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## **Patients' and general practitioners' attitudes and perceptions towards the initiation of preventive drugs for primary prevention of cardiovascular disease: protocol for a systematic review of qualitative studies**

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**TITLE**

**Patients' and general practitioners' attitudes and perceptions towards the initiation of preventive drugs for primary prevention of cardiovascular disease: protocol for a systematic review of qualitative studies**

**AUTHORS**

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**KEYWORDS**

systematic review; qualitative research; cardiovascular disease; attitudes; perceptions; drug initiation; statins; antihypertensive drugs; primary prevention

**WORD COUNT**

2307 words (excluding title page, abstract, references, figures and tables).

## ABSTRACT

**Introduction:** Lipid lowering drugs and antihypertensive agents can be prescribed for the primary prevention of cardiovascular disease. In some cases, eligible patients are not started on preventive drugs. We aim to systematically review qualitative studies assessing general practitioners' and patients' attitudes and perceptions towards drug initiation for primary prevention of cardiovascular disease.

**Methods and analysis:** MEDLINE, MEDLINE In Process, EMBASE, PsychINFO, CINAHL and Applied Social Sciences Index and Abstracts (ASSIA), Conference Proceedings Citation Index (Web of Science), Healthcare Management Information Consortium (HMIC) and Open Grey will be searched without restrictions on date or language of publication. Searches will be limited to studies of qualitative design, standalone or in the context of a mixed-method design, focusing on cardiovascular drug initiation for primary prevention. The primary outcome is the attitudes of general practitioners and patients towards preventive drug initiation. Two reviewers will independently carry out the study selection, data extraction and quality assessment. The Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist will be used to assess the quality of included studies. The findings will be analysed using thematic synthesis.

**Ethics and dissemination:** This systematic review does not require ethical approval as primary data will not be collected. The results of the study will be published in a peer-reviewed journal and presented at relevant conferences.

**Systematic review registration:** PROSPERO CRD42018095346

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- This review will utilize a systematic approach to summarize qualitative evidence on preventive drug initiation in primary care settings
- It will provide a better understanding of what influences GPs' and patients' decisions regarding initiation of preventive treatment.
- The study will not review studies addressing the initiation of aspirin for the primary prevention of cardiovascular disease.

## INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of deaths worldwide <sup>1</sup>. It accounts for 26% of deaths in the United Kingdom and 31% of deaths globally <sup>1 2</sup>. One of the ways to prevent CVD is through prescribing drugs for primary prevention. National and international guidelines recommend primary preventive treatment for patients at an increased risk of developing a cardiovascular event <sup>3-6</sup>. Patients considered at an increased risk include patients who have a 10-year CVD risk of 10% or more or patients with clinically measured blood pressure of 140/90 mmHg or higher <sup>4 6</sup>. The recommendations are supported by evidence from clinical trials demonstrating the beneficial effects of lipid lowering drugs and antihypertensive agents in the primary prevention of CVD <sup>7-10</sup>. However, studies have reported low prescribing rates of preventive drugs <sup>11-14</sup>. Patients eligible for statins are undertreated <sup>13 14</sup>; one study has reported that 50% of patients with a CVD risk  $\geq 20\%$  were not prescribed statins for primary prevention <sup>14</sup>. In addition, the detection and treatment of hypertension remains low in parts of the world <sup>15 16</sup>. 49% of adults with hypertension aged 35-84 years were treated in Japan compared to 80% in the United States <sup>15</sup>. However, the initiation rate for antihypertensive drugs in younger eligible adults in the United States is suboptimal <sup>17</sup>. A study that explored antihypertensive drug initiation among young adults with regular access to primary care found that only 34% of patients aged 18-39 years were started on antihypertensive drugs compared to 44% of patients aged 40-59 years <sup>17</sup>.

The suboptimal prescribing patterns may be a result of GPs' poor adherence to guideline recommendations. A study conducted in German general practices estimated that around 50% of GPs did not adhere to the guidelines <sup>18</sup>. GPs have expressed concerns regarding the evidence the guidelines were based on and whether following the guidelines will allow them to meet their patients' needs <sup>19 20</sup>. Nevertheless, the variation in prescribing patterns indicates that there are patient- and GP-related barriers to initiating primary preventive treatment. Previous research identified GP-related barriers such as concerns about patient adherence to medication, over-medicalization of healthy individuals and side effects <sup>21</sup>. With respect to patient-related barriers, a study reported that patients preferred making lifestyle changes and had concerns about the side effects of taking medication <sup>22</sup>. In

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2  
3 addition, patients' trust in their GP's medical judgment played a role in accepting  
4 preventive treatments<sup>22</sup>.  
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7 We are interested in studies that explore the attitudes of GPs and patients towards  
8 initiating treatments for the primary prevention of CVD. A scoping search was carried  
9 out to identify existing literature and to estimate the volume of studies available on  
10 our topic of interest. The majority of published studies address the issue of  
11 adherence to medication or prescribing drugs for secondary prevention<sup>23 24</sup>.  
12  
13 However, the search retrieved a number of qualitative studies that investigate patient  
14 and health professional-related factors influencing drug prescribing for primary  
15 prevention. The search retrieved a systematic review published in 2012 that  
16 assessed qualitative literature about initiating and adhering to preventive drugs for  
17 CVD. The review discussed factors associated with initiating preventive medication  
18 and reported that initiation was influenced by the health professional-patient  
19 relationship and the organizational structure of the clinical environment<sup>25</sup>. The  
20 authors focused on starting and adhering to preventive medication with no  
21 differentiation between primary and secondary prevention. In addition, studies were  
22 excluded from the review based on quality assessment. Our review will consider all  
23 primary studies addressing our topic of interest regardless of quality to capture all  
24 available evidence regarding prescribing cardiovascular drugs for primary  
25 prevention. Furthermore, the search retrieved one recently published systematic  
26 review that explored patients' attitudes towards taking statins. However, the review  
27 did not explore the attitudes of GPs towards statins and was restricted to studies in  
28 the English language<sup>26</sup>. The authors explored attitudes only towards statin uptake  
29 without differentiating between primary and secondary prevention. The reasons  
30 behind taking statins might be different in patients who had a CVD event and  
31 patients who are yet to experience a CVD event. Our review will explore a wider  
32 range of cardiovascular preventive drugs. We will focus on the uptake of such drugs  
33 for primary prevention because initiating therapy in relatively asymptomatic patients  
34 can be challenging for both the health professional and the patient and attitudes  
35 relating to this preventive approach needs to be identified for successful primary care  
36 preventive prescribing. Both reviews did not explore grey literature. Our review aims  
37 to explore grey literature databases to maximize the chances of capturing relevant  
38 studies.  
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3 The decision-making process involved in initiating preventive treatments is complex  
4 and influenced by multiple factors that relate to both the GP and the patient. Thus,  
5 an up-to-date, methodologically robust systematic review aiming to identify the  
6 attitudes and perceptions of GPs and patients towards the initiation of preventive  
7 drugs for the primary prevention of CVD is warranted.  
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### 11 12 13 14 **Objectives**

- 15 • Explore GPs' and nurse practitioners' attitudes and perceptions in relation to  
16 initiating preventive drugs for primary prevention of CVD in primary care  
17 settings.  
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- 19 • Explore patients' attitudes and perceptions towards initiating preventive drugs  
20 for primary prevention of CVD in primary care settings.  
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### 27 **METHODS AND ANALYSIS**

28 This protocol will use the Preferred Reporting Items for Systematic Review and  
29 Meta-Analysis Protocols (PRISMA-P) guidelines to ensure comprehensive reporting  
30 of study items<sup>27</sup>. The protocol is registered with PROSPERO (CRD42018095346).  
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32 The systematic review will follow the reporting guidelines formulated in the  
33 Enhancing transparency in reporting the synthesis of qualitative research (ENTREQ)  
34 statement<sup>28</sup>.  
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#### 42 **Information sources and search strategy**

43 The Sample, Phenomenon of Interest, Design, Evaluation, Research type (SPIDER)  
44 tool is considered an alternative to PICOS when addressing a qualitative review  
45 question and will be used in the proposed systematic review to formulate the search  
46 strategy<sup>29</sup>. The search strategy will include a combination of free text words and  
47 index terms relating to (drug initiation OR prescription OR decision making) and  
48 (attitudes OR experiences OR perceptions OR views OR behaviour) and  
49 cardiovascular disease. The formulated search strategy will be applied to MEDLINE  
50 database (including MEDLINE In Process) then adapted with necessary adjustments  
51 for use in other databases. We will search EMBASE, PsychINFO, CINAHL and  
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3 Applied Social Sciences Index and Abstracts (ASSIA) for published studies. In  
4 addition, the following grey literature sources will be searched: Conference  
5 Proceedings Citation Index (Web of Science), Healthcare Management Information  
6 Consortium (HMIC) and Open Grey. The reference lists of included studies will be  
7 checked to identify additional eligible studies which were not retrieved by the  
8 formulated search strategy. There will be no restriction on date or language of  
9 publication. The search will be limited to studies of qualitative design.  
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### 17 **Eligibility criteria**

#### 18 *Sample*

19 We will include studies of primary care health professionals (GPs and nurse  
20 practitioners), in any country, who prescribe cardiovascular preventive drugs. In  
21 addition, we will include studies that target patients who are offered a prescription for  
22 statins or antihypertensive drugs in a primary care setting. Studies that focus on  
23 practitioners or patients involved in the process of decision making or initiation of  
24 cardiovascular drugs will be included. Any study that examines practitioners who  
25 prescribe preventive drugs and patients who receive such prescriptions for  
26 secondary prevention of CVD will be excluded. Studies conducted in secondary care  
27 settings will be excluded.  
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#### 35 *Phenomenon of interest*

36 Studies will be considered for inclusion if they assess patient or practitioner factors  
37 associated with the initiation of cardiovascular preventive drugs in primary care  
38 settings. Initiation refers to the prescription of preventive drugs by the practitioner  
39 and the patient agreeing to take medication for preventive purposes. Therefore,  
40 studies that focus on decision making or discuss barriers and facilitators to  
41 prescription for primary prevention of CVD will be included. We will exclude studies  
42 that focus on adherence and continuation of cardiovascular preventive drugs.  
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#### 49 *Design / Research type*

50 Our review aims to look at aspects such as attitudes and perceptions. These are  
51 best explored through a qualitative approach. Therefore, any qualitative studies,  
52 stand alone or in the context of a mixed-method design, focusing on cardiovascular  
53 drug prescription for primary prevention will be included. A summary of Sample,  
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Phenomenon of Interest, Design, Evaluation, Research type (SPIDER) is provided in Table 1.

**Table 1. Summary of Sample, Phenomenon of Interest, Design, Evaluation, Research type (SPIDER)**

Sample	<ul style="list-style-type: none"> <li>- General practitioners or nurse practitioners who prescribe statins or antihypertensive drugs.</li> <li>- Patients eligible for cardiovascular preventive drugs or offered a prescription of statin or an antihypertensive drug for primary prevention of cardiovascular disease.</li> </ul>
Phenomenon of Interest	The initiation or prescription of statins or antihypertensive drugs.
Design	Studies including qualitative data collection or analysis methods.
Evaluation	Attitudes, perceptions, views or experiences of general practitioners, nurse practitioners or patients related to the initiation of cardiovascular preventive drugs.
Research type	Qualitative and mixed methods studies.

### *Evaluation*

Studies that address the attitudes, perceptions, views or experiences of GPs, nurse practitioners or patients involved in the process of cardiovascular preventive drug initiation will be considered for inclusion. To adhere to the European guidelines, we will include studies that target the prescription of statins or antihypertensive drugs (4-6). We will exclude studies that target the prescription of aspirin as its use for primary prevention is not recommended by several guidelines (5, 27). In addition, studies that assess the attitudes and perceptions of practitioners or patients towards the prescribing of fibrates, niacin, bile acid sequestrants and Omega-3 fatty acid compounds will be excluded as these drugs are not recommended for the primary prevention of CVD<sup>4 5</sup>. In some countries, a polypill that contains a lipid lowering agent and a blood pressure lowering agent is prescribed for CVD risk reduction<sup>30</sup>. Thus, we will consider studies that assess GPs' and patients' attitudes towards polypills.

### **Selection process**

The literature search results will be imported into Endnote X8 (Thomson Reuters, New York), to ensure efficient management of references and to facilitate the study selection process. The process of selecting studies will be carried out in two stages by two independent reviewers. The reviewers will follow explicit inclusion/exclusion criteria to minimize potential bias and to ensure minimal influence of the reviewers' preconceptions. The inclusion/exclusion form is presented in (Appendix 1). The first stage of selection will include screening the titles and abstracts of all identified records against the inclusion criteria. If a study addresses our topic but the abstract lacks sufficient information to assess eligibility for inclusion, the full text will be retrieved to make a definitive decision. In the second stage of selection the two reviewers will retrieve the full texts of included studies and assess them for eligibility. Any disagreements during the selection process will be resolved through discussion. If the two reviewers fail to reach an agreement, a third independent reviewer will be involved for an unbiased decision. The reviewers will keep a record for each article that they have assessed and justify their decision for either inclusion or exclusion. The selection process will be piloted on a small number of studies by the main reviewer to ensure the reliability of the inclusion criteria. The selection process will be illustrated using a PRISMA flow diagram<sup>27</sup>.

### **Data extraction process**

An electronic standardised data extraction form will be developed to ensure adequate and consistent extraction of all required information. The form will be piloted using a small number of studies to ensure reliability and validity and adjusted if necessary. The electronic form will be used to record extracted data on study characteristics, participants' details, theoretical approach, data collection methods, data analysis and findings (Appendix 2). Once extraction is completed by the two reviewers, the forms will be reviewed, and any discrepancies will be resolved through discussion. If the two reviewers fail to reach agreement, a third reviewer will be involved.

### **Critical appraisal**

Two independent reviewers will appraise the quality of the included studies using the Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist<sup>31</sup>. The assessment of quality will be based on the study aims, methodology, study design, sample recruitment, reflexivity, data collection, data analysis, findings, value of research and ethics. The reviewers will keep a record of the quality assessment for each study with an explanation of their decision. Any disagreements will be resolved by discussion or referral to a third independent reviewer. Studies will not be excluded from the review based on quality.

### **Data synthesis**

The NVivo10 software will be used to analyse qualitative data. We will adopt a method of thematic synthesis defined by Thomas and Harden for synthesising qualitative data in systematic reviews<sup>32</sup>. Thematic synthesis includes three stages: First, line by line examination of studies' findings and assigning codes to each line of text based on the meaning and content. Second, codes are then grouped into a hierarchical structure and organized as descriptive themes. Finally, analytical themes will be generated to provide interpretations that surpass the findings of the primary studies and ultimately answer our review question. The thematic synthesis will be carried out by two independent reviewers. The reviewers will discuss the codes and themes with an advisory team and then agree on the analytical stage of thematic synthesis.

### **Patient and public involvement**

This protocol was completed without patient or public involvement. Patients were not invited to contribute to the development of this protocol.

### **DISCUSSION**

The GP's decision to prescribe a preventive drug and the patient's willingness to start treatment for preventive purposes is a multifactorial process. It is essential to understand this process of decision making from a qualitative perspective to enable a more effective approach to cardiovascular disease prevention. This review will summarize the qualitative evidence available on healthcare professionals' and patients' attitudes towards drug initiation. The findings will help us to understand the complex interaction that occurs during the consultation visit between the patient and

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3 their GP and provide evidence to inform healthcare professionals and policy makers  
4 regarding barriers and facilitators to primary care cardiovascular preventive  
5 prescribing.  
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## 8 **ETHICS AND DISSEMINATION**

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10 This review will utilize information available from primary studies. Data will not be  
11 collected from individuals therefore ethical approval is not required. We aim to  
12 disseminate the findings of our review through publication in a peer-reviewed journal  
13 and presentation at a relevant conference.  
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## 17 **AUTHORS' CONTRIBUTIONS**

18  
19 OQ formulated the research question, performed the scoping search and wrote the  
20 first draft. OQ and DB refined research question and search strategy. TM, DB, NA  
21 reviewed and revised the draft. All authors read and approved the final manuscript.  
22  
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26  
27 OQ is funded by a governmental scholarship, the study is sponsored by the  
28 University of Birmingham.  
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## 31 **COMPETING INTERESTS**

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33 None declared.  
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For peer review only

1 **APPENDICES**

2  
3 **Appendix 1. Inclusion/exclusion form for study selection**

	<b>Include</b>	<b>Yes</b>	<b>No</b>	<b>Unclear</b>	<b>Exclude</b>
<b>Research type</b>	<ul style="list-style-type: none"> <li>▪ Qualitative study, standalone</li> <li>▪ Qualitative study in the context of mixed method</li> <li>▪ Review of qualitative studies</li> <li>▪ Other, specify:</li> </ul>	<input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>	<input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>	<input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Quantitative study</li> <li>▪ Clearly commentary/letter with no data from primary studies</li> <li>▪ Other, specify:</li> </ul>
<b>If clearly excluded on study design – STOP HERE</b>					
<b>Sample</b>	<ul style="list-style-type: none"> <li>▪ Primary care Health professionals</li> <li>- General practitioner</li> <li>- Nurse practitioner</li> <li>- Other, specify:</li> <li>▪ Patients treated in primary care</li> </ul>	<input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>	<input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>	<input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Secondary or tertiary care health professionals</li> <li>▪ Patients treated in Secondary or tertiary care</li> </ul>
<b>Phenomenon of Interest</b>	<ul style="list-style-type: none"> <li>▪ Lipid lowering drugs initiation or prescription</li> <li>▪ Antihypertensive drugs initiation or prescription</li> <li>▪ Drug initiation or prescription for primary prevention of CVD</li> </ul>	<input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>	<input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>	<input type="checkbox"/>  <input type="checkbox"/>  <input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Initiation or prescription of:                             <ul style="list-style-type: none"> <li>- Aspirin</li> <li>- Fibrates</li> <li>- Niacin</li> <li>- Bile acid sequestrants</li> <li>- Omega-3 fatty acid compounds</li> </ul> </li> <li>▪ Adherence to medication</li> <li>▪ Discontinuation of medication</li> <li>▪ Other, specify:</li> </ul>
<b>Design</b>	<ul style="list-style-type: none"> <li>▪ Qualitative data collection, specify:</li> <li>▪ Qualitative data analysis, specify:</li> </ul>	<input type="checkbox"/>  <input type="checkbox"/>	<input type="checkbox"/>  <input type="checkbox"/>	<input type="checkbox"/>  <input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Quantitative data collection or analysis with no qualitative component</li> </ul>

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<p><b>Evaluation</b></p>	<p style="text-align: right;">□ □ □</p> <ul style="list-style-type: none"> <li>▪ Attitudes, perceptions, views, experiences, patient or health professional related Factors influencing cardiovascular drug initiation or prescription for primary prevention</li> </ul>	<ul style="list-style-type: none"> <li>▪ Attitudes, perceptions, views, experiences, patient or health professional related factors influencing cardiovascular drug initiation or prescription for secondary prevention <span style="float: right;">□</span></li> <li>▪ Factors influencing drug adherence or discontinuation <span style="float: right;">□</span></li> <li>▪ Other, specify:</li> </ul>
--------------------------	--	--

If "NO" in any of the categories, exclude

<p><b>Comments</b></p>	
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## Appendix 2. Data collection form

<b>Reviewer name (collecting data)</b>		
<b>Data collection date</b>	Click or tap to enter a date.	
<b>Reviewer name (reviewing collected data)</b>		
<b>Data review date</b>	Click or tap to enter a date.	
<b>Amendments</b>		
<b>Date of amendment</b>	Click or tap to enter a date.	
<b>Notes</b>		
<b>Study Bibliographic details</b>		
<b>First author</b>		
<b>Publication date</b>	Click or tap to enter a date.	
<b>Country</b>		
<b>Study characteristics</b>		
<b>Study type</b>	<input type="checkbox"/> Qualitative <input type="checkbox"/> Mixed method	
<b>Study aim</b>	What was the purpose or aim of the study	
<b>Theoretical approach</b>	What theoretical perspective is the study based on?	
<b>Setting</b>	What is the geographical location and setting of the study?	
<b>Participants</b>		
<b>Type of participants</b>	Who was included in the study	<input type="checkbox"/> Patient <input type="checkbox"/> General practitioner <input type="checkbox"/> Nurse practitioner
<b>Recruitment</b>	How were participants recruited?	
<b>Participants excluded</b>	Were there any participants excluded?	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Reason of exclusion:	
<b>Total number of participants</b>		

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3	<b>Number of males</b>		
4	<b>Number of females</b>		
5	<b>Age of participants</b>		
6			
7	<b>Methods</b>		
8	<b>Method of data collection</b>	How was data collected?	<input type="checkbox"/> Interview
9			<input type="checkbox"/> Survey
10			<input type="checkbox"/> Questionnaire
11			<input type="checkbox"/> Focus group
12			<input type="checkbox"/> Other
13			
14	<b>Additional details about data collection</b>		
15			
16	<b>Data collection duration</b>	What is the start and end date of the data collection?	
17			
18	<b>Method of data analysis</b>	How was the data analysed?	
19			
20	<b>Additional details about data analysis</b>		
21			
22	<b>Findings</b>		
23			
24	<b>Main findings</b>	What are the main findings of the study?	
25			
26	<b>Descriptive themes</b>	What descriptive themes were reported?	
27			
28	<b>Author interpretation</b>	What are the interpretations of results provided by the authors?	
29			
30	<b>Study strengths and weakness</b>	What are the key strengths and weaknesses of the study?	
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**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item
<b>ADMINISTRATIVE INFORMATION</b>		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments
Support:		
Sources	5a	Indicate sources of financial or other support for the review
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
<b>INTRODUCTION</b>		
Rationale	6	Describe the rationale for the review in the context of what is already known
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)
<b>METHODS</b>		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated
Study records:		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review

5	Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)
7	Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators
9	Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications
11	Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale
13	Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis
15	Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised
16		15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )
17		15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)
18		15d	If quantitative synthesis is not appropriate, describe the type of summary planned
20	Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)
21	Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

# BMJ Open

**Patients' and health professionals' attitudes and perceptions towards the initiation of preventive drugs for primary prevention of cardiovascular disease: protocol for a systematic review of qualitative studies**

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-025587.R1
Article Type:	Protocol
Date Submitted by the Author:	27-Jan-2019
Complete List of Authors:	Qadi, Olla; Institute of Applied Health Research, University of Birmingham, ; Marshall, Tom; University of Birmingham, Public Health and Epidemiology Adderley, Nicola; Institute of Applied Health Research, University of Birmingham Bem, Danai; University of Birmingham, Institute of Applied Health Research
<b>Primary Subject Heading</b>:	Public health
Secondary Subject Heading:	Public health, Qualitative research
Keywords:	systematic review, QUALITATIVE RESEARCH, cardiovascular disease, attitudes, drug initiation, primary prevention

SCHOLARONE™  
Manuscripts

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3 1 **TITLE**  
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7 3 **Patients' and health professionals' attitudes and perceptions**  
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9 4 **towards the initiation of preventive drugs for primary prevention of**  
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11 5 **cardiovascular disease: protocol for a systematic review of**  
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13 6 **qualitative studies**  
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17 8 **AUTHORS**

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19 9 Olla Qadi<sup>1</sup>, Tom Marshall<sup>1</sup>, Nicola Adderley<sup>1\*</sup>, Danai Bem<sup>1</sup>

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32 14 **KEYWORDS**

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35 15 systematic review; qualitative research; cardiovascular disease;  
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37 16 attitudes; perceptions; drug initiation; statins; antihypertensive drugs;  
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39 17 primary prevention  
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44 19 **WORD COUNT**

45  
46 20 2507 words (excluding title page, abstract, references, figures and  
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48 21 tables).  
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## 28 **ABSTRACT**

29 **Introduction:** Lipid lowering drugs and antihypertensive agents can be prescribed  
30 for the primary prevention of cardiovascular disease. In some cases, patients eligible  
31 for primary prevention of cardiovascular disease according to the European  
32 guidelines are not always started on preventive drugs. Existing research explores the  
33 attitudes of health professionals and patients towards cardiovascular preventive  
34 drugs but does not always differentiate between the attitudes towards drug initiation  
35 for primary or secondary prevention. We aim to systematically review qualitative  
36 studies assessing health professionals' and patients' attitudes and perceptions  
37 towards drug initiation for primary prevention of cardiovascular disease.

38 **Methods and analysis:** MEDLINE, MEDLINE In Process, EMBASE, PsychINFO,  
39 CINAHL and Applied Social Sciences Index and Abstracts (ASSIA), Conference  
40 Proceedings Citation Index (Web of Science), Healthcare Management Information  
41 Consortium (HMIC) and Open Grey will be searched without restrictions on date or  
42 language of publication. Searches will be limited to studies of qualitative design,  
43 standalone or in the context of a mixed-method design, focusing on cardiovascular  
44 drug initiation for primary prevention. The primary outcome is the attitudes of health  
45 professionals and patients towards drug initiation for primary prevention of  
46 cardiovascular disease. Two reviewers will independently carry out the study  
47 selection, data extraction and quality assessment. The Critical Appraisal Skills  
48 Programme (CASP) Qualitative Research Checklist will be used to assess the  
49 quality of included studies. The findings will be analysed using thematic synthesis.

50 **Ethics and dissemination:** This systematic review does not require ethical approval  
51 as primary data will not be collected. The results of the study will be published in a  
52 peer-reviewed journal and presented at relevant conferences.

53 **Systematic review registration:** PROSPERO CRD42018095346

54

## 55 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

- 56 ▪ This review will utilize a systematic approach to summarize qualitative  
57 evidence on preventive drug initiation in primary care settings.

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3 58     ▪ This review will focus on summarizing existing evidence regarding drug  
4 59     initiation for primary prevention of cardiovascular as recommended by the  
5 60     European guidelines.  
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7 61     ▪ It will provide a better understanding of what influences health professionals'  
8 62     and patients' decisions regarding initiation of preventive treatment.  
9  
10 63     ▪ The study will not review attitudes towards drug initiation in secondary or  
11 64     tertiary care settings.  
12  
13 65     ▪ The study will not review studies addressing the initiation of aspirin for the  
14 66     primary prevention of cardiovascular disease.

## 67 INTRODUCTION

68 Cardiovascular disease (CVD) is the leading cause of deaths worldwide <sup>1</sup>. It accounts  
69 for 26% of deaths in the United Kingdom and 31% of deaths globally <sup>1 2</sup>. One of the  
70 ways to prevent CVD is through prescribing drugs for primary prevention. National and  
71 international guidelines recommend primary preventive treatment for patients at an  
72 increased risk of developing a cardiovascular event <sup>3-6</sup>. Patients considered at an  
73 increased risk include patients who have a 10-year CVD risk of 10% or more or  
74 patients with clinically measured blood pressure of 140/90 mmHg or higher <sup>4 6</sup>. The  
75 recommendations are supported by evidence from clinical trials demonstrating the  
76 beneficial effects of lipid lowering drugs and antihypertensive agents in the primary  
77 prevention of CVD <sup>7-10</sup>. However, studies have reported low prescribing rates of  
78 preventive drugs <sup>11-14</sup>. Patients eligible for statins are undertreated <sup>13 14</sup>; one study has  
79 reported that 50% of patients with a CVD risk  $\geq 20\%$  were not prescribed statins for  
80 primary prevention <sup>14</sup>. In addition, the detection and treatment of hypertension remains  
81 low in parts of the world <sup>15 16</sup>. 49% of adults with hypertension aged 35-84 years were  
82 treated in Japan compared to 80% in the United States <sup>15</sup>. However, the initiation rate  
83 for antihypertensive drugs in younger eligible adults in the United States is suboptimal  
84 <sup>17</sup>. A study that explored antihypertensive drug initiation among young adults with  
85 regular access to primary care found that only 34% of patients aged 18-39 years were  
86 started on antihypertensive drugs compared to 44% of patients aged 40-59 years <sup>17</sup>.

87 The suboptimal prescribing patterns may be a result of health professionals' poor  
88 adherence to guideline recommendations. A study conducted in German general  
89 practices estimated that around 50% of general practitioners (GPs) did not adhere to  
90 the guidelines <sup>18</sup>. GPs have expressed concerns regarding the evidence the guidelines

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3 91 were based on and whether following the guidelines will allow them to meet their  
4 patients' needs <sup>19 20</sup>. Nevertheless, the variation in prescribing patterns indicates that  
5 92 there are patient- and GP-related barriers to initiating primary preventive treatment.  
6  
7 93 Previous research identified GP-related barriers such as concerns about patient  
8 94 adherence to medication, over-medicalization of healthy individuals and side effects  
9 95 <sup>21</sup>. With respect to patient-related barriers, a study reported that patients preferred  
10 96 making lifestyle changes and had concerns about the side effects of taking medication  
11 97 <sup>22</sup>. In addition, patients' trust in their GP's medical judgment played a role in accepting  
12 98 preventive treatments <sup>22</sup>.  
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19 100 We are interested in studies that explore the attitudes of health professionals and  
20 101 patients towards initiating treatments for the primary prevention of CVD. A scoping  
21 102 search was carried out to identify existing literature and to estimate the volume of  
22 103 studies available on our topic of interest. The majority of published studies address  
23 104 the issue of adherence to medication or prescribing drugs for secondary prevention <sup>23</sup>  
24 105 <sup>24</sup>. However, the search retrieved a number of qualitative studies that investigate  
25 106 patient and health professional-related factors influencing drug prescribing for primary  
26 107 prevention. The search retrieved a systematic review published in 2012 that assessed  
27 108 qualitative literature about initiating and adhering to preventive drugs for CVD. The  
28 109 review discussed factors associated with initiating preventive medication and reported  
29 110 that initiation was influenced by the health professional-patient relationship and the  
30 111 organizational structure of the clinical environment <sup>25</sup>. The authors focused on starting  
31 112 and adhering to preventive medication with no differentiation between primary and  
32 113 secondary prevention. In addition, studies were excluded from the review based on  
33 114 quality assessment. Our review will consider all primary studies addressing our topic  
34 115 of interest regardless of quality to capture all available evidence regarding prescribing  
35 116 cardiovascular drugs for primary prevention. Furthermore, the search retrieved one  
36 117 recently published systematic review that explored patients' attitudes towards taking  
37 118 statins. However, the review did not explore the attitudes of health professionals  
38 119 towards statins and was restricted to studies in the English language <sup>26</sup>. The authors  
39 120 explored attitudes only towards statin uptake without differentiating between primary  
40 121 and secondary prevention. Both reviews did not explore grey literature. In this review  
41 122 we aim to explore grey literature databases to maximize the chances of capturing  
42 123 relevant studies.  
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3 124 Our review will add valuable information to the existing knowledge about CVD  
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5 125 prevention. The existing reviews either assess the initiation of a specific drug, such as  
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7 126 statins, or focus on the initiation of cardiovascular preventive drugs without  
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9 127 differentiating between primary and secondary prevention. In this review we will  
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11 128 include all preventive drugs to provide a comprehensive summary of evidence  
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13 129 regarding health professionals' and patients' attitudes towards any cardiovascular  
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15 130 drug recommended by the European guidelines for primary prevention. In addition, we  
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17 131 choose to focus on drug initiation for primary prevention of CVD because the reasons  
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19 132 behind taking cardiovascular preventive drugs such as statins might be different in  
20  
21 133 patients who had a CVD event and patients who are yet to experience a CVD event.  
22  
23 134 The initiation of preventive drugs in a relatively asymptomatic patient can be  
24  
25 135 challenging for both the health professional and the patient, and attitudes relating to  
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27 136 this preventive approach need to be identified for successful primary care preventive  
28  
29 137 prescribing. The decision-making process involved in initiating preventive treatments  
30  
31 138 is complex and influenced by multiple factors that relate to both the health professional  
32  
33 139 and the patient. Thus, an up-to-date, methodologically robust systematic review  
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35 140 aiming to identify the attitudes and perceptions of health professionals and patients  
36  
37 141 towards the initiation of preventive drugs for the primary prevention of CVD is  
38  
39 142 warranted.

143

## 144 **Objectives**

- 145 • Explore health professionals' attitudes and perceptions in relation to initiating  
146 preventive drugs for primary prevention of CVD in primary care settings.
- 147 • Explore patients' attitudes and perceptions towards initiating preventive drugs  
148 for primary prevention of CVD in primary care settings.

149

## 150 **METHODS AND ANALYSIS**

151 This protocol will use the Preferred Reporting Items for Systematic Review and Meta-  
152 Analysis Protocols (PRISMA-P) guidelines to ensure comprehensive reporting of  
153 study items <sup>27</sup>. The protocol is registered with PROSPERO (CRD42018095346). The  
154 systematic review will follow the reporting guidelines formulated in the Enhancing

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3 155 transparency in reporting the synthesis of qualitative research (ENTREQ) statement  
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5 156 <sup>28</sup>.

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## 8 9 158 **Information sources and search strategy**

10 159 The Sample, Phenomenon of Interest, Design, Evaluation, Research type (SPIDER)  
11  
12 160 tool is considered an alternative to PICOS when addressing a qualitative review  
13  
14 161 question and will be used in the proposed systematic review to formulate the search  
15  
16 162 strategy <sup>29</sup>. The search strategy will include a combination of free text words and index  
17  
18 163 terms relating to (drug initiation OR prescription OR decision making) and (attitudes  
19  
20 164 OR experiences OR perceptions OR views OR behaviour) and cardiovascular  
21  
22 165 disease. Each element from the SPIDER tool will be included in the search strategy  
23  
24 166 and potential alternative search terms will be included to maximize the chances of  
25  
26 167 retrieving relevant studies. The formulated search strategy will be applied to MEDLINE  
27  
28 168 database (including MEDLINE In Process) then adapted with necessary adjustments  
29  
30 169 for use in other databases. The search strategy for MEDLINE is presented in  
31  
32 170 (Appendix 1). We will search EMBASE, PsychINFO, CINAHL and Applied Social  
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34 171 Sciences Index and Abstracts (ASSIA) for published studies. In addition, the following  
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36 172 grey literature sources will be searched: Conference Proceedings Citation Index (Web  
37  
38 173 of Science), Healthcare Management Information Consortium (HMIC) and Open Grey.  
39  
40 174 The reference lists of included studies will be checked to identify additional eligible  
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42 175 studies which were not retrieved by the formulated search strategy. There will be no  
43  
44 176 restriction on date or language of publication. The search will be limited to studies of  
45  
46 177 qualitative design.

47 178

## 48 179 **Eligibility criteria**

### 49 180 *Sample*

50  
51 181 We will include studies of primary care health professionals (GPs and nurse  
52  
53 182 practitioners), in any country, who prescribe cardiovascular preventive drugs. In  
54  
55 183 addition, we will include studies that target patients who are offered a prescription for  
56  
57 184 statins or antihypertensive drugs in a primary care setting. However, studies assessing  
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59 185 drug initiation in older patients aged 85 or over will not be included as the  
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186 considerations for primary prevention of CVD in an older age group are different with

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3 187 additional factors that complicate drug prescription, such as multimorbidity and  
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5 188 polypharmacy. Studies that focus on practitioners or patients involved in the process  
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7 189 of decision making or initiation of cardiovascular drugs will be included. Any study that  
8  
9 190 examines practitioners who prescribe preventive drugs and patients who receive such  
10  
11 191 prescriptions for secondary prevention of CVD will be excluded. Studies conducted in  
12  
13 192 secondary care settings will be excluded.

#### 14 193 *Phenomenon of interest*

15  
16 194 Studies will be considered for inclusion if they assess patient or practitioner factors  
17  
18 195 associated with the initiation of cardiovascular preventive drugs in primary care  
19  
20 196 settings. Initiation refers to the prescription of preventive drugs by the practitioner and  
21  
22 197 the patient agreeing to take medication for preventive purposes. Therefore, studies  
23  
24 198 that focus on decision making or discuss barriers and facilitators to prescription for  
25  
26 199 primary prevention of CVD will be included. We will exclude studies that focus on  
27  
28 200 adherence and continuation of cardiovascular preventive drugs.

#### 29 201 *Design / Research type*

30  
31 202 Our review aims to look at aspects such as attitudes and perceptions. These are best  
32  
33 203 explored through a qualitative approach. Therefore, any qualitative studies, stand  
34  
35 204 alone or in the context of a mixed-method design, focusing on cardiovascular drug  
36  
37 205 prescription for primary prevention will be included. A summary of Sample,  
38  
39 206 Phenomenon of Interest, Design, Evaluation, Research type (SPIDER) is provided in  
40  
41 207 table 1.

42 208  
43  
44 209 **Table 1. Summary of Sample, Phenomenon of Interest, Design, Evaluation,**  
45  
46 210 **Research type (SPIDER)**

Sample	<ul style="list-style-type: none"> <li>- Health professionals (General practitioners or nurse practitioners) who prescribe statins or antihypertensive drugs.</li> <li>- Patients eligible for cardiovascular preventive drugs or offered a prescription of statin or an antihypertensive drug for primary prevention of cardiovascular disease.</li> </ul>
Phenomenon of Interest	The initiation or prescription of statins or antihypertensive drugs.
Design	Studies including qualitative data collection or analysis methods.

Evaluation	Attitudes, perceptions, views or experiences of health professionals or patients related to the initiation of cardiovascular preventive drugs.
Research type	Qualitative and mixed methods studies.

211

212 *Evaluation*

213 Studies that address the attitudes, perceptions, views or experiences of health  
 214 professionals or patients involved in the process of cardiovascular preventive drug  
 215 initiation will be considered for inclusion. To adhere to the European guidelines, we  
 216 will include studies that target the prescription of statins or antihypertensive drugs<sup>4 6</sup>.  
 217 We will exclude studies that target the prescription of aspirin as its use for primary  
 218 prevention is not recommended by several guidelines<sup>5 30</sup>. In addition, studies that  
 219 assess the attitudes and perceptions of practitioners or patients towards the  
 220 prescribing of fibrates, niacin, bile acid sequestrants and Omega - 3 fatty acid  
 221 compounds will be excluded as these drugs are not recommended for the primary  
 222 prevention of CVD<sup>4 5</sup>. In some countries, a polypill that contains a lipid lowering agent  
 223 and a blood pressure lowering agent is prescribed for CVD risk reduction<sup>31</sup>. Thus, we  
 224 will consider studies that assess health professionals' and patients' attitudes towards  
 225 polypills.

226

227 **Selection process**

228 The literature search results will be imported into Endnote X8 (Thomson Reuters, New  
 229 York), to ensure efficient management of references and to facilitate the study  
 230 selection process. The process of selecting studies will be carried out in two stages by  
 231 two independent reviewers. The reviewers will follow explicit inclusion/exclusion  
 232 criteria to minimize potential bias and to ensure minimal influence of the reviewers'  
 233 preconceptions. The inclusion/exclusion form is presented in (Appendix 2). The first  
 234 stage of selection will include screening the titles and abstracts of all identified records  
 235 against the inclusion criteria. If a study addresses our topic but the abstract lacks  
 236 sufficient information to assess eligibility for inclusion, the full text will be retrieved to  
 237 make a definitive decision. In the second stage of selection the two reviewers will  
 238 retrieve the full texts of included studies and assess them for eligibility. Any  
 239 disagreements during the selection process will be resolved through discussion. If the

1  
2  
3 240 two reviewers fail to reach an agreement, a third independent reviewer will be involved  
4  
5 241 for an unbiased decision. The reviewers will keep a record for each article that they  
6  
7 242 have assessed and justify their decision for either inclusion or exclusion. The selection  
8  
9 243 process will be piloted on a small number of studies by the main reviewer to ensure  
10  
11 244 the reliability of the inclusion criteria. The selection process will be illustrated using a  
12  
13 245 PRISMA flow diagram <sup>27</sup>.

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15 246

### 16 247 **Data extraction process**

17  
18 248 An electronic standardised data extraction form will be developed to ensure adequate  
19  
20 249 and consistent extraction of all required information. The form will be piloted using a  
21  
22 250 small number of studies to ensure reliability and validity and adjusted if necessary.  
23  
24 251 The electronic form will be used to record extracted data on study characteristics,  
25  
26 252 participants' details, theoretical approach, data collection methods, data analysis and  
27  
28 253 findings (Appendix 3). Once extraction is completed by the two reviewers, the forms  
29  
30 254 will be reviewed, and any discrepancies will be resolved through discussion. If the two  
31  
32 255 reviewers fail to reach agreement, a third reviewer will be involved.

33 256

### 34 35 257 **Critical appraisal**

36  
37 258 Two independent reviewers will appraise the quality of the included studies using the  
38  
39 259 Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist <sup>32</sup>. The  
40  
41 260 assessment of quality will be based on the study aims, methodology, study design,  
42  
43 261 sample recruitment, reflexivity, data collection, data analysis, findings, value of  
44  
45 262 research and ethics. The reviewers will keep a record of the quality assessment for  
46  
47 263 each study with an explanation of their decision. Any disagreements will be resolved  
48  
49 264 by discussion or referral to a third independent reviewer. Studies will not be excluded  
50  
51 265 from the review based on quality.

52 266

### 53 54 267 **Data synthesis**

55  
56 268 The NVivo10 software will be used to analyse qualitative data. We will adopt a method  
57  
58 269 of thematic synthesis defined by Thomas and Harden for synthesising qualitative data  
59  
60 270 in systematic reviews <sup>33</sup>. Thematic synthesis includes three stages: First, line by line

1  
2  
3 271 examination of studies' findings and assigning codes to each line of text based on the  
4  
5 272 meaning and content. Second, codes are then grouped into a hierarchical structure  
6  
7 273 and organized as descriptive themes. Finally, analytical themes will be generated to  
8  
9 274 provide interpretations that surpass the findings of the primary studies and ultimately  
10  
11 275 answer our review question. The thematic synthesis will be carried out by two  
12  
13 276 independent reviewers. The reviewers will discuss the codes and themes with an  
14  
15 277 advisory team and then agree on the analytical stage of thematic synthesis.  
16  
17 278

### 18 279 **Patient and public involvement**

19  
20 280 This protocol was completed without patient or public involvement. Patients were not  
21  
22 281 invited to contribute to the development of this protocol. There are no plans to  
23  
24 282 include patients in any stage of this systematic review. However, the findings of the  
25  
26 283 review will be available to healthcare professionals, policy makers and the public.  
27  
28 284

### 29 30 285 **DISCUSSION**

31  
32 286 The health professional's decision to prescribe a preventive drug and the patient's  
33  
34 287 willingness to start treatment for preventive purposes is a multifactorial process. It is  
35  
36 288 essential to understand this process of decision making from a qualitative perspective  
37  
38 289 to enable a more effective approach to cardiovascular disease prevention. This review  
39  
40 290 will summarize the qualitative evidence available on healthcare professionals' and  
41  
42 291 patients' attitudes towards drug initiation. The findings will help us to understand the  
43  
44 292 complex interaction that occurs during the consultation visit between the patient and  
45  
46 293 their health professional and provide evidence to inform healthcare professionals and  
47  
48 294 policy makers regarding barriers and facilitators to primary care cardiovascular  
49  
50 295 preventive prescribing.  
51  
52 296

### 53 297 **ETHICS AND DISSEMINATION**

54  
55 298 This review will utilize information available from primary studies. Data will not be  
56  
57 299 collected from individuals therefore ethical approval is not required. We aim to  
58  
59 300 disseminate the findings of our review through publication in a peer-reviewed journal  
60  
301 and presentation at a relevant conference.

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2  
3 302 **AUTHORS' CONTRIBUTIONS**

4  
5 303 OQ formulated the research question, performed the scoping search and wrote the  
6  
7 304 first draft. OQ and DB refined research question and search strategy. TM, DB, NA  
8  
9 305 reviewed and revised the draft. All authors read and approved the final manuscript.  
10

11 306

12  
13 307 **FUNDING**

14  
15 308 OQ is funded by a governmental scholarship, the study is sponsored by the  
16  
17 309 University of Birmingham.  
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22 311 **COMPETING INTERESTS**

23  
24 312 None declared.  
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25 334 [monitoring-antihypertensive-drug-treatment-including-blood-pressure-targets-](https://www.nice.org.uk/guidance/cg127/chapter/1-Guidance#initiating-and-monitoring-antihypertensive-drug-treatment-including-blood-pressure-targets-2)  
26 335 [2](https://www.nice.org.uk/guidance/cg127/chapter/1-Guidance#initiating-and-monitoring-antihypertensive-drug-treatment-including-blood-pressure-targets-2) accessed 1 April 2018.
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## APPENDICES

### Appendix 1. Medline search strategy

#### Search term

1	Health personnel.mp.
2	Doctor*.mp.
3	Healthcare professional*.mp.
4	GENERAL PRACTITIONERS/ or FAMILY NURSE PRACTITIONERS/ or NURSE PRACTITIONERS/ or Practitioner*.mp.
5	Physician*.mp.
6	Prescriber*.mp.
7	Patient*.mp.
8	General Practice.mp. or General Practice/
9	Primary Health Care.mp. or Primary Health Care/
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11	(Prescrib* adj2 (lipid lowering drug* or Statin* or Ezetimibe or Blood pressure lowering drug* or Antihypertensive drug* or Angiotensin Converting Enzyme Inhibitor or ACE or Angiotensin Receptor Blocker or ARB or Calcium Channel Blocker* or Beta Blocker* or variation*)).mp.
12	((Drug or medication) adj2 (start* or tak* or receiv* or initiation or utilization or prescrib* or choice)).mp.
13	Decision making.mp. or Decision Making/
14	Preventive drug*.mp.
15	Preventive therap*.mp.
16	Antihypertensive Agents/tu [Therapeutic Use]
17	Hydroxymethylglutaryl-CoA Reductase Inhibitors/tu [Therapeutic Use]
18	Statin*.mp.
19	Practice Patterns, Physicians/
20	Physician-Patient Relations/
21	(Preventive adj2 (drug* or therap* or treatment* or medication)).mp.
22	Preventive Medicine/mt [Methods]
23	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24	Cardiovascular Diseases/dt, pc [Drug Therapy, Prevention & Control]
25	(Cardiovascular adj3 primary prevention).mp.
26	(Cardiovascular preventive adj2 (drug* or therap* or treatment* or medication)).mp.
27	24 or 25 or 26
28	10 and 23 and 27
29	limit 28 to "qualitative (best balance of sensitivity and specificity)"
30	Qualitative.mp.
31	Mixed methods.mp.
32	Focus Groups*.mp.
33	Interview*.mp.
34	"Surveys and Questionnaires"/
35	Nursing Methodology Research/
36	30 or 31 or 32 or 33 or 34 or 35
37	"Attitude of Health Personnel"/
38	Attitude to Health/
39	Attitude*.mp.
40	Perception*.mp.
41	Prespective*.mp.
42	Behavio?r.mp.
43	View*.mp.

44	Experience*.mp.
45	Expectation*.mp.
46	Belie*.mp.
47	37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46
48	36 or 47
49	28 and 48
50	29 or 49

For peer review only

## Appendix 2. Inclusion/exclusion form for study selection

	Include	Yes	No	Unclear	Exclude
<b>Research type</b>	<ul style="list-style-type: none"> <li>▪ Qualitative study, standalone</li> <li>▪ Qualitative study in the context of mixed method</li> <li>▪ Review of qualitative studies</li> <li>▪ Other, specify:</li> </ul>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Quantitative study</li> <li>▪ Clearly commentary/letter with no data from primary studies</li> <li>▪ Other, specify:</li> </ul>
If clearly excluded on study design – STOP HERE					
<b>Sample</b>	<ul style="list-style-type: none"> <li>▪ Primary care Health professionals</li> <li>- General practitioner</li> <li>- Nurse practitioner</li> <li>- Other, specify:</li> <li>▪ Patients treated in primary care</li> </ul>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Secondary or tertiary care health professionals</li> <li>▪ Patients treated in Secondary or tertiary care</li> </ul>
<b>Phenomenon of Interest</b>	<ul style="list-style-type: none"> <li>▪ Lipid lowering drugs initiation or prescription</li> <li>▪ Antihypertensive drugs initiation or prescription</li> <li>▪ Drug initiation or prescription for primary prevention of CVD</li> </ul>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Initiation or prescription of:               <ul style="list-style-type: none"> <li>- Aspirin</li> <li>- Fibrates</li> <li>- Niacin</li> <li>- Bile acid sequestrants</li> <li>- Omega-3 fatty acid compounds</li> </ul> </li> <li>▪ Adherence to medication</li> <li>▪ Discontinuation of medication</li> <li>▪ Other, specify:</li> </ul>
<b>Design</b>	<ul style="list-style-type: none"> <li>▪ Qualitative data collection, specify:</li> <li>▪ Qualitative data analysis, specify:</li> </ul>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Quantitative data collection or analysis with no qualitative component</li> </ul>
<b>Evaluation</b>	<ul style="list-style-type: none"> <li>▪ Attitudes, perceptions, views, experiences, patient or health</li> </ul>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Attitudes, perceptions, views, experiences,</li> </ul>

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	<p>professional related Factors influencing cardiovascular drug initiation or prescription for primary prevention</p>	<p>patient or health professional related factors influencing cardiovascular drug initiation or prescription for secondary prevention</p> <ul style="list-style-type: none"> <li>▪ Factors influencing drug adherence or discontinuation <input type="checkbox"/></li> <li>▪ Other, specify:</li> </ul>
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If "NO" in any of the categories, exclude

<p>Comments</p>	
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For peer review only

### Appendix 3. Data collection form

<b>Reviewer name (collecting data)</b>		
<b>Data collection date</b>	Click or tap to enter a date.	
<b>Reviewer name (reviewing collected data)</b>		
<b>Data review date</b>	Click or tap to enter a date.	
<b>Amendments</b>		
<b>Date of amendment</b>	Click or tap to enter a date.	
<b>Notes</b>		
<b>Study Bibliographic details</b>		
<b>First author</b>		
<b>Publication date</b>	Click or tap to enter a date.	
<b>Country</b>		
<b>Study characteristics</b>		
<b>Study type</b>	<input type="checkbox"/> Qualitative <input type="checkbox"/> Mixed method	
<b>Study aim</b>	What was the purpose or aim of the study	
<b>Theoretical approach</b>	What theoretical perspective is the study based on?	
<b>Setting</b>	What is the geographical location and setting of the study?	
<b>Participants</b>		
<b>Type of participants</b>	Who was included in the study	<input type="checkbox"/> Patient <input type="checkbox"/> General practitioner <input type="checkbox"/> Nurse practitioner
<b>Recruitment</b>	How were participants recruited?	
<b>Participants excluded</b>	Were there any participants excluded?	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Reason of exclusion:	
<b>Total number of participants</b>		

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<b>Number of males</b>		
<b>Number of females</b>		
<b>Age of participants</b>		
<b>Methods</b>		
<b>Method of data collection</b>	How was data collected?	<input type="checkbox"/> Interview <input type="checkbox"/> Survey <input type="checkbox"/> Questionnaire <input type="checkbox"/> Focus group <input type="checkbox"/> Other
<b>Additional details about data collection</b>		
<b>Data collection duration</b>	What is the start and end date of the data collection?	
<b>Method of data analysis</b>	How was the data analysed?	
<b>Additional details about data analysis</b>		
<b>Findings</b>		
<b>Main findings</b>	What are the main findings of the study?	
<b>Descriptive themes</b>	What descriptive themes were reported?	
<b>Author interpretation</b>	What are the interpretations of results provided by the authors?	
<b>Study strengths and weakness</b>	What are the key strengths and weaknesses of the study?	

**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item	Reported on page/line
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1/5
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2/53
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1/9-12
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	11/302-305
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	NA
Support:			
Sources	5a	Indicate sources of financial or other support for the review	11/308
Sponsor	5b	Provide name for the review funder and/or sponsor	11/309
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	
<b>INTRODUCTION</b>			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5/100-142
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5/144-148, 7-8/209-211
<b>METHODS</b>			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	6-8/179-225
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6/158-177
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Appendix 1

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	8/228
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	8-9/230-245
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	9/247-255
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Appendix 3
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Appendix 3
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	9/257-265
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	NA
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )	NA
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	NA
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	9-10/267-277
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	NA
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

# BMJ Open

**Patients' and health professionals' attitudes and perceptions towards the initiation of preventive drugs for primary prevention of cardiovascular disease: protocol for a systematic review of qualitative studies**

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<b>Primary Subject Heading</b>:	Public health
Secondary Subject Heading:	Public health, Qualitative research
Keywords:	systematic review, QUALITATIVE RESEARCH, cardiovascular disease, attitudes, drug initiation, primary prevention

SCHOLARONE™  
Manuscripts

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3 1 **TITLE**  
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7 3 **Patients' and health professionals' attitudes and perceptions**  
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9 4 **towards the initiation of preventive drugs for primary prevention of**  
10  
11 5 **cardiovascular disease: protocol for a systematic review of**  
12  
13 6 **qualitative studies**  
14  
15

16 7  
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29  
30 13

31  
32 14 **KEYWORDS**

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34  
35 15 systematic review; qualitative research; cardiovascular disease;  
36  
37 16 attitudes; perceptions; drug initiation; statins; antihypertensive drugs;  
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39 17 primary prevention  
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44 19 **WORD COUNT**

45  
46 20 2617 words (excluding title page, abstract, references, figures and  
47  
48 21 tables).  
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## 28 **ABSTRACT**

29 **Introduction:** Lipid lowering drugs and antihypertensive agents can be prescribed  
30 for the primary prevention of cardiovascular disease. In some cases, patients eligible  
31 for primary prevention of cardiovascular disease according to the European  
32 guidelines are not always started on preventive drugs. Existing research explores the  
33 attitudes of health professionals and patients towards cardiovascular preventive  
34 drugs but does not always differentiate between the attitudes towards drug initiation  
35 for primary or secondary prevention. We aim to systematically review qualitative  
36 studies assessing health professionals' and patients' attitudes and perceptions  
37 towards drug initiation for primary prevention of cardiovascular disease.

38 **Methods and analysis:** MEDLINE, MEDLINE In Process, EMBASE, PsychINFO,  
39 CINAHL and Applied Social Sciences Index and Abstracts (ASSIA), Conference  
40 Proceedings Citation Index (Web of Science), Healthcare Management Information  
41 Consortium (HMIC) and Open Grey will be searched without restrictions on date or  
42 language of publication. Searches will be limited to studies of qualitative design,  
43 standalone or in the context of a mixed-method design, focusing on cardiovascular  
44 drug initiation for primary prevention. The primary outcome is the attitudes of health  
45 professionals and patients towards drug initiation for primary prevention of  
46 cardiovascular disease. Two reviewers will independently carry out the study  
47 selection, data extraction and quality assessment. The Critical Appraisal Skills  
48 Programme (CASP) Qualitative Research Checklist will be used to assess the  
49 quality of included studies. The findings will be analysed using Thomas and Harden's  
50 thematic synthesis approach.

51 **Ethics and dissemination:** This systematic review does not require ethical approval  
52 as primary data will not be collected. The results of the study will be published in a  
53 peer-reviewed journal and presented at relevant conferences.

54 **Systematic review registration:** PROSPERO CRD42018095346

## 56 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

- 57 **▪** This review will utilize a systematic approach to summarize qualitative  
58 evidence on preventive drug initiation in primary care settings.

- 1  
2  
3 59     ▪ This review will focus on summarizing existing evidence regarding drug  
4 60     initiation for primary prevention of cardiovascular disease as recommended by  
5 61     the European guidelines.  
6  
7 62     ▪ It will provide a better understanding of what influences health professionals'  
8 63     and patients' decisions regarding initiation of preventive treatment.  
9  
10 64     ▪ The study will not review attitudes towards drug initiation in secondary or  
11 65     tertiary care settings.  
12  
13 66     ▪ The study will not review studies addressing the initiation of aspirin for the  
14 67     primary prevention of cardiovascular disease.

## 68 INTRODUCTION

69 Cardiovascular disease (CVD) is the leading cause of deaths worldwide <sup>1</sup>. It accounts  
70 for 26% of deaths in the United Kingdom and 31% of deaths globally <sup>1 2</sup>. One of the  
71 ways to prevent CVD is through prescribing drugs for primary prevention. National and  
72 international guidelines recommend primary preventive treatment for patients at an  
73 increased risk of developing a cardiovascular event <sup>3-6</sup>. Patients considered at an  
74 increased risk include patients with clinically measured blood pressure of  $\geq 140/90$   
75 mmHg or patients who have a 10-year CVD risk of 10% or more <sup>4 6</sup>. A patients' risk of  
76 developing CVD within the next 10 years can be predicted using a risk assessment  
77 tool such as QRISK2. The QRISK2 assessment tool calculates an individual CVD risk  
78 taking into account factors such as age, ethnicity, smoking status, systolic blood  
79 pressure, cholesterol/HDL ratio and Body Mass Index (BMI) <sup>7</sup>. The recommendations  
80 are supported by evidence from clinical trials demonstrating the beneficial effects of  
81 lipid lowering drugs and antihypertensive agents in the primary prevention of CVD <sup>8-</sup>  
82 <sup>11</sup>. However, studies have reported low prescribing rates of preventive drugs <sup>12-15</sup>.  
83 Patients eligible for statins are undertreated <sup>14 15</sup>; one study has reported that 50% of  
84 patients with a CVD risk  $\geq 20\%$  were not prescribed statins for primary prevention <sup>15</sup>.  
85 In addition, the detection and treatment of hypertension remains low in parts of the  
86 world <sup>16 17</sup>. 49% of adults with hypertension aged 35-84 years were treated in Japan  
87 compared to 80% in the United States <sup>16</sup>. However, the initiation rate for  
88 antihypertensive drugs in younger eligible adults in the United States is suboptimal <sup>18</sup>.  
89 A study that explored antihypertensive drug initiation among young adults with regular  
90 access to primary care found that only 34% of patients aged 18-39 years were started  
91 on antihypertensive drugs compared to 44% of patients aged 40-59 years <sup>18</sup>. This

1  
2  
3 92 variation in drug initiation observed across countries can be due to multiple factors,  
4 93 including health system, health professional and patient factors. The healthcare  
5 94 system can influence the patients' ability to access health services and the affordability  
6 95 of preventive drugs. The suboptimal prescribing patterns may be a result of health  
7 96 professionals' poor adherence to guideline recommendations. A study conducted in  
8 97 German general practices estimated that around 50% of general practitioners (GPs)  
9 98 did not adhere to the guidelines<sup>19</sup>. GPs have expressed concerns regarding the  
10 99 evidence the guidelines were based on and whether following the guidelines will allow  
11 100 them to meet their patients' needs<sup>20 21</sup>. Nevertheless, the variation in prescribing  
12 101 patterns indicates that there are patient- and GP-related barriers to initiating primary  
13 102 preventive treatment. Previous research identified GP-related barriers such as  
14 103 concerns about patient adherence to medication, over-medicalization of healthy  
15 104 individuals and side effects<sup>22</sup>. With respect to patient-related barriers, a study reported  
16 105 that patients preferred making lifestyle changes and had concerns about the side  
17 106 effects of taking medication<sup>23</sup>. In addition, patients' trust in their GP's medical  
18 107 judgment played a role in accepting preventive treatments<sup>23</sup>.

19 108 We are interested in studies that explore the attitudes of health professionals and  
20 109 patients towards initiating treatments for the primary prevention of CVD. A scoping  
21 110 search was carried out to identify existing literature and to estimate the volume of  
22 111 studies available on our topic of interest. The majority of published studies address  
23 112 the issue of adherence to medication or prescribing drugs for secondary prevention<sup>24</sup>  
24 113<sup>25</sup>. However, the search retrieved a number of qualitative studies that investigate  
25 114 patient and health professional-related factors influencing drug prescribing for primary  
26 115 prevention. The search retrieved a systematic review published in 2012 that assessed  
27 116 qualitative literature about initiating and adhering to preventive drugs for CVD. The  
28 117 review discussed factors associated with initiating preventive medication and reported  
29 118 that initiation was influenced by the health professional-patient relationship and the  
30 119 organizational structure of the clinical environment<sup>26</sup>. The authors focused on starting  
31 120 and adhering to preventive medication with no differentiation between primary and  
32 121 secondary prevention. In addition, studies were excluded from the review based on  
33 122 quality assessment. Our review will consider all primary studies addressing our topic  
34 123 of interest regardless of quality to capture all available evidence regarding prescribing  
35 124 cardiovascular drugs for primary prevention. Furthermore, the search retrieved one

1  
2  
3 125 recently published systematic review that explored patients' attitudes towards taking  
4  
5 126 statins. However, the review did not explore the attitudes of health professionals  
6  
7 127 towards statins and was restricted to studies in the English language <sup>27</sup>. The authors  
8  
9 128 explored attitudes only towards statin uptake without differentiating between primary  
10  
11 129 and secondary prevention. Both reviews did not explore grey literature. In this review  
12  
13 130 we aim to explore grey literature databases to maximize the chances of capturing  
14  
15 131 relevant studies.

16 132 Our review will add valuable information to the existing knowledge about CVD  
17  
18 133 prevention. The existing reviews either assess the initiation of a specific drug, such as  
19  
20 134 statins, or focus on the initiation of cardiovascular preventive drugs without  
21  
22 135 differentiating between primary and secondary prevention. In this review we will  
23  
24 136 include all preventive drugs to provide a comprehensive summary of evidence  
25  
26 137 regarding health professionals' and patients' attitudes towards any cardiovascular  
27  
28 138 drug recommended by the European guidelines for primary prevention. In addition, we  
29  
30 139 choose to focus on drug initiation for primary prevention of CVD because the reasons  
31  
32 140 behind taking cardiovascular preventive drugs such as statins might be different in  
33  
34 141 patients who had a CVD event and patients who are yet to experience a CVD event.  
35  
36 142 The initiation of preventive drugs in a relatively asymptomatic patient can be  
37  
38 143 challenging for both the health professional and the patient, and attitudes relating to  
39  
40 144 this preventive approach need to be identified for successful primary care preventive  
41  
42 145 prescribing. The decision-making process involved in initiating preventive treatments  
43  
44 146 is complex and influenced by multiple factors that relate to both the health professional  
45  
46 147 and the patient. Thus, an up-to-date, methodologically robust systematic review  
47  
48 148 aiming to identify the attitudes and perceptions of health professionals and patients  
49  
50 149 towards the initiation of preventive drugs for the primary prevention of CVD is  
51  
52 150 warranted.

53  
54 151

## 55 152 **Objectives**

- 56 153 • Explore health professionals' attitudes and perceptions in relation to initiating  
57 154 preventive drugs for primary prevention of CVD in primary care settings.
- 58 155 • Explore patients' attitudes and perceptions towards initiating preventive drugs  
59 156 for primary prevention of CVD in primary care settings.

157

## 158 **METHODS AND ANALYSIS**

159 This protocol will use the Preferred Reporting Items for Systematic Review and Meta-  
160 Analysis Protocols (PRISMA-P) guidelines to ensure comprehensive reporting of  
161 study items <sup>28</sup>. The protocol is registered with PROSPERO (CRD42018095346). The  
162 systematic review will follow the reporting guidelines formulated in the Enhancing  
163 transparency in reporting the synthesis of qualitative research (ENTREQ) statement  
164 <sup>29</sup>.

165

### 166 **Information sources and search strategy**

167 The Sample, Phenomenon of Interest, Design, Evaluation, Research type (SPIDER)  
168 tool is considered an alternative to PICOS when addressing a qualitative review  
169 question and will be used in the proposed systematic review to formulate the search  
170 strategy <sup>30</sup>. The search strategy will include a combination of free text words and index  
171 terms relating to (drug initiation OR prescription OR decision making) and (attitudes  
172 OR experiences OR perceptions OR views OR behaviour) and cardiovascular  
173 disease. Each element from the SPIDER tool will be included in the search strategy  
174 and potential alternative search terms will be included to maximize the chances of  
175 retrieving relevant studies. The formulated search strategy will be applied to MEDLINE  
176 database (including MEDLINE In Process) then adapted with necessary adjustments  
177 for use in other databases. The search strategy for MEDLINE is presented in  
178 (Appendix 1). We will search EMBASE, PsychINFO, CINAHL and Applied Social  
179 Sciences Index and Abstracts (ASSIA) for published studies. In addition, the following  
180 grey literature sources will be searched: Conference Proceedings Citation Index (Web  
181 of Science), Healthcare Management Information Consortium (HMIC) and Open Grey.  
182 The reference lists of included studies will be checked to identify additional eligible  
183 studies which were not retrieved by the formulated search strategy. There will be no  
184 restriction on date or language of publication. The search will be limited to studies of  
185 qualitative design and mixed methods design with a qualitative component.

186

## 187 **Eligibility criteria**

### 188 *Sample*

189 We will include studies of primary care health professionals (GPs and nurse  
190 practitioners), in any country, who prescribe cardiovascular preventive drugs. In  
191 addition, we will include studies that target patients who are offered a prescription for  
192 statins or antihypertensive drugs in a primary care setting. However, studies that  
193 specifically focus on drug initiation in older patients will not be included as the  
194 considerations for primary prevention of CVD in an older age group are different with  
195 additional factors that complicate drug prescription, such as multimorbidity and  
196 polypharmacy. Studies that focus on practitioners or patients involved in the process  
197 of decision making or initiation of cardiovascular drugs will be included. Any study that  
198 examines practitioners who prescribe preventive drugs and patients who receive such  
199 prescriptions for secondary prevention of CVD will be excluded. Studies conducted in  
200 secondary care settings will be excluded.

### 201 *Phenomenon of interest*

202 Studies will be considered for inclusion if they assess patient or practitioner factors  
203 associated with the initiation of cardiovascular preventive drugs in primary care  
204 settings. Initiation refers to the prescription of preventive drugs by the practitioner and  
205 the patient agreeing to take medication for preventive purposes. Therefore, studies  
206 that focus on decision making or discuss barriers and facilitators to prescription for  
207 primary prevention of CVD will be included. We will exclude studies that focus on  
208 adherence and continuation of cardiovascular preventive drugs.

### 209 *Design / Research type*

210 Our review aims to look at aspects such as attitudes and perceptions. These are best  
211 explored through a qualitative approach. Therefore, any qualitative studies, stand  
212 alone or in the context of a mixed-method design, focusing on cardiovascular drug  
213 prescription for primary prevention will be included. A summary of Sample,  
214 Phenomenon of Interest, Design, Evaluation, Research type (SPIDER) is provided in  
215 table 1.

216

217 **Table 1. Summary of Sample, Phenomenon of Interest, Design, Evaluation,**  
 218 **Research type (SPIDER)**

Sample	<ul style="list-style-type: none"> <li>- Health professionals (General practitioners or nurse practitioners) who prescribe statins or antihypertensive drugs.</li> <li>- Patients eligible for cardiovascular preventive drugs or offered a prescription of statin or an antihypertensive drug for primary prevention of cardiovascular disease.</li> </ul>
Phenomenon of Interest	The initiation or prescription of statins or antihypertensive drugs.
Design	Studies including qualitative data collection or analysis methods.
Evaluation	Attitudes, perceptions, views or experiences of health professionals or patients related to the initiation of cardiovascular preventive drugs.
Research type	Qualitative and mixed methods studies.

219

### 220 *Evaluation*

221 Studies that address the attitudes, perceptions, views or experiences of health  
 222 professionals or patients involved in the process of cardiovascular preventive drug  
 223 initiation will be considered for inclusion. To adhere to the European guidelines, we  
 224 will include studies that target the prescription of statins or antihypertensive drugs <sup>4 6</sup>.  
 225 We will exclude studies that target the prescription of aspirin as its use for primary  
 226 prevention is not recommended by several guidelines <sup>5 31</sup>. In addition, studies that  
 227 assess the attitudes and perceptions of practitioners or patients towards the  
 228 prescribing of fibrates, niacin, bile acid sequestrants and Omega - 3 fatty acid  
 229 compounds will be excluded as these drugs are not recommended for the primary  
 230 prevention of CVD <sup>4 5</sup>. In some countries, a polypill that contains a lipid lowering agent  
 231 and a blood pressure lowering agent is prescribed for CVD risk reduction <sup>32</sup>. Thus, we  
 232 will consider studies that assess health professionals' and patients' attitudes towards  
 233 polypills.

234

### 235 **Selection process**

236 The literature search results will be imported into Endnote X8 (Thomson Reuters, New  
 237 York), to ensure efficient management of references and to facilitate the study

1  
2  
3 238 selection process. The process of selecting studies will be carried out in two stages by  
4  
5 239 two independent reviewers. The reviewers will follow explicit inclusion/exclusion  
6  
7 240 criteria to minimize potential bias and to ensure minimal influence of the reviewers'  
8  
9 241 preconceptions. The inclusion/exclusion form is presented in (Appendix 2). The first  
10  
11 242 stage of selection will include screening the titles and abstracts of all identified records  
12  
13 243 against the inclusion criteria. If a study addresses our topic but the abstract lacks  
14  
15 244 sufficient information to assess eligibility for inclusion, the full text will be retrieved to  
16  
17 245 make a definitive decision. In the second stage of selection the two reviewers will  
18  
19 246 retrieve the full texts of included studies and assess them for eligibility. Any  
20  
21 247 disagreements during the selection process will be resolved through discussion. If the  
22  
23 248 two reviewers fail to reach an agreement, a third independent reviewer will be involved  
24  
25 249 for an unbiased decision. The reviewers will keep a record for each article that they  
26  
27 250 have assessed and justify their decision for either inclusion or exclusion. The selection  
28  
29 251 process will be piloted on a small number of studies by the main reviewer to ensure  
30  
31 252 the reliability of the inclusion criteria. The selection process will be illustrated using a  
32  
33 253 PRISMA flow diagram <sup>28</sup>.

254

### 255 **Data extraction process**

256 An electronic standardised data extraction form will be developed to ensure adequate  
257 and consistent extraction of all required information. The form will be piloted using a  
258 small number of studies to ensure reliability and validity and adjusted if necessary.  
259 The electronic form will be used to record extracted data on study characteristics,  
260 participants' details, theoretical approach, data collection methods, data analysis and  
261 findings (Appendix 3). Once extraction is completed by the two reviewers, the forms  
262 will be reviewed, and any discrepancies will be resolved through discussion. If the two  
263 reviewers fail to reach agreement, a third reviewer will be involved.

264

### 265 **Critical appraisal**

266 Two independent reviewers will appraise the quality of the included studies using the  
267 Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist <sup>33</sup>. The  
268 assessment of quality will be based on the study aims, methodology, study design,  
269 sample recruitment, reflexivity, data collection, data analysis, findings, value of

1  
2  
3 270 research and ethics. The reviewers will keep a record of the quality assessment for  
4  
5 271 each study with an explanation of their decision. Any disagreements will be resolved  
6  
7 272 by discussion or referral to a third independent reviewer. Studies will not be excluded  
8  
9 273 from the review based on quality.

10  
11 274

### 12 13 275 **Data synthesis**

14  
15 276 The NVivo10 software will be used to analyse qualitative data. We will adopt a method  
16  
17 277 of thematic synthesis defined by Thomas and Harden for synthesising qualitative data  
18  
19 278 in systematic reviews<sup>34</sup>. Thematic synthesis includes three stages: First, line by line  
20  
21 279 examination of studies' findings and assigning codes to each line of text based on the  
22  
23 280 meaning and content. Second, codes are then grouped into a hierarchical structure  
24  
25 281 and organized as descriptive themes. Finally, analytical themes will be generated to  
26  
27 282 provide interpretations that surpass the findings of the primary studies and ultimately  
28  
29 283 answer our review question. The thematic synthesis will be carried out by two  
30  
31 284 independent reviewers. The reviewers will discuss the codes and themes with an  
32  
33 285 advisory team and then agree on the analytical stage of thematic synthesis.

34  
35 286

### 36 37 287 **Patient and public involvement**

38  
39 288 This protocol was completed without patient or public involvement. There were no  
40  
41 289 funds or time allocated for patient and public involvement. Therefore, patients were  
42  
43 290 not invited to contribute to the development of this protocol. There are no plans to  
44  
45 291 include patients in any stage of this systematic review. However, the findings of the  
46  
47 292 review will be available to healthcare professionals, policy makers and the public.

48  
49 293

## 50 51 294 **DISCUSSION**

52  
53 295 The health professional's decision to prescribe a preventive drug and the patient's  
54  
55 296 willingness to start treatment for preventive purposes is a multifactorial process. It is  
56  
57 297 essential to understand this process of decision making from a qualitative perspective  
58  
59 298 to enable a more effective approach to cardiovascular disease prevention. This review  
60  
300 299 will summarize the qualitative evidence available on healthcare professionals' and  
patients' attitudes towards drug initiation. The findings will help us to understand the

1  
2  
3 301 complex interaction that occurs during the consultation visit between the patient and  
4  
5 302 their health professional and provide evidence to inform healthcare professionals and  
6  
7 303 policy makers regarding barriers and facilitators to primary care cardiovascular  
8  
9 304 preventive prescribing.

10  
11 305

## 12 13 306 **ETHICS AND DISSEMINATION**

14  
15 307 This review will utilize information available from primary studies. Data will not be  
16  
17 308 collected from individuals therefore ethical approval is not required. We aim to  
18  
19 309 disseminate the findings of our review through publication in a peer-reviewed journal  
20  
21 310 and presentation at a relevant conference.

22  
23 311

## 24 25 312 **AUTHORS' CONTRIBUTIONS**

26  
27 313 OQ formulated the research question, performed the scoping search and wrote the  
28  
29 314 first draft. OQ and DB refined research question and search strategy. TM, DB, NA  
30  
31 315 reviewed and revised the draft. All authors read and approved the final manuscript.

32  
33 316

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36  
37 318 OQ is funded by a governmental scholarship, the study is sponsored by the  
38  
39 319 University of Birmingham.

40  
41 320

## 42 43 321 **COMPETING INTERESTS**

44  
45 322 None declared.

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## APPENDICES

### Appendix 1. Medline search strategy

#### Search term

1	Health personnel.mp.
2	Doctor*.mp.
3	Healthcare professional*.mp.
4	GENERAL PRACTITIONERS/ or FAMILY NURSE PRACTITIONERS/ or NURSE PRACTITIONERS/ or Practitioner*.mp.
5	Physician*.mp.
6	Prescriber*.mp.
7	Patient*.mp.
8	General Practice.mp. or General Practice/
9	Primary Health Care.mp. or Primary Health Care/
10	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
11	(Prescrib* adj2 (lipid lowering drug* or Statin* or Ezetimibe or Blood pressure lowering drug* or Antihypertensive drug* or Angiotensin Converting Enzyme Inhibitor or ACE or Angiotensin Receptor Blocker or ARB or Calcium Channel Blocker* or Beta Blocker* or variation*)).mp.
12	((Drug or medication) adj2 (start* or tak* or receiv* or initiation or utilization or prescrib* or choice)).mp.
13	Decision making.mp. or Decision Making/
14	Preventive drug*.mp.
15	Preventive therap*.mp.
16	Antihypertensive Agents/tu [Therapeutic Use]
17	Hydroxymethylglutaryl-CoA Reductase Inhibitors/tu [Therapeutic Use]
18	Statin*.mp.
19	Practice Patterns, Physicians/
20	Physician-Patient Relations/
21	(Preventive adj2 (drug* or therap* or treatment* or medication)).mp.
22	Preventive Medicine/mt [Methods]
23	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24	Cardiovascular Diseases/dt, pc [Drug Therapy, Prevention & Control]
25	(Cardiovascular adj3 primary prevention).mp.
26	(Cardiovascular preventive adj2 (drug* or therap* or treatment* or medication)).mp.
27	24 or 25 or 26
28	10 and 23 and 27
29	limit 28 to "qualitative (best balance of sensitivity and specificity)"
30	Qualitative.mp.
31	Mixed methods.mp.
32	Focus Groups*.mp.
33	Interview*.mp.
34	"Surveys and Questionnaires"/
35	Nursing Methodology Research/
36	30 or 31 or 32 or 33 or 34 or 35
37	"Attitude of Health Personnel"/
38	Attitude to Health/
39	Attitude*.mp.
40	Perception*.mp.
41	Prespective*.mp.
42	Behavio?r.mp.
43	View*.mp.

44	Experience*.mp.
45	Expectation*.mp.
46	Belie*.mp.
47	37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46
48	36 or 47
49	28 and 48
50	29 or 49

For peer review only

## Appendix 2. Inclusion/exclusion form for study selection

	Include	Yes	No	Unclear	Exclude
<b>Research type</b>	<ul style="list-style-type: none"> <li>▪ Qualitative study, standalone</li> <li>▪ Qualitative study in the context of mixed method</li> <li>▪ Review of qualitative studies</li> <li>▪ Other, specify:</li> </ul>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Quantitative study</li> <li>▪ Clearly commentary/letter with no data from primary studies</li> <li>▪ Other, specify:</li> </ul>
If clearly excluded on study design – STOP HERE					
<b>Sample</b>	<ul style="list-style-type: none"> <li>▪ Primary care Health professionals</li> <li>- General practitioner</li> <li>- Nurse practitioner</li> <li>- Other, specify:</li> <li>▪ Patients treated in primary care</li> </ul>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Secondary or tertiary care health professionals</li> <li>▪ Patients treated in Secondary or tertiary care</li> </ul>
<b>Phenomenon of Interest</b>	<ul style="list-style-type: none"> <li>▪ Lipid lowering drugs initiation or prescription</li> <li>▪ Antihypertensive drugs initiation or prescription</li> <li>▪ Drug initiation or prescription for primary prevention of CVD</li> </ul>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Initiation or prescription of:               <ul style="list-style-type: none"> <li>- Aspirin</li> <li>- Fibrates</li> <li>- Niacin</li> <li>- Bile acid sequestrants</li> <li>- Omega-3 fatty acid compounds</li> </ul> </li> <li>▪ Adherence to medication</li> <li>▪ Discontinuation of medication</li> <li>▪ Other, specify:</li> </ul>
<b>Design</b>	<ul style="list-style-type: none"> <li>▪ Qualitative data collection, specify:</li> <li>▪ Qualitative data analysis, specify:</li> </ul>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Quantitative data collection or analysis with no qualitative component</li> </ul>
<b>Evaluation</b>	<ul style="list-style-type: none"> <li>▪ Attitudes, perceptions, views, experiences, patient or health</li> </ul>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<ul style="list-style-type: none"> <li>▪ Attitudes, perceptions, views, experiences,</li> </ul>

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	<p>professional related Factors influencing cardiovascular drug initiation or prescription for primary prevention</p>	<p>patient or health professional related factors influencing cardiovascular drug initiation or prescription for secondary prevention</p> <ul style="list-style-type: none"> <li>▪ Factors influencing drug adherence or discontinuation <input type="checkbox"/></li> <li>▪ Other, specify:</li> </ul>
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If "NO" in any of the categories, exclude

<p>Comments</p>	
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For peer review only

## Appendix 3. Data collection form

<b>Reviewer name (collecting data)</b>		
<b>Data collection date</b>	Click or tap to enter a date.	
<b>Reviewer name (reviewing collected data)</b>		
<b>Data review date</b>	Click or tap to enter a date.	
<b>Amendments</b>		
<b>Date of amendment</b>	Click or tap to enter a date.	
<b>Notes</b>		
<b>Study Bibliographic details</b>		
<b>First author</b>		
<b>Publication date</b>	Click or tap to enter a date.	
<b>Country</b>		
<b>Study characteristics</b>		
<b>Study type</b>	<input type="checkbox"/> Qualitative <input type="checkbox"/> Mixed method	
<b>Study aim</b>	What was the purpose or aim of the study	
<b>Theoretical approach</b>	What theoretical perspective is the study based on?	
<b>Setting</b>	What is the geographical location and setting of the study?	
<b>Participants</b>		
<b>Type of participants</b>	Who was included in the study	<input type="checkbox"/> Patient <input type="checkbox"/> General practitioner <input type="checkbox"/> Nurse practitioner
<b>Recruitment</b>	How were participants recruited?	
<b>Participants excluded</b>	Were there any participants excluded?	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Reason of exclusion:	
<b>Total number of participants</b>		

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<b>Number of males</b>		
<b>Number of females</b>		
<b>Age of participants</b>		
<b>Methods</b>		
<b>Method of data collection</b>	How was data collected?	<input type="checkbox"/> Interview <input type="checkbox"/> Survey <input type="checkbox"/> Questionnaire <input type="checkbox"/> Focus group <input type="checkbox"/> Other
<b>Additional details about data collection</b>		
<b>Data collection duration</b>	What is the start and end date of the data collection?	
<b>Method of data analysis</b>	How was the data analysed?	
<b>Additional details about data analysis</b>		
<b>Findings</b>		
<b>Main findings</b>	What are the main findings of the study?	
<b>Descriptive themes</b>	What descriptive themes were reported?	
<b>Author interpretation</b>	What are the interpretations of results provided by the authors?	
<b>Study strengths and weakness</b>	What are the key strengths and weaknesses of the study?	

**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item	Reported on page/line
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1/5
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	NA
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2/54
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1/9-12
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	11/312-315
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	NA
Support:			
Sources	5a	Indicate sources of financial or other support for the review	11/318
Sponsor	5b	Provide name for the review funder and/or sponsor	11/319
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	
<b>INTRODUCTION</b>			
Rationale	6	Describe the rationale for the review in the context of what is already known	4-5/108-150
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	5/152-156, 8/217-219
<b>METHODS</b>			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	7-8/187-233
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	6/166-185
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	Appendix 1

Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	8/236-238
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	9/238-253
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	9/255-263
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	Appendix 3
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	Appendix 3
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	9/265-273
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	NA
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )	NA
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	NA
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	10/275-285
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	NA
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	NA

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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