPG on the primary prevention of ASCVD. The guideline will address counselling of adult patients with no clinically manifested or established diagnosis of ASCVD on prevention of cardiovascular events. It will include recommendations on whether a patient should be offered counselling, how to calculate the (untreated) global cardiovascular risk and what are the available options to reduce this risk (ie, lifestyle changes, medical treatment) and desirable and undesirable effects of these options. Finally, the guideline will include strategies to improve the communication of the recommendations to patients, including optimal ways to explain the risks, offer preventive options, discuss uncertainties and support patients in the implementation of their health-related decisions. Our systematic guideline review aims to inform the German guideline, but may also be helpful for other guideline developers as well as clinicians. The review question is: 'What are the recommendations of national and international guidelines regarding the primary prevention of ASCVD in adults in primary care?' Special consideration will be given to the individualisation of recommendations for different age groups, ethnicity, sex, and gender, and for persons living with diabetes, multimorbidity (including frailty) and polypharmacy.

METHODS AND ANALYSIS

We will conduct a systematic review of CPGs based on the systematic guideline review methodology described by Muth *et al*.[27 28] The present protocol has followed the Preferred Reporting System Items for Systematic Review and Meta-Analysis Protocols checklist[29] (see online supplemental file 1). The protocol of this review has been registered with PROSPERO (CRD42023394605) and will be updated in case of any future changes.

Inclusion and exclusion criteria

Type of records

We will include CPGs providing recommendations for the primary prevention of cardiovascular events (ie, myocardial infarction, stroke or death) in adults without a diagnosis of CVD. We will consider eligible CPGs that are informed by a systematic review of evidence, provide references for the evidence underlying their recommendations and an assessment of the benefits and harms of alternative care options.[30] As we aim to focus on evidence that has emerged since the last update of the German guideline in 2016, we will include guidelines in English, Spanish, German or Dutch languages that have been published or updated since 2016. We will exclude expired guidelines as established by their developers. We will also exclude guidelines that were not published on behalf of a professional organisation, and guidelines that do not apply a global CVD risk assessment approach.[31]

Target population

We will include guidelines providing recommendations on the management of cardiovascular risk factors (eg, type 2 diabetes, hypertension, smoking, dyslipidaemia, obesity, physical inactivity, unhealthy diet) for persons 18 years of age or older, without a diagnosis of manifested ASCVD (ie, without symptoms of coronary heart disease, peripheral arterial disease, heart failure and cerebrovascular disease, including transient ischaemic attack). We will exclude guidelines focusing on specific target populations (ie, pregnant women) and specific healthcare processes (eg, bridging in preparing for surgery), as well as disease or condition-specific guidelines unless primary prevention of ASCVD is within the scope of the guideline.

Type of intervention

We will include guidelines on all types of primary care interventions aimed at the primary prevention of cardiovascular events, such as risk assessment, risk communication, counselling, decision-making, and non-pharmacological and pharmacological prevention.

Scope of the included guidelines

We include guidelines that encompass the primary prevention of ASCVD in their scope. The algorithm for the inclusion and exclusion criteria is presented in online supplemental file 2.

Literature search and selection

Information sources

We will search MEDLINE via PubMed using a combination of Medical Subject Headings (MeSH) (eg, cardiovascular diseases, primary prevention, clinical practice guideline) and keywords (eg, cardiovascular, prevent, guideline), and also the 'Turning Research Into Practice' (TRIP) database using keywords (eg, cardiovascular disease, primary prevention, guideline), filtering both databases for publication date from 2016 onwards. For the full search strategy in Medline and TRIP, please see online supplemental file 3. In addition, we will search guideline-specific databases

(eg, Scottish Intercollegiate Guidelines Network) and websites of guidelines-producing societies in the fields of cardiology, hypertension, diabetes and primary care (eg, the US Preventive Services Task Force). Therefore, our search strategy will be strengthened by using the code for CPGs, in addition to the PubMed filter, and by searching guideline-specific resources. The full list of guideline-specific databases and websites is provided in online supplemental file 4.

Study records

Data management

Bibliographic details of all records identified in MEDLINE and TRIP will be downloaded as RIS files and uploaded into the reference manager, Zotero.[32] Subsequently, they will be imported into a systematic review platform, Covidence,[33] for duplicate elimination and screening. The retrieval of full texts will be performed using Zotero, while screening for eligibility and assessing the guideline quality will be carried out and documented using Covidence.

Selection of records

Two researchers will independently screen titles and abstracts for eligibility. Prior to the screening, a stepwise calibration test will be performed on a sample of 30 records, with the aim of achieving 80% agreement between reviewers.[34] If an 80% agreement is not achieved, our inclusion and exclusion criteria will be refined, and the calibration will be repeated until the threshold is met. We will report changes to the inclusion and exclusion criteria that result from the calibration test as deviations from the published protocol. Two reviewers will then independently assess the full texts of potentially relevant guidelines for eligibility to be included in the review. Any discrepancy will be resolved through discussion and consensus. If needed, a third reviewer will be involved.

The guideline repositories and the societies' websites will be handsearched independently by two reviewers, and the search will be documented. References of included guidelines will be checked for possible inclusion of additional CPGs in this review.

Dealing with duplicate and associated records

CPGs identified from the search will be saved in the reference manager, including their full-text version and any related documents (eg, methodological and evidence reports, journal publications, executive summaries). All documents associated with a particular guideline will be grouped and treated as one unit of observation (ie, as a 'guideline document set'). We will join the records revealed by the manual search of the guideline repositories and the societies' websites with the records found by searching PubMed and TRIP, and will eliminate duplicates.

Data collection and data items

Two review authors will extract data from the included guidelines in two subsequent stages[27 28]:

First, the characteristics of the complete guideline document set will be revised and the following items will be extracted using the data extraction form in MS Excel developed for this study: (1) guideline identification (ie, name, year of publication, country of origin), (2) target audience (eg, primary care professionals), (3) target population and (4) outcomes addressed.

Second, individual recommendations will be extracted from each guideline using the ATLAS.ti software, to be further subjected to qualitative data analysis.[35] The consistency analysis will be performed in an Excel file. Recommendations that are out of the scope of primary ASCVD prevention will not be included. The analysis of recommendations will require extraction of the following data items: (1) clinically relevant question addressed, (2) scope and directionality of recommendation, (3) grade of recommendation, (4) level of evidence, (5) guideline authors' evaluation of the evidence and (6) cited literature. We will use a code system in ATLAS.ti to identify text segments that are relevant to the type of interventions included in our review, based on a predefined framework. Hence, the main categories of the code system will be risk assessment, risk communication, counselling, decision-making, and non-pharmacological and pharmacological interventions. The categories in the code system will also be provided for the subgroups of the population included in our review (ie, persons with diabetes, multimorbidity, polypharmacy, different age groups and persons of different ethnicity, gender and sex, including non-binary sex and gender categories). Women's health issues such as menopause, hormone replacement therapy or previous pregnancy-related complications will be included in the assessment. The definition of ethnicity will be based on the approach used in individual international guidelines. If the guideline does not make a clear distinction between ethnicities, a publishing region will be used as a proxy for ethnicity. For German guidelines, 'persons with a migration background' will be used as a definition of non-German ethnicity.

Information on particular interventions referring to specific populations will be double-coded. Coding will then allow for the targeted retrieval and synopsis of all text segments belonging to specific categories.[35] One researcher will code the data and another researcher will check the output for errors and plausibility.

Assessment of quality

The quality of the CPGs will be appraised by two researchers using the MiChe list.[36 37] This checklist consists of eight specific questions and two holistic items. The overall assessment is rated on a Likert scale ranging from '1' (very good) to '7' (very poor) (see online supplemental file 5). The results of the quality assessment will be presented in a tabular form. Any discrepancy in the quality assessment will be resolved through discussion and consensus, with the involvement of a third reviewer, if needed.

Consistency analysis and validation

Recommendations put forward in the included CPGs will be assessed by consistency analysis.[27] Two reviewers will compare the content (ie, scope and directionality) and cited literature (ie, level of evidence and grading) of the recommendations on similar interventions provided by different included guidelines. The findings will be categorised into six types of categories based on their external consistency and evidence base (ie, four types of consistency and two types of inconsistency (major and minor)). Any discrepancy will be solved by a third reviewer.

In addition, two reviewers will validate the quality of evidence by the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) criteria,[38] and any discrepancy will be solved by a third reviewer if needed.

Data synthesis

Key findings, such as the extracted recommendations, will be presented in tables. The narrative synthesis of our findings will be structured according to the clinically relevant questions defined by the qualitative text analysis of the data.[39]

All extracted data on population subgroups (eg, persons living with multimorbidity) will be categorised by subgroups and in relation to specific interventions (ie, non-pharmacological or pharmacological). We will conclude by pointing out the knowledge gaps that require further research to optimise guidelines on the primary prevention of ASCVD in Germany.

Patient and public involvement

Advisory panels of patients and of GPs will be involved in the guideline development project. They will be invited to participate in the interpretation of findings from the systematic guideline review and to propose additional perspectives for complementary literature searches.

ETHICS AND DISSEMINATION

This study does not require ethical approval.

We will disseminate the results of this study through publications in peer-reviewed journals and presentations at local, national and international conferences. The updated guideline will be published on the AWMF website, registry no. 053-024: (https://www.awmf.org), together with a comprehensive report presenting the included evidence. Supporting materials will include an executive summary, decision aids, materials for patients in several languages, and a guide for teaching activities for students and practitioners, and will therefore contribute to knowledge dissemination.

The project data files (data extraction files, ATLAS.ti files, etc), along with study protocol and full search strategies, will be stored at the repository of Phillips University, Marburg (data_UMR) and will be accessible according to the FAIR principles (https://www.go-fair.org/fair-principles).

Contributors LS and MB wrote the initial draft of the protocol. JH and CM developed the concept and are the guarantors of the review. AIG-G, SP, VvdW, JH and CM are co-supervisors of the project, provided advice through the development of the protocol, and contributed to the revision of the manuscript. All authors read and approved the final manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

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