Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Supplementary material

Incidence and Predictors of reCurrent Restenosis After Drug-coated Balloon Angioplasty for Restenosis of a drUg-eluting Stent: the ICARUS Cooperation

Table 1 of the supplementary material

PRISMA-IPD Checklist of Items to Include When Reporting a Systematic Review and Meta-analysis of Individual Participant Data

PRISMA-IPD Section/topic	Item No.	Checklist item	Reported on page
Title			
Title	1	Identify the report as a systematic review and meta-analysis of individual participant data.	1
Abstract			
Structured summary	2	Provide a structured summary including as applicable:	2
		Background: state research question and main objectives, with information on participants, interventions, comparators, and outcomes.	

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

		Methods: report eligibility criteria; data sources including dates of last bibliographic search or elicitation, noting that IPD were sought; methods of assessing risk of bias.	
		Results: provide number and type of studies and participants identified and number (%) obtained; summary effect estimates for main outcomes (benefits and harms) with confidence intervals and measures of statistical heterogeneity. Describe the direction and size of summary effects in terms meaningful to those who would put findings into practice.	
		Discussion**:** state main strengths and limitations of the evidence, general interpretation of the results and any important implications.	
		Other**:** report primary funding source, registration number and registry name for the systematic review and IPD meta-analysis.	
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of the questions being addressed with reference, as applicable, to participants, interventions, comparisons, outcomes and study design (PICOS). Include any hypotheses that relate to particular types of participant-level subgroups.	5

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Methods			
Protocol and registration	5	Indicate if a protocol exists and where it can be accessed. If available, provide registration information including registration number and registry name. Provide publication details, if applicable.	Not applicable
Eligibility criteria	6	Specify inclusion and exclusion criteria including those relating to participants, interventions, comparisons, outcomes, study design and characteristics (eg, years when conducted, required minimum follow-up). Note whether these were applied at the study or individual level ie, whether eligible participants were included (and ineligible participants excluded) from a study that included a wider population than specified by the review inclusion criteria. The rationale for criteria should be stated.	6
Identifying studies - information sources	7	Describe all methods of identifying published and unpublished studies including, as applicable: which bibliographic databases were searched with dates of coverage; details of any hand searching including of conference proceedings; use of study registers and agency or company databases; contact with the original research team and experts in the field; open adverts and surveys. Give the date of last search or elicitation.	7
Identifying studies - search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	S-5

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Study selection processes	9	State the process for determining which studies were eligible for inclusion.	6
Data collection processes	10	Describe how IPD were requested, collected and managed, including any processes for querying and confirming data with investigators. If IPD were not sought from any eligible study, the reason for this should be stated (for each such study).	6
		If applicable, describe how any studies for which IPD were not available were dealt with. This should include whether, how and what aggregate data were sought or extracted from study reports and publications (such as extracting data independently in duplicate) and any processes for obtaining and confirming these data with investigators.	
Data items	11	Describe how the information and variables to be collected were chosen. List and define all study level and participant level data that were sought, including baseline and follow-up information. If applicable, describe methods of standardizing or translating variables within the IPD datasets to ensure common scales or measurements across studies.	6-7
IPD integrity	A1	Describe what aspects of IPD were subject to data checking (such as sequence generation, data consistency and completeness, baseline imbalance) and how this was done.	Not applicable

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Risk of bias assessment in individual studies	12	Describe methods used to assess risk of bias in the individual studies and whether this was applied separately for each outcome. If applicable, describe how findings of IPD checking were used to inform the assessment. Report if and how risk of bias assessment was used in any data synthesis.	6-7
Specification of outcomes and effect measures	13	State all treatment comparisons of interests. State all outcomes addressed and define them in detail. State whether they were prespecified for the review and, if applicable, whether they were primary/main or secondary/additional outcomes. Give the principal measures of effect (such as risk ratio, hazard ratio, difference in means) used for each outcome.	6-7
Synthesis methods	14	Describe the meta-analysis methods used to synthesize IPD. Specify any statistical methods and models used. Issues should include (but are not restricted to): • Use of a 1-stage or 2-stage approach. • How effect estimates were generated separately within each study and combined across studies (where applicable). • Specification of 1-stage models (where applicable) including how clustering of patients within studies was accounted for. • Use of fixed or random effects models and any other model assumptions, such as proportional hazards. • How (summary) survival curves were generated (where applicable). • Methods for quantifying statistical heterogeneity (such as I^2 and τ^2). • How studies providing IPD and not providing IPD were analyzed together (where applicable). • How missing data within the IPD were dealt with (where applicable).	7-8

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Exploration of variation in effects	A2	If applicable, describe any methods used to explore variation in effects by study or participant level characteristics (such as estimation of interactions between effect and covariates). State all participant-level characteristics that were analyzed as potential effect modifiers, and whether these were prespecified.	8
Risk of bias across studies	15	Specify any assessment of risk of bias relating to the accumulated body of evidence, including any pertaining to not obtaining IPD for particular studies, outcomes or other variables.	6
Additional analyses	16	Describe methods of any additional analyses, including sensitivity analyses. State which of these were prespecified.	Not applicable
Results			
Study selection and IPD obtained	17	Give numbers of studies screened, assessed for eligibility, and included in the systematic review with reasons for exclusions at each stage. Indicate the number of studies and participants for which IPD were sought and for which IPD were obtained. For those studies where IPD were not available, give the numbers of studies and participants for which aggregate data were available. Report reasons for nonavailability of IPD. Include a flow diagram.	23

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Study characteristics	18	For each study, present information on key study and participant characteristics (such as description of interventions, numbers of participants, demographic data, unavailability of outcomes, funding source, and if applicable duration of follow-up). Provide (main) citations for each study. Where applicable, also report similar study characteristics for any studies not providing IPD.	S-10
IPD integrity	A3	Report any important issues identified in checking IPD or state that there were none.	Not applicable
Risk of bias within studies	19	Present data on risk of bias assessments. If applicable, describe whether data checking led to the up-weighting or down-weighting of these assessments. Consider how any potential bias impacts on the robustness of meta-analysis conclusions.	9
Results of individual studies	20	For each comparison and for each main outcome (benefit or harm), for each individual study report the number of eligible participants for which data were obtained and show simple summary data for each intervention group (including, where applicable, the number of events), effect estimates and confidence intervals. These may be tabulated or included on a forest plot.	9

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Results of syntheses	21	Present summary effects for each meta-analysis undertaken, including confidence intervals and measures of statistical heterogeneity. State whether the analysis was prespecified, and report the numbers of studies and participants and, where applicable, the number of events on which it is based.	9
		When exploring variation in effects due to patient or study characteristics, present summary interaction estimates for each characteristic examined, including confidence intervals and measures of statistical heterogeneity. State whether the analysis was prespecified. State whether any interaction is consistent across trials.	
		Provide a description of the direction and size of effect in terms meaningful to those who would put findings into practice.	
Risk of bias across studies	22	Present results of any assessment of risk of bias relating to the accumulated body of evidence, including any pertaining to the availability and representativeness of available studies, outcomes or other variables.	S-8
Additional analyses	23	Give results of any additional analyses (eg, sensitivity analyses). If applicable, this should also include any analyses that incorporate aggregate data for studies that do not have IPD. If applicable, summarize the	9-10

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

		main meta-analysis results following the inclusion or exclusion of studies for which IPD were not available.	
Discussion			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome.	10
Strengths and limitations	25	Discuss any important strengths and limitations of the evidence including the benefits of access to IPD and any limitations arising from IPD that were not available.	12-13
Conclusions	26	Provide a general interpretation of the findings in the context of other evidence.	13
Implications	A4	Consider relevance to key groups (such as policy makers, service providers and service users). Consider implications for future research.	12-13
Funding			
Funding	27	Describe sources of funding and other support (such as supply of IPD), and the role in the systematic review of those providing such support.	

IPD, individual participant data.

A1–A3 denote new items that are additional to standard PRISMA items. A4 was created as a result of rearranging content of the standard PRISMA statement to suit the way that systematic review IPD meta-analyses are reported. ©Reproduced with permission of the PRISMA-IPD Group, which encourages sharing and reuse for noncommercial purposes.[1]

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Search strategy: MEDLINE (PubMed)

(drug-coated[All Fields] AND balloon[All Fields] OR drug-eluting[All Fields] AND balloon[All Fields])) AND (paclitaxel-eluting[All Fields] AND balloon[All Fields] OR paclitaxel-coated[All Fields] AND balloon[All Fields])) AND ("drug-eluting stents"[MeSH Terms] OR ("drug-eluting"[All Fields] AND "stents"[All Fields]) OR "drug-eluting stents"[All Fields] OR ("drug"[All Fields] AND "eluting"[All Fields] AND "stent"[All Fields]) OR "drug eluting stent"[All Fields]) AND restenosis[All Fields])) AND ("clinical trials as topic"[MeSH Terms] OR ("clinical"[All Fields] AND "trials"[All Fields] AND "topic"[All Fields]) OR "clinical trials as topic"[All Fields] OR "trial"[All Fields]) AND ("random allocation"[MeSH Terms] OR ("random"[All Fields] AND "allocation"[All Fields]) OR "random allocation"[All Fields] OR "randomized"[All Fields])

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Table 2 of the supplementary material

Assessment of Risk of Bias

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Trial	Random sequence generation	Allocation concealment	Blinding of participants	Blinding of outcome assessment	Description of incomplete outcome data	Selective outcome reporting	Sample size calculation	Sponsor
Habara et al.[2]	Yes (computer-generated)	Yes (sealed envelopes)	No	Yes	Yes (flow diagram)	No	No	Investigator-initiated
Habara et al.[3]	Yes (computer-generated, block)	N/R	No	Yes	Yes (flow diagram)	No	Yes (superiority design)	Investigator-initiated
ISAR DESIRE 3[4]	Yes (computer-generated)	Yes (sealed envelopes)	No	Yes	Yes (flow diagram)	No	Yes (noninferiority and superiority design)[a]	Investigator-initiated
PEPCAD China ISR[5]	Yes	N/R	No	Yes	Yes (flow diagram)	No	Yes (noninferiority design)	Industry-initiated

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

PEPCAD DES[6]	Yes	N/R	No	Yes	No	No	Yes (superiority design)	Investigator-initiated
RIBS IV[7]	Yes (computer-generated)	No	No	Yes	Yes (flow diagram)	No	Yes (superiority design)[b]	Investigator-initiated

[a]For the angiographic comparison of drug-coated balloon vs paclitaxel-eluting stent and of drug-coated-balloon and paclitaxel-eluting stent vs plain old balloon angioplasty, respectively

[b]For the angiographic comparison of everolimus-eluting stent vs drug-coated balloon.

ISAR-DESIRE 3, Randomized Trial of Paclitaxel-Eluting Balloon, Paclitaxel-Eluting Stent and Plain Balloon Angioplasty for Restenosis in "-Limus"-Eluting Coronary Stents; PEPCAD China ISR, A Multicenter, Randomized, Active Controlled Clinical Study to Evaluate the Safety and Efficacy of the Treatment of In-stent Restenosis Lesion by Paclitaxel-eluting PTCA-Balloon Catheter Vs Paclitaxel-eluting Stent; PEPCAD DES, Treatment of DES-In-Stent Restenosis With SeQuent Please Paclitaxel Eluting PTCA Catheter; RIBS IV, Restenosis Intrastent of Drug-eluting Stents: Paclitaxel-eluting Balloon vs Everolimus-eluting Stent). A Prospective, Multicenter and Randomized Clinical Trial.

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Table 3 of the supplementary material

Main Features of Patients With DES restenosis Assigned to DCB Angioplasty in Each Included Trial

Trial	Patients, n	Age, y	Male sex, %	Diabetes mellitus, %	Stable angina, %	Lesions, n
Habara et al.[2]	25	69.9	76	56	100	25
Habara et al.[3]	53	69.4	83	58	94	56
ISAR DESIRE 3[4]	137	67.7	77	41	81	172
PEPCAD China ISR[5]	110	61.8	88	44	37	114
PEPCAD DES[6]	72	69.8	72.2	36.1	95.8	72
RIBS IV[7]	149	66.0	82	49	48	149

Data are presented as counts, proportions or means.

DCB, drug-coated balloon;DES, drug-eluting stent; ISAR-DESIRE 3, Randomized Trial of Paclitaxel-Eluting Balloon, Paclitaxel-Eluting Stent and Plain Balloon Angioplasty for Restenosis in "-Limus"-Eluting Coronary Stents; PEPCAD China ISR, A Multicenter, Randomized, Active Controlled Clinical Study to Evaluate the Safety and Efficacy of the Treatment of In-stent Restenosis Lesion by Paclitaxel-eluting PTCA- Balloon Catheter Vs Paclitaxel-eluting Stent; PEPCAD DES, Treatment of DES-In-Stent Restenosis With SeQuent Please Paclitaxel Eluting PTCA Catheter; RIBS IV, Restenosis Intrastent of Drug-eluting Stents: Paclitaxel-eluting Balloon vs Everolimus-eluting Stent). A Prospective, Multicenter and Randomized Clinical Trial.

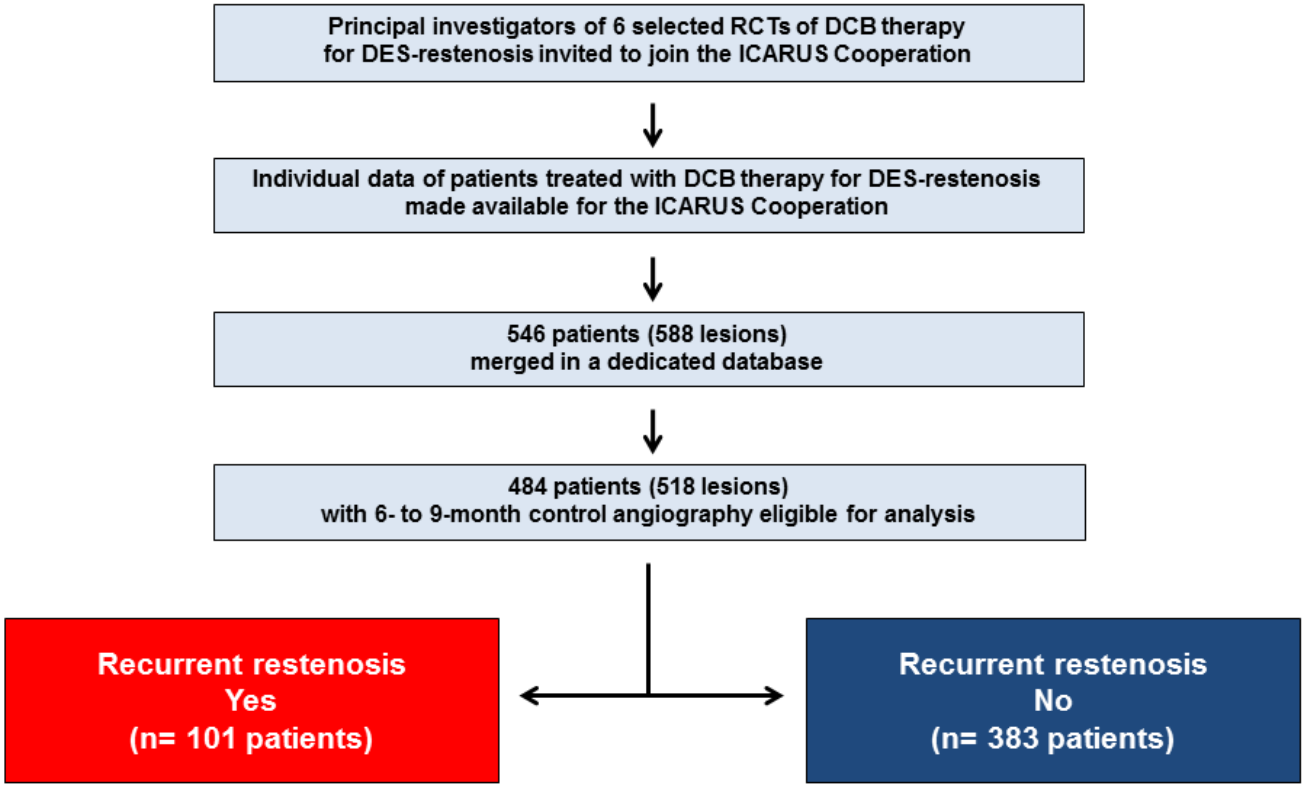
Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

Figure of the supplementary material

Flow diagram of the study

DCB, drug-coated balloon; DES, drug-eluting stent, RCT, randomized controlled trial.

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.



S-Figure

Document downloaded from http://www.elsevier.es, day 09/02/2026. This copy is for personal use. Any transmission of this document by any media or format is strictly prohibited.

REFERENCES OF THE SUPPLEMENTARY MATERIAL

1. Stewart LA, Clarke M, Rovers M, et al.; PRISMA-IPD Development Group. Preferred Reporting Items for Systematic Review and Meta-Analyses of individual participant data: the PRISMA-IPD Statement. *JAMA.* 2015;313:1657-1665.

2. Habara S, Mitsudo K, Kadota K, et al. Effectiveness of paclitaxel-eluting balloon catheter in patients with sirolimus-eluting stent restenosis. *JACC Cardiovasc Interv.* 2011;4:149-154.

3. Habara S, Iwabuchi M, Inoue N, et al. A multicenter randomized comparison of paclitaxel-coated balloon catheter with conventional balloon angioplasty in patients with bare-metal stent restenosis and drug-eluting stent restenosis. *Am Heart J.* 2013;166:527-533.

4. Byrne RA, Neumann FJ, Mehilli J, et al.; investigators I-D. Paclitaxel-eluting balloons, paclitaxel-eluting stents, and balloon angioplasty in patients with restenosis after implantation of a drug-eluting stent (ISAR-DESIRE 3): a randomised, open-label trial. Lancet. 2013;381:461-467.

5. Xu B, Gao R, Wang J, et al.; Investigators PCIT. A prospective, multicenter, randomized trial of paclitaxel-coated balloon versus paclitaxel-eluting stent for the treatment of drug-eluting stent in-stent restenosis: results from the PEPCAD China ISR trial. *JACC Cardiovasc Interv.* 2014;7:204-211.

6. Rittger H, Brachmann J, Sinha AM, et al. A randomized, multicenter, single-blinded trial comparing paclitaxel-coated balloon angioplasty with plain balloon angioplasty in drug-eluting stent restenosis: the PEPCAD-DES study. *J Am Coll Cardiol.* 2012;59:1377-1382.

7. Alfonso F, Perez-Vizcayno MJ, Cardenas A, et al.; Investigators RIS. A Prospective Randomized Trial of Drug-Eluting Balloons Versus Everolimus-Eluting Stents in Patients With In-Stent Restenosis of Drug-Eluting Stents: The RIBS IV Randomized Clinical Trial. *J Am Coll Cardiol.* 2015;66:23-33.