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MODIFIABLE RISK FACTORS IN SECONDARY PREVENTION OF MYOCARDIAL INFARCTION AND ISCHEMIC STROKE IN ATHEROSCLEROSIS: A SYSTEMATIC REVIEW

FATORES DE RISCO MODIFICÁVEIS NA PREVENÇÃO SECUNDÁRIA DO INFARTO DO MIOCÁRDIO E DO ACIDENTE VASCULAR CEREBRAL ISQUÊMICO NA ATEROSCLEROSE: UMA REVISÃO SISTEMÁTICA

FACTORES DE RIESGO MODIFICABLES EN LA PREVENCIÓN SECUNDARIA DEL INFARTO DE MIOCARDIO Y DEL ACCIDENTE CEREBROVASCULAR ISQUÉMICO EN LA ATEROSCLEROSIS: UNA REVISIÓN SISTEMÁTICA

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ABSTRACT

Cardiovascular diseases impose a substantial burden on global health, remaining a leading cause of morbidity and premature death. This systematic review aimed to describe and compare the reported prevalence of key modifiable cardiovascular risk factors among patients undergoing secondary prevention for myocardial infarction and ischemic stroke. The literature search identified 2831 published studies. After removing duplicates, screening the titles and abstracts, and evaluating the potentially eligible studies, 49 epidemiological studies were included, assessing the prevalence of these factors. Given the substantial heterogeneity among the included studies, a meta-analysis was not performed; findings were synthesized narratively. Median prevalences and interquartile ranges were used as the principal descriptive measures, and Pearson's correlation coefficient was applied exploratorily to study-level prevalence estimates. Dyslipidemia and hypertension were reported in all 17 myocardial infarction studies, with median prevalences of 54.6% (IQR: 40.7–63.4) and 48.2% (IQR: 41.1–57.2), respectively, showing a moderate-to-strong positive correlation between their prevalences (r = 0.61, p = 0.007). For ischemic stroke, hypertension and dyslipidemia showed median prevalences of 73% (IQR: 55–77.1) and 45.9% (IQR: 32–60.7), respectively. Our findings show that dyslipidemia, hypertension, smoking, and diabetes mellitus were the most consistently reported modifiable cardiovascular risk factors in secondary prevention populations. Dyslipidemia was frequently documented across studies involving both myocardial infarction and ischemic stroke, highlighting the relevance of lipid assessment within comprehensive cardiovascular risk management.

KEYWORDS: *Secondary prevention. Cardiovascular risk factors. Myocardial infarction. Ischemic stroke.*

RESUMO

As doenças cardiovasculares impõem uma carga substancial à saúde global, permanecendo como uma das principais causas de morbidade e morte prematura. Esta revisão sistemática objetivou descrever e comparar a prevalência relatada dos principais fatores de risco cardiovasculares modificáveis entre pacientes em prevenção secundária após infarto do miocárdio e acidente vascular cerebral isquêmico.

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A busca na literatura identificou 2.831 estudos publicados. Após remoção de duplicatas, a triagem de títulos e resumos e a avaliação dos estudos potencialmente elegíveis, foram incluídos 49 estudos. Devido à heterogeneidade entre os estudos, não foi realizada metanálise, e os achados foram sintetizados narrativamente. As medianas das prevalências e os intervalos interquartis foram utilizados como principais medidas descritivas, e o coeficiente de correlação de Pearson foi aplicado de forma exploratória. A dislipidemia e a hipertensão foram relatadas em todos os 17 estudos sobre infarto do miocárdio, com prevalências medianas de 54,6% (IIQ: 40,7–63,4) e 48,2% (IIQ: 41,1–57,2), respectivamente, apresentando correlação positiva moderada a forte entre suas prevalências (r = 0,61; p = 0,007). Para o acidente vascular cerebral isquêmico, a hipertensão e a dislipidemia apresentaram medianas de 73,0% (IIQ: 55,0–77,1) e 45,9% (IIQ: 32,0–60,7), respectivamente. Nossos achados mostram que dislipidemia, hipertensão, tabagismo e diabetes mellitus foram os fatores de risco cardiovasculares relatados de forma mais consistente nas populações em prevenção secundária. A dislipidemia foi frequentemente documentada nos estudos envolvendo ambos os contextos clínicos, destacando a relevância da avaliação do perfil lipídico no manejo abrangente do risco cardiovascular.

PALAVRAS-CHAVE: Prevenção secundária. Fatores de risco cardiovascular. Infarto do miocárdio. Acidente vascular cerebral isquêmico.

RESUMEN

Las enfermedades cardiovasculares representan una carga sustancial para la salud mundial y continúan siendo una de las principales causas de morbilidad y muerte prematura. Esta revisión sistemática tuvo como objetivo describir y comparar la prevalencia reportada de los principales factores de riesgo cardiovascular modificables entre pacientes en prevención secundaria tras un infarto de miocardio o un accidente cerebrovascular isquémico. La búsqueda bibliográfica identificó 2.831 estudios publicados. Tras la eliminación de duplicados, la revisión de títulos y resúmenes y la evaluación de los estudios potencialmente elegibles, se incluyeron 49 estudios epidemiológicos que evaluaron la prevalencia de estos factores. Debido a la heterogeneidad sustancial entre los estudios incluidos, no se realizó un metanálisis y los hallazgos se sintetizaron de forma narrativa. Las medianas de las prevalencias y los rangos intercuartílicos se utilizaron como principales medidas descriptivas, y el coeficiente de correlación de Pearson se aplicó de forma exploratoria a las estimaciones de prevalencia a nivel de estudio. La dislipidemia y la hipertensión fueron reportadas en los 17 estudios sobre infarto de miocardio, con prevalencias medianas del 54,6% (RIC: 40,7–63,4) y del 48,2% (RIC: 41,1–57,2), respectivamente, mostrando una correlación positiva de moderada a fuerte entre sus prevalencias (r = 0,61; p = 0,007). Para el accidente cerebrovascular isquémico, la hipertensión y la dislipidemia presentaron prevalencias medianas del 73,0% (RIC: 55,0–77,1) y del 45,9% (RIC: 32,0–60,7), respectivamente. Nuestros hallazgos muestran que la dislipidemia, la hipertensión, el tabaquismo y la diabetes mellitus fueron los factores de riesgo cardiovascular modificables reportados de manera más consistente en las poblaciones en prevención secundaria. La dislipidemia fue documentada con frecuencia en los estudios que incluyeron tanto infarto de miocardio como accidente cerebrovascular isquémico, destacando la relevancia de la evaluación del perfil lipídico dentro del manejo integral del riesgo cardiovascular.

PALABRAS CLAVE*: Prevención secundaria. Factores de riesgo cardiovascular. Infarto de miocardio. Accidente cerebrovascular isquémico.*

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INTRODUCTION

Cardiovascular diseases (CVD) impose a substantial burden on global health, remaining a leading cause of morbidity and premature death, with an estimated annual mortality of around 17.9 million in 2019, primarily driven by atherosclerotic cardiovascular disease (ASCVD), especially ischemic heart disease (IHD) and stroke. IHD accounts for around 49.2% of CVD-related deaths, while stroke represents about a quarter, with nearly half of these stroke cases being of ischemic origin. The impact of CVDs on the working-age population is higher, as it is estimated that economic loss due to CVD in low- and middle-income countries from 2011-2030 is projected at $7.1 trillion (US$ 2010), which represents nearly half of the global CVD economic burden (Roth *et al.*, 2020; Ahmed, Guo and Jalal, 2023; Fernando, Pamela and Alejandra, 2014; Bovet and Paccaud, 2011; Nedkoff *et al.*, 2023; GBD 2013 Mortality and Causes of Death Collaborators, 2015; GBD 2016 Causes of Death Collaborators, 2017). The rising numbers of CVD may be attributed to the significant growth levels of modifiable risk factors closely related to atheromatous plaques formation (Poznyak *et al.*, 2022; Vaduganathan *et al.*, 2022), including dyslipidemia, diabetes, hypertension, obesity, and smoking, which are pervasive across high-, low-, and middle-income countries, but with important disparities between them. Low- and middle-income countries exhibit the highest rate of cardiovascular deaths, accounting for 80% of global deaths (Rao *et al.*, 2022; Karunathilake and Ganegoda, 2018).

Evidence suggests that lipid-lowering therapies, which reduce low-density lipoprotein cholesterol (LDL-c), along with lifestyle modifications, play a crucial role in preventing myocardial infarction (MI) and ischemic stroke (Caldwell *et al.*, 2019; Masson *et al.*, 2020; Sanin, Pfetsch and Koenig, 2017; Xiao *et al.*, 2016). However, the dissemination of evidence-based information on risk factors and measures for secondary prevention is often fragmented, and there is a lack of comparative studies analyzing these key aspects.

Secondary prevention aims to mitigate risks in patients with ASCVD, implementing practices to prevent disease progression, permanent damage, and death (Karunathilake and Ganegoda, 2018). A systematic review demonstrated that patients submitted to secondary prevention strategies after suffering from MI had a lower overall risk of mortality (odds ratio [OR] 0.74; 95% confidence interval [95%CI] 0.58-0.95) and a reduced risk of reinfarction (OR 0.53, 95%CI 0.38-0.76) (Lawler, Filion and Eisenberg, 2011), compared to those with lower attendance rates. Another study showed that acute coronary syndrome patients who received secondary prevention measures, such as medication adherence follow-up, experienced a significant reduction in LDL-c levels (median: -25.73 vs. -0.2538, p = 0.0071), compared to those who did

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not receive these measures (Casper *et al.*, 2019). The complexity of secondary prevention in CVD stems from the need to manage multiple risk factors and ensure long-term adherence to treatment and lifestyle modifications. Effective secondary prevention relies on a multifaceted, patient-centered approach to reduce the long-term impacts of ASCVD.

It is worth highlighting that LDL-c is widely recognized as a causal risk factor for the development of MI and other cardiovascular diseases, including ischemic stroke. The results of the Stroke Prevention by Aggressive Reduction in Cholesterol Level (SPARCL) trial revealed that patients who achieved an LDL-c level of less than 70 mg per deciliter (1.8 mmol per liter) experienced a 28% lower relative risk of stroke compared to those who achieved a level of 100 mg per deciliter (2.6 mmol per liter) (Amarenco *et al.*, 2020; Mortensen and Nordestgaard, 2020).

It is also important to distinguish causal risk factors from clinical markers and study-level variables used to describe patient characteristics. Following Kraemer *et al.* (1997), a causal risk factor is one for which empirical evidence, typically from experimental or intervention studies, shows that manipulating the factor changes the risk of the outcome, whereas a marker (fixed or variable) is associated with risk without such evidence of a causal, manipulable relationship. An associated condition or comorbidity that precedes the outcome may technically satisfy the minimal definition of a risk factor, but this precedence alone does not establish whether the condition is causally implicated in the outcome or merely a marker of underlying risk. In observational studies, these categories may nevertheless be grouped together as “risk factors,” even though they represent different clinical and epidemiological concepts (Kraemer *et al.*, 1997).

Moreover, modifiable risk factors are not measured uniformly in clinical practice. Self-reported information, clinical or laboratory measurements, and medical records capture different manifestations of the same condition and may therefore produce different prevalence estimates. Self-reported data depends on participants’ awareness, memory, and understanding of their diagnosis, whereas examination-based data may identify previously undiagnosed abnormalities, and medical records depend on healthcare access, diagnostic practices, and the completeness of clinical documentation. A previous systematic comparison has shown that self-reported data may underestimate the prevalence of hypertension and elevated cholesterol compared with examination-based measurements, and that differences in diagnostic thresholds and medication-based definitions can further affect comparability across studies (Paalanen *et al.*, 2018).

Despite the abundance of evidence regarding individual risk factors and treatment strategies, there is still a lack of systematic reviews that synthesize and compare the prevalence of major modifiable cardiovascular risk factors, including dyslipidemia (encompassing elevated LDL-c and/or total cholesterol, as variably defined across primary studies), hypertension,

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diabetes, and smoking, in the specific context of secondary prevention for both MI and ischemic stroke. Most existing reviews focus on isolated outcomes, primary prevention, or treatment efficacy. To address this gap, a systematic review was conducted to describe and compare the reported prevalence of these key modifiable risk factors, with particular attention to lipid-related measures given their well-established causal role in atherosclerotic disease, in the secondary prevention of MI and ischemic stroke in ASCVD patients.

METHODS

This systematic review was conducted in accordance with the Cochrane Handbook for Systematic Reviews of Interventions (Higgins and Green, 2011). Additionally, it was registered on Open Science Framework (OSF) (October 29th, 2024; https://doi.org/10.17605/OSF.IO/RFJWY) and its report was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (Page *et al.*, 2021).

Eligibility criteria

The scientific articles eligible for inclusion in this systematic review were peer-reviewed prospective or retrospective observational studies aimed at investigating the comparative prevalence of LDL-c, dyslipidemia, or total cholesterol levels compared to other modifiable cardiovascular risk factors in the secondary prevention of MI and ischemic stroke. Studies with other primary objectives that also reported on the prevalence of these risk factors among patients undergoing secondary prevention were also considered.

Inclusion and exclusion criteria

For the purpose of this systematic review, predefined inclusion and exclusion criteria were established by the authors. Only peer-reviewed studies were included. Consequently, other types of scientific articles were excluded, such as systematic reviews, non-systematized reviews, randomized controlled trials comparing treatments, abstracts, editorials, proceedings, and commentary articles. Regarding the scope of the analyzed records, studies that evaluated LDL-c, dyslipidemia or total cholesterol levels and at least one additional modifiable cardiovascular risk factor, such as those related to hypertension (blood pressure, systolic blood pressure, and diastolic blood pressure), diabetes (glycated hemoglobin), obesity (body mass index), smoking, and others were included. The term “modifiable” here refers to the nature of the risk factors, and not to the inclusion of studies assessing the efficacy of interventions to modify them. Included

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studies investigated cardiovascular events and/or major adverse cardiovascular events, with the prerequisite that they incorporated analyses of MI and ischemic stroke. Furthermore, studies examining adult patients in secondary prevention were considered for inclusion. Studies that did not analyze LDL-c (or related risk factors) or that focused on patients without previous cardiovascular conditions, or that assessed another type of cardiovascular disease, were excluded. Additionally, studies that specified the type of stroke were selected, as ischemic stroke is significantly associated with ASCVD (Nedkoff *et al.*, 2023; Vaduganathan *et al.*, 2022).

PECO question

Considering the following question: “What is the reported prevalence of dyslipidemia and other modifiable cardiovascular risk factors among adults in secondary prevention after myocardial infarction or ischemic stroke in ASCVD patients?”, the PECO framework was used to guide study selection and the definition of search terms. The Population (P) comprised adults with a history of myocardial infarction or ischemic stroke in the context of secondary prevention. The Exposure (E) comprised dyslipidemia, used as an overarching term encompassing LDL-c abnormalities, elevated total cholesterol, and clinically diagnosed dyslipidemia, as variably reported in the primary studies. The Comparison (C) consisted of other modifiable cardiovascular risk factors, including hypertension, diabetes mellitus, obesity, and smoking. The Outcome (O) was the reported prevalence of these factors in the included populations.

Literature search and information sources

A reproducible and comprehensive search was performed in the electronic databases MEDLINE and EMBASE. All synonyms, medical subject heading (MeSH) terms, similar terms, and variants of the keywords were considered, ensuring broad coverage for finding the eligible scientific articles (Table S1). A publication-year restriction was applied to include studies published between 2014 and 2024. This period was selected to prioritize contemporary evidence generated under more comparable diagnostic practices, risk-factor definitions, and secondary prevention strategies, which have evolved over time. The restriction also reduced the temporal heterogeneity of the included evidence and ensured that the synthesis reflected the most recent decade available at the time of the search. The last search was carried out in August 2024.

Study selection

Duplicates were removed with EndNote 20 software (EndNote 20, Thomson Reuters, New York, NY) and titles and abstracts of the records were screened to exclude out-of-scope

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studies. Subsequently, full texts of the remaining articles were retrieved and reviewed based on the eligibility criteria. The selection steps were independently conducted by two reviewers, and any disagreement was resolved through consensus. The entire study-selection process was conducted with the Rayyan QCRI software (Ouzzani *et al.*, 2016).

Data collection process and data items

The information and data extracted were collected through Excel (Microsoft Corp, Washington, USA) spreadsheets by two reviewers. For each study included in this systematic review, the following data were extracted: authors, year of publication, study design and location, number and age of patients, sex/gender distribution, follow-up period, and analyzed risk factors.

Risk of bias assessment

The Newcastle-Ottawa scale for observational studies was applied by two authors independently to assess the methodological quality of the included studies (Wells *et al.*, 2000). This tool consisted of eight questions dispersed across the three domains: Selection (four questions), Comparability (one question), and Outcome (three questions). Usually, the highest possible score for the scale is nine points (Wells *et al.*, 2000; Manchanda *et al.*, 2023). However, in this systematic review, an adapted version of the tool was applied. The Selection item "Demonstration that outcome of interest was not present at start of study" could not be meaningfully scored because, by the eligibility criteria of the primary studies themselves, all cohort members had already experienced the outcome of interest (MI or ischemic stroke) at baseline; these are secondary-prevention populations by definition, not incidence cohorts. The Comparability domain, which in the original scale assesses whether a cohort study controls for confounding between an exposed and an unexposed comparison group, was not applicable to the design of the present review, since the included studies report the prevalence of risk factors within a single population of patients already undergoing secondary prevention, without an internal unexposed comparator group; this adaptation was specified in the protocol registered on OSF prior to data collection. Studies that attained the maximum adapted score (6/6) were descriptively classified as low risk of bias, whereas studies that did not meet at least one of the applicable criteria (score 4-5) were classified as moderate risk of bias; these categories represent a descriptive convention adopted for this review rather than a validated categorical cut-off; converting Newcastle-Ottawa Scale scores into quality categories warrants cautious interpretation, as this practice may yield arbitrary results (Stang, 2010). Any disagreements

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between the two reviewers over the bias assessment were resolved, if necessary, by discussion and consensus with a third reviewer.

Data analysis

The data analysis for this systematic review was conducted after extracting quantitative information on each identified risk factor from the included studies. Given the heterogeneity of study designs, populations, and reporting formats, a meta-analysis was not feasible. Therefore, a narrative synthesis strategy was adopted. The synthesis focused on assessing the reported prevalence of major modifiable cardiovascular risk factors in the context of secondary prevention, allowing for a comparative understanding across studies.

Quantitative data extraction focused on the prevalence of modifiable cardiovascular risk factors reported in each included study. For each risk factor, the proportion of patients with the condition (denoted as “Y” in the data matrix) and without the condition (“N”) was extracted when available. However, only the values referring to the presence of the condition (“Y”) were used in the analysis. When studies reported stratified results (e.g., by sex or age), only the overall values for the total population were included to ensure consistency. All prevalence values were extracted as originally reported by the authors and were used in descriptive analyses and correlation testing. Box plots were generated to describe the distribution, central tendency, variability, and outliers of the reported prevalence values. Simple arithmetic means were calculated solely as descriptive summaries of study-level prevalences. Because the included studies differed in sample size, population characteristics, definitions, and ascertainment methods, these values were not weighted by sample size and should not be interpreted as pooled prevalence estimates. Pearson’s correlation coefficient was applied as an exploratory study-level analysis to examine whether the reported prevalences of the main risk factors varied together across studies. These correlations represent ecological associations between aggregated study-level prevalences and do not indicate individual-level associations or co-occurrence of risk factors. Data management was performed in Microsoft Excel, and statistical analyses were conducted in R using the base package stats.

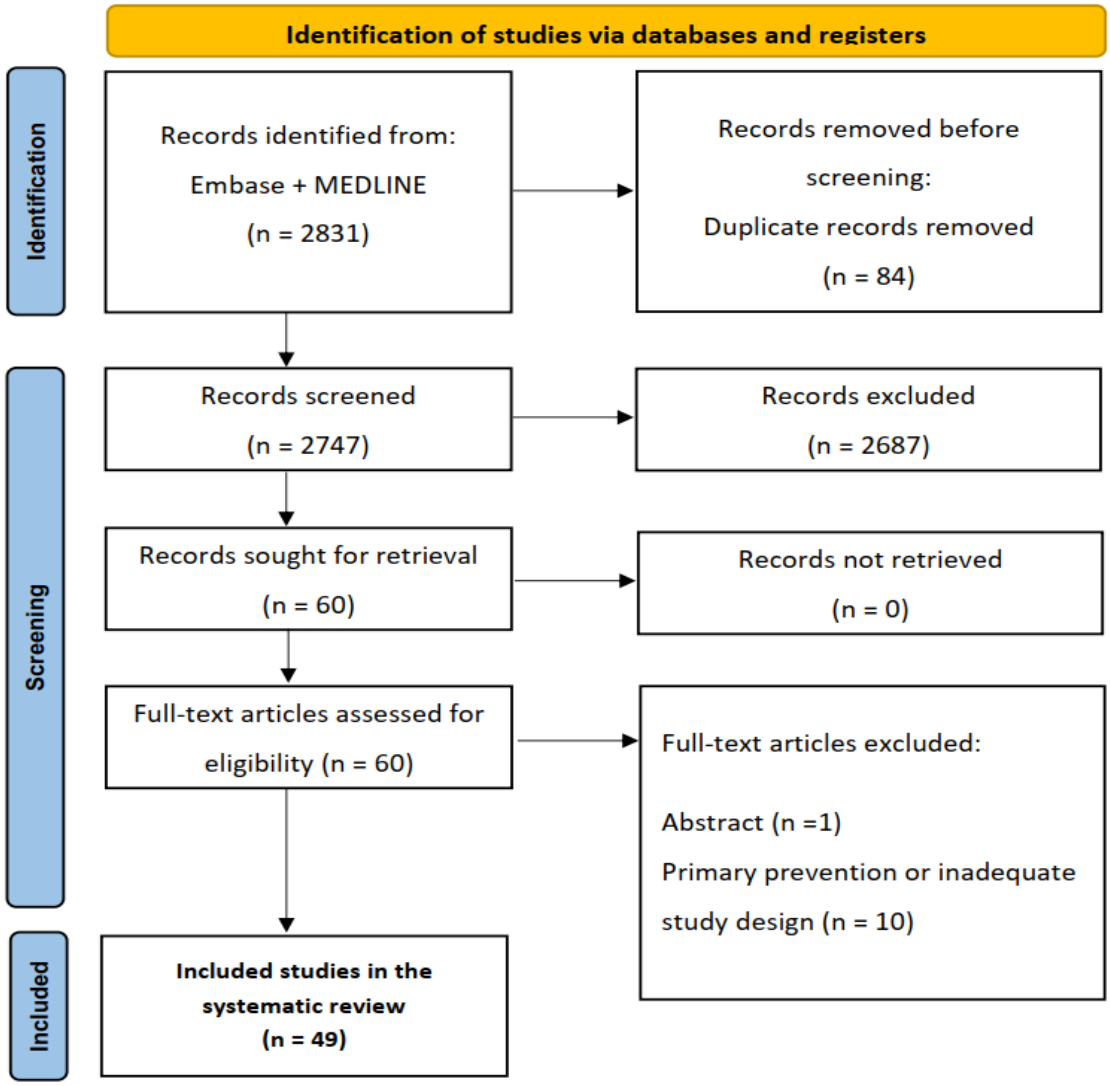
RESULTS AND DISCUSSION

The literature search identified 2831 published studies. After removing duplicates, 2747 records were screened by title and abstract; 2687 were excluded as ineligible, and 60 reports were sought for retrieval. All 60 reports were successfully retrieved and assessed for eligibility. In

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the full-text analysis step, 11 studies were excluded: an abstract published in conference proceedings, seven studies of primary prevention, and three studies with inadequate design (out of scope), as they analyzed inflammatory markers in patients with MI, the relationship between diagonal earlobe creases and stroke, and discussed radiological evaluations of Doppler images related to possible risk factors. Finally, 49 epidemiological studies were included. Figure 1 represents the PRISMA flow-chart for studies identification.

Figure 1. PRISMA flow-chart of study selection.

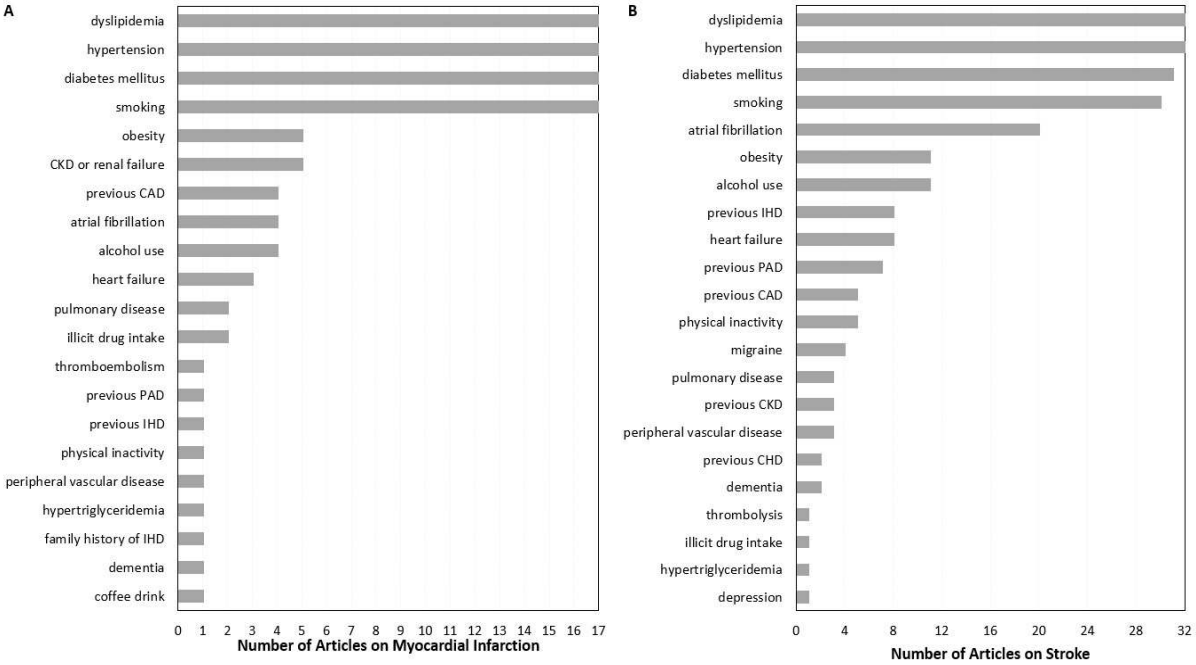


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Of the 49 studies retrieved, 17 focused on patients with MI, and 32 on patients with stroke (all focused on the ischemic stroke subtype), all published between 2014 and 2024. These studies exhibit considerable diversity in terms of study design, objectives, and geographic locations. Additionally, different cardiovascular risk factors were considered in the respective epidemiological analyses. Detailed information about the design of included studies and patient characteristics is provided in Table S2.

Among the 49 included studies, the most frequently analyzed risk factors were dyslipidemia, hypertension, diabetes, and smoking, which were the main four in studies on both MI and ischemic stroke. This is an expected outcome, as these modifiable risk factors are well-established contributors to the development of ASCVD. Following these, among the risk factors analyzed in three or more articles, MI studies also considered obesity, chronic kidney disease or renal failure, previous coronary artery disease (CAD), atrial fibrillation, alcohol use, and heart failure were also analyzed. In stroke-related articles, atrial fibrillation, obesity, alcohol use, heart failure, previous IHD, previous peripheral artery disease, previous CAD, physical inactivity, migraine, pulmonary disease, previous chronic kidney disease, and previous peripheral vascular disease were also considered by the authors (Figure 2).

Figure 2. Risk factors frequency in articles on MI (A) and ischemic stroke (B).

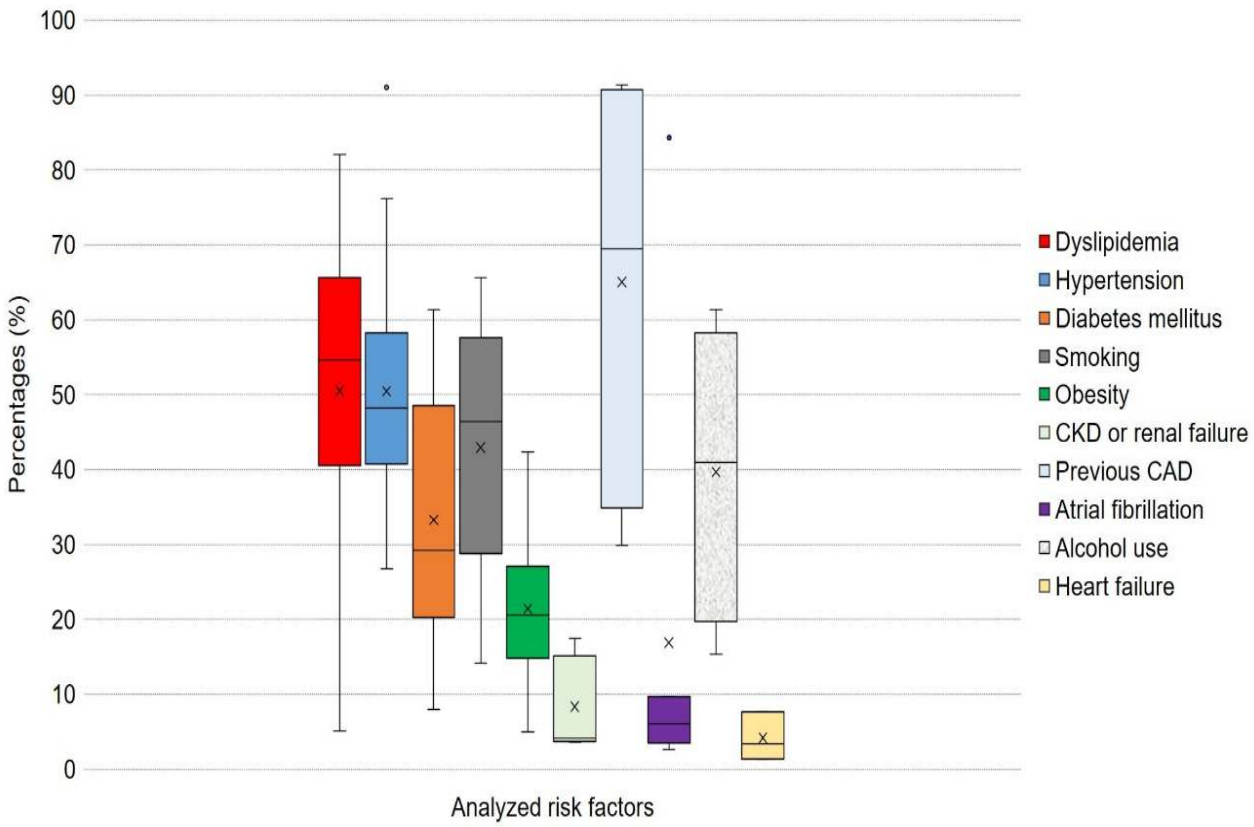


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A detailed overview of the prevalence of risk factors identified in the included studies, presented as percentages, is provided. Due to the extensive range of factors identified, the data are organized into four tables, focusing on those included in three or more studies (Tables S3–S6). Given the substantial heterogeneity among the included studies, a meta-analysis was not performed; findings were synthesized narratively.

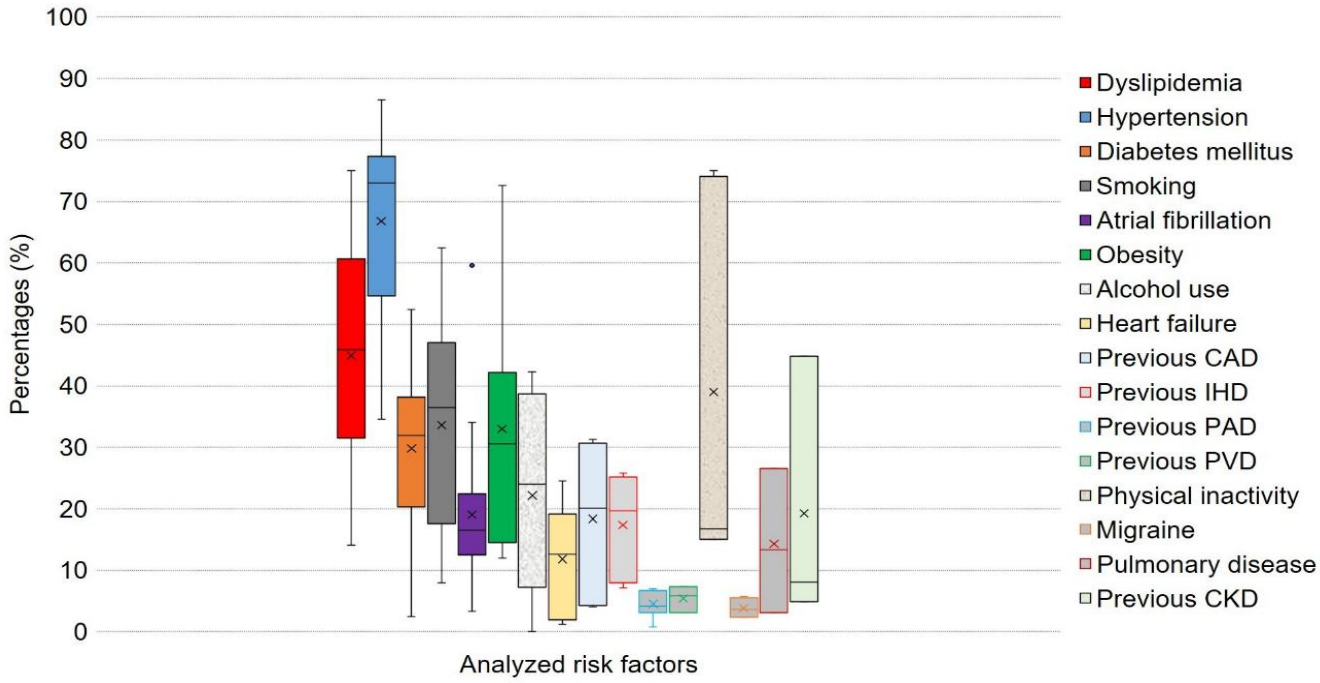
Box plots were generated to provide a clearer understanding of the analyzed risk factors in the context of MI (Figure 3) and ischemic stroke (Figure 4) research.

Figure 3. Analyzed risk factors related to myocardial infarction, expressed as percentages (%). The X inside each boxplot indicates the mean, and the dots represent the outliers.



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Figure 4. Analyzed risk factors related to ischemic stroke, expressed as percentages (%). The X inside each boxplot indicates the mean, and the dots represent the outliers.



For MI, dyslipidemia and hypertension were reported in all 17 included studies and showed median prevalences of 54.6% (IQR: 40.65–63.4) and 48.2% (IQR: 41.05–57.15), respectively. Smoking was evaluated in 16 studies and had a median prevalence of 46.45% (IQR: 30.5–56.28), whereas diabetes mellitus was reported in all 17 studies, with a median prevalence of 29.2% (IQR: 21.4–47.7). These four factors were the most consistently assessed across the included studies. Previous CAD and alcohol use showed median prevalences of 69.5% and 41%, respectively; however, these findings should be interpreted cautiously because each factor was reported in only four studies and showed substantial variability across estimates. Overall, the median prevalences of all factors analyzed ranged from 3.4% to 69.5% (Figure 3).

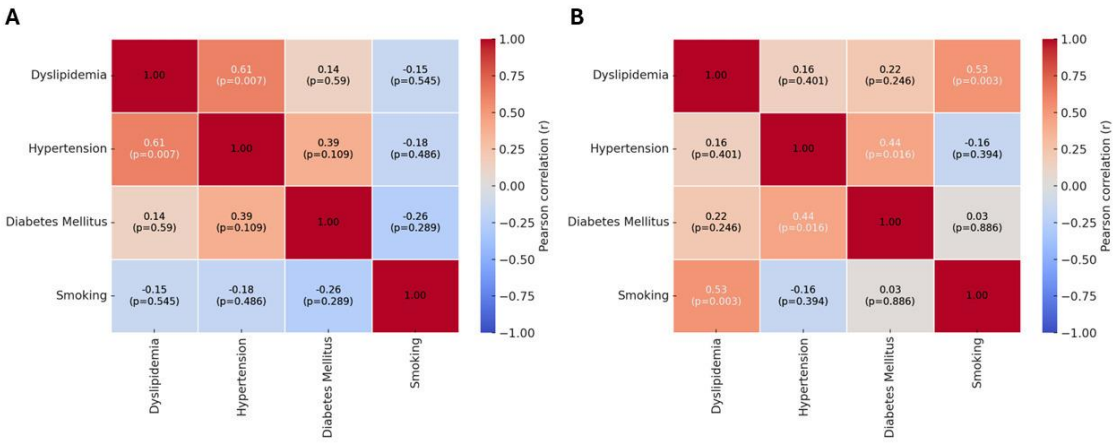
For ischemic stroke, dyslipidemia and hypertension were reported in all 32 included studies and showed median prevalences of 45.85% (IQR: 32.02–60.7) and 73% (IQR: 55.02–77.1), respectively. Diabetes mellitus was evaluated in 31 studies and had a median prevalence of 31.9% (IQR: 20.9–38.2), whereas smoking was reported in 30 studies, with a median prevalence of 36.45% (IQR: 18.6–46.9). These four factors were the most consistently assessed across the included studies. Physical inactivity and obesity showed median prevalences of 16.7%

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and 30.6%, respectively; however, these estimates should be interpreted cautiously because physical inactivity was assessed in only 5 studies and obesity in 11 studies, with substantial variability across estimates. Overall, the median prevalences of all factors analyzed ranged from 3.6% to 73% (Figure 4).

Considering the main risk factors identified across the included studies, an exploratory Pearson correlation analysis was conducted using study-level prevalence estimates. For MI, a statistically significant positive correlation was observed between the reported prevalences of dyslipidemia and hypertension (r = 0.61, p = 0.007), indicating that these prevalences tended to vary in the same direction across studies. The remaining correlations were weak or inverse and were not statistically significant. In studies on ischemic stroke, significant positive correlations were observed between the reported prevalences of dyslipidemia and smoking (r = 0.53, p = 0.003) and between hypertension and diabetes mellitus (r = 0.44, p = 0.016). These findings represent ecological associations at the study level and should not be interpreted as evidence of individual-level co-occurrence or causal relationships between risk factors (Figure 5).

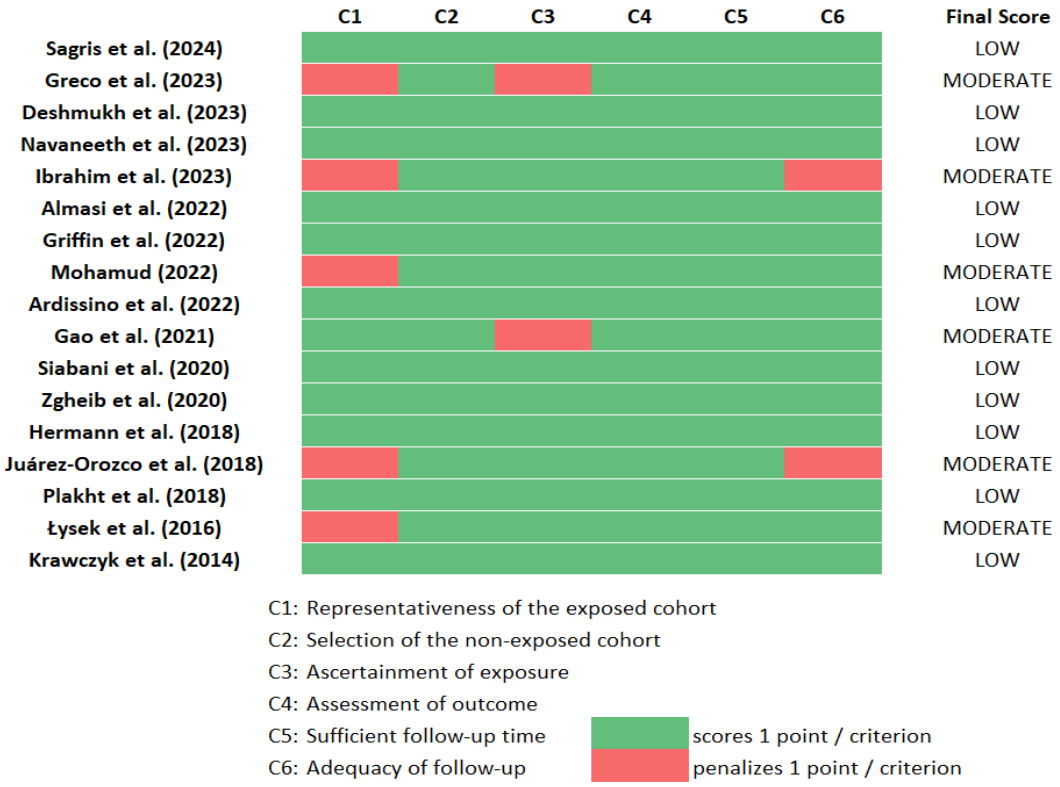
Figure 5. Pearson correlation matrices for the main cardiovascular risk factors across the included studies. (A) Studies on myocardial infarction. (B) Studies on ischemic stroke. Each cell represents the Pearson correlation coefficient (r) and the corresponding p-value between pairs of risk factors. Statistically significant correlations are highlighted in white font.



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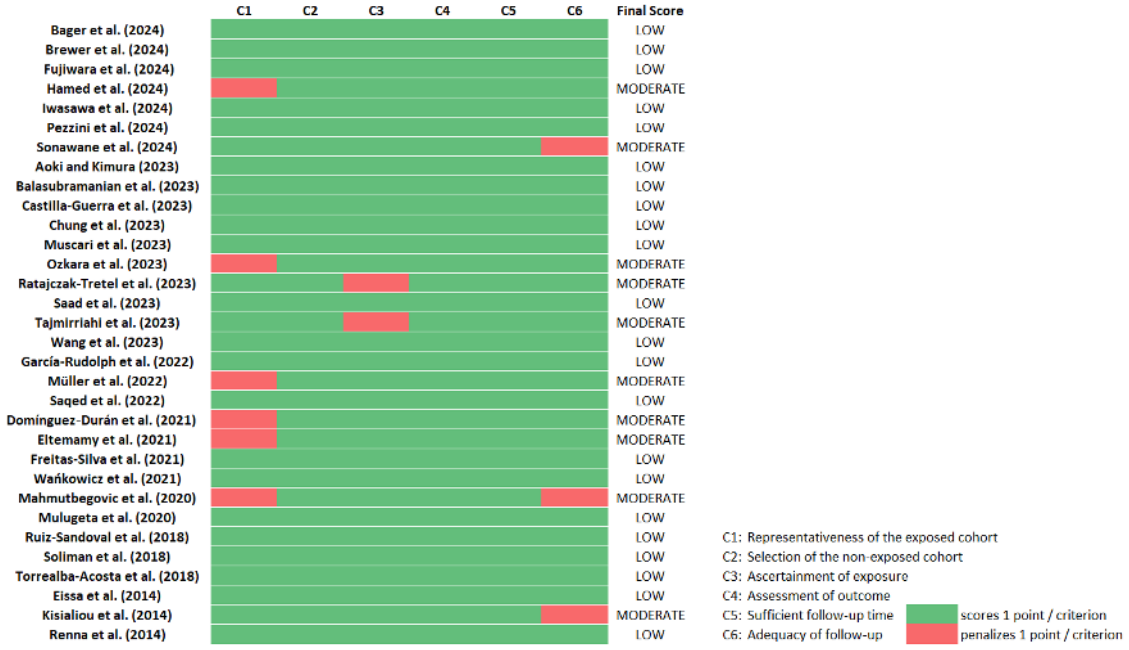
Figures 6 and 7 present the risk of bias analysis for the articles included in the systematic review, assessed using the Newcastle-Ottawa Scale. The scores ranged from 4 to 6 points, with the majority receiving the maximum score of 6, indicating a low risk of bias. Studies that did not achieve the maximum score lost points on the following criteria: 'Representativeness of the Exposed Cohort,' due to the small sample size of patients; 'Ascertainment of Exposure,' as they did not provide specific descriptions of how exposure to risk factors was confirmed; and 'Adequacy of Follow-up,' for studies that did not provide information on the duration of the study period. Consequently, studies that lost points on these criteria can be considered to have a moderate risk of bias, as these limitations may affect the reliability of the findings. The risk of bias analysis is also represented in tables (Table S7 and Table S8).

Figure 6. Assessment of risk of bias of myocardial infarction studies using the adapted Newcastle-Ottawa scale.



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Figure 7. Assessment of risk of bias of ischemic stroke studies using the adapted Newcastle-Ottawa scale.



Our systematic review emphasizes that dyslipidemia, hypertension, diabetes mellitus, and smoking are the most consistently reported modifiable cardiovascular risk factors among patients undergoing secondary prevention following MI and ischemic stroke. These factors were evaluated in nearly all of the 49 studies included in our analysis, highlighting their central role in the clinical characterization and management of patients with established cardiovascular disease.

Among studies of patients with MI, dyslipidemia and hypertension were reported in all 17 studies and showed median prevalences of 54.6% (IQR: 40.7–63.4) and 48.2% (IQR: 41.1–57.2), respectively. Pearson's correlation coefficient analysis indicated a moderate to strong positive correlation between the study-level reported prevalences of dyslipidemia and hypertension in studies of patients with MI ($r = 0.61$, $p = 0.007$). Despite the heterogeneity in populations, geographic settings, diagnostic criteria, and ascertainment methods across studies, this tendency to covary indicates that the reported prevalences of dyslipidemia and hypertension varied together across studies of patients with MI. However, because the analysis was based on aggregated prevalence estimates, it cannot confirm that these conditions co-occurred within the same individuals or establish a causal relationship between them.

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For ischemic stroke, hypertension showed the highest median prevalence at 73% (IQR: 55.02–77.1), followed by dyslipidemia at 45.85% (IQR: 32.02–60.7). For this context, no significant study-level correlation between the reported prevalences of dyslipidemia and hypertension was observed. This absence of correlation indicates that the aggregated prevalences of these factors did not vary together consistently across the included studies. It should not be interpreted as evidence that their simultaneous management is less relevant among patients with ischemic stroke. Differences in population characteristics, stroke mechanisms, diagnostic definitions, and ascertainment methods may have influenced this finding.

The study-level correlation observed among studies of patients with MI should not be interpreted as direct evidence of the clinical benefit of simultaneously managing dyslipidemia and hypertension. Nevertheless, integrated control of lipid levels and blood pressure is an established component of secondary cardiovascular prevention. Evidence from randomized clinical trials indicates that polypill strategies combining lipid-lowering and blood pressure-lowering agents can improve treatment adherence and may contribute to reducing the risk of major adverse cardiovascular events (De Cates *et al.*, 2014; Di Fusco *et al.*, 2023).

Following dyslipidemia and hypertension, our findings showed that smoking and diabetes mellitus were also frequently reported modifiable risk factors in studies of cardiovascular secondary prevention. For MI, smoking had a median prevalence of 46.5% (IQR: 30.5–56.3), whereas diabetes mellitus had a median prevalence of 29.2% (IQR: 21.4–47.7). For ischemic stroke, smoking had a median prevalence of 36.45%, and diabetes mellitus had a median prevalence of 31.9%.

This convergence between our findings and global estimates highlights the consistency of key risk factors across different populations. The main risk factors reported for secondary prevention in our systematic review are also among the top fifteen contributors to cardiovascular disease, according to the Global Burden analysis by Mensah et al. (2023).

This systematic review has limitations that should be acknowledged. Restricting inclusion to studies published between 2014 and 2024 prioritized contemporary evidence and reduced temporal heterogeneity but may have excluded relevant earlier studies. The search was restricted to MEDLINE and EMBASE and did not include other databases (e.g., Web of Science, Scopus, CENTRAL) or gray literature; although these two databases provide broad coverage of the clinical and epidemiological literature relevant to this topic, this restriction may have limited the comprehensiveness of study identification. The analysis relied on study-level prevalence estimates without access to individual participant data or standardized definitions. Risk factors were identified through different methods, including self-report, clinical or laboratory

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measurements, previous diagnoses, medication use, and medical records, which limit direct comparability across studies. Simple arithmetic means were initially used as descriptive summaries but assigned equal weight to studies with markedly different sample sizes. Medians and interquartile ranges were therefore adopted as the principal descriptive measures. Weighting by sample size would not resolve heterogeneity in populations, definitions, and ascertainment methods and could imply unsupported precision. Pearson correlations were based on aggregated study-level prevalences and should not be interpreted as evidence of individual-level association, co-occurrence, or causality. Subgroup analyses were not performed, and publication or reporting bias may be present. Finally, this descriptive synthesis does not provide pooled prevalence estimates or longitudinal associations with recurrent cardiovascular outcomes.

Taken together, our findings support the importance of dyslipidemia in secondary prevention, particularly among patients with MI, in whom its reported prevalence showed a positive study-level relationship with hypertension. This evidence supports the importance of interpreting lipid abnormalities within a broader framework of integrated cardiovascular risk management. Accordingly, early and sustained LDL-c reduction through appropriate therapy remains a central component of secondary prevention and is associated with improved cardiovascular outcomes (Linton *et al.*, 2000; Santangelo *et al.*, 2022).

CONCLUSIONS

This systematic review showed that dyslipidemia, hypertension, smoking, and diabetes mellitus were the most consistently reported modifiable cardiovascular risk factors among patients undergoing secondary prevention for MI and ischemic stroke. Dyslipidemia was frequently documented in both clinical contexts, reinforcing the relevance of lipid assessment within integrated cardiovascular risk management. Comprehensive secondary prevention should therefore address multiple modifiable risk factors in high-risk populations, while recognizing that the evidence synthesized in this review derives from observational studies with heterogeneous definitions and ascertainment methods and does not provide standardized or pooled prevalence estimates.

DECLARATIONS

Ethics approval and consent to participate: Not applicable.
Consent for publication: Not applicable.

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Authors' contributions: Ione Ayala Gualandi de Oliveira conceived of this study; André Ferreira Azeredo da Silva supervised this research; Daniela Debone and Bruna Muhlinberg Vetromilla participated in the collection of the data; Daniela Debone and Bruna Muhlinberg Vetromilla analyzed the data; Daniela Debone and Bruna Muhlinberg Vetromilla, André Ferreira Azeredo da Silva, and Ione Ayala Gualandi de Oliveira drafted and revised the manuscript; and all authors have read and approved the final version of the manuscript.

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