

# BMJ Open Global prevalence of dyslipidaemia in adult populations: a systematic review protocol

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## ABSTRACT

**Introduction** Dyslipidaemia is one of the established risk factors for cardiovascular disease. Evidence from large-scale trials showed that effective treatment of dyslipidaemia can reduce all-cause and coronary mortality. To date, there is no published systematic review on the worldwide prevalence of dyslipidaemia in adults. We propose to perform a systematic review on the global prevalence of dyslipidaemia in adults 18 years and older.

**Methods and analysis** We will identify observational studies through comprehensive literature searches. We will search: MEDLINE, Cochrane Central Register of Controlled Trials for published studies and trial registries including the WHO International Trial Registry Platform and ClinicalTrials.gov. Two reviewers will independently screen the titles and abstracts, attain full text of eligible articles, extract data, and appraise the quality and bias of the included studies. Disagreement among the authors will be resolved by discussion leading to a consensus. Next, we will perform a narrative synthesis of the study results. Study heterogeneity will be assessed using  $I^2$  statistics. If  $I^2$  is high ( $\geq 75\%$ ), and plausible heterogeneity contributors are found, we will divide the studies into appropriate subgroups for pooling of results or assess the association of plausible covariates and the prevalence estimates using meta-regression. If  $I^2 < 75\%$ , we will undertake meta-analysis using the random-effects model and transform all prevalence estimates using the Freeman-Tukey transformation for pooling, to obtain a synthesised point estimate of prevalence with its 95% confidence. We will then back-transform the point estimate, and report our results using the back-transformed figures.

**Ethics and dissemination** Ethics approval is not a requirement as this study is based on available published data. Results of this systematic review will be presented at conferences, shared with relevant health authorities, and published in a peer-reviewed journal. These results may help quantify the magnitude of dyslipidaemia globally, and guide preventative and therapeutic interventions.

**PROSPERO registration number** CRD42020200281

## INTRODUCTION

Dyslipidaemia refers to lipid abnormalities consisting of either one or any combination of the following: elevated total cholesterol (TC), elevated low-density lipoprotein cholesterol (LDL-c), elevated triglycerides

## Strengths and limitations of this study

- This is the first systematic review on the global prevalence of dyslipidaemia in adult populations.
- The overall pooled prevalence of dyslipidaemia, as well as the prevalence in different geographical regions and settings will help provide the baseline risk and absolute risk difference in studies assessing interventions for dyslipidaemia.
- Possible limitation of this systematic review could be the lack of studies and data on the subtypes of dyslipidaemia.

(TG) or low high-density lipoprotein cholesterol (HDL-c).<sup>1</sup> Dyslipidaemia is one of the established risk factors for cardiovascular disease.<sup>1</sup> Extensive reviews had concluded that elevated LDL-c is a significant contributor to atherosclerotic cardiovascular disease (CVD).<sup>2-4</sup> Low HDL-c had also been found to be associated with CVD.<sup>5-8</sup> However, recent studies had questioned the role of high TC and LDL-c, in the development of atherosclerosis and CVD.<sup>9-10</sup> The protective role of increasing HDL-c in CVD had also been challenged,<sup>11</sup> while some studies had shown that non-HDL-c predicts CV risk better than LDL-c.<sup>12-14</sup>

The WHO's estimates from 2008 showed that the prevalence of hypercholesterolaemia in adults were the highest in Europe (53.7%) and America (47.7%), while South East Asia (30.3%) and Africa (23.1%) had much lower prevalence.<sup>15</sup> However, Lin *et al* reported marked prevalence differences between different Asia Pacific countries, ranging from 9% in Indonesia to 46.9% in the Philippines.<sup>16</sup> For high LDL-c, high TG and low HDL-c, the prevalence ranges from 7.8% to 47.2%, 13.9% to 38.6% and 10.1% to 71.3%, respectively.<sup>16</sup> Noubiap *et al* in their 2018 systematic review of dyslipidaemia in Africa, reported the prevalence of elevated TC,

elevated LDL-c, elevated TG and low HDL-c as 25.5%, 28.6%, 17% and 37.4%, respectively.<sup>17</sup>

Vigorous evidence from large-scale randomised trials showed that effective treatment of dyslipidaemia can reduce all-cause mortality and coronary mortality.<sup>18</sup> LDL-c reduction of 1 mmol/L with statin treatment can lower the 5-year incidence of stroke, coronary revascularisation and major coronary events by around one fifth.<sup>2 18</sup>

To date, there is no published systematic review on the worldwide prevalence of dyslipidaemia in adults and we aim to address this evidence gap. Hence, the objective of this systematic review is to determine the global prevalence of dyslipidaemia in adults 18 years old and older.

Here, we present the protocol for this systematic review, prepared according to the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols 2015 guidelines.

## METHODS AND ANALYSIS

### Actual start date of study

1st September 2020.

### Anticipated end date of study

28 February 2022.

### Patient and public involvement

No patient involved.

### Study design

This will be a systematic review with meta-analysis if suitable data are available for pooling.

### Search strategy

We will search PubMed/MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL) for published studies and trial registries including the WHO International Trial Registry Platform and ClinicalTrials.gov for ongoing studies. There will be no restrictions applied on the publication period and language. The main search strategy is shown in [table 1](#).

### Participants/population

This systematic review will include adults 18 years or older with dyslipidaemia (elevated TC, elevated LDL-c, elevated TG, low HDL-c).

### Inclusion and exclusion criteria

We will include all cross-sectional and longitudinal observational studies reporting on the prevalence of elevated serum TC, elevated LDL-c, elevated TG and low HDL-c in adults above 18 years old. We will exclude studies of children or individuals with familial hypercholesterolaemia in this review. We will also exclude editorials, commentaries, reviews, letters, case series with less than 50 patients, and studies without primary data or explicit description of methods. When a study is published in two or more reports, the most comprehensive one with the largest sample size will be included.

**Table 1** Search strategy

**Search strategy PubMed/MEDLINE (adapted for CENTRAL)**

Search	Search terms
1	dyslipid*[Title/Abstract]
2	dyslipidemia[MeSH Terms]
3	hyperlipid*[Title/Abstract]
4	hyperlipidemia[MeSH Terms]
5	hypercholesterol*[Title/Abstract]
6	essential hypercholesterolemia[MeSH Terms]
7	hypertriglycerid*[Title/Abstract]
8	hypertriglyceridemia[MeSH Terms]
9	"lipid disorder"[Title/Abstract]
10	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9
11	prevalence[Title/Abstract]
12	prevalence[MeSH Terms]
13	#11 OR #12
14	#10 AND #13

CENTRAL, Cochrane Central Register of Controlled Trials.

### Data extraction (selection and coding)

Two review authors will independently screen the titles and abstracts of the articles retrieved from the literature search. These citations will be imported into the Endnote software, with duplicate articles being omitted. Any studies excluded from the review will be documented with justification. Full texts of potentially eligible articles will be attained and further evaluated for final inclusion. Any disagreement among the review authors will be resolved by discussion leading to a consensus, with referral to a third review author if necessary. We will seek professional translation services for abstracts and full articles that are not available in English.

Two review authors will independently extract relevant data from individual studies using a pro forma designed specifically for this review. The following data will be extracted: first author's name, publication year, study design, country, locality (rural vs urban), setting (community or hospital-based), sample size, mean/median age, age range, proportion of men/women, any disease specific to the study population, dyslipidaemia subtypes included (ie, elevated TC, elevated LDL-c, elevated TG, low HDL-c), diagnostic cut-off levels and the number of participants with dyslipidaemia. We will consider the most frequently used cut-off for the diagnosis of dyslipidaemia. Any disagreement among the review authors will be resolved by discussion leading to a consensus, with referral to a third review author if necessary.

### Risk of bias (quality) assessment

We will evaluate all included studies for quality and bias using an adapted version of the Risk of Bias Tool for

Prevalence Studies developed by Hoy *et al*<sup>19</sup> or the Joanna Briggs Institute's Checklist for Prevalence Studies,<sup>20</sup> pending team deliberation and piloting if required.

### Strategy for data synthesis

First, we will perform a narrative (descriptive) synthesis of the study results. We will assess the degree of heterogeneity in the estimates among studies as measured by the  $I^2$  statistics, which denotes the percentage of variation in estimate that is not attributable to sampling error and will be relevant only if there are more than one included study in the analysis. We adopt an  $I^2$  level of 75% to indicate a substantial degree of heterogeneity.<sup>21</sup> As heterogeneity is inherent among prevalence studies, we adopt a higher threshold of  $I^2$  estimate compared with that in a systematic review of randomised studies.

If  $I^2$  of the pool of studies is below 75%, we will undertake meta-analysis using the random-effects model, to take into account of the inherent heterogeneity present among different prevalent studies. To address the limitations of current meta-analysis of prevalence studies, in which studies with very low or very high prevalence tends to be assigned disproportionately high weight due to the marked reduction of their inferred variance towards 0, we will transform all prevalence estimates using the Freeman-Tukey transformation (arcsine square root transformation)<sup>22</sup> for pooling, to obtain a synthesised point estimate of prevalence with its 95% CI,<sup>23</sup> using the MetaXL software as an add-in of Excel (EpiGear International, Queensland, Australia). We will then back-transform the point estimate and 95% CI, and report our results using the back-transformed figures to facilitate interpretation.

If the  $I^2$  is 75% or above, which indicates substantial level of heterogeneity, we will explore possible contributors of heterogeneity by assessing variation between studies in terms of the following: (i) population characteristics, including geographical location, age group and sex, (ii) definition and measurement of the target condition of dyslipidaemia, including the data collection methods (eg, self-completed questionnaire vs interview or testing (clinical assessment and/or objective test), (iii) risk of bias of the included studies, divided by low or high risks of bias in participation and outcome measurement. If we find plausible contributors of heterogeneity, we will divide the studies into appropriate subgroups for pooling of results or assess the association of plausible covariates and the prevalence estimates using meta-regression (Stata 13 software).

### Sensitivity analysis

If sufficient data are available, we will perform sensitivity analysis to assess the impact of excluding studies with an overall high risk of bias.

### Certainty of evidence

As there is not yet an established tool to rate the certainty of evidence for prevalence studies, we will discuss our findings by incorporating our assessment of the risk of

bias of included studies and our findings in sensitivity analysis.

### Limitation of study

The main potential limitation of this systematic review could be the lack of studies on the prevalence of dyslipidaemia in specific regions around the world such as South America, Australia and the Pacific Islands. In view of our limitations in time and manpower, we have opted to focus on the databases with the highest relevant yields from our experience in our search strategy, which are PubMed/MEDLINE and CENTRAL. These databases cover most relevant articles to be screened and additional databases such as Web of Science and Scopus may yield little additional relevant information amidst a large body of non-relevant articles. Hence, there is a possibility of potentially missing articles with this approach.

### ETHICS AND DISSEMINATION

As the current study is based on available published data, ethics approval is not a requirement. We plan to disseminate the findings from this systematic review at relevant international conferences. Then, we will submit the final report in the form of an article to a peer-reviewed journal for publication. We also plan to share the findings with the relevant health authorities such as the WHO and guideline development bodies. Finally, we plan to update the review in the future as more relevant publications are produced.

**Contributors** M-SM-Y and NML conceived and designed the protocol. M-SM-Y drafted the manuscript. M-SM-Y, NB, SA-R, ASR and NML revised the manuscript for methodological and clinical content. All authors read and approved the final manuscript.

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**Competing interests** None declared.

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**Patient consent for publication** Not applicable.

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