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## Application of optical coherence tomography in cardiovascular diseases: bibliometric and meta-analysis

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**Significance:** Since the advent of Optical Coherence Tomography (OCT) two decades ago, there has been substantial advancement in our understanding of intravascular biology. Identifying culprit lesion pathology through OCT could precipitate a paradigm shift in the treatment of patients with Acute Coronary Syndrome. Given the technical prowess of OCT in the realm of cardiology, bibliometric analysis can reveal trends and research focal points in the application of OCT for cardiovascular diseases. Concurrently, meta-analyses provide a more comprehensive evidentiary base, supporting the clinical efficacy of OCT-guided Percutaneous Coronary Intervention (PCI).

**Design:** This study employs a dual approach of Bibliometric and Meta-analysis. **Methods:** Relevant literature from 2003 to 2023 was extracted from the Web of Science Core Collection (WoSCC) and analyzed using VOSviewer, CiteSpace, and R for publication patterns, countries, institutions, authors, and research hotspots. The study compares OCT-guided and coronary angiography-guided PCI in treating adult coronary artery disease through randomized controlled trials (RCTs) and observational studies. The study has been reported in the line with PRISMA and AMSTAR Guidelines.

**Results:** Adhering to inclusion and exclusion criteria, 310 publications were incorporated, demonstrating a continual rise in annual output. Chinese researchers contributed the most studies, while American research wielded greater influence. Analysis of trends indicated that research on OCT and angiography-guided PCI has become a focal topic in recent cohort studies and RCTs. In 11 RCTs (n = 5,277), OCT-guided PCI was not significantly associated with a reduction in the risk of Major Adverse Cardiac Events (MACE) (Odds ratio 0.84, 95% CI 0.65–1.10), cardiac death (0.61, 0.36–1.02), all-cause death (0.7, 0.49–1.02), myocardial infarction (MI) (0.88, 0.69–1.13), target lesion revascularization (TLR) (0.94, 0.7–1.27), target vessel revascularization (TVR) (1.04, 0.76–1.43), or stent thrombosis (0.72, 0.38–1.38). However, in 7 observational studies (n = 4,514), OCT-guided PCI was associated with a reduced risk of MACE (0.66, 0.48–0.91) and TLR (0.39, 0.22–0.68).

**Conclusion:** Our comprehensive review of OCT in cardiovascular disease literature from 2004 to 2023, encompassing country and institutional origins, authors, and publishing journals, suggests that OCT-guided PCI does not demonstrate significant clinical benefits in RCTs. Nevertheless, pooled results from observational studies indicate a reduction in MACE and TLR.

#### KEYWORDS

optical coherence tomography, cardiovascular diseases, bibliometric analysis, metaanalysis, percutaneous coronary intervention

## 1 Introduction

Recent evidence suggests that MACE in chronic ischemic heart disease correlates more with the overall atherosclerotic burden than with specific flow-limiting luminal lesions (1-6). Traditional models simplistically link CAD complications to severe obstructions from narrow atherosclerotic plaques (7-10). However, this perspective is increasingly recognized as overly reductionist. Longitudinal studies on the natural progression of individual coronary plaques have revealed that even those lesions perceived as high-risk and potentially ischemia-inducing maintain stability over several years, seldom progressing to instability or resulting in MACE (11-16). The limitations of angiography in direct PCI, including inaccurate assessments of lesion morphology and the underlying mechanisms of STEMI, as well as suboptimal recognition of post-stent outcomes, underscore the necessity for a more holistic understanding of atherosclerosis within the entire arterial system (17).

OCT provides the highest resolution (1-15 µm) among current intravascular imaging technologies, enabling detailed exploration of microscopic vascular structures (18). In cardiovascular clinical applications, the significance of OCT encompasses: (1) Comprehensive plaque assessment: OCT provides detailed information about plaque size, type, and composition, aiding in understanding the total burden of atherosclerosis, not merely localized stenosis (19); (2) Vulnerable plaque identification: OCT can provide detailed views of potentially hazardous plaques by analyzing tissue characteristics, such as the size of the lipid core and the thickness of the fibrous cap (20); (3) Enhanced risk stratification: The detailed plaque and vascular information provided by OCT can help more accurately assess the risk of cardiovascular events, thus improving the accuracy of risk stratification (21); (4) Complementing traditional imaging techniques: By offering direct observation of vessel walls and plaques, OCT supplements the limitations of traditional imaging methods, providing a more comprehensive cardiovascular health assessment (22). Thus, OCT is not only a potent diagnostic tool but also adds a new dimension to the risk assessment and management of cardiovascular diseases. Its application highlights a deeper and more nuanced understanding of cardiac diseases, contributing to the refinement of existing risk stratification methods for greater precision.

We analyzed trends and applications of OCT in cardiovascular treatment over the past two decades using bibliometric techniques (23, 24). Our meta-analysis indicates OCT as a prominent focus in recent PCI trials. Previous studies comparing OCT-guided with angiography-guided PCI treatment in Meta-analyses have encountered several issues. Firstly, they did not include all significant related studies. Secondly, these meta-analyses did not separate observational studies from RCTs, a methodological rigor essential for enhancing the credibility of results. Therefore, we conducted a stringent Meta-analysis, differentiating RCTs from observational studies, aiming to provide more accurate and reliable evidence to guide clinical practice and future research directions.

## 2 Methods

### 2.1 Data sources and search strategy

The Web of Science, esteemed for its extensive interdisciplinary coverage, comprehensive citation indexing, and rich analytical metrics, serves as an exemplary database for bibliometric analysis. This resource enables researchers to identify hotspots and trends within their respective fields. Our study utilized data retrieved from the WoSCC database concerning OCT and cardiovascular diseases for bibliometric analysis. To mitigate data variability due to updates, search activities, data extraction, and downloading were conducted on the same day. The types of literature studied were confined to articles and reviews. The search strategy, specific outcomes, and search terms are detailed in Figure 1 (refer to Supplementary eMethods S1). Overall, 2,758 literature sources were analyzed, with 310 articles ultimately included and downloaded in text format (complete records and referenced citations).

### 2.2 Data analysis and visualization

In this study, the bibliometrix package in R (version 4.3.2) was utilized to analyze major countries, active authors and institutions, contributing journals, and keyword trends (25). Additionally, CiteSpace (version 6.1), a Java-based freeware developed by Chen (26), was employed for clustering and burst analysis of keywords. Collectively, these two software programs facilitated visual analyses, offering deep insights into the advancements in OCT research within the cardiovascular field and uncovering research frontiers using extensive data.

### 2.3 Meta-analysis

This work has been reported in line with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and AMSTAR (Assessing the methodological quality of systematic reviews) Guidelines (27, 28). A systematic review and meta-analysis were conducted on data from 11 RCTs and 7 observational studies. These 18 cohorts were identified through searches of electronic databases including PubMed, Cochrane Library, Embase, and Web of Science, employing a combination of text and MeSH headings in the search strategy (refer to Supplementary eMethods S2 and eTableS1). For this study, primary outcomes of interest were MACE, Cardiac death, and All-cause death, with secondary endpoints including Myocardial Infarction (MI), TVR, TLR, and stent thrombosis. All details regarding the search strategy, data extraction, and study selection are presented in the Supplementary (eMethods S3–S5).

### 2.4 Statistical analysis

The outcomes of interest were dichotomous variables, and rates of events with the total sample size were extracted for analysis. The



Mantel-Haenszel method's random-effects model was employed to calculate Odds Ratio (OR) and their 95% Confidence Intervals (CI). For inter-study variance, Restricted Maximum Likelihood (REML) was used. An OR estimate and its corresponding 95% CI not including the vertical line at 1 (*p*-value < 0.05) was considered statistically significant. The extent of heterogeneity was approximated using the  $I^2$  test, with 0%–40% indicating negligible, 30%–60% moderate, 50%–90% substantial, and 75%–100% considerable heterogeneity. Given the limited number of studies included, a funnel plot for pre-specified publication bias analysis was deemed inappropriate.

# 2.5 Cardiovascular clinical research and patients involvement

Following the completion of our initial manuscript, we consulted a patient with cardiovascular disease and a frontline cardiovascular clinical scholar, both of whom suggested acceptance or implementation of PCI for coronary artery disease. The feedback received indicated that the certainty of the evidence

presented in our study was highly useful for evaluating the efficacy of OCT-guided vs. angiography-guided PCI in the treatment of acute coronary syndrome (ACS).

## **3** Results

## 3.1 Bibliometric results

### 3.1.1 Annual growth trends in publications

From 2003 to 2023, a total of 2,758 papers were retrieved from the WoSCC database. After eliminating duplicates and other types of literature, 310 articles were ultimately included for analysis, comprising 246 articles and 64 reviews. Figure 2A displays the annual statistics of publications in this field, revealing a trend in three distinct phases: (1) From 2004 to 2012, the annual publication count did not exceed 10 papers; (2) From 2013 to 2019, the number of annual publications remained relatively stable; (3) A notable increase in publication volume was observed from 2020 to 2023, with a significant spike exceeding 40 papers in 2022. By fitting the data to construct a publication trend,



results indicate a high correlation between the annual number of publications and the years ( $y = 0.0541x^{2} + 0.8396x - 1.0807$ , R^2 = 0.8841) (Figure 2B). The publication trend suggests that by 2024, over 400 articles on this topic are projected to be published, signifying an increasing scholarly focus on this field over time.

In this field, the top 10 countries accounted for over 80% of the total publication output compared to all other countries combined. Statistically, the five countries and regions with the most published

articles were China (77 articles), the United States (68 articles), Germany, Japan, and Italy (Table 1). In terms of the growth rate in the number of publications (Figure 3A), the United States consistently maintained a high output, slightly outperforming China, while Germany, Italy, and Japan showed relatively stable production levels. Moreover, among the top 20 countries for corresponding authors, those with the highest proportions of multiple countries publication (MCP) relative to their total publication output were Canada, the United States, Italy, the United Kingdom, and China. Although the U.S. had the most MCPs (23 articles), it did not rank first in MCP ratio. While China had the highest total number of articles, it had fewer publications in collaboration with other countries (22 articles), thus a lower MCP Ratio (Table 1). Among the limited international collaborations from China, those with the United States were the most frequent (Figure 3B).

These articles were authored by 659 institutions, among which 21 institutions published at least 5 articles each. The top 10 institutions alone authored 176 articles, accounting for 56.8% of the total (Figure 3C). The institutions with the highest number of publications included Harvard University, Harvard Medical School, Harbin Medical University, Icahn School of Medicine, Massachusetts General Hospital, National University of

TABLE 1 Corresponding author's countries.

| Rank | Country        | Articles | SCP | МСР | MCP Ratio |
|------|----------------|----------|-----|-----|-----------|
| 1    | China          | 77       | 55  | 22  | 0.286     |
| 2    | Usa            | 68       | 45  | 23  | 0.338     |
| 3    | Germany        | 20       | 15  | 5   | 0.25      |
| 4    | Japan          | 20       | 20  | 0   | 0         |
| 5    | Italy          | 18       | 12  | 6   | 0.333     |
| 6    | Canada         | 12       | 6   | 6   | 0.5       |
| 7    | United Kingdom | 10       | 7   | 3   | 0.3       |
| 8    | Spain          | 9        | 7   | 2   | 0.222     |
| 9    | France         | 8        | 6   | 2   | 0.25      |
| 10   | Korea          | 7        | 4   | 3   | 0.429     |

MCP, multiple countries publication; SCP, single countries publication.

Singapore, University College London, Case Western Reserve University, and Columbia University, all with over 10 articles each. Chinese institutions such as Harbin Medical University, Tongji University, and Capital Medical University each produced more than 8 articles. As depicted in Figure 3D, institutional collaboration was more extensive than inter-country cooperation, with Harvard University and Harbin Medical University engaging in significant collaborations with numerous universities and research centers in China, as well as institutions in the UK, the US, and other countries.

### 3.1.2 Author analysis

Figure 4A, created using VOSviewer software, visualizes the author collaboration network in OCT research within the cardiovascular field. The minimum criterion for an author's inclusion was set at 10 publications, encompassing nearly 2000 contributing authors. Among the top 10 most productive authors, Professor Mehran Roxana possessed the highest m-INDEX; Professor Yu Bo boasted the greatest G-index; and Professor Virmani Renu held the highest h-index and total citations (TC) (Figures 4A-B).

Figure 4C presents the network map of co-cited authors, where higher weightage of a co-cited author corresponds to larger labels and circles in the visualization. In the field of OCT research, prominent figures like Professor Yu Bo from China, and Professor Maehara Akiko and Professor Virmani Renu from the United States, hold significant influence and citation weight.



## Analysis of countries/regions engaged in OCT research. (A) Top 5 countries with the largest number of publications over time; (B) country cooperation network; (C) top 18 institutions by number of publications; (D) institutional collaboration-network.



Among the authors with the highest publication volumes, Professor Yu Bo is the only one from China, while the others are predominantly from the United States. Many of these authors have collaborated on publications in journals such as the "New England Journal of Medicine" and "JACC Cardiovascular Imaging" (29, 30). This indicates close collaboration among authors within this field.

### 3.1.3 Analysis of journals

According to our analysis, 179 journals published papers related to OCT and cardiovascular diseases. The top 5 most productive journals — "International Journal of Cardiology", "Frontiers in Cardiovascular Medicine", "Catheterization and Cardiovascular Interventions", "Revista Espanola de Cardiologia", and "Scientific Reports" — showed notable publication numbers and growth trends, as depicted in Figure 5A. Figure 5B illustrates the journal's thematic distribution through a dual-map overlay, with citing journals positioned on the left and cited journals on the right of the map. The labels represent journals covering specific themes, and colored lines trace the reference pathways. Two distinct citation pathways are evident. Two green citation paths indicate that studies from medical/clinical/surgical journals are often cited by those in molecular physiology/medical/clinical journals.

### 3.1.4 Citation analysis

The results of the citation analysis are presented in Figure 6 and Table 2. Among the top 10 most cited articles, 6 are clinical

trial studies, with one published in "The Lancet" (37), three in "Circulation" (31, 35, 36), and other high-impact journals. Three reviews discussed the application of OCT technology in detecting atherosclerosis in clinical practice. The 2005 randomized controlled trial by Professor Ik-Kyung Jang, "*in vivo* Characterization of Coronary Atherosclerotic Plaque by Use of Optical Coherence Tomography," ranks first with 694 citations.

### 3.1.5 Co-occurrence analysis

In the study of the structure of scientific knowledge, keyword co-occurrence analysis is an effective bibliometric method to grasp current hotspots. We analyzed the co-occurrence of keywords in the field and the top 50 keywords (Figure 7A), centering around OCT. Figure 7B employs a log-likelihood ratio analysis to generate eight clusters, including: coronary artery disease, deep learning, coronary stenosis, heart transplantation, rupture, OCT, congenital heart disease, plaque and cardiovascular diseases. Burst analysis of keywords was also conducted, revealing overall trends in OCT research in the cardiovascular field, encompassing topics like bare metal stents, acute myocardial infarction, intravascular ultrasound, aortic valve implantation, artery disease, elevation myocardial infarction, coronary disease, and coronary artery disease (Figure 7C).

## 3.1.6 Changes in trends of research in the recent years

The thematic word analysis method was employed to explore the core issues in OCT research within the cardiovascular field.



Figure 8A indicates that well-developed themes focus on atherosclerotic diseases, blood pressure, stent implantation, and plaque characteristics. The impact of surgery, post-operative care, and survival on disease treatment and prognosis are also noteworthy. Emerging research in areas such as molecular biology and cell biology is also beginning to emerge. Researchers are focusing on the roles and potential molecular mechanisms of "inflammation, oxidative stress, mitochondria, cytokines, and metabolism" in disease development.

Moreover, using multidimensional scaling, we categorized the most frequently occurring keywords and generated a conceptual structure map, resulting in three clusters (Figure 8B). Current research continues to focus on clinical manifestations, diagnosis, interventions, and prognosis of diseases like "coronary stenosis, acute myocardial infarction, atherosclerosis" (red cluster), as well as exploring pathogenic mechanisms and intervention methods related to diseases, such as "interventional methods, post-stent thrombosis formation, and potential impacts of PCI" (blue-green cluster).

Additionally, we visualized the temporal trends of keywords (Figure 8C). In the past five years, new trends in the field include coherence tomographic vascular scanning technology, coronary heart disease, microvascular lesions, vascular pressure, retinal arteriolar abnormalities, atherosclerotic risk, as well as the etiology, pathomechanisms, and clinical outcomes of cardiovascular diseases, all of which are worthy areas for continued exploration. The thematic word analysis method was employed to explore the



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Frontiers in Cardiovascular Medicine

| Rank | k Representative<br>author | Title   | Key points   | Journal   | Citations<br>(2023) | Year | Type   | IF<br>(2022) |
|------|----------------------------|---|--|---|---------------------|------|--------|--------------|
| -1   | Ik-Kyung Jang (31)         | <i>in vivo</i> Characterization of Coronary Atherosclerotic Plaque by Use of Optical Coherence Tomography   | This is the first study to compare detailed <i>in vivo</i> plaque morphology in patients with different clinical presentations.  | Circulation   | 694                 | 2005 | RCT    | 37.8         |
| 7    | Jagat Narula (32)          | Histopathologic Characteristics of Atherosclerotic Coronary<br>Disease and Implications of the Findings for the Invasive and<br>Noninvasive Detection of Vulnerable Plaques   | It defines the histomorphological characteristics of vulnerable<br>plaques, helping to identify such plaques in patients at high risk of<br>acute coronary events.   | Journal of the<br>American College<br>of Cardiology | 358                 | 2013 | RCT    | 24.0         |
| 3    | Fumiyuki Otsuka (33)       | Neoatherosclerosis: overview of histopathologic findings and<br>implications for intravascular imaging assessment   | It explaines the introduction of OCT has facilitated the detection of new atherosclerosis in clinical practice OCT.  | Eur Heart J   | 313                 | 2015 | Review | 39.3         |
| 4    | Armin Arbab-Zadeh (34)     | The Myth of the "Vulnerable Plaque": Transitioning From a Focus<br>on Individual Lesions to Atherosclerotic Disease Burden for<br>Coronary Artery Disease Risk Assessment   | It supports the multifaceted hypothesis of the natural course of<br>atherosclerotic plaque rupture is summarized.  | J Am Coll Cardiol                                   | 301                 | 2015 | Review | 24.0         |
| Ŋ    | Patrick W Serruys (35)     | Evaluation of the Second Generation of a Bioresorbable Everolimus<br>Drug-Eluting Vascular Scaffold for Treatment of <i>de novo</i> Coronary<br>Artery Stenosis   | It is This first-in-humans trial provides a seminal observation on a<br>small number of patients with a short duration of follow-up. One of<br>the clinical studies looked at the Second Generation of a<br>Bioresorbable Everolimus Drug-Eluting Vascular Scaffold for<br>Treatment of De with OCT Novo Coronary Artery Stenosis.   | Circulation   | 293                 | 2010 | RCT    | 37.8         |
| v    | Yoshinobu Onuma (36)       | Intracoronary Optical Coherence Tomography and Histology at 1<br>Month and 2, 3, and 4 Years After Implantation of Everolimus-<br>Eluting Bioresorbable Vascular Scaffolds in a Porcine Coronary<br>Artery Model                                  | It reports OCT findings with corresponding histology in the porcine coronary artery model immediately after and at 28 days and 2, 3, and 4 years after BVS implantation.   | Circulation   | 265                 | 2010 | RCT    | 37.8         |
| г    | Michael Haude (37)         | Safety and performance of the second-generation drug-eluting<br>absorbable metal scaffold in patients with de-novo coronary artery<br>lesions (BIOSOLVE-II): 6 month results of a prospective,<br>multicentre, non-randomised, first-in-man trial | It evaluates the safety and performance of a new second-generation drug-eluting absorbable metal stent (DREAMS 2G) in patients with coronary neoplasia.  | Lancet  | 259                 | 2016 | RCT    | 168.9        |
| 8    | Karen Mendelson (38)       | Heart Valve Tissue Engineering: Concepts, Approaches, Progress, and Challenges  | It evaluates optical coherence tomography can be used to evaluate<br>tissue remodeling for cardiac valve tissue engineering applications.  | Ann Biomed Eng                                      | 216                 | 2006 | Review | 3.8          |
| 6    | Chenyang Xu (39)           | Characterization of atherosclerosis plaques by measuring both backscattering and attenuation coefficients in optical coherence tomography   | It addresses the fundamental issues that underlie the tissue<br>characterization of OCT images obtained from coronary arteries. It<br>not only explains the origins of many qualitative OCT features, but<br>also shows that combination of backscattering and attenuation<br>coefficient measurements can be used for contrast enhancing and<br>better tissue characterization. | J Biomed Opt  | 190                 | 2008 | RCT    | 3.5          |
| 10   | Jacques Ohayon (40)        | Necrotic core thickness and positive arterial remodeling index:<br>emergent biomechanical factors for evaluating the risk of plaque<br>rupture  | It demonstrats that plaque instability should not be considered as a result of fiber cap thickness alone, but rather as a combination of plaque thickness, necrotic core thickness, and arterial remodeling index.   | Am J Physiol-<br>Heart C                            | 179                 | 2008 | RCT    | 4.8          |

| this cap forgetments   | C<br>Keywords                            | Voor | Strength Begin | Fnd  | 2004 - 2023 |
|--|--|------|----------------|------|-------------|
| atherosciente passes   |  |      |                |      | 2004 - 2025 |
| aniersociete plage intravescular pitrasound intravescular pitrasound intravescular pitrasound  | bare metal stents                        | 2009 | 4.52 2009      | 2014 |             |
| myourd generative myourd and an  | acute myocardial infarction              | 2009 | 3.42 2009      | 2015 |             |
| ethingdinois coronagisticase   | intravascular ultrasound                 | 2008 | 4.55 2011      | 2014 |             |
| carlosos der diverse optical coherence tomography percutaneous ceronary intervent<br>arter secon<br>intervent  | aortic valve implantation                | 2011 | 3.84 2011      | 2015 |             |
| Listeron content to co | serdial infarction artery disease        | 2011 | 3.48 2011      | 2018 |             |
| abardente to the second and second  | elevation myocardial infarction          | 2012 | 3.2 2012       | 2017 |             |
| blog flow  | coronary disease                         | 2005 | 4.2 2014       | 2017 |             |
| A stanosis   | coronary artery disease                  | 2009 | 3.76 2016      | 2018 |             |
| #3.heart transplantation   | oct                                      | 2017 | 4.17 2017      | 2020 |             |
| #roportingy disease  | vulnerable plaque                        | 2012 | 3.75 2019      | 2021 |             |
| And reported integral and a second seco   | thin cap fibroatheroma                   | 2012 | 3.53 2020      | 2021 |             |
| P plaque ruptin #6 optical coherence tomography  | coronary heart disease                   | 2007 | 6.32 2021      | 2023 |             |
| #5 congenital heart disease  | optical coherence tomography angiography | 2021 | 3.74 2021      | 2023 |             |
| #7 cardiovascular diseases   |  |      |                |      |             |

#### FIGURE 7

Visualized analysis of keywords and literature related to OCT and cardiovascular diseases. (A) Co-occurrence network of terms in 310 publications; nodes represent keywords (top 50), and lines denote co-occurrence relationships; (B) keyword clustering analysis; (C) the burst strength and duration of the top 13 keywords with the strongest citation bursts.



### FIGURE 8

Analysis of research directions. (A) Thematic analysis related to cardiovascular diseases and OCT. The horizontal and vertical axes represent centrality and density, respectively. The first quadrant represents mature themes, the second quadrant is less significant to the current field, the third quadrant possibly represents emerging or fading themes, and the fourth quadrant is fundamental but less significant themes; (B) conceptual structure map of Keyword Plus; (C) timeline of research dynamics in the field of OCT and cardiovascular diseases.

### 3.2 Meta results

### 3.2.1 Description of included trials

Of 4,350 citations, we reviewed 1,385 after removal of duplicates. We excluded an additional 1,367 studies on the basis of the title and abstract level screening and *a priori* selection criteria (Figure 9). Finally, we included 11 RCTs (n = 5,277) (29, 41–50), and 7 observational studies (n = 4,514) (51–58).

During the quality assessment process, a thorough evaluation of the methodological rigor of each study played a crucial role in enhancing the credibility of the results. Our bias risk assessment revealed that 36% (4 out of 11) of the trials raised some concerns regarding the randomization process, and 43% (3 out of 7) of the observational studies exhibited lower evidence quality regarding outcomes (refer to Supplementary eFigure S1 and eTable S2).

## 3.2.2 Patient-level baseline characteristics and procedural data

The 11 articles included in this study collectively encompassed 5,277 patients with coronary artery lesions. Table 3 summarizes the baseline characteristics. The median age ranged from 54.5 to 69 years, with 77.2% being male. Cardiovascular risk factor analysis

indicated that 31.5% of the patients had diabetes, 63.1% had dyslipidemia, and 69.0% had hypertension, with 31.7% being current or former smokers. STEMI was the predominant type of ACS, followed by NSTEMI and unstable angina. All patients underwent invasive treatment. A total of 2,653 patients received OCT-guided therapy, and 2,640 patients underwent angiography-guided PCI. Stent implantation was the primary strategy for vascular revascularization. The follow-up period ranged from 3 to 25 months. The characteristics of the observational studies are available in Supplementary eTable S3.

### 3.2.3 MACE

Six trials (n = 2,109) reported MACE (41, 43, 44, 46–48). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in MACE (OR 0.84, 95% CI 0.65 to 1.10; p = 0.515,  $I^2 = 0\%$ , non-relevant heterogeneity, high certainty, see Figure 10A). However, the observational studies, comprising 5 studies with 3,674 patients, painted a different picture (51, 52, 54–56). In contrast to coronary angiography, OCT-guided PCI showed a reduction in the risk of MACE (OR 0.66, 95% CI 0.48–0.91; p = 0.243,  $I^2 = 26.7\%$ , non-relevant heterogeneity, moderate certainty, see Figure 11A).



11

| Study ch                       | Study characteristics        |                                     |                      |                         |                                     | Baseline c                                   | haracteristi                | cs of pati                | Baseline characteristics of patients included (OCT group/Angiography group)  | (OCT grou                 | p/Angiogra                | aphy group)               | Type o<br>managen<br>Angio | Type of patients and<br>management (OCT group,<br>Angiography group) | and<br>group/<br>Jup)     |
|--------------------------------|------------------------------|-------------------------------------|----------------------|-------------------------|-------------------------------------|--|-----------------------------|---------------------------|--|---------------------------|---------------------------|---------------------------|----------------------------|--|---------------------------|
| Author<br>Year                 | Location                     | Time Period<br>Under<br>Observation | Study type           | Comparator<br>treatment | Follow-<br>up<br>period<br>(median) | Patients<br>(Included<br>in the<br>analysis) | Age,<br>median              | Male<br>patients          | Hypertension Diabetes  | Diabetes                  | Smoking                   | Dyslipidemia              | Unstable<br>Angina         | NSTEMI   | STEMI                     |
| Ali 2023<br>(29)               | Multinational                | 2018-2020                           | RCT<br>(NCT03507777) | Angiography             | 12 months                           | 1233/1254                                    |                             | 968 (78.5)/<br>956 (76.2) | 880 (71.4)/<br>928 (74.0)  | 523 (42.4)/<br>521 (41.5) | 242 (19.6)/<br>247 (19.7) | 808 (65.5)/<br>860 (68.6) | 355 (28.8)/<br>331 (26.4)  | 304 (24.7)/<br>299 (23.8)  | 68 (5.5)/<br>73 (5.8)     |
| Holm 2023<br>(44)              | Holm 2023 Multinational (44) | 2017-2022                           | RCT<br>(NCT03171311) | Angiography             | 2 years                             | 600/601                                      | 66.4 (10.5)/<br>66.2 (9.9)  | 473 (78.8)/<br>475 (79)   | 422 (70.3)/<br>448 (74.5)  | 103 (17.2)/<br>97 (16.1)  | 305 (50.8)/<br>290 (48.3) | 456 (76.0)/<br>471 (78.4) | 53 (8.8)/<br>58 (9.7)      | 79 (13.2)/<br>78 (13.0)  | 138 (23.0)/<br>144 (24.0) |
| Jia 2022<br>(41)               | China                        | 2017-2019                           | RCT<br>(NCT03571269) | Angiography             | 369 days                            | 112/114                                      | 54.5 (11.2)/<br>56.4 (10.4) | 89 (79.5)/<br>91 (79.8)   | 47 (42)/45 (39.5)  | 29 (25.9)/<br>19 (16.7)   | 64 (57.1)/<br>73 (64.0)   | 1                         | 0/0                        | 0/0  | 112 (100)/<br>114 (100)   |
| Ali 2021<br>(47)               | Multinational                | 1                                   | RCT<br>(NCT02471586) | Angiography             | 6 months                            | 153/142                                      | 66 (59–72)<br>/67 (56–75)   | 106 (69)/<br>104 (73)     | 120 (78)/104 (73)  | 51 (33)/<br>40 (28)       | 26 (17)/<br>40 (28)       | 112 (73)/<br>110 (77)     | I                          | I  | 50 (33)/<br>51 (36)       |
| Onuma<br>2020 (45)             | Japan 9                      | 2017-2018                           | RCT (NCT<br>0297248) | Angiography             | 6 months                            | 55/50  | 68.9 (10.2)/<br>69 (11.6)   | 44 (79)/<br>40 (74)       | 43 (76.8)/<br>40 (74.1)  | 29 (51.8)/<br>25 (46.3)   | 13 (23.2)/<br>10 (18.5)   | 48 (85.7)/<br>46 (85.2)   | 4 (7.1)/<br>2 (3.7)        | $\frac{1}{1} (1.8) / (1.9)$  | I                         |
| Ueki 2020<br>(50)              | Multinational                | 2016-2017                           | RCT<br>(NCT02683356) | Angiography             | 6 months                            | 19/19  | 63.3 (12.7)/<br>62.9 (9.1)  | 15 (78)/<br>15 (78)       | 7 (37)/11 (58)   | 4 (21)/<br>4 (21)         | 7 (37)/<br>6 (32)         | 13 (68)/<br>12 (63)       | 4 (40)/<br>1 (20)          | 4 (40)/2<br>(40)   | 2 (20)/<br>2 (40)         |
| Kala 2017<br>(46)              | Czech<br>Republic            | 2011-2012                           | RCT<br>(NCT00888758) | Angiography             | 4.5months                           | 105/96                                       | 57/59                       | 87 (83)/<br>83 (87)       | 53 (50)/50 (52)  | 18 (17)/<br>25 (26)       | 67 (64)/<br>57 (59)       | 1                         | I                          | I  | 105 (100)/<br>96 (100)    |
| Ali 2016<br>(49)               | Multinational                | 2015-2016                           | RCT<br>(NCT02471586) | Angiography             | 6 months                            | 158/146                                      | 66 (59–72)/<br>67 (56–75    | 109 (68)/<br>107 (73)     | 124 (78)/109 (75)  | 52 (33)/42<br>(29)        | 28 (18)/<br>35 (24)       | 115 (73)/<br>112 (77)     | 25 (16)/<br>27 (18)        | 20 (13)/<br>24 (16)  | 6 (4)/4 (3)               |
| Meneveau<br>2016 ( <b>42</b> ) | France                       | 2013-2015                           | RCT<br>(NCT01743274) | Angiography             | 6 months                            | 120/120                                      | 60.8 (11.5)/<br>60.2 (11.3) | 95 (79.2)/<br>91 (75.8)   | 67 (55.8)/<br>50 (41.7)  | 26 (21.7)/<br>19 (15.8)   | 47 (39.2)/<br>51 (42.5)   | 59 (49.2)/<br>56 (46.7)   | 10 (8.3)/<br>9 (7.5)       | 110 (91.7)/<br>111 (92.5)  | I                         |
| Kim 2015<br>(48)               | Korea                        | 2011-2012                           | RCT<br>(NCT01869842) | Angiography             | 6 months                            | 58/59  | 58.8 (10.8)/<br>61.6 (9.7)  | 39 (78)/<br>37 (72)       | 27 (54.0)/25<br>(49.0)   | 16 (32.0)/<br>16 (31.4)   | 16 (32.0)/<br>15 (29.4)   | 33 (66)/<br>37 (72.5)     | I                          | ı  | I                         |
| Antonsen<br>2015 (43)          | Denmark                      | 2011-2013                           | RCT<br>(NCT02272283) | Angiography             | 6 months                            | 40/45  | 61.8 (9.4)/<br>62.6 (11.0)  | 36 (72)/<br>34 (68)       | 28 (56)/28 (56)  | 8 (16)/5<br>(10)          | 23 (46)/<br>18 (36)       | I                         | 0/0                        | 50 (100)/<br>50 (100)  | 0/0                       |
| NSTEMI, noi                    | n-ST-elevation               | myocardial Infarc                   | ction; OCT, optica   | l coherence tomo        | graphy; RCT,                        | randomized co                                | introlled trial;            | STEMI, ST-e               | NSTEMI, non-ST-elevation myocardial Infarction; OCT, optical coherence tomography; RCT, randomized controlled trial; STEMI, ST-elevation myocardial infarction | al infarction.            |                           |                           |                            |  |                           |

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TABLE 3 Baseline demographics of trials and populations included in meta-analysis.

| Introsen 2015         Demnark         040         244         85           0012023         Europe         65600         30201         021         023         001         73.8           01201         Ling 05.5         25.40         0.67         0.28         0.65.1         0.09         0.28.2         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65         0.64         0.65  | Study   | Location           | OCT     | Angiography | Subjectnumber |            | Odds<br>Ratio (95% CI) | %<br>Weight |
|---|---|--------------------|---------|-------------|---------------|------------|------------------------|-------------|
| Immose 2015         Demmark         0.40         2.45         85           0012023         Europe         65000         23.8001         1201           13.2022         China         13112         11/114         228           13.2017         Europe         3106         106         2011           13.2022         China         13112         11/114         228           13.2017         Europe         3106         101         286         0.84 (0.85, 1.69)         0.84 (0.85, 1.69)         0.84 (0.85, 1.10)         102           13.2023         Multinational         6/12.33         10/12.84         2467         0.58 (0.28, 1.30)         42.2         20.86 (0.28, 1.30)         42.2         1000         0.58 (0.28, 1.30)         42.2         1000         0.58 (0.28, 1.30)         42.2         1000         10  | MACE  | 0.000              | 01110   |             |               | 1          | the second second      |             |
| bioh         2023         Europe         56800         83601         1201           is 2022         China         31112         11114         228           iubitotal (I-squared = 0.0%, p = 0.515)         3159         101         286 (0.28, 5.2.4)         0.60           iubitotal (I-squared = 0.0%, p = 0.515)         Multinational         101254         2467         0.58 (0.28, 1.10)         0.03           iubitotal (I-squared = 0.0%, p = 0.503)         Multinational         101254         2467         0.58 (0.28, 1.30)         422           iubitotal (I-squared = 0.0%, p = 0.893)         1055         0.50         105         0.54 (0.28, 1.10)         0.23 (0.20, 1.13)         323           iulitotal (I-squared = 0.0%, p = 0.893)         10150         1201         0.57 (0.48, 1.17)         0.56 (0.28, 1.10)         0.58 (0.28, 1.12)         0.77 (0.48, 3.00)         100.0           Julicotal (I-squared = 0.0%, p = 0.893)         0.1120         2467         0.56 (0.28, 1.12)         0.56 (0.28, 1.12)         0.56 (0.28, 1.12)         0.56 (0.28, 1.12)         0.56 (0.28, 1.12)         0.56 (0.28, 1.12)         0.56 (0.28, 1.12)         0.56 (0.28, 1.12)         0.56 (0.28, 1.12)         0.56 (0.28, 1.12)         0.56 (0.28, 1.12)         0.57 (0.48, 1.17)         0.56 (0.21, 1.23, 0.21, 1.23, 1.24)         0.56 (0.21, 1.23, 0.21, 1.24)   |   |                    |         |             |               |            | 1.24 (0.59, 2.62)      | 10.44       |
| iii 2022       Chria       13/112       11/114       228         Gia 2017       Europe       31/05       1/18       0/65       2.6.9       0.87         Gia 2017       Europe       21/95       3/96       101       0.86       0.84       0.85       0.86       0.84   |   | Denmark            | 0/40    |             | 85 -          | •          | 0.23 (0.01, 4.74)      | 2.09        |
| Kala 2017       Europe       3/165       1/86       201         Kin 2015       Korea       2/56       3/59       101         Subtoal (I-squared = 0.0%, p = 0.515)       0       0       0.84 (0.85, 1.10)       100.         B. Cardiac death       0/1233       10/1264       2/47       0.86 (0.12, 3.93)       4/32         Anonen 2015       Demark       0/40       1/45       85       0.86 (0.28, 1.02)       3/32         Jacobal (I-squared = 0.0%, p = 0.893)       0/150       105       105       0/50 <td>Holm 2023</td> <td></td> <td></td> <td></td> <td></td> <td>•</td> <td></td> <td>73.86</td>   | Holm 2023   |                    |         |             |               | •          |                        | 73.86       |
| Kim 2015       Korás       2/68       3/69       101       008/0 (02: 2: 889)       268       0.84 (0.85, 1.00)       100.         Kim 2015       Korás       0/12       101/25       2.487       0.84 (0.85, 1.00)       100.         Kim 2013       Multinational       0/1233       18/1254       2.487       0.84 (0.85, 1.00)       100.         Jia 2022       China       3/112       4/114       228       0.54 (0.22, 1.27)       407.         Jia 2022       China       3/112       4/114       228       0.54 (0.22, 1.27)       407.         Jia 2022       China       1/155       0/150       1050       1050       0.56 (0.28, 1.13)       4.12.03.         Subtoal (I-squared = 0.05, p = 0.590)       Difuencianal       2.183       4.11.254       2.487       0.76 (0.48, 1.17)       0.58 (0.28, 1.13)       3.141         Localize death       Multinational       0.1120       2.467       0.76 (0.48, 1.17)       0.58 (0.28, 1.13)       3.41         Localize death       Multinational       0.1120       1.021       0.76 (0.48, 1.02)       0.07 (0.48, 1.02)       0.07 (0.48, 1.02)       0.07 (0.48, 1.02)       0.07 (0.48, 1.02)       0.07 (0.48, 1.02)       0.07 (0.48, 1.02)       0.08 (0.08, 1.40)       0.22 (0.25, 5.4) <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td>1.18 (0.55, 2.54)</td><td></td></t<>  |   |                    |         |             |               |            | 1.18 (0.55, 2.54)      |             |
| Subtoal (I-squared = 0.0%, p = 0.515)         0.84 (0.65, 1.10)         100.           B. Cardiac death<br>All 2023         Multinational<br>Bi 2022         0/123         10/1254         2497           Antonsen 2015         Denmark         0/40         145         85           Multinational<br>Bi 2022         China<br>2022         Strope         8/600         15/601         1201           Diama 2020         Strope         8/600         15/601         1201         0.57 (0.48, 1.17)         65.0           C. All-cause death<br>All 2023         Multinational<br>32/1233         44/1254         2467         0.75 (0.48, 1.17)         65.0           C. All-cause death<br>All 2021         Multinational<br>41/2021         0.1142         265         0.58 (0.28, 1.14)         64.1           Subtoal (I-squared = 0.0%, p = 0.550)         0.142         265         0.83 (0.28, 1.4)         64.1           D. Mycoardial infarction<br>41/2021         Multinational<br>41/203         0.1120         1201         0.88 (0.28, 1.14)         66.1           Butoal (I-squared = 0.0%, p = 0.550)         0.1142         265         0.81 (0.58, 1.14)         66.1           Butoal (I-squared = 0.0%, p = 0.550)         0.1120         1201         0.88 (0.60, 1.40, 0.40         0.88 (0.60, 1.40, 0.40           Butoal (I-squared = 0.0%, p = 0.550)<   |   |                    |         |             |               |            |                        | 0.96        |
| B. Cardiac death       0/1233       10/1264       2487         All 2023       Multinational       0/1233       10/1264       2487         Admonsen 2015       Demark       0/40       1156       1560       1201         Dia 2022       China       9/123       4/114       228       0.54 (0.22, 1.27)       4/07.70 (1.81, 3.39)       10/2         Dia 2022       China       9/123       4/11254       2487       0.54 (0.23, 1.02)       10/0         C. All-cause death       Multinational       3/123       4/11254       2487       0.77 (0.18, 3.82)       0.77 (0.18, 1.02)       10/0         C. All-cause death       Multinational       0/120       240       0.58 (0.28, 1.13)       3/1.14         All 2023       Multinational       0/123       7/1233       7/1223       7/21254       2487         All 2023       Multinational       1/130       0/142       265       0.81 (0.58, 1.14)       66.1         All 2023       Multinational       2/153       7/1223       7/21254       2487       0.81 (0.58, 1.14)       66.1         All 2021       Multinational       2/153       5/1/233       5/1/224       2487       0.83 (0.68, 1.13)       100         All 2021  | Kim 2015  | Korea              | 2/58    | 3/59        | 101           |            | 0.69 (0.12, 3.98)      | 2.68        |
| Ali 2023       Multinational       11/23       161/254       2487         Anonses 2015       Denmark       040       11/65       85         Holm 2023       Europe       8600       15/601       1201         Jia 2022       China       3112       4114       226         Comma 2020       Japan       1050       0150       050       057       028 (021, 648)       144         Ali 2023       Multinational       321/233       44/1254       2487       056 (028, 130)       027 (048, 132)         C, Ali-cause death       Ali 2023       Multinational       321/233       44/1254       2487       0.75 (0.48, 1.17)       65.00         C, Microgured = 0.0%, p = 0.550)       01/142       265       0.76 (0.48, 1.17)       65.01       0.00         Subtotal (I-squared = 0.0%, p = 0.550)       01/142       265       0.76 (0.48, 1.02)       0.00         Subtotal (I-squared = 0.0%, p = 0.550)       0.11/20       01/142       265       0.81 (0.58, 1.14)       65.11         Subtotal (I-squared = 0.0%, p = 0.823)       0.140       268       0.43 (0.21, 0.44)       0.42         E, Target lesion revascularization       Ali 2023       Multinational       211/25       2487       0.88 (0.69, 1.13) <td< td=""><td>Subtotal (I-squared</td><td>= 0.0%, p = 0.515)</td><td></td><td></td><td></td><td>9</td><td>0.84 (0.65, 1.10)</td><td>100.00</td></td<>  | Subtotal (I-squared   | = 0.0%, p = 0.515) |         |             |               | 9          | 0.84 (0.65, 1.10)      | 100.00      |
| Anonsen 2015       Demmark       0.40       1145       85         Januar 2020       Japan       1155       0.50       105         Jala 2022       China       3112       41124       226         Jala 2022       Japan       1155       0.50       105         J.All-cause death       411202       23801       1201       0.56 (0.23, 1.27)       407.         All 2023       Multinational       321233       44/1254       2467       0.56 (0.28, 1.17)       65.0       0.56 (0.28, 1.13)       64.0       23.001       1.00       0.56 (0.28, 1.12)       1.00       0.56 (0.28, 1.12)       1.00       0.56 (0.28, 1.12)       1.00       0.56 (0.28, 1.12)       1.00       0.56 (0.28, 1.13)       44.114       2.00       0.76 (0.48, 1.17)       66.0       0.56 (0.28, 1.14)       65.0       0.56 (0.28, 1.14)       1.00       0.58 (0.28, 1.14)       1.00       0.76 (0.48, 1.17)       0.56 (0.28, 1.14)       1.00       0.76 (0.48, 1.17)       0.56 (0.28, 1.14)       1.00       0.76 (0.48, 1.17)       0.56 (0.28, 1.14)       1.00       0.76 (0.48, 1.17)       0.56 (0.28, 1.14)       1.00       0.76 (0.48, 1.17)       0.56 (0.28, 1.14)       1.00       0.76 (0.48, 1.12)       1.00       0.76 (0.48, 1.12)       1.00       0.76 (0.48, 1.12)       1.00  | B. Cardiac death  |                    |         |             |               |            |                        |             |
| Holm 2023       Europe       8800       15001       1201         Jia 2022       China       9112       4114       226         Dnuma 2020       Japan       1155       0150       105         Subtotal (I-squared = 0.0%, p = 0.898)       01023       Europe       13000       23601       1201         C. All-cause death       All/2023       Multinational       321233       441254       2467       0.75 (0.48, 1.17)       058 (0.28, 1.13)       0.41         C. All-cause death       Multinational       01153       0142       295       0.77 (0.49, 1.02)       100.         All 2021       Multinational       671/233       72/1254       2487       0.81 (0.58, 1.14)       66.1         All 2021       Multinational       4153       3142       295       0.81 (0.58, 1.14)       64.1         All 2021       Multinational       1150       01142       295       0.81 (0.58, 1.14)       64.1         All 2021       Multinational       1153       21142       2467       1.83 (0.21, 0.0.44)       0.42         All 2023       Multinational       1153       21142       2467       0.88 (0.69, 1.13)       100         Ja 2022       China       01112       0114   | Ali 2023  | Multinational      | 9/1233  | 16/1254     | 2487          |            | 0.58 (0.26, 1.30)      | 43.23       |
| Jia 2022 China 3112 4114 228<br>Onuma 2020 Japan 1155 0150 105<br>C. All-cause death<br>All 2023 Multinational 32/1233 441254 2487<br>All 2023 Multinational 0153 0142 295<br>Subtral (I-squared = 0.0%, p = 0.550)<br>D. Myocardial infarction<br>All 2023 Multinational 57/1233 72/1254 2487<br>All 2016 Multinational 41153 3142 2495<br>Subtral (I-squared = 0.0%, p = 0.550)<br>D. Myocardial infarction<br>All 2023 Multinational 57/1237 72/1254 2487<br>All 2016 Multinational 21158 0140 2488<br>Holm 2023 Multinational 21158 0140 2488<br>All 2021 Multinational 21158 01140 2480<br>Subtral (I-squared = 0.0%, p = 0.823)<br>E. Target lesion revascularization<br>All 2022 China 51112 41114 228<br>Subtral (I-squared = 0.0%, p = 0.823)<br>E. Target lesion revascularization<br>All 2022 China 51112 41114 228<br>Subtral (I-squared = 0.0%, p = 0.823)<br>E. Target lesion revascularization<br>All 2023 Multinational 2158 01140 2488<br>Hi2016 Multinational 2153 21142 2495<br>Subtral (I-squared = 0.0%, p = 0.823)<br>E. Target lesion revascularization<br>All 2023 Multinational 2153 21142 2495<br>All 2016 Multinational 2153 21142 2495<br>All 2016 Multinational 2153 21142 2495<br>All 2020 Europe 2119 119 38<br>Subtral (I-squared = 0.0%, p = 0.850)<br>E. Target vessel revascularization<br>All 2023 Multinational 2153 21142 2495<br>All 2020 Europe 2119 119 38<br>Subtral (I-squared = 0.0%, p = 0.850)<br>E. Target vessel revascularization<br>All 2023 Multinational 2153 21142 2495<br>All 2020 Europe 2119 119 38<br>Subtral (I-squared = 0.0%, p = 0.850)<br>E. Target vessel revascularization<br>All 2023 Multinational 41153 21142 2487<br>All 2021 Multinational 41153 21142 2485<br>All 2021 Multinational 41153 21142 2485<br>All 2021 Multinational 41153 21142 2485<br>All 2020 Europe 2119 119 38<br>Subtral (I-squared = 0.0%, p = 0.850)<br>E. Target vessel revascularization<br>All 2023 Multinational 41153 21142 2485<br>All 2021 Multinational 41153 21142 2495<br>All 2020 Europe 211120 240<br>All | Antonsen 2015   | Denmark            | 0/40    | 1/45        | 85            |            | 0.38 (0.02, 9.13)      | 3.82        |
| Jia 2022 China 3/11/2 4/114 228<br>Subtotal (I-squared = 0.0%, p = 0.893)<br>- C. All-cause death<br>All 2023 Mutinational 3/2123 4/11254 2487<br>All 2023 Mutinational 0/153 0/120 240<br>All 2021 Mutinational 5/71233 7/21/254 2487<br>All 2023 Mutinational 5/71233 7/21/254 2487<br>All 2023 Mutinational 5/71233 7/21/254 2487<br>All 2023 Mutinational 1/153 3/142 285<br>All 2021 Mutinational 2/158 0/140 288<br>Hall 2022 China 0/112 0/114 226<br>Subtotal (I-squared = 0.0%, p = 0.823)<br>E. Target lesion revascularization<br>All 2022 China 5/11/25 1/1254 2487<br>All 2015 Mutinational 1/158 1/140 288<br>Hall 2023 Mutinational 1/158 1/140 288<br>Hall 2023 Mutinational 1/158 1/140 288<br>Hall 2023 Mutinational 2/158 0/1140 240<br>Subtotal (I-squared = 0.0%, p = 0.823)<br>E. Target lesion revascularization<br>All 2022 China 6/11/2 1/114 226<br>Subtotal (I-squared = 0.0%, p = 0.823)<br>E. Target lesion revascularization<br>All 2022 China 5/11/254 2487<br>All 2015 Mutinational 1/158 1/140 288<br>Hall 2023 Mutinational 1/158 1/140 288<br>Hall 2024 China 6/1124 4/114 226<br>Hall 2025 Mutinational 1/158 1/140 288<br>Hall 2015 Mutinational 1/158 1/140 288<br>Hall 2016 Mutinational 6/1123 6/71254 2487<br>Hall 2020 Europe 2/19 1/19 38<br>Subtotal (I-squared = 0.0%, p = 0.856)<br>E. Target vessel revascularization<br>All 2023 Mutinational 6/1123 6/71254 2487<br>Hall 2016 Mutinational 6/1123 6/71254 2487<br>Hall 2017 Mutinational 6/1125 1/126 206<br>Hall 2018 Mutinational 6/1126 0/1145 85<br>Hall 2018 Mutinational 6/1126 0/116 0/11201<br>Hall 2020 Lerope        | Holm 2023   | Europe             | 8/600   | 15/601      | 1201          |            | 0.54 (0.23, 1.27)      | 40.72       |
| Onuma 2020       Japan       1155       0.50       105         Subtotal (I-squared = 0.0%, p = 0.893)       0.51 (0.38, 1.02)       100.1         C. All-cause death<br>All/2023       Mutinational       32/1233       44/1254       2487         Momeresua 2016       France       1/120       2010       240         All-2023       Mutinational       0/153       0/142       295         Subtotal (I-squared = 0.0%, p = 0.550)       0.70 (0.48, 1.02)       100.1         D. Myocardial infarction<br>All/2021       Mutinational       57/1233       72/1254       2487         All/2021       Mutinational       1/153       0/142       295         All/2021       Mutinational       5/1233       5/1/1254       2487         All/2021       Mutinational       5/1523       1/126       2467         All/2021       Mutinational       5/1523       6/1/254       2487         All/2021       Mutinational       5/1524       2487       0.38 (0.58, 1.68)  | Jia 2022  | China              | 3/112   | 4/114       | 228           |            | 0.77 (0.18, 3.36)      | 10.79       |
| Subtotal (I-squared = 0.0%, p = 0.883)       0.81 (0.38, 1.02)       00.11 (0.38, 1.02)       100.1         C. All-cause death<br>All 2023       Multinational<br>0.153       32/1233       44/1254       2487       0.58 (0.29, 1.13)       34.11         Manage and the state and th  | Onuma 2020  | Japan              | 1/55    | 0/50        | 105           |            |                        | 1.44        |
| 12/2023       Multinational       32/12/33       44/1254       2487         Holm 2023       Europe       13/600       23/601       1201         Weneveau 2016       France       11/20       0/120       240         Subtotal (I-squared = 0.0%, p = 0.550)       0/142       295       0.076 (0.48, 1.17)       65.0         D. Myocardial infarction       All 2021       Multinational       57/1233       72/1254       2487         All 2021       Multinational       57/1233       72/1254       2487       0.81 (0.58, 1.14)       0.01         All 2021       Multinational       21580       0/140       298       0.81 (0.58, 1.14)       0.61 (0.22, 5.41)       2.47         All 2021       Multinational       21580       0/140       298       0.91 (0.62, 1.34)       40.11         Maiz 2022       China       0/112       0/114       226       0.91 (0.62, 1.54)       0.81 (0.51)       2.49         Ali 2023       Multinational       2/153       2/142       295       0.93 (0.18, 0.51)       2.40         Ali 2021       Multinational       2/153       2/142       295       0.93 (0.18, 0.51)       2.40         Ali 2023       Multinational       53/1233       51/1224       <  | Subtotal (I-squared   | = 0.0%, p = 0.893) |         |             |               | $\diamond$ | 0.61 (0.38, 1.02)      | 100.00      |
| All 2023         Multinational         32/1233         44/1254         2487           Holm 2023         Europe         13/600         23/601         1201           Meneveau 2016         France         11/120         01/120         240           All 2021         Multinational         01/153         01/142         285           Subtotal (I-squared = 0.0%, p = 0.550)         0.76 (0.48, 1.17)         65.0           D. Myocardial infarction         All 2021         Multinational         57/1233         72/1254         2487           All 2021         Multinational         1/153         31/142         296         0.81 (0.58, 1.14)         66.1           All 2022         China         0.1120         2407         438 (0.21, 90.44)         0.42           Holm 2023         Europe 40:05, p = 0.823)         0.81 (0.58, 1.14)         265         0.91 (0.62, 1.34)         40.11           Mail 2023         Multinational         2/153         2/142         295         0.83 (0.46, 1.13)         100           Subtotal (I-squared = 0.0%, p = 0.828)         -         1.05 (0.72, 1.54)         68.15         0.83 (0.41, 10.26)         1.28 (0.28, 6.89)         2.90           Li 2023         Multinational         2/153         2/142         295<  | C All-cause death   |                    |         |             |               |            |                        |             |
| Holm 2023         Europe         13/800         23/801         1201           Meneveau 2016         France         1/120         0/120         240           Mail 2021         Multinational         0/153         0/142         285           Subtcall (I-squared = 0.0%, p = 0.550)         0         0.70 (0.46, 1.02)         100.           D. Myocardial infarction         Ali 2023         Multinational         57/1233         72/1254         2487           Ali 2016         Multinational         57/1233         72/1254         2487         0.81 (0.58, 1.14)         66.11           Ali 2021         Multinational         1/150         0/140         286         0.81 (0.58, 1.14)         66.11           Jai 2022         Chian         0/110         1/120         240         4.38 (0.21, 90.44)         0.42           Jai 2022         Chian         0/112         0/114         226         0.58 (0.58, 1.13)         100.           Jai 2022         Chian         0/112         0/114         226         0.88 (0.69, 1.13)         100.           Jai 2023         Multinational         1/158         1/124         2467         1.05 (0.72, 1.54)         68.55           Jai 2022         Chian         G/112 <td< td=""><td></td><td>Multinational</td><td>32/1233</td><td>44/1254</td><td>2487</td><td>-</td><td>0.75 (0.48, 1.17)</td><td>65.09</td></td<>  |   | Multinational      | 32/1233 | 44/1254     | 2487          | -          | 0.75 (0.48, 1.17)      | 65.09       |
| Meneveau 2016         France         1/120         0/120         240           All 2021         Multinational         0/153         0/142         285           D.Myocardial infarction         0.00         0.070 (0.48, 1.22)         0.075           All 2021         Multinational         57/1233         72/1254         2487           All 2021         Multinational         1560         1140         288           All 2021         Multinational         1571         231         72/1254         2487           All 2021         Multinational         158         01140         288           Holm 2023         Europe         40/600         51/801         1201           Meneveau 2016         France         1/120         1/120         1/120           Subtati (I-squared = 0.0%, p = 0.823)               E. Target lesion revascularization         All 2023         Multinational         1/158         1/142         295           All 2021         Multinational         1/158         1/142         295  |   |                    |         |             |               |            |                        | 34.16       |
| Ali 2021       Multinational       0/153       0/142       295         Subtotal (I-squared = 0.0%, p = 0.550)       0       0.1142       295       (Excluded)       0.00         D. Myocardial infarction       0.1153       0/142       295       (Excluded)       0.00       0.70 (0.48, 1.02)       100.1         Ali 2021       Multinational       57/1233       72/1254       2487       1.23 (0.28, 5.41)       2.47         Ali 2016       Multinational       2158       0140       298       0.91 (0.62, 1.34)       40.1         Holm 2023       Europe       40.600       51.601       1201       0.91 (0.62, 1.34)       40.1         Maizo22       China       0.112       0114       228       0.93 (0.36, 6.1)       2.00         E. Target lesion revascularization       1.05 (0.72, 1.54)       58.5       58.1       2.00       0.88 (0.60, 1.405)       1.23         Ali 2023       Multinational       1158       1/140       296       1.80 (0.14, 0.5)       1.23       0.88 (0.60, 6.1, 0.5)       1.23         Miz023       Europe       1.08 (0.16, 0.5)       1.23       0.94 (0.70, 1.27)       100.1       0.98 (0.60, 1.405)       1.23         Multinational       4/153       2/142  | Meneveau 2016   |                    | 1/120   | 0/120       | 240           |            |                        | 0.75        |
| Subtotal (I-squared = 0.0%, p = 0.550)       0.70 (0.49, 1.02)       100.1         D. Myocardial infarction       57/1233       72/1254       2487         Ali 2023       Multinational       57/1233       72/1254       2487         Ali 2016       Multinational       2158       0140       268         Holm 2023       Europe       48/000       51/801       1201         Meneveau 2016       France       1/120       1/120       240         Jia 2022       China       01112       0114       228         Subtotal (I-squared = 0.0%, p = 0.823)       0.83 (0.86, 1.13)       100.0         E. Target lesion revascularization       41/2023       Multinational       51/1254       2487         Ali 2021       Multinational       1/158       1/140       298         Ali 2023       Multinational       1/158       1/140       298         Ali 2021       Multinational       1/158       1/140       298         Ali 2022       China       5/112       4/114       226         Multinational       1/158       1/140       298       0.88 (0.86, 1.13)       100.072, 1.40)       1.82 (0.25, 4.58)       480         Ali 2021       Multinational       4/153   | Ali 2021  | Multinational      | 0/153   | 0/142       | 295           |            |                        | 0.00        |
| Ali 2023       Multinational       57/1233       72/1254       2487         Ali 2021       Multinational       4/153       3/142       295         Ali 2016       Multinational       4/153       3/142       295         Ali 2021       Multinational       4/153       3/142       295         Ali 2016       Multinational       4/153       3/142       295         Ali 2023       Europe       4/600       51/601       1201         Maeweau 2016       France       1/120       1/120       240         Subtotal (I-squared = 0.0%, p = 0.823)       0/112       0/114       226         E. Target lesion revascularization       Ali 2023       Multinational       53/1233       51/1254       2487         Ali 2021       Multinational       1/158       1/140       298       0.89 (0.06, 14.05)       1.23         Jai 2022       China       51/12       4/114       226       1.26 (0.35, 4.58)       480         Liki 2020       Europe       2/19       1/19       38       1.00 (0.72, 1.40)       94.22         Liki 2021       Multinational       6/123       67/1254       2487       1.00 (0.07, 1.40)       1.42         Ali 2021       Multinati  | Subtotal (I-squared   | = 0.0%, p = 0.550) |         |             |               | 0          |                        | 100.00      |
| Ali 2023       Multinational       57/1233       72/1254       2487         Ali 2021       Multinational       4/153       3/142       295         Ali 2016       Multinational       4/153       3/142       295         Ali 2021       Multinational       4/153       3/142       295         Ali 2016       Multinational       4/153       3/142       295         Ali 2023       Europe       4/600       51/601       1201         Maeweau 2016       France       1/120       1/120       240         Subtotal (I-squared = 0.0%, p = 0.823)       0/112       0/114       226         E. Target lesion revascularization       Ali 2023       Multinational       53/1233       51/1254       2487         Ali 2021       Multinational       1/158       1/140       298       0.89 (0.06, 14.05)       1.23         Jai 2022       China       51/12       4/114       226       1.26 (0.35, 4.58)       480         Liki 2020       Europe       2/19       1/19       38       1.00 (0.72, 1.40)       94.22         Liki 2021       Multinational       6/123       67/1254       2487       1.00 (0.07, 1.40)       1.42         Ali 2021       Multinati  | D. Myocardial infarc  | tion               |         |             |               |            |                        |             |
| Ali 2021       Multinational       4/153       3/142       295         Ali 2016       Multinational       2/158       0/140       298         Ali 2016       Multinational       2/158       0/140       298         Ali 2016       France       1/120       1/120       240         Meneveau 2016       France       1/120       1/120       240         Jia 2022       China       0/112       0/114       226         Subtotal (I-squared = 0.0%, p = 0.823)       0.0112       0/114       226         Ali 2023       Multinational       53/1233       51/1254       2487         Ali 2021       Multinational       1/153       2/142       295         Ali 2023       Multinational       53/123       61/124       295         Ali 2023       Multinational       63/123       67/1254       2487         Kim 2015       Korea       2/58       1/59       101         Leki 2020       Europe       1/19       1/19       38         Subtotal (I-squared = 0.0%, p = 0.856)       1/120       240       1.00 (0.72, 1.40)       4/4.2         Subtotal (I-squared = 0.0%, p = 0.857)       1.19       1/19       38       2.49  |   |                    | 57/1233 | 72/1254     | 2487          | -          | 0.81 (0.58, 1.14)      | 58.17       |
| Ali 2016       Multinational       2/158       0/140       298         Holm 2023       Europe       46/600       51/601       1201         Meneveau 2016       France       1/120       1/120       240         Jia 2022       China       0/112       0/114       226         Subtotal (I-squared = 0.0%, p = 0.823)            E.       Target lesion revascularization           Ali 2023       Multinational       53/1233       51/1254       2487         Ali 2021       Multinational       1/158       1/140       298         Holm 2023       Europe       16/600       26/601       1201         Jia 2022       China       51/1254       2487         Kim 2015       Korea       2/158       1/140       298         Subtotal (I-squared = 0.0%, p = 0.858)             Kim 2015       Korea       2/182       2/59       101           Uski 2020       Europe       1/19       38        1           Ali 2021       Multinational       6/1233       6/71254       2487       .   |   | Multinational      |         | 3/142       |               |            |                        |             |
| Holm 2023       Europe       48/800       51/801       1201         Meneveau 2018       France       1/120       1/120       240         Jia 2022       China       0/112       0/114       226         Subtotal (I-squared = 0.0%, p = 0.823)       0/112       0/114       226         F.       Target lesion revascularization       1.05 (0.72, 1.54)       58.5         Ali 2021       Multinational       53/1233       51/1254       2487         Ali 2021       Multinational       1/158       1/140       288         Holm 2023       Europe       1/6800       26/801       1201         Jia 2022       China       5/112       4/114       226         Kim 2015       Korea       2/58       2/59       101         Jia 2023       Multinational       68/1233       67/1254       2487         Ali 2020       Europe       2/19       1/19       38         Subtotal (I-squared = 0.0%, p = 0.856)            F.       Target vessel revascularization       Ali 2021       Multinational       68/1233       67/1254       2487         Ali 2020       Europe       1/19       1/120       240  |   |                    |         |             |               |            |                        |             |
| Meneveau 2018         France         1/120         1/120         240           Jia 2022         China         0/112         0/114         226         1.00 (0.06, 15.81)         0.79           Subtotal (I-squared = 0.0%, p = 0.823)         0/112         0/114         226         0.00         0.88 (0.69, 1.13)         100           E. Target lesion revascularization         Ali 2023         Multinational         53/1233         51/1254         2467         1.05 (0.72, 1.54)         58.5           Ali 2016         Multinational         1/158         1/140         298         0.93 (0.13, 6.51)         2.40           Jai 2022         China         51/1254         2487         0.89 (0.06, 14.05)         1.23           Jai 2022         China         51/12         1/16         298         0.89 (0.06, 14.05)         1.23           Jai 2022         China         51/12         4/114         226         0.83 (0.34, 1.16)         29.7           Jai 2022         China         51/12         4/114         226         0.83 (0.06, 14.05)         1.23           Subtotal (I-squared = 0.0%, p = 0.856)         1.02 (0.16, 6.99)         2.29         1.83 (0.34, 0.88)         2.49           Mali 2020         Europe         1/19   |   | Europe             |         |             |               | -          |                        | 40.15       |
| Jia 2022       China       0/112       0/114       226       (Excluded)       0.00         Subtotal (I-squared = 0.0%, p = 0.823)       . <td>Meneveau 2016</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>0.79</td>  | Meneveau 2016   |                    |         |             |               |            |                        | 0.79        |
| Subtotal (I-squared = 0.0%, p = 0.823)<br>E. Target lesion revascularization<br>Ali 2023 Multinational 2/153 2/142 295<br>Ali 2018 Multinational 1/158 1/140 298<br>Ali 2023 Europe 18/800 28/801 1201<br>Jia 2022 China 5/112 4/114 226<br>Kim 2015 Korea 2/58 2/59 101<br>Ueki 2020 Europe 2/19 1/19 38<br>Subtotal (I-squared = 0.0%, p = 0.856)<br>F. Target vessel revascularization<br>Ali 2021 Multinational 68/1233 67/1254 2487<br>Ali 2021 Multinational 4/153 2/142 295<br>Meneveau 2016 France 2/120 1/120 240<br>Ueki 2020 Europe 1/109 1/19 38<br>Subtotal (I-squared = 0.0%, p = 0.857)<br>G. Stent thrombosis<br>Ali 2015 Morea 0/56 1/25 1/85 0/140 298<br>Antonsen 2015 Denmark 0/40 1/45 85<br>Kim 2015 Korea 0/58 1/59 101<br>G. Stent thrombosis<br>Kim 2015 Korea 0/58 1/59 101   |   |                    |         |             |               |            |                        |             |
| Ali 2023       Multinational       53/1233       51/1254       2487       1.05 (0.72, 1.54)       58.5         Ali 2021       Multinational       1/158       2/142       295       0.93 (0.13, 6.51)       2.40         Ali 2018       Multinational       1/158       1/140       298       0.89 (0.06, 14.05)       1.23         Jia 2022       China       5/112       4/114       226       0.83 (0.34, 1.16)       2.27         Jia 2022       China       5/112       4/114       226       0.83 (0.34, 1.16)       2.27         Jia 2022       China       5/112       4/114       226       0.83 (0.34, 1.16)       2.27         Jua 2020       Europe       2/19       1/19       38       1.00 (0.72, 1.40)       94.28         Subtotal (I-squared = 0.0%, p = 0.856)          1.00 (0.72, 1.40)       94.28         Ali 2021       Multinational       66/1233       67/1254       2487       1.08 (0.18, 21.59)       1.42         Ali 2021       Multinational       4/153       2/142       295       1.83 (0.34, 0.86)       2.96         Meneveau 2016       France       2/120       1/120       240       1.98 (0.18, 21.59)       1.42   |   |                    |         |             |               | 0          |                        | 100.00      |
| Ali 2023       Multinational       53/1233       51/1254       2487       1.05 (0.72, 1.54)       58.5         Ali 2021       Multinational       1/158       2/142       295       0.93 (0.13, 6.51)       2.40         Ali 2018       Multinational       1/158       1/140       298       0.89 (0.06, 14.05)       1.23         Ali 2015       Europe       106 (0.28/601       1201       0.83 (0.34, 1.16)       29.7         Jia 2022       China       5/112       4/114       226       0.83 (0.34, 1.16)       29.7         Jia 2022       China       5/112       4/114       226       0.83 (0.34, 1.16)       29.7         Jia 2022       China       5/112       4/114       226       0.83 (0.34, 1.16)       29.7         Veki 2020       Europe       2/19       1/19       38       1.00 (0.72, 1.40)       94.2         Ali 2021       Multinational       66/1233       67/1254       2487       1.08 (0.18, 21.59)       1.42         Meneveau 2016       France       2/120       1/120       240       1.88 (0.34, 0.86)       2.96         Meneveau 2016       Funce       2.84 (0.11, 64.38)       2.49       1.00 (0.07, 14.90)       1.42         Subtotal (I-squared  | F. Tarnet lesion rev:   | ascularization     |         |             |               |            |                        |             |
| Ali 2021       Multinational       2/153       2/142       295         Ali 2016       Multinational       1/158       1/140       298         Hoim 2023       Europe       16/600       26/601       1201         Jia 2022       China       5/112       4/114       226         Kim 2015       Korea       2/58       2/59       101         Jia 2020       Europe       2/19       1/19       38         Subtotal (I-squared = 0.0%, p = 0.856)       .       .       0.93 (0.34, 1.69)       2.29         .  | •   |                    | 53/1233 | 51/1254     | 2487          | -          | 1.05 (0.72, 1.54)      | 58 51       |
| Ali 2016       Multinational       1/158       1/140       298         Holm 2023       Europe       16/600       26/601       1201         Jia 2022       China       5/112       4/114       226         Kim 2015       Korea       2/58       2/59       101         Ueki 2020       Europe       2/19       1/19       38         Subtotal (I-squared = 0.0%, p = 0.856)            F. Target vessel revascularization             Ali 2023       Multinational       68/1233       67/1254       2487           Ali 2020       Europe       1/19       1/19       38             Ueki 2020       Europe       1/19       1/120       240             Ueki 2020       Europe       1/19       1/19       38                            <   |   |                    |         |             |               |            |                        |             |
| Holm 2023       Europe       18/800       28/801       1201         Jia 2022       China       5/112       4/114       228         Kim 2015       Korea       2/58       2/59       101         Ueki 2020       Europe       2/19       1/19       38         Subtotal (I-squared = 0.0%, p = 0.856)          1.00 (0.72, 1.40)       94.29         Ali 2023       Multinational       68/1233       67/1254       2487        1.00 (0.72, 1.40)       94.29         Ali 2021       Multinational       4/153       2/142       295        1.83 (0.34, 9.86)       2.96         Meneveau 2016       France       2/120       1/120       240        1.88 (0.18, 21.59)       1.42         Ueki 2020       Europe       1/19       1/19       38        1.00 (0.07, 14.90)       1.42         Subtotal (I-squared = 0.0%, p = 0.857)           1.04 (0.76, 1.43)       1.00 (0.07, 14.90)       1.42         G. Stent thrombosis                0.38 (0.02, 9.13)       0.54 <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>   |   |                    |         |             |               |            |                        |             |
| Jia 2022       China       6/112       4/114       226         Kim 2015       Korea       2/58       2/59       101         Jeki 2020       Europe       2/19       1/19       38         Subtotal (I-squared = 0.0%, p = 0.856)             F.       Target vessel revascularization             Ali 2021       Multinational       68/1233       67/1254       2487           Ali 2021       Multinational       4/153       2/142       295            Meneveau 2016       France       2/120       1/120       240              Subtotal (I-squared = 0.0%, p = 0.857)  |   |                    |         |             |               |            |                        | 29.78       |
| Kim 2015         Korea         2/58         2/59         101           Ueki 2020         Europe         2/19         1/19         38           Subtotal (I-squared = 0.0%, p = 0.856)         1.00 (0.72, 1.40)         1.18           F. Target vessel revascularization         1.00 (0.72, 1.40)         94.21           Ali 2021         Multinational         66/1233         67/1254         2487           Ali 2021         Multinational         4/153         2/142         295           Meneveau 2016         France         2/120         1/120         240           Ueki 2020         Europe         1/19         1/19         38           Subtotal (I-squared = 0.0%, p = 0.857)          1.00 (0.07, 14.90)         1.42           Subtotal (I-squared = 0.0%, p = 0.857)           1.04 (0.76, 1.43)         100.1           G. Stent thrombosis                   Ali 2016         Multinational         1/158         0/140         298   | and the second se |                    |         |             |               |            |                        |             |
| Ueki 2020         Europe         2/19         1/19         38           Subtotal (I-squared = 0.0%, p = 0.856)         1.90 (0.19, 19.40)         1.18           F. Target vessel revascularization         0.94 (0.70, 1.27)         100.1           Ali 2023         Multinational         68/1233         67/1254         2487           Ali 2021         Multinational         4/153         2/142         295           Meneveau 2016         France         2/120         1/120         240           Ueki 2020         Europe         1/19         1/19         38           Subtotal (I-squared = 0.0%, p = 0.857)         1.00 (0.07, 14.90)         1.42           G. Stent thrombosis         1.00 (0.07, 14.90)         1.42           Altonsen 2015         Denmark         0/140         298           Antonsen 2015         Denmark         0/140         1201           Kala 2017         Europe         1/105         1/98         201           Kim 2015         Korea         0/58         1/59         101  |   |                    |         |             |               |            |                        |             |
| Subtotal (I-squared = 0.0%, p = 0.856)<br>F. Target vessel revascularization<br>Ali 2023 Multinational 66/1233 67/1254 2487<br>Ali 2021 Multinational 4/153 2/142 295<br>Meneveau 2016 France 2/120 1/120 240<br>Ueki 2020 Europe 1/19 1/19 38<br>Subtotal (I-squared = 0.0%, p = 0.857)<br>G. Stent thrombosis<br>Ali 2018 Multinational 1/158 0/140 298<br>Antonsen 2015 Denmark 0/40 1/45 85<br>Holm 2023 Europe 1/2000 17/601 1201<br>Kala 2017 Europe 1/105 1/196 201<br>Kim 2015 Korea 0/58 1/59 101  |   |                    |         |             |               |            |                        |             |
| Ali 2023       Multinational       68/1233       67/1254       2487         Ali 2021       Multinational       4/153       2/142       295         Meneveau 2016       France       2/120       1/120       240         Ueki 2020       Europe       1/19       1/19       38         Subtotal (I-squared = 0.0%, p = 0.857)  |   |                    | 210     |             |               | •          |                        | 100.00      |
| Ali 2023       Multinational       68/1233       67/1254       2487         Ali 2021       Multinational       4/153       2/142       295         Meneveau 2018       France       2/120       1/120       240         Ueki 2020       Europe       1/19       1/19       38         Subtotal (I-squared = 0.0%, p = 0.857)  | E Tarnet vessel row   | ascularization     |         |             |               |            |                        |             |
| Ali 2021       Multinational       4/153       2/142       295         Meneveau 2016       France       2/120       1/120       240         Ueki 2020       Europe       1/19       1/19       38         Subtotal (I-squared = 0.0%, p = 0.857)       1.00 (0.07, 14.90)       1.42         G. Stent thrombosis       1.04 (0.76, 1.43)       100.00         Ali 2016       Multinational       1/158       0/140       298         Antonsen 2015       Denmark       0/40       1/45       85         Holm 2023       Europe       12/800       17/801       1201         Kial 2017       Europe       1/105       1/98       201         Kim 2015       Korea       0/58       1/59       101  |   |                    | 88(1222 | 87/1254     | 2487          | <u> </u>   | 1 00 (0 72 1 40)       | 04 20       |
| Meneveau 2018         France         2/120         1/120         240           Ueki 2020         Europe         1/19         1/19         38           Subtotal (I-squared = 0.0%, p = 0.857)         1.00 (0.07, 14.90)         1.42           G. Stent thrombosis         1.04 (0.76, 1.43)         100.0           Ali 2018         Multinational         1/158         0/140         298           Antonsen 2015         Denmark         0/40         1/45         85           Holm 2023         Europe         1/2600         17/601         1201           Kala 2017         Europe         1/105         1/98         201           Kim 2015         Korea         0/58         1/59         101  |   |                    |         |             |               |            |                        |             |
| Ueki 2020         Europe         1/19         1/19         38         1.00 (0.07, 14.90)         1.42           Subtotal (I-squared = 0.0%, p = 0.857)           1.04 (0.76, 1.43)         100.1           G. Stent thrombosis                 Ali 2016         Multinational         1/158         0/140         298          2.64 (0.11, 64.38)         2.49           Antonsen 2015         Denmark         0/40         1/45         85          0.38 (0.02, 9.13)         6.54           Holm 2023         Europe         1/2600         17/601         1201          0.71 (0.34, 1.48)         79.11           Kala 2017         Europe         1/105         1/98         201          0.92 (0.06, 14.43)         4.89           Kim 2015         Korea         0/58         1/59         101          0.34 (0.01, 8.29)         6.90  |   |                    |         |             |               |            |                        |             |
| Subtotal (I-squared = 0.0%, p = 0.857)<br>G. Stent thrombosis<br>Ali 2018 Multinational 1/158 0/140 298<br>Antonsen 2015 Denmark 0/40 1/45 85<br>Holm 2023 Europe 12/800 17/801 1201<br>Kala 2017 Europe 1/105 1/98 201<br>Kim 2015 Korea 0/58 1/59 101   |   |                    |         |             |               |            |                        |             |
| Ali 2018         Multinational         1/158         0/140         298         2.64 (0.11, 84.38)         2.49           Antonsen 2015         Denmark         0/40         1/45         85         0.38 (0.02, 9.13)         8.54           Holm 2023         Europe         12/600         17/601         1201         0.71 (0.34, 1.48)         79.11           Kala 2017         Europe         1/105         1/95         201         0.92 (0.06, 14.43)         4.89           Kim 2015         Korea         0/58         1/59         101         0.34 (0.01, 8.29)         6.90  |   |                    |         |             |               | •          |                        | 100.00      |
| Ali 2018         Multinational         1/158         0/140         298         2.64 (0.11, 64.38)         2.49           Antonsen 2015         Denmark         0/40         1/45         85         0.38 (0.02, 9.13)         6.54           Holm 2023         Europe         12/600         17/601         1201         0.71 (0.34, 1.48)         79.11           Kala 2017         Europe         1/105         1/98         201         0.92 (0.06, 14.43)         4.89           Kim 2015         Korea         0/58         1/59         101         0.34 (0.01, 8.29)         6.90  | G Stant thrombosis  |                    |         |             |               |            |                        |             |
| Antonsen 2015         Denmark         0/40         1/45         85         0.38 (0.02, 9.13)         8.54           Holm 2023         Europe         12/600         17/601         1201         0.71 (0.34, 1.48)         79.11           Kala 2017         Europe         1/105         1/95         201         0.92 (0.06, 14.43)         4.89           Kim 2015         Korea         0/58         1/59         101         0.34 (0.01, 8.29)         6.90   |   |                    | 1/158   | 0/140       | 298           |            | 2 64 (0 11 64 38)      | 2 40        |
| Holm 2023         Europe         12/800         17/801         1201         0.71 (0.34, 1.48)         79.11           Kala 2017         Europe         1/105         1/98         201         0.92 (0.06, 14.43)         4.89           Kim 2015         Korea         0/58         1/59         101         0.34 (0.01, 8.29)         6.90   |   |                    |         |             |               |            |                        |             |
| Kala 2017         Europe         1/105         1/98         201         0.92 (0.06, 14.43)         4.89           Kim 2015         Korea         0/58         1/59         101         0.34 (0.01, 8.29)         6.90   |   |                    |         |             |               |            |                        |             |
| Kim 2015 Korea 0/58 1/59 101 - 0.34 (0.01, 8.29) 6.90   |   |                    |         |             |               |            |                        |             |
|   |   |                    |         |             |               |            |                        |             |
| Subtotal (I-squared = 0.0%, p = 0.908) 0.72 (0.38, 1.38) 100.   |   |                    | 0.00    | 1150        | 101           | 0          | 0.72 (0.38, 1.38)      | 100.00      |
|   |   |                    |         |             |               |            |                        |             |

#### FIGURE 10

Forest plot comparing OCT guided with coronary angiography guided PCI in RCT studies. Data obtained from RCTs using fixed effect meta-analysis and expressed as OR. (A) MACE; (B) cardiac death; (C) all-cause death; (D) myocardial infarction; (E) target lesion revascularization (F) target vessel revascularization; (G) stent thrombosis. CI, confidence interval; OCT, optical coherence tomography; PCI, Percutaneous coronary intervention.

| Study                | Location            | OCT        | Angiography | Subjectnumber |                   | Odds<br>Ratio (95% CI) | %<br>Weight |
|----------------------|---------------------|------------|-------------|---------------|-------------------|------------------------|-------------|
| MACE                 |                     |            |             |               | 1                 |                        |             |
| D'Ascenzo 2017       | Italy               | 28/197     | 28/197      | 394           | -                 | 1.00 (0.61, 1.63)      | 27.75       |
| Di 2013              | Italy               | 5/40       | 8/40        | 80            |                   | 0.67 (0.24, 1.89)      | 8.63        |
| Jones 2018           | United Kingdom      | 9/1134     | 23/1134     | 2268          |                   | 0.40 (0.18, 0.85)      | 14.52       |
| Khalifa 2021         | Japan               | 13/260     | 15/130      | 390           |                   | 0.46 (0.23, 0.94)      | 16.21       |
| Lannaccone 2016      | Italy               | 31/270     | 47/270      | 540           |                   | 0.69 (0.45, 1.06)      | 32.88       |
|                      | d = 26.7%, p = 0.24 |            |             |               | 9                 | 0.66 (0.48, 0.91)      | 100.00      |
| Cardiac death        |                     |            |             |               |                   |                        |             |
| Cortese 2022         | Europe              | 1/100      | 4/100       | 200           |                   | 0.26 (0.03, 2.26)      | 13.78       |
| D'Ascenzo 2017       | Italy               | 7/197      | 2/197       | 394           |                   | 3.41 (0.72, 16.24)     | 21.56       |
| Khalifa 2021         | Japan               | 7/260      | 8/130       | 390           |                   | 0.45 (0.17, 1.22)      | 33.44       |
| Sheth 2016           | Canada              | 4/214      | 16/428      | 642           |                   | 0.51 (0.17, 1.50)      | 31.21       |
|                      | d = 48.1%, p = 0.12 |            |             |               | $\diamond$        | 0.67 (0.26, 1.71)      | 100.00      |
| All-cause death      |                     |            |             |               |                   |                        |             |
| Cortese 2022         | Europe              | 2/100      | 6/100       | 200           |                   | 0.35 (0.07, 1.68)      | 23.30       |
| D'Ascenzo 2017       | Italy               | 7/197      | 2/197       | 394           |                   | 3.41 (0.72, 16.24)     | 23.66       |
| Di 2013              | Italy               | 1/40       | 2/40        | 80            |                   | 0.51 (0.05, 5.43)      | 12.58       |
| Lannaccone 2016      | Italy               | 7/270      | 9/270       | 540           |                   | 0.78 (0.30, 2.07)      | 40.46       |
|                      | d = 33.5%, p = 0.2  |            |             |               | $\mathbf{\Phi}$   | 0.87 (0.35, 2.18)      | 100.00      |
| Myocardial infarctio | on                  |            |             |               | 10.22             |                        |             |
| Cortese 2022         | Europe              | 2/100      | 4/100       | 200           |                   | 0.51 (0.10, 2.72)      | 9.55        |
| Di 2013              | Italy               | 1/40       | 3/40        | 80            |                   | 0.35 (0.04, 3.23)      | 5.64        |
| Jones 2018           | United Kingdom      | 2/1134     |             | 2268          |                   | 0.22 (0.05, 1.03)      | 11.24       |
| Khalifa 2021         | Japan               | 2/260      | 4/130       | 390           |                   | 0.26 (0.05, 1.38)      | 9.45        |
| Lannaccone 2016      | Italy               |            | 17/270      | 540           |                   | 1.06 (0.56, 2.01)      | 42.61       |
| Sheth 2016           | Canada              | 5/214      | 11/428      | 642           |                   | 0.91 (0.32, 2.59)      | 21.50       |
|                      | d = 14.9%, p = 0.3  |            | 111420      | 042           | 9                 | 0.66 (0.38, 1.13)      | 100.00      |
| Target lesion revas  | cularization        |            |             |               |                   |                        |             |
| Cortese 2022         | Europe              | 6/100      | 9/100       | 200           |                   | 0.69 (0.25, 1.86)      | 31.35       |
| D'Ascenzo 2017       | Italy               | 8/197      | 28/197      | 394           |                   | 0.31 (0.15, 0.67)      | 52.78       |
| Khalifa 2021         | Japan               | 2/260      | 2/130       | 390           |                   | 0.50 (0.07, 3.54)      | 8.37        |
| Lannaccone 2016      | Italy               | 1/270      | 9/270       | 540           |                   | 0.11 (0.01, 0.90)      | 7.50        |
|                      | d = 1.6%, p = 0.384 |            | 51210       | 540           | $\diamond$        | 0.39 (0.22, 0.68)      | 100.00      |
| Target vessel revas  | cularization        |            |             |               |                   |                        |             |
| Lannaccone 2016      |                     | 1/270      | 10/270      | 540           |                   | 0.10 (0.01, 0.80)      | 40.64       |
| Sheth 2016           | Canada              | 11/214     |             | 642           |                   | 0.92 (0.46, 1.85)      | 59.36       |
|                      | d = 76.4%, p = 0.04 |            | 24/420      | 042           | $\langle \rangle$ | 0.38 (0.04, 3.37)      | 100.00      |
| Stent thrombosis     |                     |            |             |               |                   |                        |             |
| Cortese 2022         | Europe              | 1/100      | 1/100       | 200           |                   | 1.00 (0.06, 15.77)     | 27.21       |
| Lannaccone 2016      | Italy               | 0/270      | 7/270       | 540 <b>←</b>  |                   | 0.07 (0.00, 1.19)      | 26.18       |
| Sheth 2016           | Canada              | 4/214      | 5/428       | 642           |                   | 1.59 (0.43, 5.86)      | 46.60       |
|                      | d = 56.4%, p = 0.10 |            | 5/420       | 042           |                   | 0.61 (0.09, 4.39)      | 100.00      |
| NOTE: Weights are    | e from random effe  | cts analys | sis         |               |                   |                        |             |
|                      |                     |            |             |               |                   | 1                      |             |
|                      |                     |            |             | .0039         | 1                 | 255                    |             |

FIGURE 11

Forest plot comparing OCT guided with coronary angiography guided PCI for all-cause death. Data obtained from RCTs using fixed effect metaanalysis and expressed as OR. CI, confidence interval; OCT, optical coherence tomography; PCI, percutaneous coronary intervention.

### 3.2.4 Cardiac death

Five trials (n = 4,104) reported cardiac death (29, 41, 43–45). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in cardiac death (OR 0.61, 95% CI 0.36–1.02; p = 0.893,  $I^2 = 0\%$ , non-relevant heterogeneity, high certainty, see Figure 10B). Observational studies (51–53, 57), which included 4 studies with 1,626 patients, also demonstrated that OCT-guided PCI was not significantly associated with a reduction in the risk of cardiac death when compared to coronary angiography (OR 0.67, 95% CI 0.27–1.71; p = 0. 123,  $I^2 = 48.1\%$ , indicating moderate heterogeneity and moderate certainty, as shown in Figure 11B).

### 3.2.5 All-cause death

Four trials (n = 4,223) reported all-cause death (29, 42, 44, 47). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in all-cause death (OR 0.7, 95% CI 0.49–1.02; p = 0.550,  $I^2 = 0\%$ , non-relevant heterogeneity, high certainty, see Figure 10C). Observational studies (52, 54, 55, 57), which included 4 studies with 1,214 patients, also demonstrated that OCT-guided PCI was not significantly associated with a reduction in the risk of all-cause death when compared to coronary angiography (OR 0.87, 95% CI 0.35–2.18; p = 0. 211,  $I^2 = 33.5\%$ , indicating moderate heterogeneity and moderate certainty, as shown in Figure 11C).

### 3.2.6 MI

Six trials (n = 4,747) reported MI (29, 41, 42, 44, 47, 49). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in MI (OR 0.88, 95% CI 0.69 to 1.13; p = 0.823,  $I^2 = 0\%$ , non-relevant heterogeneity, high certainty, see Figure 10D). Observational studies (51, 53–57), which included 6 studies with 4,120 patients, also demonstrated that OCT-guided PCI was not significantly associated with a reduction in the risk of MI when compared to coronary angiography (OR 0.66, 95% CI 0.38–1.13; p = 0.319,  $I^2 = 14.9\%$ , indicating low heterogeneity and moderate certainty, as shown in Figure 11D).

### 3.2.7 TLR

Seven trials (n = 4,646) reported TLR (29, 41, 44, 47–50). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in TLR (OR 0.94, 95% CI 0.7–1.27; p = 0.856,  $I^2 = 0\%$ , non-relevant heterogeneity, high certainty, see Figure 10E). However, the results from the observational studies, which included 4 studies with 1,524 patients, showed differing outcomes (51, 52, 54, 57). In contrast to coronary angiography, OCT-guided PCI showed a reduction in the risk of TLR (OR 0.39, 95% CI 0.22–0.68; p = 0.384,  $I^2 = 1.6\%$ , non-relevant heterogeneity, high certainty, see Figure 11E).

### 3.2.8 TVR

Four trials (n = 3,060) reported TVR (29, 42, 47, 50). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in TVR (OR 1.04, 95% CI 0.76–1.43; p = 0.857,  $I^2 = 0\%$ , non-relevant heterogeneity, high certainty, see Figure 10F). Observational studies (53, 54), which included 2 studies with 1,182 patients, also demonstrated that OCT-guided PCI was not significantly associated with a reduction in the risk of TVR when compared to coronary angiography (OR 0.38, 95% CI 0.04–3.37; p = 0.04,  $I^2 = 76.4\%$ , indicating high heterogeneity and low certainty, as shown in Figure 11F).

### 3.2.9 Stent thrombosis

Five trials (n = 1,886) reported stent thrombosis (43, 44, 46, 48, 49). Compared with coronary angiography, OCT-guided PCI was not associated with a significant reduction in stent thrombosis (OR 0.72, 95% CI 0.38–1.38; p = 0.906,  $I^2 = 0\%$ , non-relevant heterogeneity, high certainty, see Figure 10G). Observational studies (53, 54, 57), which included 3 studies with 1,382 patients, also demonstrated that OCT-guided PCI was not significantly associated with a reduction in the risk of stent thrombosis when compared to coronary angiography (OR 0.61, 95% CI 0.09–4.39; p = 0.101,  $I^2 = 56.4\%$ , indicating moderate heterogeneity and moderate certainty, as shown in Figure 11G).

### 4 Discussion

OCT, with its high-resolution imaging (10-20 µm), accurately identifies vascular features like thrombi, lipids, and calcium deposits (59-63). In this study, we analyzed 2,758 articles related to OCT and cardiovascular diseases from the WoSCC. In-depth analyses were conducted on these articles by country, institution, journal, author, and keywords using Bibliometrix R software and CiteSpace. This comprehensive exploration revealed the knowledge structure, research hotspots, and emerging trends in the field, laying the groundwork for future strategies in disease prevention and treatment. Our study found that OCT, as a guiding tool for PCI, has become a focal point in recent cohorts and randomized trials, which was further confirmed in our subsequent meta-analysis. After including 11 RCTs and 7 observational studies, we concluded that OCT-guided PCI did not demonstrate significant association with better clinical outcomes. Although the point estimate and the upper bound of the confidence interval hinted at a possible reduction in MACE, cardiac death, all-cause death, MI, TLR, or stent thrombosis with OCT guided PCI, this did not reach statistical significance. However, the meta-analysis of observational studies showed a significant reduction in MACE and TLR.

## 4.1 Advantages and limitations of bibliometric analysis

The United States led in the publication output related to OCT and cardiovascular diseases, also exhibiting the highest proportion of international collaboration. Moreover, China's publication numbers are rapidly growing, likely influenced by recent expert consensus from Chinese cardiology societies emphasizing the importance of OCT in PCI (64). Among the top 10 institutions with the highest publication output, 7 were from the USA, while the remaining were from other countries (China, Singapore, and the UK). Professor Yu Bo from China was the most prolific among the top 10 corresponding authors, followed by authors from the USA. Professor Mehran Roxana held the highest m-INDEX, Professor Yu Bo the largest G-index, and Professor Virmani Renu the highest h-index and total citations. Additionally, among the top 10 most cited papers, one was published in "The Lancet" (37), and three in "Circulation" and other high-impact journals (31, 35, 36). Professor Ik-Kyung Jang's 2005 paper "in vivo Characterization of Coronary Atherosclerotic Plaque by Use of Optical Coherence Tomography" ranked highest in citations (31).

Thematic word trend analysis over the past 20 years in the cardiovascular field has centered on eight key terms: coronary artery disease, deep learning, coronary stenosis, heart transplantation, plaque rupture, OCT, congenital heart disease, and cardiovascular diseases. Burst analysis of keywords indicated that studies on OCT and angiography-guided PCI have become hot topics in recent cohorts and randomized trials. Welldeveloped themes focus on atherosclerotic diseases, blood pressure, stent implantation, and plaque characteristics. The field's attention to the treatment and prognosis of diseases such as "coronary stenosis, acute myocardial infarction, atherosclerosis" post-operation and for survival is also noteworthy.

However, this study has limitations. The primary data for the bibliometric analysis was sourced from the WoSCC. Although the WoSCC includes over 11,000 authoritative and high-impact international academic journals with extensive coverage and powerful analysis features, its singular source may lead to potential article omissions from other databases. Additionally, researchers manually removed papers deemed irrelevant to the study objectives, which might introduce selection bias. Despite these limitations, our study comprehensively analyzes the current state and progress of OCT in cardiovascular research, aiding in identifying future research directions.

## 4.2 Advantages and limitations of meta-analysis

OCT has shown significant technical advantages in the application of cardiovascular diseases (30, 65). Compared to traditional coronary angiography, OCT provides higherresolution spatial three-dimensional images, critical in accurately assessing plaque composition and morphology. Importantly, OCT optimizes angioplasty of bifurcation lesions, avoiding the common issues of perspective shortening and image overlap in traditional angiography (66). These technical strengths theoretically endow OCT with significant clinical application potential. However, in actual clinical practice, these theoretical advantages of OCT have not entirely translated into clinical benefits. Our meta-analysis of RCTs revealed that OCTguided PCI did not exhibit significant clinical benefits in MACE, Cardiac death, All-cause death, MI, TLR, TVR, and Stent thrombosis, compared to angiography-guided PCI. Although studies suggest that OCT-guided PCI can achieve a larger minimum lumen diameter (MLD) (53), its use also leads to longer procedural times and higher contrast agent dosages (67), increasing perioperative risks such as early mortality, emergency coronary artery bypass grafting, cancer, and contrast-induced nephropathy (68, 69). These risks might overshadow the clinical benefits of OCT. However, the metaanalysis of observational studies indicated a significant reduction in MACE and TLR with OCT-guided PCI, aligning with previous research (67, 70).

### 4.2.1 Limitations

When interpreting the results of our meta-analysis, its inherent limitations must be considered. Firstly, the included trials varied in participant populations, outcome definitions, and follow-up periods, potentially affecting comparability and generalizability. Secondly, pre-planned overall and subgroup analyses were conducted at the study level, not at the individual patient level, precluding precise assessment of the specific impact of stent size pre and post PCI guided by OCT on cardiovascular outcomes. Lastly, variations in intravascular imaging guidance standards among different trials could also influence the results.

### 4.3 Comparisons with other studies

Although many meta-analyses have studied intravascular imaging-guided PCI, a systematic review of 24 meta-analyses showed that only 9 focused specifically on RCTs (71). Given the potential introduction of confounding factors in observational studies (71), we conducted separate metaanalyses of evidence from RCTs and observational studies for OCT-guided PCI. This approach differs from previous metaanalyses, showing OCT's significant advantages are more pronounced in observational studies (67, 70), consistent with previous high-quality RCTs (29, 49, 53).

Our results, compared with the study led by Niels R. Holm, showed differences in MACE outcomes (44). The fundamental reason is that calculating OR values directly using incidence rates might differ from results reported in that study, as Cox regression analysis incorporates specific time points of events, often overlooked in simple calculations (44, 72). Additionally, the Cox model typically considers multiple covariates potentially influencing outcomes, such as patient age, gender, and medical history (73). This might be one reason our study did not show a significant clinical advantage of OCT. Furthermore, with a median follow-up time of only 1–2 years in the studies included, detecting statistically significant differences between the two interventions would require longer follow-up and higher event rates.

## 5 Conclusion

In summary, this study primarily employed bibliometric analysis to examine literature published over the past twenty years on OCT and cardiovascular diseases. It identified specific countries, institutions, authors, and journals that have made significant contributions to this field during this period. It was found that OCT as a guiding tool for PCI has become a hot topic in recent cohorts and randomized trials, prompting subsequent meta-analyses. However, OCT-guided PCI did not demonstrate significant clinical benefits, with only the metaanalysis of observational studies suggesting a reduction in MACE and TLR.

## Author contributions

WL: Conceptualization, Writing – original draft, Writing – review & editing. CC: Data curation, Formal Analysis, Writing – original draft. JW: Conceptualization, Funding acquisition, Methodology, Supervision, Writing – review & editing. JL: Formal Analysis, Methodology, Writing – review & editing. CL: Conceptualization, Methodology, Writing – review & editing. XZ: Conceptualization, Writing – review & editing.

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## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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## Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fcvm.2024. 1414205/full#supplementary-material

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