



Limus- Versus Paclitaxel-Coated Balloons for In-Stent Restenosis Treatment: A Systematic Review and Study-Level Meta-Analysis of Randomized Controlled Trials

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Drug-coated balloons are the preferred treatment for in-stent restenosis (ISR), avoiding the need for a second metallic layer. While both paclitaxel-coated balloons (PCB) and limus-coated balloons (LCB, typically sirolimus or biolimus) are used, direct comparative evidence is limited, particularly regarding their long-term angiographic efficacy and clinical safety. We conducted a systematic review and study-level meta-analysis of studies comparing LCB with PCB for coronary ISR. A comprehensive search was performed across PubMed, Embase, Cochrane, Scopus, Web of science for randomized controlled trials. Outcomes were compared using risk ratios (RR) for categorical data and mean differences for continuous data in a random-effects model. Heterogeneity was assessed using the I^2 statistic. Six randomized controlled trials involving 1,038 patients were included (552 in the LCB group and 481 in the PCB group). Compared with PCB, LCB were associated with a significantly higher risk of clinically driven target lesion revascularization (RR: 1.48; 95% CI: 1.02 to 2.14; $p = 0.04$; $I^2 = 0\%$) and target lesion failure (RR: 1.19; 95% CI: 0.87 to 1.62; $p = 0.27$; $I^2 = 0\%$). In contrast, both platforms demonstrated no differences in all-cause mortality (RR: 0.98; $p = 0.96$), myocardial infarction (RR: 0.73; $p = 0.46$), stent thrombosis (RR: 0.66; $p = 0.57$), or MACE (RR: 1.09; $p = 0.58$). Angiographic outcomes were comparable, including late lumen loss (mean differences: -0.00 mm; $p = 0.65$; $I^2 = 74.7\%$) and minimal lumen diameter (mean differences: -0.12 mm; $p = 0.07$). In patients with ISR, PCB reduced repeat revascularization compared with LCB. These data suggest a modest advantage for PCB in preventing restenosis following drug-coated balloon angioplasty for ISR.

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Abbreviations: ISR, In-Stent Restenosis; LCB, Limus-Coated Balloon; PCB, Paclitaxel-Coated Balloon; PRISMA, Systematic Review and Meta-analysis; PROSPERO, International Prospective Register of Systematic Reviews; ROBINS-I, Risk Of Bias In Non-randomised Studies

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Despite the advances achieved with second- and third-generation drug-eluting stents (DES), *in-stent restenosis* (ISR) remains a clinically relevant complication, with an estimated incidence of 5% to 10% of all percutaneous cardiovascular interventions procedures, depending on lesion complexity and patient profile.^{1,2} The management of ISR seeks to balance antiproliferative efficacy with the preservation of

vascular function. The conventional “stent-in-stent” approach restores luminal flow promptly but adds another metallic layer, increasing the risk of late thrombosis, impairing vasomotion, and complicating future reinterventions. In this context, “leave-nothing-behind” strategies have emerged as physiologically conservative alternatives, avoiding metal accumulation and promoting functional vessel restoration.³

Drug-coated balloons (DCBs) and coronary brachytherapy allow treatment of ISR without additional stent layers. Unlike DES, DCBs deliver antiproliferative agents locally without leaving a permanent implant, thereby reducing inflammation and improving endothelial healing.⁴ The European Society of Cardiology (2024) guidelines and the European Association of Percutaneous Cardiovascular Interventions (2023) consensus recommend DCBs as first-line therapy for ISR, with a *Class I recommendation* and *Level of Evidence A*, although DES are preferred over DCB for DES ISR.^{5,6}

There is controversy on the angiographic efficacy and clinical safety of limus- versus paclitaxel-coated DCBs in ISR. Published studies had methodological variability, differences in lesion preparation, coating technologies, and endpoint definitions, as well as small sample sizes and short follow-up durations (<12 months). Previous meta-analyses were limited by small sample sizes with limited power for clinical outcomes and focused primarily on angiographic outcomes like late lumen loss (LLL).

Methods

We performed a systematic review and study-level meta-analysis of randomized controlled trials (RCTs) comparing limus-coated-balloons (sirolimus or biolimus-coated) versus paclitaxel-coated balloons for the treatment of coronary in-stent restenosis. The study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines⁷ and registered in PROSPERO (CRD420261285762).

Search strategy and study selection

A comprehensive search was conducted across PubMed, Embase, Cochrane Central Register of Controlled Trials, Scopus, and Web of Science (WOS) databases from January 2000 to October 2025. The final search was performed on October 15, 2025. The following medical subject heading were used ([“Sirolimus” OR “Sirolimus-eluting”] AND [“Paclitaxel” OR “Paclitaxel-eluting”]) AND [“In-stent restenosis” OR ISR OR “coronary stenosis”] AND [“Percutaneous Coronary Intervention” OR PCI OR “Coronary Angioplasty”]. We identified a total of 948 records, of which 706 were removed as duplicates. Two reviewers independently conducted the search, screened titles and abstracts, and assessed full-text articles, resolving disagreements through consensus. References of all included studies were manually reviewed to identify additional eligible studies, though gray literature was not searched. Data extraction was performed independently by 3 reviewers using a standardized extraction form, and inconsistencies were resolved by discussion.

Eligibility criteria and endpoints

Studies were eligible for inclusion if they RCTs that compared limus-coated balloons with paclitaxel-coated balloons for the treatment of coronary in-stent restenosis in adult patients undergoing percutaneous coronary intervention. Only studies that reported at least one angiographic or clinical outcome of interest, such as late lumen loss, percentage diameter stenosis, minimal lumen diameter, target lesion revascularization (TLR) defined as Repeat percutaneous intervention or surgical bypass of the original target lesion, target lesion failure (TLF), myocardial infarction, cardiac death, or major

adverse cardiovascular events, were included. Studies with overlapping populations from the same recruitment centers, conference abstracts, case reports, editorials, reviews, animal or laboratory investigations, or those without extractable quantitative outcomes were excluded. When essential information was missing or unclear, attempts were made to contact study authors for clarification.

Regarding the definition of clinical endpoints, revascularization was defined as clinically driven in the majority of contemporary trials, such as REFORM, BIO ASCEND ISR, and SIBLINT-ISR.^{8–10} In contrast, the Mohd Ali (2019) and Scheller (2022) trials utilized mandatory 6-month angiographic follow-up to assess their primary endpoint of late lumen loss. In these studies, any reintervention performed at the time of the scheduled angiogram, even in the absence of worsening symptoms, was recorded as a TLR. This ‘angiographic trigger’ likely contributed to higher overall revascularization rates in these specific cohorts compared to trials using purely symptom-driven criteria.

Bias assessment

To ensure the internal validity of the included studies, we performed a rigorous assessment of the risk of bias using the Cochrane Risk of Bias 2 (RoB 2) tool for randomized controlled trials. This assessment was conducted independently by 2 reviewers, with any discrepancies resolved through consensus or by consultation with a third senior investigator. The RoB 2 tool was applied across 5 essential domains to evaluate the integrity of the trial results. Each domain was classified as having a “low risk of bias,” “some concerns,” or a “high risk of bias.” Finally, an overall risk of bias was assigned to each trial based on these criteria to determine the strength of the evidence generated by our meta-analysis.¹¹

Statistical analysis

Continuous outcomes were compared using mean differences (MD) with 95% confidence intervals, while categorical outcomes were compared using risk ratios (RR) with 95% confidence intervals. A random-effects model was chosen a priori due to anticipated heterogeneity in study populations, devices, and angiographic methodologies. Heterogeneity was assessed using the Cochran Q test and the I^2 statistic. To evaluate the robustness of the primary findings and ensure that the results were not driven by a single outlier, sensitivity analyses were performed using the leave-one-out method. This involved iteratively recalculating the pooled effect size by omitting one study at a time to assess the stability of the RRs and MDs. Finally, potential publication bias and small-study effects were visually inspected using funnel plots. The symmetry of these plots was evaluated to determine the likelihood of missing or unpublished data affecting the validity of the meta-analytical results. All statistical analyses were performed using R version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria) and the meta package.¹²

Results

Study selection and characteristics

The study selection process is shown in Figure 1. A total of 948 records were identified through the systematic database search. After removal of duplicate records (242 studies) and ineligible studies by title and abstract, 60 remained and were fully reviewed. Ultimately, 6 studies (6 RCTs) met the inclusion criteria and were incorporated into the final analysis.^{8–10,13–15} Tables 1 and 2 summarize 6 studies (2017 to 2022) comparing Limus versus PCB, with 50 to 280 patients

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

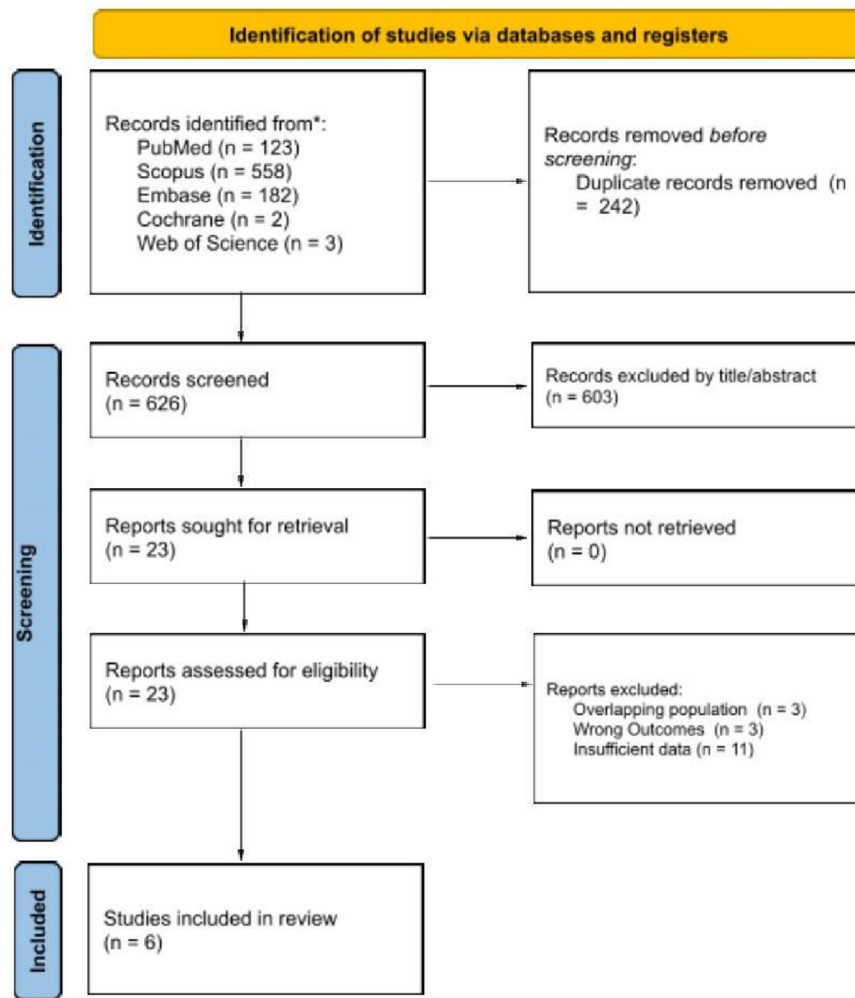


Figure 1. PRISMA flow diagram.

per study (about 1,038 total, 552 in the LCB group and 481 in the PCB group); populations were predominantly male (about 73% to 97%) and mean age was similar between groups (about 59 to 70 years). Previous MI (A clinical condition defined by the presence of acute myocardial injury detected by abnormal cardiac biomarkers) prevalence varied widely (about 16% to 100%). Most studies assessed angiographic primary endpoints, mainly late lumen loss at 6 to 12 months or percent diameter stenosis at 6 months, while one study reported cardiac death. Overall, follow-up percent diameter stenosis and late lumen loss were broadly comparable between LCB and PCB,

but in-stent restenosis was heterogeneous, notably higher with LCB in Byrne (2025) (33.9% vs 9.3%), whereas other studies showed more similar rates when reported (about 11% to 32% vs 13% to 30%).

Clinical outcomes

Clinical outcomes were comparable between the 2 technologies across most safety and efficacy parameters. As compared with PCB, LCB demonstrated similar rates of all-cause mortality (RR 0.98; 95% CI: 0.35 to 2.70; $p = 0.96$; $I^2 = 0\%$, Figure 3), TLF (RR 1.19; 95% CI: 0.87

Table 1
Characteristics of the included studies

Authors (year)	Country	Study design (year range)	N total (LCB/PCB)	Age, mean (LCB/PCB)	Male, n (%) LCB/PCB	Limus coated balloon type
REFORM STUDY (2025) ⁸	6 countries	RCTs (2020–2022)	202 (135/67)	68.9/68.3	110 (81.5)/52 (77.6)	Biolimus
BIO ASCEND ISR (2024) ⁹	China	RCTs (2020–2022)	280 (138/137)	63.64/64.24	103 (74.6)/101 (73.7)	Biolimus
SIBLINT-ISR (2025) ¹⁰	-	RCTs (2020–2021)	260 (132/128)	63.8/63.7	95 (73.1)/97 (75.8)	Sirolimus
Mohd (2019) ¹³	-	RCTs (2020–2021)	50 (25/25)	58.6/61.6	19 (79)/22 (88)	Sirolimus
TIS 2 STUDY (2025) ¹⁴	Czech Republic	RCTs (2019–2022)	145 (72/73)	69.7/68.0	56 (77.8)/59 (80.8)	Sirolimus
Scheller (2022) ¹⁵	Malaysia and German-Swiss	RCTs (2017–2020)	101 (50/51)	67/63	43 (86)/39 (76)	Sirolimus

Table 2
Baseline characteristics of the patients in each study

Authors (year)	Previous MI, n (%) LCB/PCB	Primary end point	Follow-up, %DS in segment (LCB/PCB)	Follow-up, %DS in stent (LCB/PCB)	Follow-up, LLL in segment (LCB/PCB)	Follow-up, %DS in stent (LCB/PCB)	Binary restenosis in stent (LCB/PCB)
REFORM STUDY (2025) ⁸	69 (51.1)/37 (55.2)	% diameter stenosis at 6 months	43.25 ± 22.87/31.4 ± 17.7	42.76 ± 22.90/27.9 ± 19.49	0.54 ± 0.62/0.20 ± 0.54	0.69 ± 0.62/0.31 ± 0.54	41 (33.9%)/5 (9.3%)
BIO ASCEND ISR (2024) ⁹	22 (15.9)/33 (24.1)	Late lumen loss at 9 months	32.59 ± 18.78/31.61 ± 16.9	31.25 ± 19.31/29.54 ± 17.3	0.25 ± 0.40/0.27 ± 0.39	0.26 ± 0.42/0.29 ± 0.40	17 (11.3%)/20 (13.1%)
SIBLINT-ISR (2025) ¹⁰	132 (100)/128 (100)	Late lumen loss at 9 months	31.81 ± 20.92/31.46 ± 8.44	27.99 ± 21.62/28.77 ± 18.72	0.37 ± 0.48/0.30 ± 0.38	0.35 ± 0.47/0.31 ± 0.36	20 (17.9%)/18 (15%)
Mohd (2019) ¹³	9 (36)/8 (32)	Late lumen loss at 6 months	-	16.1 ± 15.5/17.8 ± 20.9	0.21 ± 0.54/0.17 ± 0.55	0.28 ± 0.51/0.25 ± 0.58	-
TIS 2 STUDY (2025) ¹⁴	48 (66.7)/50 (68.5)	Late lumen loss at 12 months	-	32 (3%)/38 (15%)	-	0.45 ± 0.77/0.50 ± 0.56	25 (31.6%)/24 (30.4%)
Scheller (2022) ¹⁵	50 (100)/51 (100)	Late lumen loss at 6 months	-	20.8 ± 22.9/18.3 ± 18.0	0.26 ± 0.43/0.25 ± 0.42	0.30 ± 0.47/0.30 ± 0.47	7 (13.5%)/4 (7.7%)

LCB = limus-coated balloon; PCB = paclitaxel coated balloon.

to 1.62; $p = 0.27$; $I^2 = 0\%$, Figure 4) and MACE (A standard composite clinical endpoint used to evaluate the cumulative safety and efficacy of cardiovascular interventions. It is defined as cardiovascular death, non-fatal myocardial infarction, and stroke, though some protocols may include target lesion revascularization [TLR]) (RR 1.09; 95% CI: 0.81 to 1.47; $p = 0.58$; $I^2 = 0\%$, Figure 5). Regarding secondary safety endpoints, no significant differences were observed in the incidence of myocardial infarction (RR 0.73; 95% CI: 0.31 to 1.70; $p = 0.46$, Figure 6) or stent thrombosis (RR 0.66; 95% CI: 0.15 to 2.81; $p = 0.57$, Figure 7), with 0 heterogeneity ($I^2 = 0\%$) across all safety analyzes.

In contrast, treatment with LCB was associated with significantly higher TLR compared with PCB (RR 1.48; 95% CI: 1.02 to 2.14; $p = 0.04$; $I^2 = 0\%$, Figure 2).

Angiographic outcomes

From an angiographic perspective, both platforms performed similarly. There were no significant differences in acute luminal gain (MD -0.03 mm; 95% CI: -0.12 to 0.05 ; $p = 0.46$, Figure 8) or late lumen loss (MD -0.00 mm; 95% CI: -0.07 to 0.06 ; $p = 0.65$, Figure 9). Although minimal lumen diameter was numerically higher in the PCB group, this did not reach statistical significance (MD -0.12 mm; 95% CI: -0.24 to 0.01 ; $p = 0.07$, Figure 10).

Sensitivity analysis

Sensitivity analysis using the leave-one-out method confirmed the robustness of the primary findings. Notably, the exclusion of the REFORM study from the Minimal Lumen Diameter analysis eliminated the observed moderate heterogeneity (reducing I^2 from 33% to 0%) and resulted in a revised mean difference of -0.06 mm (95% CI: -0.16 to 0.04). Although the effect size was slightly attenuated, the lack of statistical significance for MLD (Minimal Luminal Diameter A quantitative coronary angiography (QCA) parameter representing the smallest diameter of the vessel lumen within a stenotic lesion) remained consistent with the primary analysis, confirming that the angiographic equivalence between LCB and PCB is a stable finding across the remaining randomized evidence. The authors conducted comprehensive subgroup analyzes comparing specific drug-eluting stents (Sirolimus vs Paclitaxel and Biolimus vs Paclitaxel), as shown in Supplementary Figures S1 to S17. The results of these subgroup analyzes remained consistent with the findings of the primary general analysis. This consistency reinforces the robustness of the study's conclusions across different stent platforms, suggesting that the observed clinical outcomes are not significantly altered by the specific type of limus-analog utilized.

Quality assessment

For the 6 randomized controlled trials, we applied the RoB 2 tool across 5 domains, with results summarized in a table and visualized in Supplementary Figure S18 (traffic-light plot). For bias arising from the randomization process (Domain 1), 3 studies—Ali (2019), Scheller (2022), and Pleva (2025)—were judged high risk, whereas t3—Chen (2024), Liv (2025), and Byrne (2025)—were low risk. Bias due to deviations from intended interventions (Domain 2) was predominantly low risk (5 studies), with 1 high-risk study (Byrne, 2025). For missing outcome data (Domain 3), 5 studies had some concerns and 1 (Liv, 2025) was low risk. Measurement of outcomes (Domain 4) was low risk in all 6 trials. Selection of the reported result (Domain 5) showed some concerns in 5 trials, with 1 low-risk study (Ali, 2019). Overall, 3 trials—Scheller (2022), Pleva (2025), and Byrne (2025)—were judged high risk of bias, and 3—Ali (2019), Chen (2024), and Liv (2025)—had some concerns; none were at low overall risk.

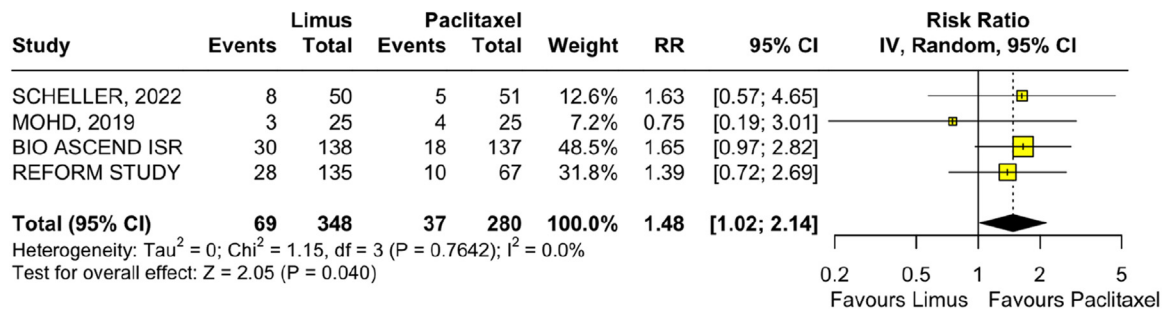


Figure 2. Forest plot of target lesion revascularization comparing limus and PCB in ISR.

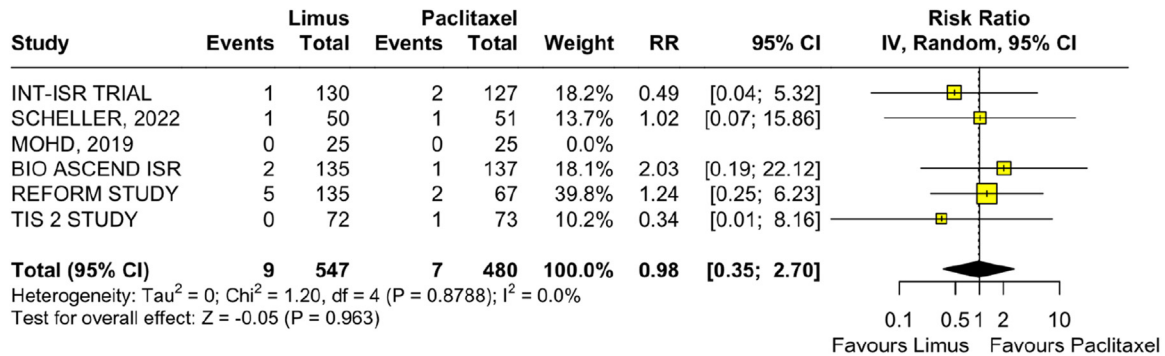


Figure 3. Forest plot of all-cause death comparing limus and PCB in ISR.

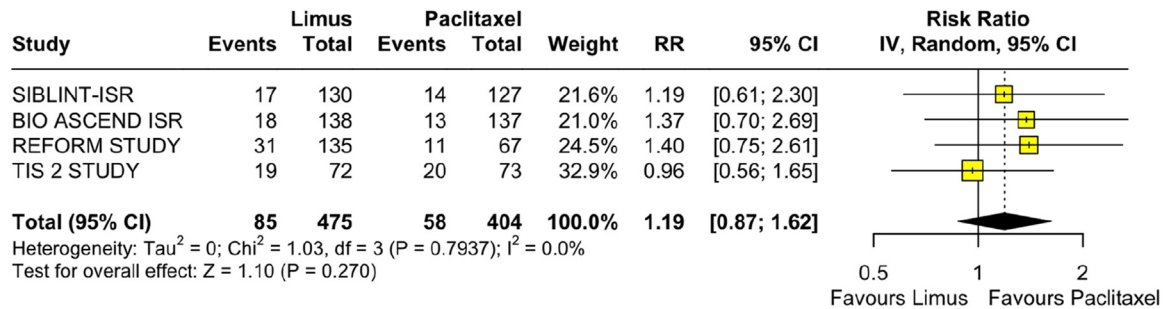


Figure 4. Forest plot of target lesion failure comparing limus and PCB in ISR.

Discussion

In this systematic review and meta-analysis of 6 RCTs, we found that treatment of coronary ISR with PCB decreased the risk of TLR compared with LCB. Distinct from prior meta-analyses that often pooled heterogeneous data, our study is characterized by its focus on the ISR population and the strict inclusion of only RCTs. In contrast, no significant differences were observed between LCB and PCB in

hard endpoints including all-cause mortality, myocardial infarction, TLF, stent thrombosis, or MACE, as well as angiographic measures (late lumen loss, minimal lumen diameter).

ISR results from aggressive neointimal proliferation.¹⁶ Our findings suggest that the antiproliferative effect of paclitaxel may be more effective at suppressing neointima than that of sirolimus or biolimus in this setting.¹⁷ This contrasts with prior data in ISR: for example, a recent head-to-head RCT of a new biolimus DCB

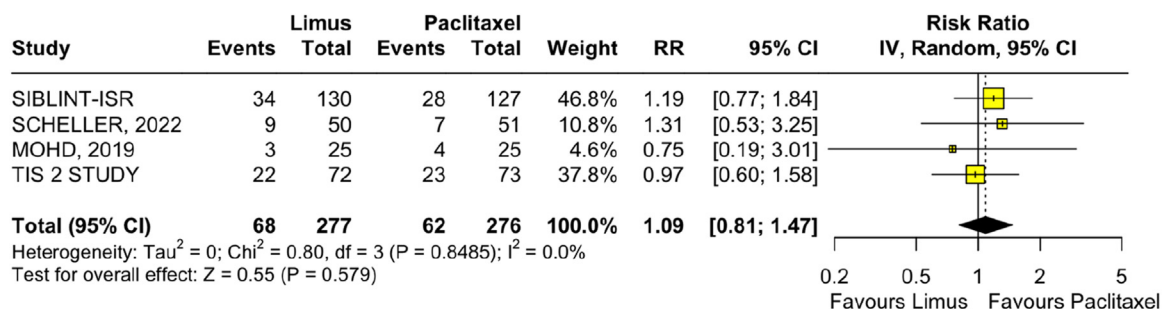


Figure 5. Forest plot of MACE events comparing limus and PCB in ISR.

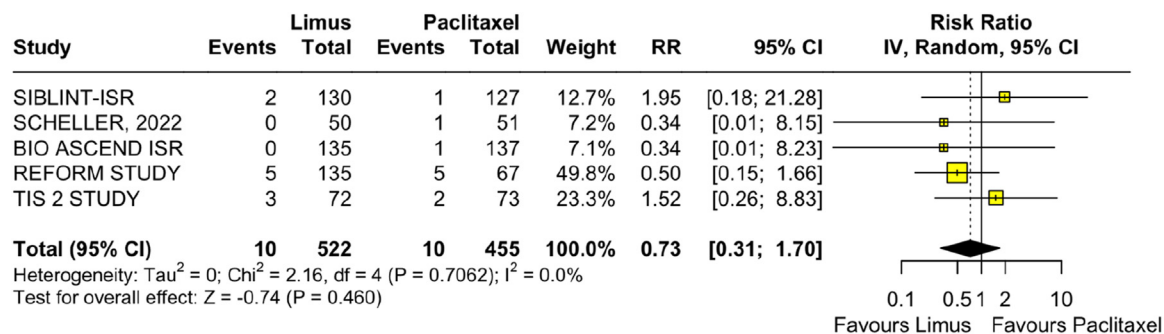


Figure 6. Forest plot of myocardial infarction comparing limus and PCB in ISR.

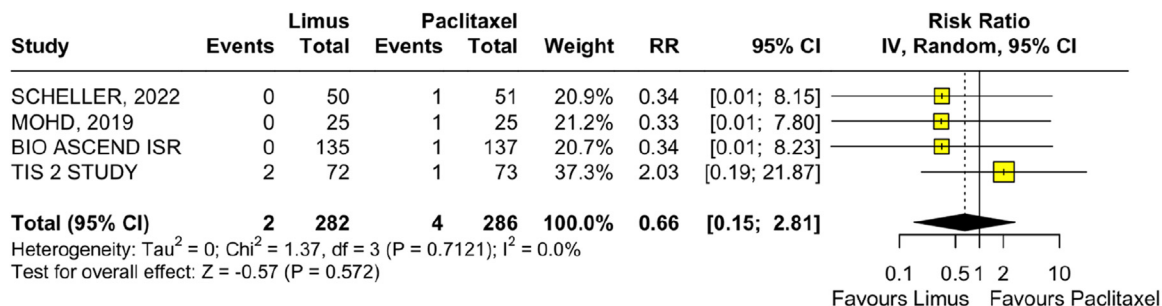


Figure 7. Forest plot of stent thrombosis comparing limus and PCB in ISR.

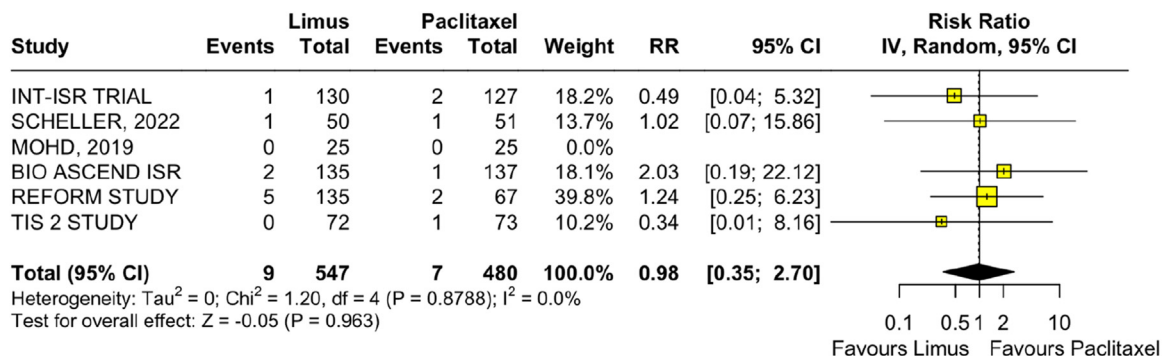


Figure 8. Forest plot of acute luminal gain comparing limus and PCB in ISR.

versus a well-established paclitaxel DCB in DES-ISR found essentially equivalent angiographic outcomes at 9 months.⁹ Our meta-analytic results of higher repeat revascularization after LCB contrasts with these reports, suggesting that even subtle differences in lesion biology or device performance may tip the balance in favor of paclitaxel in preventing restenosis. In any case, both LCB and PCB produced high overall success, and our observed TLR

benefit with PCB needs to be weighed against the similar hard-event rates.

By contrast, we found no signal that LCBs and PCBs differ in death, MI, MACE or stent thrombosis. This concurs with prior analyses. A recent network meta-analysis of DCB angioplasty (over 10,000 patients) found no significant difference in MACE (or its components) between limus- and paclitaxel-coated balloons. Our findings

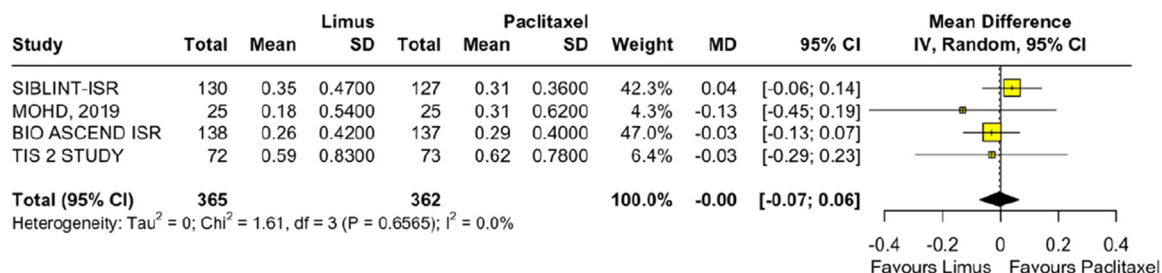


Figure 9. Forest plot of late lumen loss comparing limus and PCB in ISR.

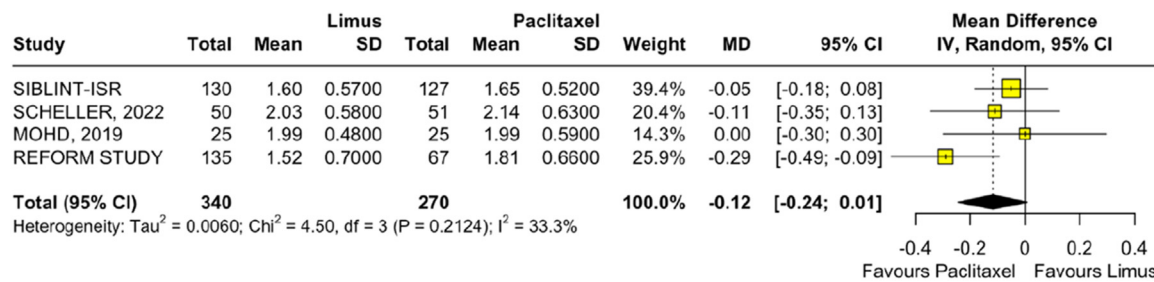


Figure 10. Forest plot of minimal lumen diameter comparing limus and PCB in ISR.

differentiate themselves from previous meta-analyses in several ways. First, by excluding de novo lesions and focusing exclusively on ISR, we isolated the performance of these devices in the most challenging coronary environment. Second, unlike prior reviews that included observational data, our strict inclusion of only RCTs.¹⁸ Likewise, the real-world REFORM trial cited above showed statistically indistinguishable 12-month mortality, MI and TLR between the new limus- and paclitaxel-coated device. Our results reinforce that the choice of coating did not impact these clinical endpoints. Angiographically, acute gain, late lumen loss and final lumen diameter were also comparable between groups, apart from substantial heterogeneity in late loss; this variability may reflect differences in procedural technique and follow-up timing among trials. In short, apart from the higher TLR with LCB, all other efficacy and safety metrics were essentially equivalent, and this parallels the literature showing generally similar outcomes for limus- versus paclitaxel-based DCB in CAD.^{8,19}

The discordance between comparable angiographic parameters (LLL and MLD) and the clinical superiority of PCB in reducing TLR suggests a multifactorial dynamic. Although the absolute difference in MLD was marginal (-0.12 mm; $p = 0.07$), such variations can disproportionately impact outcomes in small-caliber vessels, where minor luminal loss more readily crosses the threshold for functional ischemia.

Furthermore, the potential for surveillance bias inherent in trials with mandatory late imaging (e.g., Mohd Ali, Scheller, and TIS 2)^{13–15} must be considered. In these settings, angiographically-driven interventions may inflate TLR rates by identifying lesions that might otherwise remain asymptomatic. However, as the included trials predominantly utilized clinically-driven TLR, requiring objective evidence of ischemia, the observed benefit of PCB likely reflects a genuine efficacy advantage in maintaining vessel patency rather than a discrepancy in clinical decision-making. This interpretation is supported by the comparable incidence of hard safety endpoints, such as myocardial infarction and cardiac death, which accounts for the lack of statistical significance in TLF while confirming a robust safety profile for both technologies.

Preclinical and molecular studies suggest intrinsic differences between drugs used in DCBs. Paclitaxel is highly lipophilic and achieves rapid vessel-wall uptake and sustained retention, whereas sirolimus delivery tends to be slower and more washout-prone.²⁰ Paclitaxel induces apoptotic death of smooth muscle cells, whereas sirolimus causes cell-cycle arrest without apoptosis.²¹ In 1 comparative study, only paclitaxel blocked smooth muscle migration at nanomolar levels and drove vascular cells into apoptosis.²² In animal histology paclitaxel DCBs produced greater smooth-muscle cell loss than a sirolimus balloon (reflecting higher local drug effect).²³ Thus, the more pronounced antiproliferative potency of paclitaxel might underlie the lower TLR seen in our analysis, whereas the broader safety profile and prohealing effects of sirolimus manifest in similar MACE and lumen outcomes.

Clinically, these findings suggest that PCB angioplasty may offer an advantage in reducing the risk of repeat revascularization for ISR, although both devices provide favorable results overall. Current

guidelines already endorse DCB as a first-line therapy for ISR based on Class I evidence of efficacy.¹ Our data indicate that while both platforms maintain a comparable safety profile—with low and statistically indistinguishable rates of death, MI, and stent thrombosis—device selection may be influenced by the specific goal of maximizing efficacy against restenosis. Given the observed reduction in TLR with paclitaxel-based platforms in this analysis, PCB remains a highly effective standard for ISR treatment. However, further research is required to determine if specific lesion characteristics or patient subsets might derive differential benefits from one coating over the other

Limitations

Our study has limitations. First, the ‘limus’ category was not uniform across the included trials, as it aggregated diverse pharmacological agents (such as sirolimus, biolimus, or pimecrolimus) utilizing distinct coating technologies and drug-delivery platforms. Notably, none of the included trials utilized the Selution SLR DCB, which currently possesses the most extensive published clinical data among limus-based balloons. This lack of data on high-performance platforms may further explain the observed differences compared to established paclitaxel coatings. Second, the complexity of the treated lesions and the timing of clinical and angiographic follow-up varied significantly among studies. Differences in lesion preparation protocols, the prevalence of multivessel disease, and follow-up intervals (ranging from 6 to 12 months) may have influenced the observed rates of TLR and vessel healing. Third, intravascular imaging (IVI) was not mandatory across the included trials. Evidence from trials like the Intravascular Ultrasound Guided Drug Eluting Stents Implantation in “All-Comers” Coronary Lesions (ULTIMATE) and RENASCENT III has shown that IVUS and OCT are essential for identifying mechanical causes of ISR, such as stent underexpansion, and for optimizing lesion preparation. In the analyzed RCTs, IVI was largely left to operator discretion. Furthermore, we acknowledge that Target Lesion Revascularization (TLR) as a clinical endpoint may be influenced by operator judgment, potentially contributing to the divergence observed between revascularization rates and composite safety outcomes. Finally, there were few events for some of the clinical safety endpoints, which limits the statistical power to detect differences between the study groups.

Conclusion

This systematic review demonstrates that PCB may offer a modest clinical advantage, primarily driven by a significant reduction in the rate of repeat revascularizations compared to LCB. However, both technologies showed comparable performance regarding procedural success and hard clinical safety endpoints, including mortality, myocardial infarction, and stent thrombosis. These findings suggest that while PCB remains a highly effective standard for reducing recurrence, the choice between drug-coating platforms does not appear to impact overall safety. This nuanced distinction highlights the need

for larger, adequately powered head-to-head trials in ISR. Regardless, the evidence continues to support the use of DCB as a first-line therapy for ISR, with device selection increasingly informed by these emerging efficacy data.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

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Supplementary materials

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