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REVIEW

Burden of risk factors in women and men with unrecognized myocardial infarction: a systematic review and meta-analysis†

Julie A.E. van Oortmerssen [1], Noluthando Ntlapo [1], Martijn J. Tilly [1], Wichor M. Bramer [2], Hester M. den Ruijter [3], Eric Boersma [4], Maryam Kavousi [1], and Jeanine E. Roeters van Lennep [5]*; on behalf of the IMPRESS consortium

[1]Department of Epidemiology, Erasmus MC, University Medical Centre Rotterdam, PO Box 2040, 3000 CA Rotterdam, The Netherlands; [2]Medical Library, Erasmus MC, University Medical Centre Rotterdam, PO Box 2040, 3000 CA Rotterdam, The Netherlands; [3]Laboratory for Experimental Cardiology, University Medical Centre Utrecht, Utrecht University, Utrecht, The Netherlands; [4]Department of Cardiology, Erasmus MC Cardiovascular Institute, University Medical Centre Rotterdam, PO Box 2040, 3000 CA Rotterdam, The Netherlands; and [5]Department of Internal Medicine, Erasmus MC Cardiovascular Institute, University Medical Centre Rotterdam, PO Box 2040, 3000 CA Rotterdam, The Netherlands

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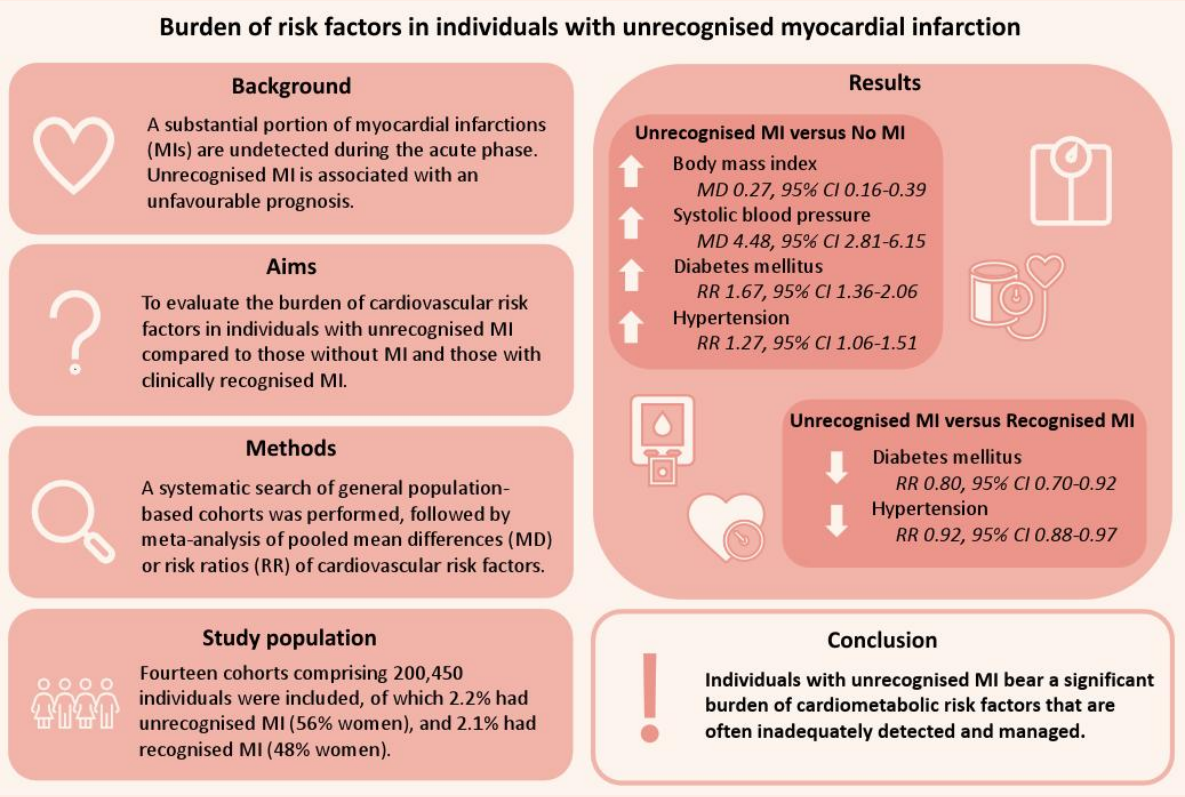
Abstract

Unrecognized myocardial infarction (MI) is an MI that remains undetected in the acute phase and is associated with an unfavourable prognosis. With this systematic review and meta-analysis, we evaluated the burden of cardiovascular risk factors in individuals with unrecognized MI. We searched general population-based cohort studies diagnosing unrecognized MI by electrocardiogram or myocardial imaging up to 24 November 2023. Pooled mean differences (MDs) or risk ratios (RRs) with 95% confidence intervals (CIs) were determined, and random-effects meta-analyses were performed. Fourteen cohort studies were included involving 200 450 individuals (mean age 62.8 ± 9.9 years, 56.0% women), among which 4322 (2.2%) experienced unrecognized MI (mean age 66.3 ± 8.2 years, 47.8% women) and 4653 (2.1%) recognized MI (mean age 68.5 ± 7.3 years, 33.8% women). Compared to individuals without MI, those with unrecognized MI had higher body mass index (MD 0.27, 95% CI 0.16–0.39) and systolic blood pressure (MD 4.48, 95% CI 2.81–6.15) levels, and higher prevalence of hypertension (RR 1.27, 95% CI 1.06–1.51) and diabetes mellitus (RR 1.67, 95% CI 1.36–2.06). Furthermore, individuals with unrecognized MI had lower prevalence of hypertension (RR 0.92, 95% CI 0.88–0.97) and diabetes mellitus (RR 0.80, 95% CI 0.70–0.92). Individuals with unrecognized MI are characterized by a substantial burden of metabolic risk factors. Our findings suggest insufficient recognition and management of cardiovascular risk factors among individuals with unrecognized MI.

* Corresponding author. Department of Internal Medicine, Erasmus MC Cardiovascular Institute, University Medical Centre, Dr. Molewaterplein 40, 3015 GD Rotterdam, The Netherlands. Tel: +31 107040704, E-mail: j.roetersvanlennep@erasmusmc.nl

† Results of this study were presented at the European Society of Cardiology Congress 2023 in a moderated poster session on 25 August 2023.

Graphical Abstract



Keywords Unrecognized myocardial infarction • Silent myocardial infarction • Asymptomatic disease • Heart disease risk factors • General population

1. Introduction

Coronary heart disease, primarily myocardial infarction (MI), is the leading cause of mortality worldwide.[1] Despite ongoing advancements in cardiovascular risk management and post-MI treatment, an estimated 20–60% of all MIs are undiagnosed in the acute phase, depending on the study population and diagnostic technique employed.[2–4] The retrospective diagnosis of unrecognized MI relies on the identification of pathological Q-waves on the electrocardiogram (ECG), myocardial imaging revealing evidence of a loss of viable myocardium, or pathological findings on autopsy.[2,5,6] It can manifest either with symptoms or without, yet is predictive of subsequent major cardiovascular events, including cardiovascular mortality.[7] This underscores the importance of identifying high-risk populations that may benefit from screening or intervention strategies.

While the absence of symptoms may explain some undiagnosed cases of MI, there remains a dearth of information on factors predisposing to unrecognized MIs, complicating the development of optimal screening or intervention strategies.[3,8] Sex-related factors may also contribute to under-recognition, as evidenced by a higher ratio of unrecognized to recognized MI cases among women compared to men.[8] Furthermore, delays in seeking healthcare among symptomatic patients have been associated with sociocultural factors, such as educational level, literacy, health literacy, and distance to healthcare. Current guidelines recommend performing a resting ECG solely in asymptomatic individuals with diabetes mellitus and hypertension.[9,10,11] However, robust evidence for this expert recommendation is lacking and the true prevalence of cardiovascular risk factors in individuals with unrecognised MI in the general population is unknown. Therefore, with this systematic review and meta-analysis, we evaluated the burden of these risk factors among individuals with unrecognised MI. We further compared these risk factors among individuals with unrecognised MI to those with recognised MI.

2. Methods

2.1 Data sources and study selection

This review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines[12] and was registered with the International Prospective Register of Systematic Reviews (PROSPERO) as ID CRD42023392597.[13] Local ethical approval was obtained for all studies included in the analysis at the time of their conduct, and participants in these studies provided informed consent before their involvement.

A comprehensive search strategy was developed by an experienced information specialist (W.M.B.) in Embase, optimized for sensitivity, and translated to other databases.[14] The search, conducted in multiple databases including Embase, Medline ALL via Ovid, and Web of Science Core Collection, was originally performed on 1 March 2022 and last updated on 24 November 2023 (see Supplementary material online, *Appendix S1*). No limitation was placed on the study publication date. No author or subject expert contacts were made, and unindexed journals were not browsed. EndNote was used to manage search results, with duplicates removed by a medical librarian. Two reviewers (J.v.O. and N.N.) independently screened references by title and abstract, followed by full-text assessment and

application of inclusion criteria for relevant studies. Discrepancies were adjudicated by a third reviewer (M.K.). Reference lists of all records deemed eligible after full-text assessment were manually checked to identify other potential studies. The methodological quality of the included studies was assessed using the Newcastle-Ottawa Quality Assessment Scale for cohort studies by at least two assessors (J.v.O., N.N., or M.T.), with discrepancies resolved by consensus.[15]

2.2 Inclusion and exclusion criteria

This study included prospective population-based cohort studies (participants aged ≥18 years) detecting unrecognized MI and reporting mean values with standard deviations (SDs), median values with interquartile ranges (IQRs), or numbers with percentages of cardiovascular risk factors in individuals with unrecognized MI vs. those without MI. Data on recognized MI, if available, were also considered. Unrecognized MI was defined as an MI that was not recognized as such during the acute phase, but eventually discovered by detection of pathological Q-waves on ECG or myocardial imaging, such as cardiac magnetic resonance imaging (MRI), revealing evidence of a loss of viable myocardium. Recognized MI involved a documented clinical history of acute MI, while no MI referred to the absence of recognized MI and ECG or myocardial imaging findings suggestive of MI. Excluded were studies lacking original data, not diagnosing unrecognized MI via resting ECG or myocardial imaging, or lacking information on risk factors present in individuals with unrecognized MI or without MI. If multiple articles were reported on the same study cohort, only the most comprehensive and recent study was included. All established risk factors for cardiovascular disease, as outlined in current guidelines, were taken into account for this study.[16,17] Risk factors were included in our analyses if data were reported for at least three cohorts. Eligible studies needed to present risk factors and MI status in a cross-sectional manner. Consequently, our analysis focused solely on assessing the burden of risk factors associated with different MI statuses rather than delving into the longitudinal trajectories of these risk factors over time and their association with the occurrence of MI.

2.3 Statistical analyses

Means and SDs were extracted from the included studies (J.v.O. and N.N.). If median and IQR were reported, SD was manually calculated by dividing IQR by 1.35 as per the Cochrane Handbook.[18] Inverse variance weighting was used for pooling, with differences reported as mean difference (MD) and 95% confidence interval (CI). Due to anticipated high heterogeneity, random-effect models were used.

To explore the observed heterogeneity among the included studies, several sensitivity analyses were conducted. Analyses were repeated excluding studies that diagnosed unrecognized MI using myocardial imaging instead of ECG. Additionally, analyses were also stratified by continent and by the timeframe during which the data were collected. The year 1994 was chosen as a stratification point because it marked the Scandinavian Simvastatin Survival Study, the first statin trial to show reduced mortality and advance cardiovascular disease prevention.[19]

Statistical significance was set at a two-tailed $P \leq 0.05$. Data management and statistical analyses were conducted using IBM SPSS Statistics for Windows, version 28.0 (IBM Corp., Armonk, NY, USA) and R: A language and environment for statistical computing, version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

3.1 Study selection and study population

Out of 4977 records identified, 2736 remained after duplicates were removed. Following title and abstract screening, 158 (5.8%) qualified for full-text review (*Figure 1*). Exclusions after full-text assessment involved studies without specified risk factors for individuals with unrecognized MI or those without MI ($n = 52$), not adhering to predefined criteria for diagnosing

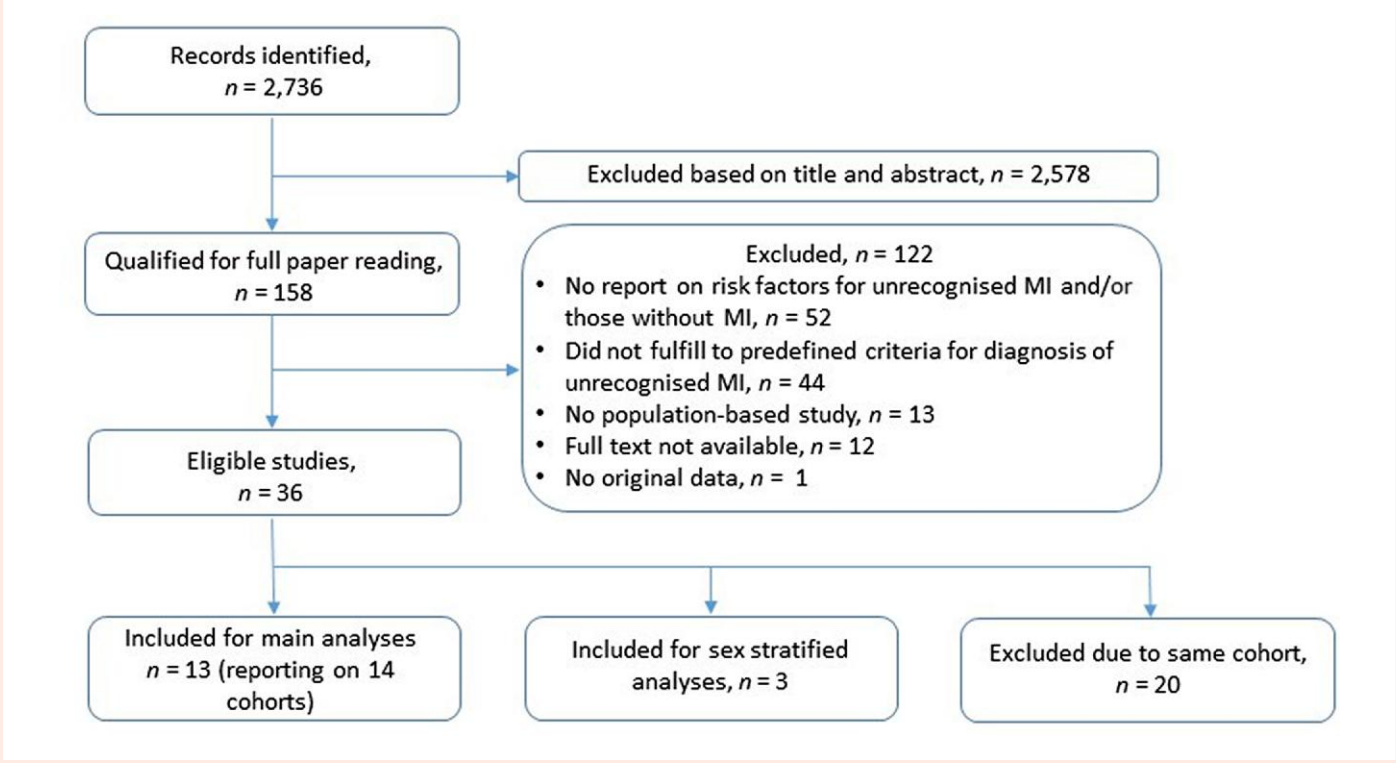


Figure 1 Flowchart of the inclusion and exclusion of studies. MI, myocardial infarction; *n*, number.

unrecognized MI ($n = 44$), non-population-based studies ($n = 13$), lack of full-text availability ($n = 12$), and studies lacking original data ($n = 1$), leaving 36 eligible studies (see Supplementary material online, *Appendix S2*). No additional relevant studies were identified through reference checking. After excluding studies reporting on the same cohort, 13 studies were included in the main analyses,[20–32] reporting on a total of 14 study cohorts as one study included 2 cohorts[20] (*Table 1*). Of these, 11 study cohorts provided data on individuals with both unrecognized MI and recognized MI.[20–23,26–31] The 14 study cohorts comprised in total 200 450 participants (mean age 62.8 ± 9.9 years, 56% women), including 4322 participants (2.2%) with unrecognized MI (mean age 66.3 ± 8.2 years, 47.8% women) and 4653 participants (2.1%) with recognized MI (mean age 68.5 ± 7.3 years, 33.8% women). In studies diagnosing unrecognized MI by ECG, the unrecognized to recognized MI ratio ranged from 0.4 to 3.2 in men and 0.6 to 2.2 in women. In studies diagnosing unrecognized MI by MRI, the unrecognized to recognized MI ratio was 3.1 to 13.5 in men and 1.8 to 11 in women. For comparisons between individuals with unrecognized MI vs. no MI, and unrecognized vs. recognized MI, we had sufficient data to analyse the following risk factors: body mass index, systolic and diastolic blood pressure, hypertension, serum total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol, diabetes mellitus, and smoking status.

Additionally, 3 out of 36 eligible studies reported data stratified by sex and were analysed to explore differences in the prevalence of cardiovascular risk factors in unrecognized MI vs. no MI among men and women[33–35] (*Table 2*). For sex-stratified analyses, 20 167 individuals (mean age 57.1 ± 16.8 years, 56.7% women) were included, with 507 participants (2.5%) having unrecognized MI (mean age 71.0 ± 9 years, 50.5% women). For sex-stratified analyses on the comparison of individuals with unrecognized MI vs. no MI, sufficient data were available to analyse the following risk factors: body mass index, hypertension, diabetes mellitus, and current smoking.

3.2 Unrecognized MI vs. no MI

Individuals with unrecognized MI had significantly higher values of body mass index (MD 0.27 kg/m^2, 95% CI 0.16–0.39) and systolic blood pressure (MD 4.48 mmHg, 95% CI 2.81–6.15) compared to those without MI (*Figure 2*). Moreover, a higher prevalence of hypertension [risk ratio (RR) 1.27 mmHg, 95% CI 1.06–1.51] and diabetes mellitus (RR 1.67, 95% CI 1.36–2.06) was observed in the unrecognized MI group. No significant differences were found in diastolic blood pressure values (MD 1.27 mmHg, 95% CI −0.55 to 3.09) or total cholesterol levels (MD −0.01 mmol/L, 95% CI −0.23 to 0.20). Similarly, no significant disparities were identified in the prevalence of dyslipidaemia (RR 1.06, 95% CI 0.84–1.35) or ever smoking (RR 1.11, 95% CI 0.88–1.40). Insufficient data were available to conduct a pooled analysis of HDL cholesterol, LDL cholesterol, or triglycerides levels.

3.3 Recognized MI vs. no MI

In individuals with recognized MI, there was a higher prevalence of hypertension (RR 1.33, 95% CI 1.08–1.63) and diabetes mellitus (RR 2.33, 95% CI 1.63–3.33) compared to those without MI (*Figure 3*). In contrast, no significant differences were found in body mass index (MD 0.23 kg/m^2, 95% CI −0.76–1.23), systolic blood pressure (MD 0.23 mmHg, 95% CI −4.98 to 5.44), diastolic blood pressure (MD −1.39 mmHg, 95% CI −4.69 to 1.91), or total cholesterol levels (MD −0.38 mmol/L, 95% CI −1.96 to 1.20). Additionally, there were no differences in the prevalence of dyslipidaemia (RR 0.86, 95% CI 0.64–1.15) or ever smoking (RR 1.22, 95% CI 0.88–1.68).

3.4 Unrecognized MI vs. recognized MI

In addition, we compared individuals with unrecognized MI to those with recognized MI (*Figure 4*). A lower prevalence of hypertension (RR 0.92, 95% CI 0.88–0.97) and diabetes mellitus (RR 0.80, 95% CI 0.70–0.92) was found in individuals with unrecognized MI. No differences were observed in body mass index (MD 0.03 kg/m^2, 95% CI −0.88 to 0.93), systolic blood pressure (MD 4.06 mmHg, 95% CI −0.03 to 11.15), diastolic blood pressure (MD 1.95 mmHg, 95% CI −2.87 to 6.77), or total cholesterol levels (MD 0.42 mmol/L, 95% CI −0.93 to 1.77) between the two groups. Furthermore, there was no difference in the prevalence of dyslipidaemia (RR 0.86, 95% CI 0.64–1.15) or ever smoking (RR 0.95, 95% CI 0.79–1.13).

3.5 Men vs. women

The only sex difference that we found was that men with unrecognized MI exhibited significantly higher levels of body mass index compared to men without MI (men: MD 0.40 kg/m^2, 95% CI 0.26–0.55; women: MD 1.62 kg/m^2, 95% CI −0.28 to 3.52) (*Figure 5*). No significant disparities in the prevalence of hypertension (men: RR 1.34, 95% CI 0.73–2.43; women: RR 1.75, 95% CI 0.57–5.41), diabetes mellitus (men: RR 2.52, 95% CI 0.83–7.66; women: RR 1.93, 95% CI 0.71–5.29), or current smoking (men: RR 1.32, 95% CI 0.60–2.90; women: RR 1.21, 95% CI 0.36–4.09) were observed among the sexes.

3.6 Sensitivity analyses

Omitting studies that diagnosed unrecognized MI by myocardial imaging instead of ECG yielded similar findings (see Supplementary material online, *Appendices S3–S5*). Stratifying the analyses by continent showed no differences in trends compared with the main analyses, although some results lost statistical significance (see Supplementary material online, *Appendices S7–S9*). Additionally, stratifying the analyses by timeframe of data collection demonstrated similar results (see Supplementary material online, *Appendices S10–S12*).

4. Discussion

In this study, we evaluated the burden of cardiovascular risk factors in men and women with unrecognized MI. Our comprehensive analysis involved 200 450 individuals from population-based cohort studies, of which 4322 experienced unrecognized MI, and 4653 experienced recognized MI. Our findings indicate that individuals with unrecognized MI had a more unfavourable cardiovascular risk profile, exhibiting higher levels of body mass index and systolic blood pressure, and higher prevalence of hypertension and diabetes mellitus, compared to individuals without MI. Additionally, individuals with recognized MI had a higher prevalence of hypertension and diabetes mellitus in contrast to those with unrecognized MI.

This study is the first systematic review and meta-analysis exploring the burden of risk factors in individuals with unrecognized MI. We conducted a comprehensive search of population-based cohort studies and included 17 studies with substantial sample sizes and robust methodology. Our findings reveal that individuals with unrecognized MI bear a significant burden of metabolic risk factors, offering opportunities for screening strategies. Additionally, we demonstrated lower rates of diagnosis of hypertension and diabetes mellitus in individuals with unrecognized MI compared to individuals with recognized MI, likely due to their covert status without prior clinical events. By laying this groundwork, we pave the way for future studies to delve deeper into this population and inform management strategies.

Our findings highlight that traditional cardiovascular risk factors, especially diabetes and hypertension, provide an opportunity for improving screening strategies to diagnose individuals with unrecognized MI. Accordingly, we underscore adherence to current guidelines, recommending to perform a resting ECG in individuals with diabetes mellitus or hypertension.[10,11] When using MRI as the gold standard, performing ECGs to detect unrecognized MI has been reported to be of low sensitivity (13.2%) but high specificity (95.7%).[7] However, the high cost and time-consuming nature of cardiac MRI restrict its clinical application.[7] Transthoracic echocardiography stands out as another potential screening modality, since it is the most commonly used method for assessing cardiac function, easily accessible without significant costs, and free of contrast-related risks. However, although screening for unrecognized MI through ECG or echocardiography is without medical complications, abnormal findings can result in increased specialist consultations, additional diagnostic procedures that are costly and potentially harmful because of radiation exposure and procedural complications.[36] Therefore, research to guide clinicians on optimal screening strategies for identifying unrecognized MI is urgently needed.

Table 1 Study characteristics of the studies included in the main analysis

First author	Year	Cohort	Country	Sample size (% women)	Mean age, years	UMI cases (% women)	RMI cases (% women)	Quality[a]
UMI determined by ECG								
Ammar	2005	Olmsted County Minnesota	USA	2035 (52.0)	62.3	80 (42.5)	101 (25.7)	Good
Cheng	2021	Atherosclerosis Risk in Communities Study (ARIC)	USA	13 725 (54.5)	54.2	513 (30.8)	441 (37.0)	Good
		The Cardiovascular Health Study (CHS)	USA	5207 (57.7)	72.3	1070 (55.3)	632 (42.7)	Good
Godsk	2012	The Copenhagen City Heart Study	Denmark	5381 (58.4)	58.1	114 (57.9)	–	Good
Ikram	2006	The Rotterdam Study	The Netherlands	6439 (59.6)	68.7	361 (56.0)	442 (31.4)	Good
Iozzia	2020	The Lifelines Cohort Study	The Netherlands	125 988 (58.8)	44.3	346 (50.0)	1068 (21.8)	Fair
Kazibwe	2023	The Multi-Ethnic Study of Atherosclerosis (MESA)	USA	6705 (52.9)	62.2	178 (31.5)	–	Good
Nadelmann	1990	The Bronx Aging Study	USA	390 (64.0)	79.0	25 (60.0)	47 (53.3)	Good
Øhrn	2018	The Tromsø Study	Norway	6128 (57.1)	63.3	502 (38.0)	326 (30.0)	Good
Rizk	2011	The REasons for Geographic And Racial Differences in Stroke (REGARDS) Study	USA	18 864 (62.3)	64.0	852 (58.7)	1365 (42.9)	Good
Sigurdsson	1995	The Reykjavík Study	Iceland	7533 (0)	50.9	53 (0)	129 (0)	Good
UMI determined by MRI								
Acharya	2018	The ICELAND-MI Study	Iceland	935 (51.7)	75.9	156 (36.5)	91 (35.2)	Fair
Barbier	2006	Prospective Investigation of the Vasculature in Uppsala Seniors (PIVUS)	Sweden	248 (49.6)	70.0	49 (44.9)	11 (18.2)	Good
Cha	2018	–	Korea	872 (6.3)	53.9	23 (0)	–	Good

RMI, recognized myocardial infarction; UMI, unrecognized myocardial infarction.
[a]Study quality was assessed using the Newcastle-Ottawa Scale: scores of 7–9 were rated as 'good,' 4–6 as 'fair,' and 0–3 as 'poor.'

Table 2 Study characteristics of the studies included in the sex-stratified analysis

First author	Year	Cohort	Country	Sample size (% women)	Mean age, years	UMI cases (% women)	RMI cases (% women)	Quality[a]
Boland	2002	Atherosclerosis Risk in Communities Study (ARIC)	USA	12 843 (56.0)	Not reported	100 (34.0)	408 (33.6)	Good
Dehghan	2014	The Rotterdam Study	The Netherlands	6534 (59.1)	69.0	370 (55.4)	437 (29.8)	Good
Lundblad	2003	Northern Sweden Monica Study	Sweden	790 (48.2)	45.2	37 (46.0)	49.0 (5.5)	Good

RMI, recognized myocardial infarction; UMI, unrecognized myocardial infarction.
[a]Study quality was assessed using the Newcastle-Ottawa Scale: scores of 7–9 were rated as 'good,' 4–6 as 'fair,' and 0–3 as 'poor.'

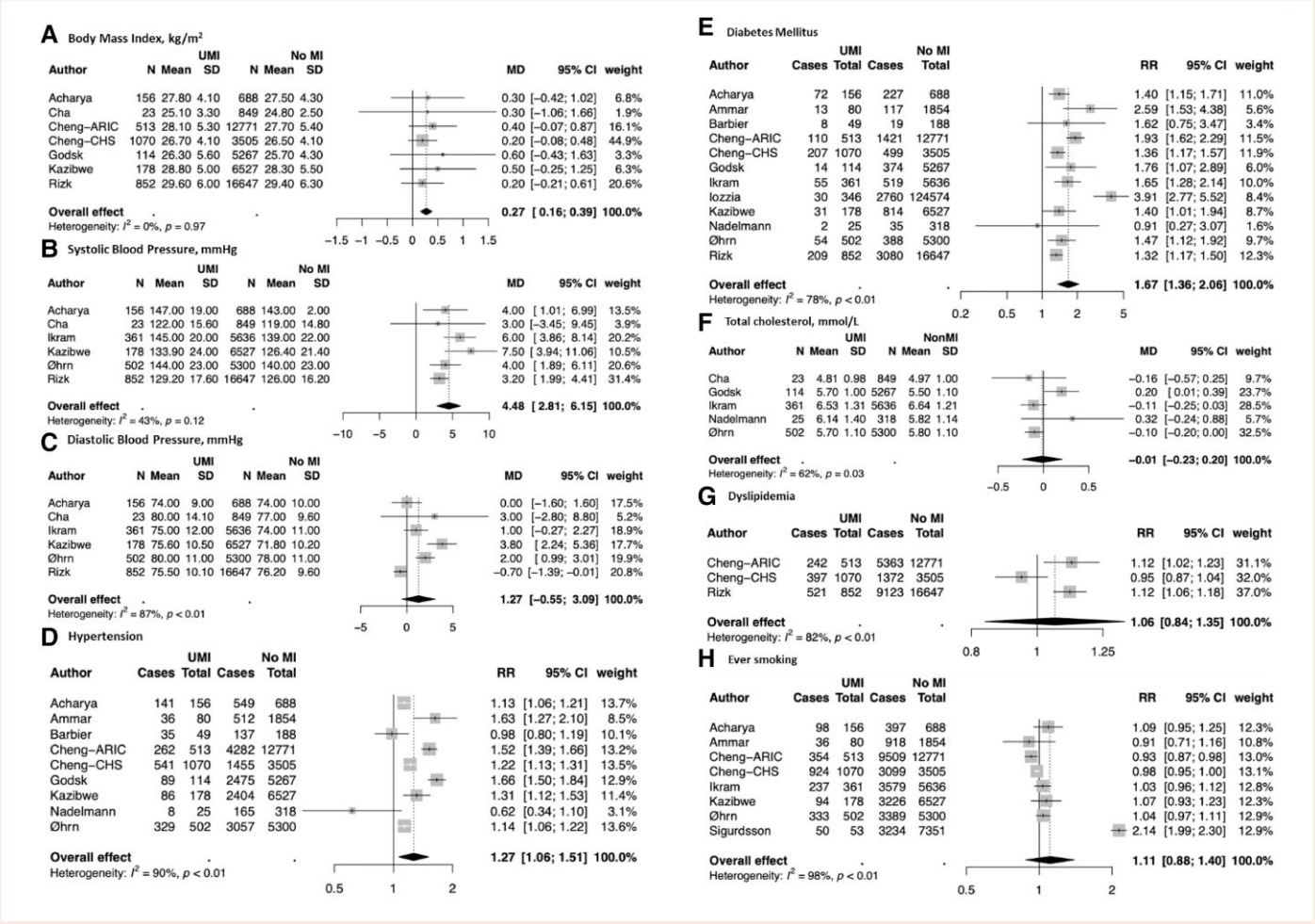


Figure 2 Forest plots of mean values/prevalence of body mass index (*A*), systolic blood pressure (*B*), diastolic blood pressure (*C*), hypertension (*D*), diabetes mellitus (*E*), total cholesterol (*F*), dyslipidaemia (*G*), and ever smoking (*H*) in individuals with unrecognized MI vs. individuals without MI. CI, confidence interval; MI, myocardial infarction; *n*, number; SD, standard deviation; MD, mean difference; RR, risk ratio.

Given the shared pathophysiology, it is reasonable to ascribe traditional cardiovascular risk factors to both unrecognized and recognized MI. A noteworthy finding of this study is the lower prevalence of diabetes mellitus and hypertension in the unrecognized MI group compared to individuals with recognized MI. Diabetes mellitus is believed to contribute to asymptomatic MI by impeding pain signals through neuropathy,[37–41] and its prevalence was therefore expected to be higher in individuals with unrecognized MI compared to individuals with recognized MI. Additionally, earlier studies suggested a robust association between hypertension and unrecognized MI; however, this observation is likely mediated by the role of hypertension in atherosclerosis progression, as there is no evidence supporting a direct link between hypertension and neuropathy.[3,37,40,42] We hypothesize these counterintuitive results are attributed to individuals with recognized MI receiving more intensive cardiovascular risk management following their clinical event, leading to increased detection of these conditions. In contrast, individuals with unrecognized MI do not receive cardiovascular risk management or (secondary) preventive treatments,[43,44] increasing their susceptibility to an unfavourable prognosis.

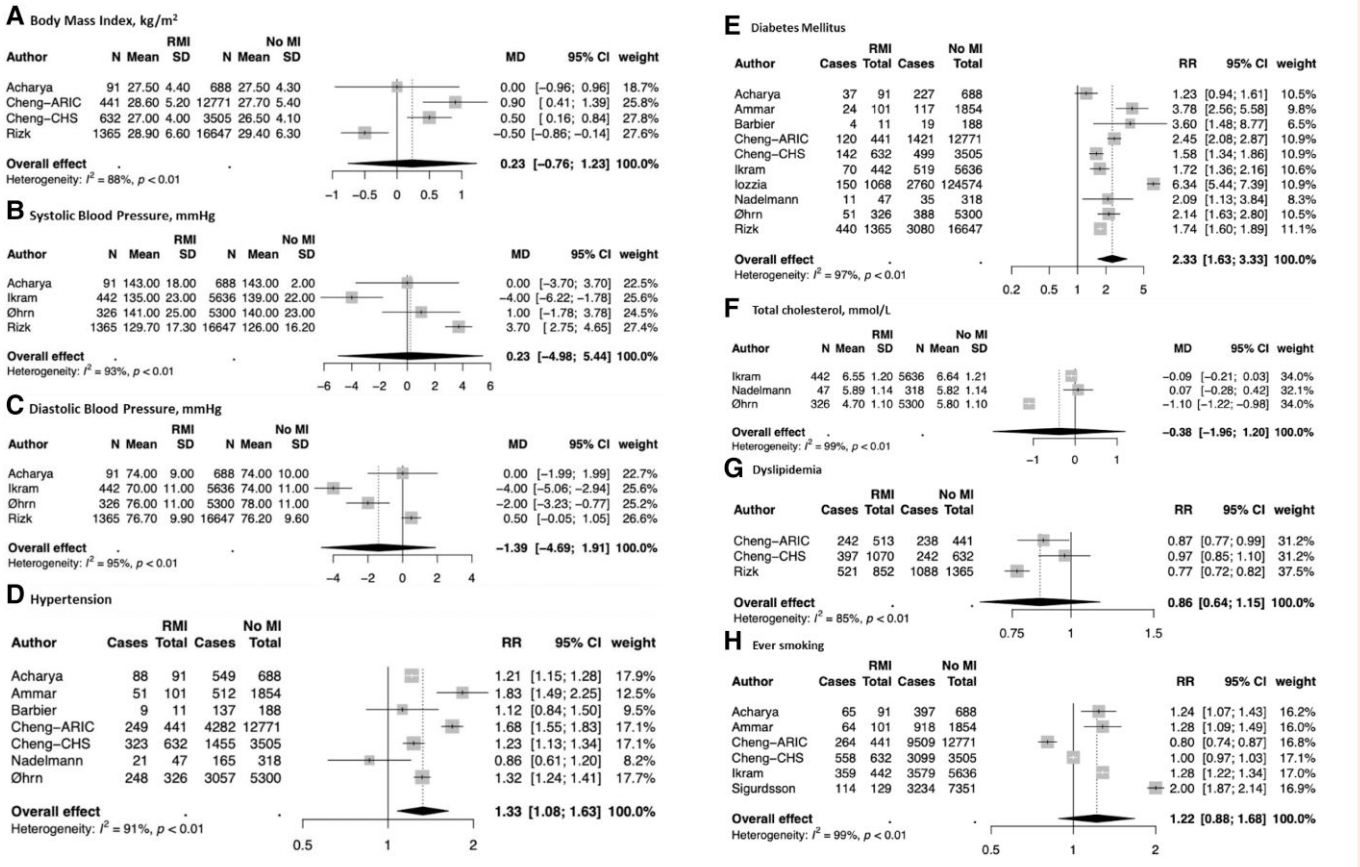


Figure 3 Forest plots of mean values/prevalence of body mass index (*A*), systolic blood pressure (*B*), diastolic blood pressure (*C*), hypertension (*D*), diabetes mellitus (*E*), total cholesterol (*F*), dyslipidaemia (*G*), and ever smoking (*H*) in individuals with recognized MI vs. individuals without MI. CI, confidence interval; MI, myocardial infarction; *n*, number; SD, standard deviation; MD, mean difference; RR, risk ratio.

Despite the historical underrepresentation of women in cardiovascular trials, most of our analysed studies enrolled more women than men, possibly due to their observational design and focus on older individuals, mirroring the demographic distribution of the general population, where women tend to have higher life expectancies.[45] The prevalence of unrecognized and recognized MI varied substantially between both sexes. Men generally showed higher absolute numbers of MI, both unrecognized and recognized, while the ratio of unrecognized to recognized MI was higher in women, consistent with existing literature.[8] Previously, misclassification bias stemming from challenges in ECG lead placement in women, primarily due to breast tissue, was suggested to overestimate unrecognized MI cases in women.[46] However, a similar trend is noted in studies using MRI for diagnosis,[21,23] undermining the notion that difficulties in ECG lead placement are the sole explanation for the increased proportion of unrecognized MIs in women vs. men. Under-recognition of MI in women may be influenced by various factors. For example, MIs in women are typically smaller, potentially resulting in more asymptomatic presentations. Additionally, attitudes of both patients and general practitioners towards cardiovascular risk may also play a role in influencing the perception of pain and symptoms. Women tend to less frequently link their chest pain to cardiac disease compared to men.[47] Furthermore, public information and medical training traditionally focused on recognizing male pattern symptoms, possibly leaving women at a greater risk of underdiagnoses.[48] Moreover, a recent study showed varying sex differences in unrecognized MI prevalence across ethnic groups, possibly due to differences in symptom recognition, interpretation, and communication.[49] Future research should explore patient- and healthcare system-related factors contributing to unrecognized MIs, including sex-specific symptoms and barriers to care for women and men from different ethnic groups.

In our sex-stratified analyses, body mass index values were significantly higher in men with unrecognized MI vs. men without MI. However, such trend was not observed in women. While our findings may imply potential sex differences, we contend that drawing valid conclusions on this matter is hindered by the insufficiency of available data. Additionally, the analysis is constrained by a limited number of studies, with one study carrying low analytical weight.[34] Given the disparity in occurrence of unrecognized vs. recognized MI between the sexes, we advocate for future research to further investigate factors contributing to this observation. This could pave the way to for more targeted and individualized screening strategies to prevent unrecognized MI in the future.

This study has three main limitations. First, significant within-study heterogeneity was observed despite our focus on population-based cohorts. Variations in timeframes of the conducted studies and population characteristics, such as age range, women to men ratio, and ethnic backgrounds, potentially have contributed to this heterogeneity. Additional heterogeneity arose from the inclusion of studies diagnosing unrecognized MI through either ECG or myocardial imaging. Moreover, in ECG studies, diagnostic criteria and methods varied, involving automated processes, physician validation, or a combination, potentially affecting the classification of unrecognized MI. To address these sources of heterogeneity, random-effect models and sensitivity analyses were employed. Unfortunately, due to limited studies reporting the prevalence of the risk factors of interest, we were unable to perform meta-regression as heterogeneity exploration strategy. Moreover, although numerous factors contribute to the

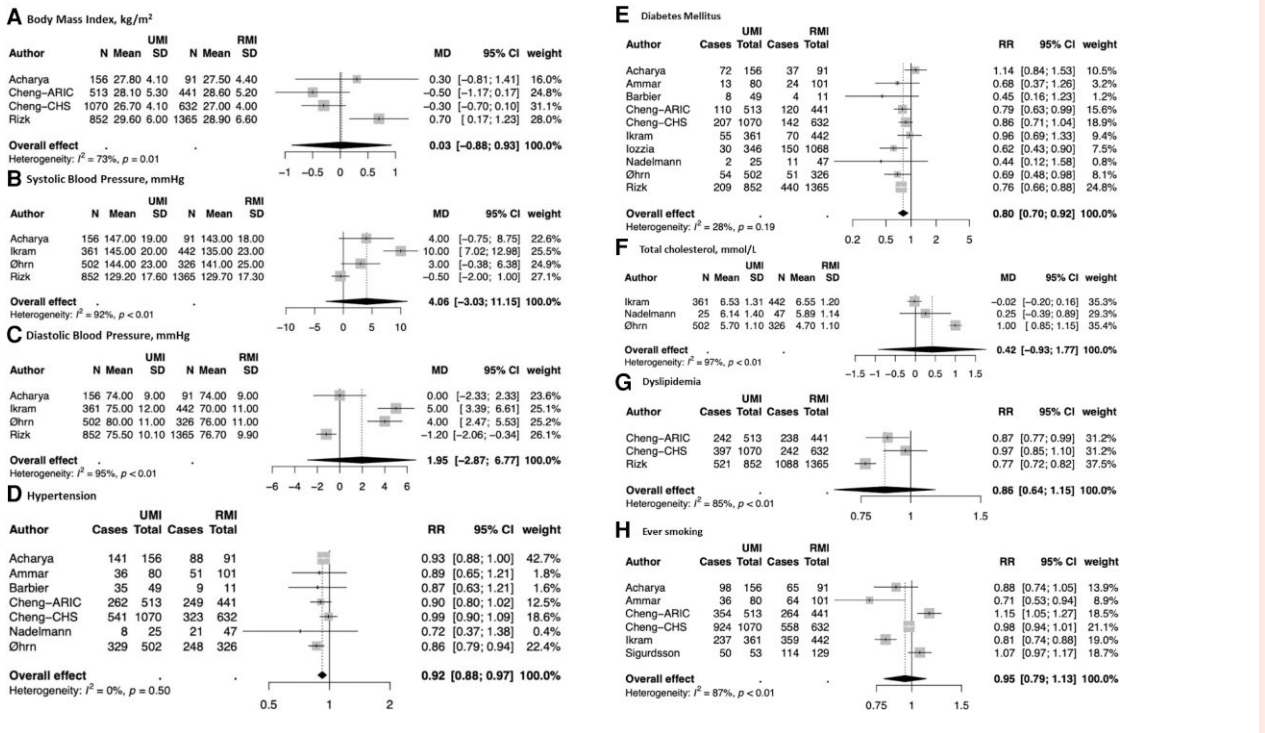


Figure 4 Forest plots of mean values/prevalence of body mass index (*A*), systolic blood pressure (*B*), diastolic blood pressure (*C*), hypertension (*D*), diabetes mellitus (*E*), total cholesterol (*F*), dyslipidaemia (*G*), and ever smoking (*H*) in individuals with unrecognized MI vs. individuals with recognized MI. CI, confidence interval; MI, myocardial infarction; *n*, number; SD, standard deviation; MD, mean difference; RR, risk ratio.

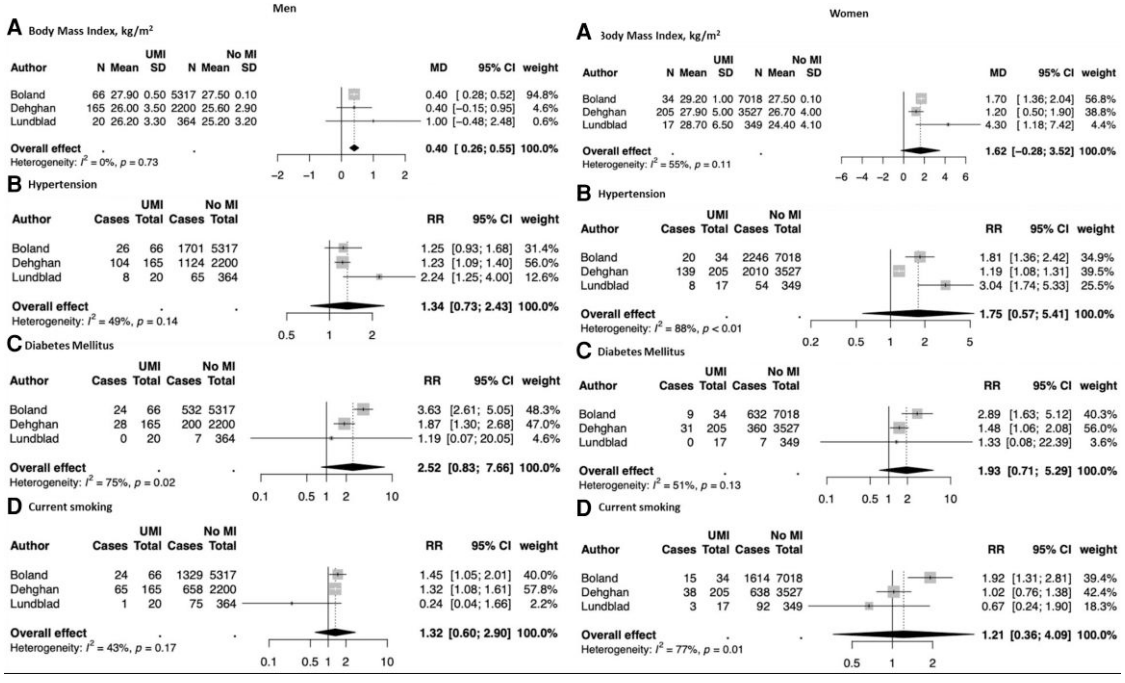


Figure 5 Forest plots of mean values/prevalence of body mass index (*A*), hypertension (*B*), diabetes mellitus (*C*), and current smoking (*D*) in individuals with unrecognized MI vs. individuals without MI, stratified for sex. CI, confidence interval; MI, myocardial infarction; *n*, number; SD, standard deviation; MD, mean difference; RR, risk ratio.

development of cardiovascular disease, our analysis was constrained by the availability of data pertaining to additional factors such as ethnic background. Second, some studies excluded participants with recognized MI, thereby constraining the statistical power of the analyses for the comparisons between recognized MI vs. no MI and recognized MI vs. unrecognized MI.[20,24,25] Nevertheless, we were still able to conduct meta-analyses on the same variables as those for unrecognized MI vs. no MI. Lastly, while we present statistically significant variances in body mass index, systolic blood pressure, and the prevalence of diabetes mellitus and hypertension among individuals with unrecognized MI and those without, the magnitude of these differences is insufficient for immediate identification of individuals as having unrecognized MI, limiting the direct impact of our study. Hence, we recommend that future research delve deeper into strategies aimed at identifying individuals who have experienced unrecognized MI and explore management strategies to mitigate their risk of future cardiovascular complications.

In conclusion, our study revealed a differential burden of traditional cardiovascular risk factors in individuals with unrecognized MI compared to those without MI and with recognized MI. The findings imply that individuals with unrecognized MI experience a deficit in diagnosis and management of risk factors, contributing to an increased risk of subsequent cardiovascular complications. Future studies should prioritize identifying predisposing factors of unrecognized MI and determining high-risk individuals that could benefit from targeted screening strategies.

Supplementary material

Supplementary material is available at *Cardiovascular Research* online.

Authors' contributions

The contributor roles of the manuscript are described according to Contributor Roles Taxonomy (CRediT): conceptualization (J.v.O., E.B., M.K., J.R.v.L.), data curation (J.v.O., N.N., M.T., M.K., J.R.v.L.), formal analysis (J.v.O.), funding acquisition (E.B., M.K., J.R.v.L.), investigation (J.v.O., N.N., M.T., E.B., M.K., J.R.v.L.), methodology (J.v.O., N.N., M.T., W.B., E.B., M.K., J.R.v.L.), project administration (J.v.O., J.R.v.L.), resources (J.v.O., N.N., W.B.), software (J.v.O., M.T.), supervision (M.K., E.B., J.R.v.L.), validation (all authors), visualization (all authors), writing—original draft (J.v.O., J.R.v.L.), and writing—review & editing (all authors). Accordingly, all listed authors agree to be accountable for all aspects of the work and ensure the accuracy and integrity of the work.

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