Review Article Long-term outcomes following ultrathin vs thin-strut drug-eluting stents for percutaneous coronary intervention: an updated systematic review and meta-analysis of randomized control trials

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Abstract: Objectives: Current thin-strut 2nd generation drug eluting stents (DES) are considered as optimal standard of care for revascularization of coronary artery disease (CAD) patients undergoing percutaneous coronary intervention (PCI). Ultrathin (< 70 µm strut thickness) strut DES have recently been shown to reduce target lesion failure (TLF) compared to thin-strut DES. Therefore, in order to assess the validity of improved outcomes associated with ultrathin-strut DES, we conducted an updated meta-analysis that includes recently published follow-ups of previously conducted randomized controlled trials (RCTs). Methods: MEDLINE and Scopus were gueried from their inception to May 2024 to identify studies comparing outcomes between ultrathin and current thin-strut 2nd generation DES groups. A random-effects meta-analysis was conducted to derive risk ratios (RR) from dichotomous data. The primary endpoint was long-term TLF defined as a composite of cardiac death, target vessel myocardial infarction (TV-MI) and clinically driven target lesion revascularization (CD-TLR). The secondary outcome was target-vessel failure (TVF) defined as a composite of cardiac death, TV-MI and clinically driven target-vessel revascularization (CD-TVR). Results: A total of 17 RCTs (n=22141) with a mean follow-up of 34 months were included. The risk of TLF was significantly lowered in the ultrathin DES group in comparison to thin-strut DES. A significant decrease was also noted in rates of TVF, CD-TLR and CD-TVR in the ultrathin DES vs thin-strut DES group. Conclusion: The results of our analysis demonstrate a significantly reduced risk of TLF in the ultrathin DES group in comparison with thin-strut DES. Ultrathin DES was also associated with a significantly decreased risk of TVF, CD-TLR and CD-TVR.

Keywords: Major adverse cardiovascular events, target lesion revascularization, drug eluting stents

Introduction

Current 2^{nd} generation thin-strut drug eluting stents (DES) are considered as the optimal standard of care for revascularization of coronary artery disease (CAD) patients undergoing percutaneous coronary intervention (PCI) [1, 2]. At long-term follow up, 1^{st} generation DES were found to be associated with late thrombotic events. A pro-inflammatory environment, mechanical injury during the implantation process and the deposition of fibrin over uncovered stent struts contributed to the thrombogenic complications observed with 1^{st} generation DES [3]. To overcome these issues, 2^{nd} generation

tion DES were introduced with upgraded stent platforms and thinner struts which led to improved efficacy, event free survival rates and a reduced need for revascularization. One study reported a statistically significant (32% and 45% respectively) reduction in target vessel failure (TVF) and major adverse cardiovascular events (MACE) with thin-strut 2nd generation DES in comparison with thick-strut 1st generation DES [4]. First generation thicker-strut DES have also shown an increase in the risk of bleeding complications due to the necessity of prolonged dual antiplatelet therapy (DAPT) [5-7]. The benefits of 2nd generation thin-strut DES have been linked to several factors such as anti-proliferative agents embedded in a polymer coating, the use of biocompatible polymers, and thinner strut stent platforms with novel metallic alloys [8-10]. Moreover, they are also found to reduce the incidence of DESinduced thrombotic complications and stent restenosis compared to their earlier counterparts [11]. Despite these advancements, 2nd generation thin-strut DES are associated with late onset of adverse complications such as very late stent related ischemic events [12].

Hence the development of ultrathin strut DES (\leq 70 µm) has emerged as a new line of treatment for PCI in patients with CAD. Several clinical trials have reported reduced incidence of outcomes such as target lesion failure (TLF) with ultrathin-strut DES compared to 2nd generation thin-strut DES. These improvements are a result of much thinner stent platforms with biodegradable polymers which reduce the risk of vascular injury during the implantation procedure, alleviate chances of inflammation, and stimulate rapid endothelialization [13].

A recent meta-analysis comparing clinical outcomes of ultrathin DES with current thin-strut 2nd generation DES over a mean follow up period of 30 months has reported a significant relative risk reduction of 15% in TLF, and a reduced risk of TVF [14]. However, since then, newly published trials including the very recent CASTLE trial [15], and data corresponding to longer follow-ups of previously published randomized control trials (RCTs) have emerged. Hence, we performed an updated meta-analysis including a total of 17 RCTs with a large sample size of 22,141 patients undergoing PCI [15-31]. We further conducted a meta-regression analysis to account for the effects of various confounders, including baseline comorbidities, on the outcomes associated with ultrathin-strut vs current 2nd generation thin-strut DES.

Methods

Data sources and search strategy

This systematic review and meta-analysis was conducted in accordance with the established methods recommended by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [32], Cochrane [33],

and Assessing the methodological quality of systematic reviews-2 (AMSTAR-2) guidelines. A PRISMA search strategy was employed, utilizing Boolean operators and PICO (Patient, Intervention, Control, and Outcomes) criteria, to conduct a search on online databases such as MEDLINE, Scopus, and Embase from inception till May 2024 to identify randomized control trials (RCTs) comparing clinical outcomes between ultrathin-strut versus. Thin-strut 2nd generation DES. We additionally performed manual searches through reference lists of original publications, review articles, and pertinent editorials. Google scholar, medrix.org, and ClinicalTrials.gov were also searched to identify grey literature, and preprints. The literature screening was performed by two independent investigators (FY and SFZ), with conflicts resolved by discussion and consensus with a third investigator (AM). The following key-words and their MeSH (medical subject headings) terms were used in this comprehensive literature search: "drug eluting stents (DES)", "ultrathin-strut DES", "very-thin DES", "thin-strut DES", "current 2nd generation DES". No filters were applied on the basis of language, author names, year of publication, and country or institution of publication. The detailed search strategy has been reported in Table S1.

Study selection

After conducting the literature search, the identified articles were exported to the Endnote Reference Library software (Version X7.5; Clarivate Analytics, Philadelphia, PA). To ensure the removal of duplicates present in multiple online databases, a duplicate filter was applied. The remaining articles were thoroughly screened based on title and abstract by two independent investigators (FY and SFZ), ensuring they met the required eligibility criteria. Any conflicts were resolved by discussion and consensus with a third investigator (AM). All randomized controlled trials (RCTs) reporting on clinical outcomes comparing ultrathin-strut DES and thin-strut DES in CAD patients undergoing PCI were included. Stents with strut thickness \leq 70 µm were defined as ultrathin whereas those > 70 µm were classified under thinstrut 2nd generation DES.

Study outcomes

The primary endpoint was long-term target lesion failure (TLF) defined as a composite of cardiac death, target-vessel myocardial infarc-

tion (TV-MI) and clinically driven target lesion revascularization (CD-TLR). The secondary outcome was target-vessel failure (TVF) defined as a composite of cardiac death, TV-MI and clinically driven target-vessel revascularization (CD-TVR). Other outcomes included the individual components of TLF and TVF, all-cause MI, definite or probable stent thrombosis (ST) defined by the Academic Research Consortium criteria [34], all-cause mortality, and non-cardiac death. If not specifically reported, non-cardiac death was calculated as the difference between all-cause mortality and cardiac death.

Data extraction

Data extraction of the relevant articles was conducted by two independent investigators (FY and SFZ). The following data was extracted from the RCTs: study name and year, study design, study duration, total number of participants, general patient characteristics including mean age, and baseline comorbidities, stent design, and all clinical outcomes of interest.

Study quality assessment

Two investigators (FY and SFZ) independently assessed the quality of the included clinical trials using the Collaboration's risk of bias tool for randomized controlled trials [35]. Studies were evaluated for random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data and selective reporting.

Statistical analysis

This meta-analysis was conducted using Review Manager (RevMan) Version 5.4 Cochrane Collaboration. A random-effects meta-analysis was conducted to derive risk ratios (RR) with 95% confidence intervals for dichotomous data at the time of latest follow-up. A p-value < 0.05 was considered statistically significant for all outcomes. The pooled results are presented as forest plots. Higgins I² value was used to evaluate heterogeneity. A value of I²=25-50% was considered mild, 50-75% moderate, and > 75% severe heterogeneity. Furthermore, a subgroup analysis assessing the effect of the type of anti-proliferative drug used on each outcome was also conducted. Studies comparing the ultrathin Orsiro DES vs the thin-strut Xience DES were subjected to a sensitivity analysis to evaluate the impact of stent type on all outcomes. A funnel plot was used to assess outcomes with potential publication bias. Lastly, meta-regression, using OpenMeta [Analyst] (version 5.26.14), was conducted to evaluate the correlation of the primary outcome with cofounders such as age, gender and several baseline comorbidities. These results were reported as coefficients (Coeff) and *P*-values.

Results

Study selection and study characteristics

A total of 453 new studies were retrieved from all databases. After checking for eligibility and excluding irrelevant articles, a total of 17 RCTs comprising 22,141 patients [15-31] with a mean follow-up of 34 months were included in this meta-analysis. This meta-analysis includes the recently published CASTLE trial [15], and latest follow-ups of previously published, SORT OUT IX trial [26], BIO-RESORT Trial [27], BIONYX Trial [28], SORT OUT VII [29], BIO-FLOW V [30], and TALENT trial [31]. The PRISMA flow chart shows the detailed search and study selection process and is represented in Figure 1. 11,606 patients were randomized to ultrathin-strut DES and 10,535 to thin-strut 2nd generation DES. The ultrathin stents utilized in the RCTs included Orsiro (n=13), MiStent (n=2), BioMime (n=1), and Supraflex (n=1). Thin-strut stents in these trials were Xience (n=11), Resolute (n=3), Nobori (n=1), BioFreedom (n=1), and Endeavor (n=1). Detailed baseline and study characteristics are demonstrated in Table S2.

Primary outcome

A total of 15 RCTs with 21,555 patients reported on the outcome of TLF. There was a significant decrease in the risk of TLF (relative risk (RR) 0.91, 95% CI 0.84-0.99, P=0.03, I^2 =0%) with ultrathin-strut DES compared to thin-strut DES as shown in **Figure 2**.

Secondary outcomes

An analysis of 13 RCTs demonstrated that the risk of TVF was significantly decreased in the ultrathin group compared to thin-strut DES (RR 0.91, 95% CI 0.83-0.99, P=0.03, I^2 =0%) (**Figure 3**). The risk of CD-TVR (RR 0.89, 95% CI 0.81-0.99, P=0.02, I^2 =0%) and CD-TLR (RR 0.83,

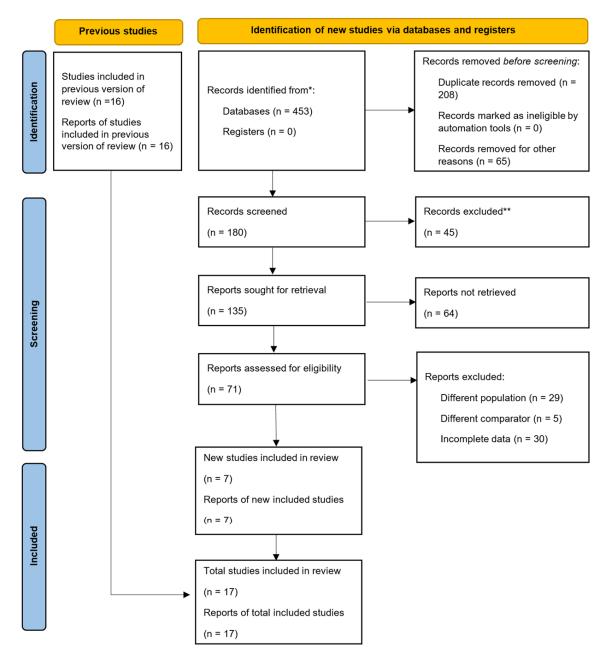


Figure 1. PRISMA flow diagram for new systematic reviews which included searches of databases and additional records.

95% CI 0.72-0.95, P=0.008, I²=15%) was also significantly decreased in the ultrathin vs thin strut DES, while no significant differences were seen with TV-MI (RR 0.95, 95% CI 0.83-1.09, P=0.47, I²=0%), all cause MI (RR 0.98, 95% CI 0.87-1.10, P=0.74, I²=0%) and definite or probable ST (RR 0.92, 95% CI 0.76-1.13, P=0.44, I²=0%) between the two groups (**Figures 4-8**). No significant differences were seen in rates of cardiac (RR 1.03, 95% CI 0.88-1.20, P=0.73,

 $l^2=0\%$), non-cardiac (RR 1.09, 95% Cl 0.91-1.30, P=0.35, $l^2=18\%$) and all-cause death (RR 1.07, 95% Cl 0.96-1.19, P=0.22, $l^2=3\%$) between ultrathin vs thin strut DES (**Figures 9-11**).

Quality assessment and publication bias

All 17 RCTs were classified as having a 'high' quality score due to their robust methodology.

	Ultrathin	DES	SecondGeneration Thir	1 DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Wijns 2015	11	123	5	61	0.6%	1.09 [0.40, 3.00]	2015	
Lefèvre 2018	30	298	19	154	2.3%	0.82 [0.48, 1.40]	2018	
Pilgrim 2018	198	1063	189	1056	20.4%	1.04 [0.87, 1.25]	2018	+
Saito 2019	14	385	8	190	0.9%	0.86 [0.37, 2.02]	2019	
Iglesias 2019	33	649	53	651	3.7%	0.62 [0.41, 0.95]	2019	
Kim 2019	11	250	9	122	0.9%	0.60 [0.25, 1.40]	2019	
Li 2020	5	220	3	220	0.3%	1.67 [0.40, 6.89]	2020	
Takahashi 2020	72	703	79	695	7.3%	0.90 [0.67, 1.22]	2020	
Ploumen (1) 2021	91	1245	88	1243	8.3%	1.03 [0.78, 1.37]	2021	
Winter 2022	57	720	66	715	5.8%	0.86 [0.61, 1.20]	2022	
Ploumen (2) 2022	113	1169	128	1173	11.5%	0.89 [0.70, 1.13]	2022	
Kandzari 2022	104	884	66	450	8.0%	0.80 [0.60, 1.07]	2022	
Nakamura 2022	43	722	41	718	3.8%	1.04 [0.69, 1.58]	2022	
Ellert Gregersen 2022	100	1579	122	1572	10.2%	0.82 [0.63, 1.05]	2022	
Hansen 2023	156	1261	166	1264	15.9%	0.94 [0.77, 1.16]	2023	
Total (95% CI)		11271		10284	100.0%	0.91 [0.84, 0.99]		•
Total events	1038		1042					
Heterogeneity: Tau ² = 0.	00; Chi ² = 1	10.05, d	f = 14 (P = 0.76); I ² = 0%				-	
Test for overall effect: Z	= 2.21 (P =	0.03)						0.2 0.5 1 2 5 Favours Ultrathin DES Favours Thin DES

Figure 2. Forest plot for the outcome of target lesion failure (TLF).

	Ultrathin	DES	SecondGeneration Th	nin DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Wijns 2015	12	123	9	61	1.2%	0.66 [0.29, 1.48]	2015	
Lefèvre 2018	45	298	19	154	3.1%	1.22 [0.74, 2.02]	2018	_ -
Pilgrim 2018	220	1063	219	1056	28.3%	1.00 [0.84, 1.18]	2018	+
Abizaid 2018	5	170	6	86	0.6%	0.42 [0.13, 1.34]	2018	
Kim 2019	18	250	11	122	1.5%	0.80 [0.39, 1.64]	2019	
Saito 2019	19	385	12	190	1.6%	0.78 [0.39, 1.58]	2019	
Iglesias 2019	39	649	61	651	5.3%	0.64 [0.44, 0.94]	2019	
Li 2020	5	220	4	220	0.5%	1.25 [0.34, 4.59]	2020	
Takahashi 2020	85	703	97	695	10.7%	0.87 [0.66, 1.14]	2020	
Ploumen (1) 2021	109	1245	112	1243	12.4%	0.97 [0.76, 1.25]	2021	-
Ploumen (2) 2022	142	1169	157	1173	17.5%	0.91 [0.73, 1.12]	2022	
Kandzari 2022	127	884	81	450	12.1%	0.80 [0.62, 1.03]	2022	
Nakamura 2022	47	722	48	718	5.2%	0.97 [0.66, 1.44]	2022	
Total (95% CI)		7881		6819	100.0%	0.91 [0.83, 0.99]		•
Total events	873		836					
Heterogeneity: Tau ² =	= 0.00; Chi ^a	= 10.02	2, df = 12 (P = 0.61); l ² =	0%				0.05 0.2 1 5 20
Test for overall effect								0.05 0.2 1 5 20 Favours Ultrathin DES Favours Thin DES

Figure 3. Forest plot for the outcome of target vessel failure (TVF).

	Ultrathin	DES	SecondGeneration Thir	DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Wijns 2015	6	123	6	61	0.8%	0.50 [0.17, 1.47]	2015	
Abizaid 2018	4	170	2	86	0.3%	1.01 [0.19, 5.41]	2018	
Lefèvre 2018	36	298	15	154	2.9%	1.24 [0.70, 2.19]	2018	
Pilgrim 2018	125	1063	123	1056	17.2%	1.01 [0.80, 1.28]	2018	+
Kim 2019	15	250	7	122	1.2%	1.05 [0.44, 2.50]	2019	
Saito 2019	12	385	5	190	0.9%	1.18 [0.42, 3.31]	2019	
Iglesias 2019	20	649	40	651	3.4%	0.50 [0.30, 0.85]	2019	
Li 2020	0	220	4	220	0.1%	0.11 [0.01, 2.05]	2020	
Takahashi 2020	51	703	62	695	7.4%	0.81 [0.57, 1.16]	2020	-
Ploumen (1) 2021	75	1245	84	1243	10.3%	0.89 [0.66, 1.20]	2021	-
Kandzari 2022	78	884	51	450	8.4%	0.78 [0.56, 1.09]	2022	
Nakamura 2022	13	722	17	718	1.8%	0.76 [0.37, 1.55]	2022	
Ploumen (2) 2022	91	1169	101	1173	12.7%	0.90 [0.69, 1.19]	2022	-
Ellert Gregersen 2022	91	1579	104	1572	12.6%	0.87 [0.66, 1.14]	2022	-
Hansen 2023	141	1261	146	1264	19.8%	0.97 [0.78, 1.20]	2023	+
Total (95% CI)		10721		9655	100.0%	0.89 [0.81, 0.99]		•
Total events	758		767					
Heterogeneity: Tau ² = 0.	00; Chi ² =	12.17, d	lf = 14 (P = 0.59); I ² = 0%					
Test for overall effect: Z								0.005 0.1 1 10 200 Favours Ultrathin DES Favours Thin DES

Figure 4. Forest plot for the outcome of clinically driven target-vessel revascularization (CD-TVR).

The details of the quality assessment are presented in <u>Table S3</u>. To determine publication bias for all outcomes, funnel plots were constructed which showed significant bias for most

	Ultrathin	DES	SecondGeneration Thin	DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Wijns 2015	4	123	2	61	0.7%	0.99 [0.19, 5.27]	2015	
Abizaid 2018	4	170	2	86	0.7%	1.01 [0.19, 5.41]	2018	
Lefèvre 2018	18	298	10	154	3.3%	0.93 [0.44, 1.97]	2018	- _
Pilgrim 2018	103	1063	97	1065	17.9%	1.06 [0.82, 1.39]	2018	+
Saito 2019	6	385	1	190	0.4%	2.96 [0.36, 24.42]	2019	
Iglesias 2019	16	649	33	651	5.1%	0.49 [0.27, 0.87]	2019	
Kim 2019	9	250	6	122	1.9%	0.73 [0.27, 2.01]	2019	
Takahashi 2020	35	703	44	695	8.7%	0.79 [0.51, 1.21]	2020	
Li 2020	0	220	1	220	0.2%	0.33 [0.01, 8.14]	2020	
Ploumen (1) 2021	55	1245	57	1243	11.5%	0.96 [0.67, 1.38]	2021	-
Nakamura 2022	6	722	7	718	1.6%	0.85 [0.29, 2.52]	2022	
Ploumen (2) 2022	55	1169	62	1173	11.9%	0.89 [0.62, 1.27]	2022	
Ellert Gregersen 2022	41	1579	80	1572	11.1%	0.51 [0.35, 0.74]	2022	
Kandzari 2022	48	884	32	450	8.7%	0.76 [0.50, 1.18]	2022	
Hansen 2023	84	1261	94	1264	16.3%	0.90 [0.67, 1.19]	2023	-
Total (95% CI)		10721		9664	100.0%	0.83 [0.72, 0.95]		•
Total events	484		528					
Heterogeneity: Tau ² = 0.	01; Chi ² =	16.44. d	f=14 (P=0.29); I ² =15%					
Test for overall effect: Z =								0.005 0.1 1 10 200 Favours Ultrathin DES Favours Thin DES

Figure 5. Forest plot for the outcome of clinically driven target-lesion revascularization (CD-TLR).

	Ultrathin	DES	SecondGeneration Thi	n DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Wijns 2015	5	123	2	61	0.8%	1.24 [0.25, 6.21]	2015	
Abizaid 2018	1	170	1	86	0.3%	0.51 [0.03, 7.99]	2018	
Lefèvre 2018	10	298	5	154	1.8%	1.03 [0.36, 2.97]	2018	
Pilgrim 2018	62	1063	69	1056	17.7%	0.89 [0.64, 1.24]	2018	
Saito 2019	13	385	6	190	2.2%	1.07 [0.41, 2.77]	2019	
Iglesias 2019	10	649	13	651	2.9%	0.77 [0.34, 1.75]	2019	
Li 2020	4	220	2	220	0.7%	2.00 [0.37, 10.81]	2020	
Takahashi 2020	22	703	17	695	5.0%	1.28 [0.69, 2.39]	2020	_
Ploumen (1) 2021	38	1245	39	1243	10.1%	0.97 [0.63, 1.51]	2021	
Ploumen (2) 2022	50	1169	50	1173	13.3%	1.00 [0.68, 1.47]	2022	+
Kandzari 2022	56	884	45	450	13.8%	0.63 [0.44, 0.92]	2022	
Nakamura 2022	31	722	28	718	7.8%	1.10 [0.67, 1.82]	2022	_ _
Ellert Gregersen 2022	43	1579	43	1572	11.2%	1.00 [0.66, 1.51]	2022	-+-
Hansen 2023	51	1261	45	1264	12.6%	1.14 [0.77, 1.68]	2023	+-
Total (95% CI)		10471		9533	100.0%	0.95 [0.83, 1.09]		•
Total events	396		365					
Heterogeneity: Tau ² = 0.	.00; Chi ² = 1	8.14, df	= 13 (P = 0.83); I ² = 0%					
Test for overall effect: Z								0.02 0.1 1 10 50 Favours Ultrathin DES Favours Thin DES

Figure 6. Forest plot for the outcome of target vessel myocardial infarction (TV-MI).

	Ultrathin	DES	SecondGeneration Thin	DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Wijns 2015	7	123	3	61	0.8%	1.16 [0.31, 4.32]	2015	
Lefèvre 2018	13	298	9	154	2.1%	0.75 [0.33, 1.71]	2018	
Pilgrim 2018	99	1063	118	1056	22.7%	0.83 [0.65, 1.07]	2018	-
Abizaid 2018	1	170	4	86	0.3%	0.13 [0.01, 1.11]	2018	
Kim 2019	1	250	3	122	0.3%	0.16 [0.02, 1.55]	2019	
Saito 2019	14	385	6	190	1.6%	1.15 [0.45, 2.95]	2019	
Iglesias 2019	24	649	20	651	4.3%	1.20 [0.67, 2.16]	2019	- -
Zivelonghi 2019	3	165	4	165	0.7%	0.75 [0.17, 3.30]	2019	
Takahashi 2020	24	703	22	695	4.5%	1.08 [0.61, 1.91]	2020	
Li 2020	4	220	2	220	0.5%	2.00 [0.37, 10.81]	2020	
Ploumen (1) 2021	54	1245	55	1243	10.8%	0.98 [0.68, 1.42]	2021	-
Ploumen (2) 2022	66	1169	60	1173	12.6%	1.10 [0.79, 1.55]	2022	+
Nakamura 2022	33	722	32	718	6.4%	1.03 [0.64, 1.65]	2022	+
Ellert Gregersen 2022	69	1579	67	1572	13.5%	1.03 [0.74, 1.42]	2022	+
Hansen 2023	94	1261	91	1264	18.9%	1.04 [0.78, 1.37]	2023	+
Total (95% CI)		10002		9370	100.0%	0.98 [0.87, 1.10]		4
Total events	506		496					
Heterogeneity: Tau ² = 0.	00; Chi ² =	10.13, d	f = 14 (P = 0.75); I ² = 0%					
Test for overall effect: Z								0.005 0.1 i 10 200 Favours Ultrathin DES Favours Thin DES

Figure 7. Forest plot for the outcome of all-cause myocardial infarction (MI).

outcomes as the studies were not symmetrically distributed around the summary effect size (Figures S1, S2, S3, S4, S5, S6, S7, S8, S9, S10).

	Ultrathin	DES	SecondGeneration Thin	DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Wijns 2015	1	123	1	61	0.5%	0.50 [0.03, 7.79]	2015	
Abizaid 2018	0	170	0	86		Not estimable	2018	
Lefèvre 2018	0	298	1	154	0.4%	0.17 [0.01, 4.22]	2018	
Pilgrim 2018	62	1063	76	1056	37.6%	0.81 [0.59, 1.12]	2018	
Kim 2019	0	250	2	122	0.4%	0.10 [0.00, 2.03]	2019	
Saito 2019	3	385	0	190	0.5%	3.46 [0.18, 66.72]	2019	
Iglesias 2019	13	649	15	651	7.3%	0.87 [0.42, 1.81]	2019	
Li 2020	0	220	0	220		Not estimable	2020	
Takahashi 2020	8	703	10	695	4.6%	0.79 [0.31, 1.99]	2020	
Ploumen (1) 2021	15	1245	7	1243	5.0%	2.14 [0.88, 5.23]	2021	
Ellert Gregersen 2022	30	1579	24	1572	14.0%	1.24 [0.73, 2.12]	2022	
Winter 2022	8	720	10	715	4.6%	0.79 [0.32, 2.00]	2022	
Ploumen (2) 2022	20	1169	19	1173	10.2%	1.06 [0.57, 1.97]	2022	-
Nakamura 2022	1	722	0	718	0.4%	2.98 [0.12, 73.11]	2022	
Hansen 2023	25	1261	31	1264	14.6%	0.81 [0.48, 1.36]	2023	
Total (95% CI)		10557		9920	100.0%	0.92 [0.76, 1.13]		•
Total events	186		196					
Heterogeneity: Tau ² = 0.	.00; Chi ² =	10.54, d	f = 12 (P = 0.57); I ² = 0%					
Test for overall effect: Z :	= 0.77 (P =	0.44)	. ,					0.005 0.1 1 10 200 Favours Ultrathin DES Favours Thin DES
		,						Favours Oliratinin DES Favours Thin DES

Figure 8. Forest plot for the outcome of probable or definite stent thrombosis (ST).

	Ultrathin	DES	SecondGeneration Thir	DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Wijns 2015	5	123	2	61	0.9%	1.24 [0.25, 6.21]	2015	
Abizaid 2018	0	170	0	86		Not estimable	2018	
Lefèvre 2018	5	298	4	154	1.4%	0.65 [0.18, 2.37]	2018	
Pilgrim 2018	81	1063	76	1056	26.2%	1.06 [0.78, 1.43]	2018	+
Iglesias 2019	19	649	21	651	6.4%	0.91 [0.49, 1.67]	2019	
Zivelonghi 2019	2	165	2	165	0.6%	1.00 [0.14, 7.01]	2019	
Saito 2019	0	385	1	190	0.2%	0.16 [0.01, 4.03]	2019	
Kim 2019	2	250	3	122	0.8%	0.33 [0.06, 1.92]	2019	
Takahashi 2020	27	703	26	695	8.5%	1.03 [0.61, 1.74]	2020	+
Li 2020	1	220	0	220	0.2%	3.00 [0.12, 73.24]	2020	
Ploumen (1) 2021	23	1245	13	1243	5.2%	1.77 [0.90, 3.47]	2021	
Ploumen (2) 2022	33	1169	40	1173	11.6%	0.83 [0.53, 1.30]	2022	
Kandzari 2022	21	884	8	450	3.7%	1.34 [0.60, 2.99]	2022	_ +- _
Nakamura 2022	6	722	7	718	2.0%	0.85 [0.29, 2.52]	2022	
Ellert Gregersen 2022	41	1579	32	1572	11.4%	1.28 [0.81, 2.01]	2022	
Hansen 2023	62	1261	66	1264	20.9%	0.94 [0.67, 1.32]	2023	+
Total (95% CI)		10886		9820	100.0%	1.03 [0.88, 1.20]		•
Total events	328		301					
Heterogeneity: Tau ² = 0	.00; Chi ² =	9.02, df	= 14 (P = 0.83); I ² = 0%					0.005 0.1 1 10 200
Test for overall effect: Z	= 0.34 (P =	0.73)	. ,					0.005 0.1 1 10 200 Favours Ultrathin DES Favours Thin DES

Figure 9. Forest plot for the outcome of cardiac death.

Meta regression

Age, male sex, follow-up time, baseline diabetes mellitus, hypertension and smoking were assessed as possible covariates having an impact on the primary outcome of TLF. Only increasing age was found to be a statistically significant predictor of increased TLF in the ultrathin group when compared with 2nd generation thin-strut DES (Coeff: 0.0812, P=0.03). Other potential confounders had no significant association with TLF (Figures S11, S12, S13, S14, S15, S16).

Subgroup analysis

A subgroup analysis based on the type of antiproliferative drug was also conducted (Figures S17, S18, S19, S20, S21, S22, S23, S24, S25,

S26). All RCTs utilized the ultrathin sirolimus DES, whereas everolimus (n=12), zotarolimus (n=3), and biolimus (n=2) were used in the thin strut DES group. For the outcome of TLF, no significant difference was observed in the sirolimus DES vs everolimus DES (RR 0.91, 95% CI 0.82-1.01, P=0.07, I²=0%), sirolimus DES vs zotarolimus DES (RR 0.99, 95% CI 0.76-1.28, P=0.91, I²=0%) and sirolimus DES vs biolimus DES (RR 0.89, 95% CI 0.76-1.04, P=0.15, I²=0%). However, the overall effect size demonstrated that the ultrathin group was significantly associated with a reduced risk of TLF compared with thin strut DES (RR 0.91, 95% CI 0.84-0.99, P=0.03, I²=0%). The ultrathin sirolimus DES was significantly associated with a reduced risk of TVF compared with everolimus thin strut DES (RR 0.90, 95% CI 0.82-0.99, P=0.04, I²=0%), whereas no significant differ-

	Ultrathin	DES	SecondGeneration Thin	DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Wijns 2015	6	123	4	61	2.0%	0.74 [0.22, 2.54]	2015	
Abizaid 2018	1	170	0	86	0.3%	1.53 [0.06, 37.08]	2018	
Lefèvre 2018	9	298	10	154	3.8%	0.47 [0.19, 1.12]	2018	
Pilgrim 2018	58	1063	29	1056	11.8%	1.99 [1.28, 3.08]	2018	
Saito 2019	6	385	3	190	1.6%	0.99 [0.25, 3.90]	2019	
Iglesias 2019	8	649	4	651	2.2%	2.01 [0.61, 6.63]	2019	
Kim 2019	7	250	1	122	0.7%	3.42 [0.43, 27.46]	2019	
Zivelonghi 2019	2	165	5	165	1.2%	0.40 [0.08, 2.03]	2019	
Li 2020	1	220	0	220	0.3%	3.00 [0.12, 73.24]	2020	
Takahashi 2020	28	703	23	695	8.6%	1.20 [0.70, 2.07]	2020	
Ploumen (1) 2021	34	1245	27	1243	9.7%	1.26 [0.76, 2.07]	2021	
Ploumen (2) 2022	59	1169	66	1173	16.1%	0.90 [0.64, 1.26]	2022	
Kandzari 2022	35	884	19	450	8.5%	0.94 [0.54, 1.62]	2022	- _
Nakamura 2022	10	722	8	718	3.5%	1.24 [0.49, 3.13]	2022	
Ellert Gregersen 2022	27	1579	32	1572	9.5%	0.84 [0.51, 1.40]	2022	
Hansen 2023	96	1261	89	1264	20.1%	1.08 [0.82, 1.43]	2023	+
Total (95% CI)		10886		9820	100.0%	1.09 [0.91, 1.30]		•
Total events	387		320					
Heterogeneity: Tau ² = 0.	.02; Chi ² =	18.37, d	f=15 (P=0.24); I ² =18%					
Test for overall effect: Z			//					0.01 0.1 1 1 10 100 Favours Ultrathin DES Favours Thin DES

Figure 10. Forest plot for the outcome of non-cardiac death.

	Ultrathin	DES	SecondGeneration Thin	DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
Wijns 2015	11	123	6	61	1.3%	0.91 [0.35, 2.34]	2015	
Lefèvre 2018	14	298	14	154	2.2%	0.52 [0.25, 1.06]	2018	
Pilgrim 2018	139	1063	105	1056	18.2%	1.32 [1.04, 1.67]	2018	-
Abizaid 2018	1	170	0	86	0.1%	1.53 [0.06, 37.08]	2018	
Kim 2019	9	250	4	122	0.9%	1.10 [0.34, 3.49]	2019	
Zivelonghi 2019	4	165	8	165	0.8%	0.50 [0.15, 1.63]	2019	
Saito 2019	6	385	4	190	0.7%	0.74 [0.21, 2.59]	2019	
Iglesias 2019	27	649	25	651	3.9%	1.08 [0.64, 1.85]	2019	_ _
Takahashi 2020	55	703	49	695	8.0%	1.11 [0.77, 1.61]	2020	+-
Li 2020	2	220	0	220	0.1%	5.00 [0.24, 103.55]	2020	
Ploumen (1) 2021	67	1245	45	1243	8.0%	1.49 [1.03, 2.15]	2021	
Ellert Gregersen 2022	68	1579	64	1572	9.7%	1.06 [0.76, 1.48]	2022	+
Ploumen (2) 2022	92	1169	106	1173	14.8%	0.87 [0.67, 1.14]	2022	
Kandzari 2022	56	884	27	450	5.6%	1.06 [0.68, 1.65]	2022	_ _
Nakamura 2022	16	722	15	718	2.3%	1.06 [0.53, 2.13]	2022	_
Hansen 2023	158	1261	155	1264	23.3%	1.02 [0.83, 1.26]	2023	+
Total (95% CI)		10886		9820	100.0%	1.07 [0.96, 1.19]		•
Total events	725		627					
Heterogeneity: Tau ² = 0.	00; Chi ² =	15.50, d	f = 15 (P = 0.42); I ² = 3%					0.01 0.1 1 10 100
Test for overall effect: Z	= 1.23 (P =	0.22)						Favours Ultrathin DES Favours Thin DES

ence was observed between the ultrathin sirolimus DES vs thin strut zotarolimus DES (RR 0.92, 95% CI 0.74-1.16, P=0.50, I²=0%). However, the overall effect size demonstrated that the ultrathin group was associated with a reduced risk of TVF compared to thin-strut DES (RR 0.91, 95% CI 0.83-0.99, P=0.03, I²=0%).

Sensitivity analysis

A sensitivity analysis was performed for all outcomes by only including studies comparing the ultrathin Orsiro DES with the thin-strut Xience DES. No significant difference was observed for the outcome of TLF between the ultrathin Orsiro and thin-strut Xience stents (RR 0.91, 95% CI 0.77-1.06, P=0.22, I²=16%), as shown in <u>Figure</u> <u>S27</u>. Similarly, there was no significant difference between the rates of TVF, CD-TLR, CD-TVR, all-cause MI, TV-MI, definite or probable ST, cardiac death, non-cardiac death and all-cause mortality between the two stent types (<u>Figures</u> <u>S28, S29, S30, S31, S32, S33, S34, S35, S36</u>).

Discussion

The principal findings of this meta-analysis report a significant decrease in the risk of TLF, TVF, CD-TVR and CD-TLR in the ultrathin stent group compared with the thin-strut DES group. No significant differences were observed for the outcomes of TV-MI, MI, definite or probable ST, cardiac death, non-cardiac death and all-cause death. This systematic review and meta-analysis, to our knowledge, is the most recent and updated study comparing outcomes between ultrathin DES versus. current 2nd generation thin-strut DES, the mostly commonly

utilized stent for PCI in the United States. Contemporary 2nd generation thin-strut DES have exhibited favorable outcomes over the years in published literature [36-38]. Regardless of the implementation of various designs. such as bioresorbable polymers, polymer-free DES, or bioresorbable scaffolds, 2nd generation DES have not shown further improvements in outcomes [39-41]. However, ultrathin stents offer several advantages due to a strut thickness of \leq 70 µm. Ultrathin stents are advantageous in terms of deliverability, as they are more flexible and trackable [42]. Additionally, they are less likely to disrupt blood flow in coronary branches, and have the benefit of promoting rapid endothelialization. A previously conducted meta-analysis by Madhavan and coworkers analyzed data from 16 trials at a mean follow-up of 30 months and found ultrathin DES to be associated with reduced relative risks of TLF, TVF, CD-TVR and CD-TLR (15%, 15%, 16% and 25%, respectively) when compared with current 2nd generation DES [14]. Another metaanalysis of 10 studies conducted by Bangalore and co-workers also demonstrated a significant 16% reduction in TLF in the ultrathin group at a mean follow-up of 12 months [43].

Our meta-analysis differs from previous metaanalyses such that we included data from the new CASTLE trial [15], recent follow-ups of previously included trials and also performed a meta-regression to evaluate potential cofounders for the primary outcome. The SORT OUT IX trial, the largest study included in this analysis, recently published data for a follow up period of 24 months and reported no significant differences between the ultrathin and 2nd generation thin-strut stents for the outcome of TLF [26]. Similarly, the CASTLE trial also reported no significant difference for the primary outcome of TLF between the two groups. However, our updated pooled analyses show TLF to be significantly reduced in patients treated with an ultrathin stent. The current study not only verifies a significant reduction in long-term TLF but also confirms a significantly reduced incidence of TVF with ultrathin-strut DES. These results align with the findings from previous meta-analyses by Madhavan and co-workers and Bangalore and co-workers [14, 43]. The studies included in the ultrathin group in our analysis predominantly utilized the Orsiro stent type, whereas Xience was used in the majority of

studies included in the thin-strut DES group. A comprehensive network meta-analysis by Taglieri and coworkers compared TLF in various types of stent designs from a total of 39 trials involving 59,855 patients, and found the Orsiro stent to be associated with a significantly lower 1-year rate of TLF compared with the Xience stent (OR: 0.84; 95% CI: 0.71 to 0.98; P=0.03) [44]. However, at a follow-up period of 50 months, no statistically significant results were obtained for these stent designs. It is important to mention that the strut thickness of the Orsiro stents in this particular study ranged from 60 μm-80 μm, which could explain the conflicting results obtained at longer follow-ups. Our sensitivity analysis demonstrated no significant difference between the Orsiro and Xience stents at a mean follow-up of 34 months for the outcome of TLF. Nevertheless, the overall analysis, comparing all stent types, demonstrated that the ultrathin group was significantly associated with a reduced risk of TLF compared with 2nd generation thin strut DES.

Our meta-analysis demonstrates a significant reduction in CD-TLR and CD-TVR in the ultrathin DES compared with current second-generation DES. It can be deduced that the reductions observed in the outcomes of TLF and TVF were driven by relative reductions of their revascularization composites (CD-TLR and CD-TVR, respectively) and not by TV-MI. No significant differences were observed for TV-MI in either of the two groups in our study. These results concord with the meta-analysis conducted by Madhavan and co-workers which also reported TLF and TVF to be decreased due to relative decreases in CD-TLR and CD-TVR, respectively, and not TV-MI [14]. However, in Bangalore and co-workers these reductions were driven by lower risks of TV-MI without any differences in revascularizations between the two stent types [43]. The risk for vascular injury, stagnation and flow separation is markedly increased with the use of thicker struts. These complications in turn modulate thrombogenicity and neointimal hyperplasia [45]. Furthermore, delayed endothelization due to thicker struts also promotes neointimal formation [46, 47]. The impact of strut thickness on angiographic neointimal hyperplasia has been demonstrated in several trials previously [48]. Our meta-analysis further confirms that the use of an even smaller strut thickness of < 70 µm will significantly decrease

the risk of repeat revascularization. Our study found no significant differences between the risk of TV-MI or any MI. similarly, there was no difference in the risk of definite or probable stent thrombosis in either of the two groups. It should be mentioned, however, that despite not reaching statistical significance, numerically lower rates of events were observed with these outcomes. These findings also reaffirm the results evaluated by Madhavan and co-workers [14].

The present meta-analysis revealed no significant differences for the risk of all-cause mortality, cardiac death and non-cardiac death between the two groups. In fact, ultrathin stents were associated with a non-significant increase in the incidence of all three outcomes. Similarly, Madhavan and co-workers also reported an 11% increase in the risk of all-cause death in the ultrathin group, however these results did not reach statistical significance [14]. Several studies have established a correlation between adverse events such as stent thrombosis. MI. and repeat revascularization, with both all cause and cardiovascular mortality [49]. Notably, Brener and co-workers analysed data from 21 trials and found significant associations of outcomes such as MI and definite stent thrombosis with all-cause mortality and cardiovascular death [50]. Similarly, in another study, the need for repeat revascularization was associated with an increased risk for all-cause and cardiac mortality (P=0.02 and P < 0.0001, respectively) [51]. Despite the significantly lower rates of CD-TLR and CD-TVR along with numerically lower incidences of MI and ST observed with ultrathin DES in our study, the plausible explanation for a numerical increase in the risk of death remains uncertain. Lastly. the regression analysis revealed increasing age to be a statistically significant predictor of increased TLF in the ultrathin group when compared with current 2nd generation DES (Coeff: 0.0812, P=0.03). Other potential confounders (male sex, follow-up time, baseline diabetes mellitus, hypertension and smokers) had no significant association with TLF.

Our meta-analysis has certain limitations that should be acknowledged. Firstly, to minimize the risk of bias, our study only included RCTs with their selective patient populations, which may raise concerns about the generalizability of our findings to broader populations. Secondly, different follow-up periods across the studies might have influenced the pooled risk ratio estimates. To address this, we performed a regression analysis to assess the impact of follow-up duration on our primary outcome of TLF and found no significant association between the two. Lastly, it is worth noting that the most commonly used stent in the ultrathin group was the Orsiro stent, which has thicker struts for stent diameters ≥ 3.5 mm. However, stents with these diameters were likely used in less than 10% of the total patient population, which may have had a relatively low effect on the overall pooled estimate.

Nevertheless, this meta-analysis is the first to combine both meta-analysis and meta-regression to compare ultrathin and current thin-strut 2nd generation DES using data from 17 trials involving 22141 patients adding to the statistical power of our analysis. Furthermore, the overall mean follow-up of our analysis was 34 months enabling us to evaluate the longestterm impact of ultrathin vs thin strut DES on clinical outcomes following PCI. The results provide further confirmation that the risk of longterm TLF and TVF is significantly reduced in the ultrathin DES group when compared to thin strut DES. This reduction in risk is likely attributed to the lower rates of CD-TVR and CD-TLR observed with ultrathin-strut DES.

Conclusion

In the current meta-analysis, the use of ultrathin DES was associated with decreased risks of TLF, TVF, CD-TLR and CD-TVR. No significant differences were observed for the outcomes of TV-MI, MI, definite or probable ST, all-cause death, cardiac and non-cardiac death between the two groups.

Disclosure of conflict of interest

None.

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PubMed 2021-2023, full texts, randomized controlled trials	((((("ultra-thin"[Title/Abstract]) OR ("very thin"[Title/Abstract])) AND (DES[Title/Abstract])) OR (Drug
	eluting stents [Title/Abstract]))
Scopus 2021-2023	(ultra-thin OR very thin) AND (DES OR Drug eluting stents)
Cochrane	(ultra-thin OR very thin) AND (DES OR Drug eluting stents)

Table S1. Detailed literature search of each database

Table S2. Study characteristics of the included trials

Author's Name	Study Name	Year	Ν	Mean Age*	Follow-up** Patient population		Ultrathin Stent Type	Conventional Stent Type	Primary outcomes
Saito	BIOFLOW-IV	2019	575	64.7 ± 9.6	12	De novo CAD in up to two native coronary arteries.	Orsiro	Xience	Target vessel failure
Kandzari	BIOFLOW-V	2020	1334	Tx: 64.5 ± 10.3 Cx: 64.6 ± 10.7	60	Percutaneous coronary intervention of no more than 3 de novo native coronary artery lesions in a maximum of 2 native target vessels.	Orsiro	Xience	Target lesion failure
Lefèvre	BIOFLOW-II	2018	452	Tx: 62.7 ± 10.4 Cx: 64.8 ± 9.2	60	De novo lesions with a maximum length of 26 mm and a reference vessel diameter from 2.25 to 4.0 mm.	Orsiro	Xience	In-stent late lumen loss
Ploumen 2	BIO-RESORT	2019	3514	63.9 ± 10.8	60	Patients with coronary artery conditions, including new and recurrent blockages, as well as those who had undergone coronary bypass surgery. There were no restrictions on the length of the blockage, the size of the blood vessels involved, or the number of blockages or vessels that could be treated.	Orsiro	Resolute	Target vessel failure
Pilgrim	BIOSCIENCE	2018	2119	Median Age: Tx: 66.7 (IQR: 33.5- 90.2) Cx: 66.6 (IQR: 38.6- 89.1)	60	Symptomatic coronary artery disease. Presence of one or more coronary artery stenoses > 50% in a native coronary artery or a saphenous bypass graft. No limitation on the number of treated lesions, and ves- sels, and lesion length.	Orsiro	Xience	Target lesion failure
Takahashi	DESSOLVE III	2020	1398	Tx: 66.4 ± 10.7 Cx: 66.3 ± 10.7	36	Patients who were at least 18 years old and had undergone percutaneous coronary intervention for a lesion with a reference vessel diameter ranging from 2.50 to 3.75 mm.	MiStent	Xience	Device oriented composite endpoint or target lesion failure
Kim	ORIENT	2019	372	65.1 ± 11.6	36	Symptomatic coronary artery disease and coronary lesions > 50%, and indicated for PCI with DES implantation.	Orsiro	Resolute Integrity	Late lumen loss (in-stent)

Zivelonghi	PRISON-IV	2019	330	Tx: 62.4 ± 10.5 Cx: 62.8 ± 9.5	36	Patients who were older than 18 years could participate in the study if they had total occlusions or chronic total occlu- sions (CTOs) that were estimated to have lasted for at least 4 weeks. The reference diameter of the target blood vessel for intervention needed to be within the range of 2.25 to 4.0 mm.	Orsiro	Xience	In-segment late luminal loss
Hansen	SORT-OUT VII	2020	2525	Tx: 66.1 ± 10.7 Cx: 64.8 ± 10.8	60	Patients who were at least 18 years old and had either chronic stable coronary ar- tery disease or acute coronary syndromes were eligible for inclusion in the study. Additionally, they needed to have at least one coronary artery lesion with a diameter stenosis greater than 50%.	Orsiro	Nobori	Target lesion failure
Abizaid	meriT-V	2018	256	Tx: 64.33 ± 9.57 Cx: 64.70 ± 8.99	9	Patients with ischaemic heart disease or myocardial ischaemia were eligible for the study if they had up to two newly developed native coronary artery lesions, and the length of each lesion was equal to or less than 44 mm. Additionally, the reference vessel diameter of the target blood vessel needed to be between ≥ 2.5 and ≤ 3.5 mm.	BioMime	Xience	In-stent late lumen loss
Li	BIOFLOW-VI	2020	440	59.1 ± 8.5	12	Eligible patients had up to 2 new native lesions with a reference vessel diameter between 2.25 mm and 4.0 mm, and a le- sion length of < 36 mm.	Orsiro	Xience	In-stent late lumen loss
Ploumen 1	BIONYX	2020	2488	64.0 ± 11.0	36	Coronary syndrome, de novo or restenotic target lesions, any lesion length, refer- ence vessel size, and number of lesions or vessels.	Orsiro	Resolute Onyx	Target vessel failure
Iglesias	BIOSTEMI	2019	1300	Tx: 62.2 ± 11.8 Cx: 63.2 ± 11.8	24	Eligible patients had acute STEMI and were referred for primary PCI within 24 hours of symptom onset. They needed to have at least one culprit coronary lesion in native target coronary vessels suitable for drug- eluting stent implantation.	Orsiro	Xience	Target lesion failure
Ellert-Gregersen	SORT-OUT IX	2020	3151	66.3 ± 10.9	12	Coronary artery disease with > 50% diam- eter stenosis.	Orsiro	BioFreedom	Target lesion failure
Winter	TALENT	2019	1,435	Median Age: Tx: 66 (IQR: 58-72) Cx: 65 (IQR: 58-72)	36	Patients aged 18 years or older, with one or more coronary artery stenoses of 50% or greater in native coronary arteries, sa- phenous venous grafts, or arterial bypass conduits, and a reference vessel diameter between 2.25 and 4.50 mm were eligible.	Supraflex	Xience	Target lesion failure

Wijns	DESSOLVE II	2015	184	Tx: 65.0 ± 10.4 Cx: 65.1 ± 10.5	9	Eligible participants had either stable an- gina pectoris or class I-IV unstable angina pectoris, as well as documented overt or silent myocardial ischemia. They also had a single, newly formed coronary artery stenosis of type A, B1, or B2, with a visual estimate of more than 50% narrowing, in a native coronary artery with a visual esti- mate of diameter between 2.5 mm and 3.5 mm. This stenosis was suitable for cover- age with a stent of up to 30 mm in length.	MiStent	Endeavor	In-stent late lumen loss
Nakamura et al.	CASTLE	2022	1440	Tx: 70.1 ± 10.4 Cx: 70.4 ± 10.1	12	Participants aged 20 years or older, with coronary artery disease (atleast 1 lesion causing more than a 50% reduction in the diameter of the native coronary artery. Indicated for coronary revascularization.	Orsiro, Biotronik	Xience	Target lesion failure

*Mean age in years (± SD). **Follow-up in months (latest follow-up). ***"Tx": Treatment group (ultrathin-strut stent); "Cx": Control group (conventional thin-strut second generation stent).

Table S3. Quality assessment of included trials

Trial	Random sequence generation	Allocation concealment	Blinding of participants & personnel	Blinding of out- come assessment	Incomplete outcome data	Selective reporting	Overall Quality*
BIOFLOW-IV	Low risk- Computer generated	Low risk Central allocation	High risk Un-blinded-Open-label.	High risk Un-blinded.	Low risk 95% completed follow-up	Low risk	High
BIOFLOW-V	Low risk- Computer generated	Low risk Central allocation	High risk Incomplete blinding. Participants not blinded.	Low risk Blinded.	Low risk 95% completed follow-up	Low risk	High
BIOFLOW-II	Low risk- Computer generated	Low risk Central allocation	High risk Incomplete blinding. Participants not blinded.	Low risk Blinded.	Low risk 95% completed follow-up	Low risk	High
BIO-RESORT	Low risk- Computer generated	Low risk Central allocation	High risk Incomplete blinding. Clinicians not blinded.	Low risk Blinded.	Low risk 95% completed follow-up	Low risk	High
BIOSCIENCE	Low risk- Computer generated	Low risk Central allocation	High risk Incomplete blinding. Clinicians not blinded.	Low risk Blinded.	Low risk Over 95% completed follow-up	Low risk	High
DESSOLVE III	Low risk- Computer generated	Low risk Central allocation	High risk Incomplete blinding. Clinicians not blinded.	Low risk Blinded.	Low risk Over 95% completed follow-up	Low risk	High
ORIENT	Low risk- Computer generated	Low risk Central allocation	High risk Un-blinded-Open-label.	Unclear	Low risk	Low risk	High
PRISON-IV	Low risk- Computer generated	Low risk Central allocation	High risk Clinicians not blinded.	Low risk Blinded.	Low risk Over 95% completed follow-up	Low risk	High

SORT-OUT VII	Low risk- Permuted blocks with an undisclosed block size	Low risk Central allocation	High risk Un-blinded-Open-label.	Low risk Blinded.	Low risk Over 99% completed follow-up	Low risk	High
meriT-V	Low risk- Computer generated	Low risk Central allocation	High risk Un-blinded-Open-label.	Unclear	Low risk Over 95% completed follow-up	Low risk	High
BIOFLOW-VI	Low risk- Computer generated	Low risk Central allocation	High risk Un-blinded-Open-label.	Unclear	Low risk Over 99% completed follow-up	Low risk	High
BIONYX	Low risk- Computer generated	Low risk Central allocation	High risk Incomplete blinding. Clinicians not blinded.	Low risk Blinded.	Low risk Over 99% completed follow-up	Low risk	High
BIOSTEMI	Low risk- Computer generated	Low risk Central allocation	High risk Un-blinded.	Low risk Blinded.	Low risk Over 95% completed follow-up	Low risk	High
SORT-OUT IX	Low risk- permuted blocks with an undisclosed block size	Low risk Central allocation	High risk Physicians un-blinded.	Low risk Blinded.	Low risk Over 99% completed follow-up	Low risk	High
TALENT	Low risk- Computer generated	Low risk Central allocation	High risk Physicians un-blinded.	Low risk Blinded.	Low risk Over 95% completed follow-up	Low risk	High
DESSOLVE II	Low risk- Computer generated	Low risk Central allocation	High risk Physicians un-blinded.	Unclear	Low risk Over 95% completed follow-up	Low risk	High
CASTLE	Low risk- Computer generated	Low risk Central allocation	High risk Physicians un-blinded.	Low risk Blinded.	Low risk Over 95% completed follow-up	Low risk	High

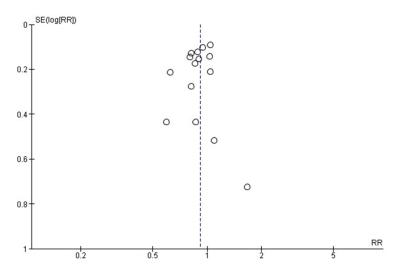


Figure S1. Funnel plot for the outcome of TLF.

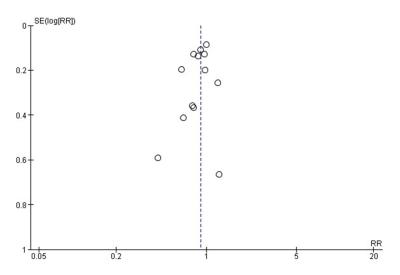


Figure S2. Funnel plot for the outcome of TVF.

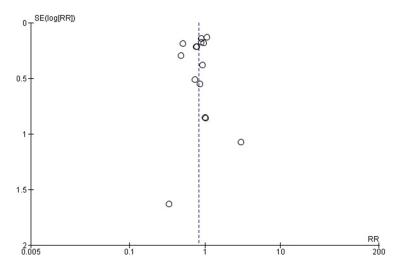


Figure S3. Funnel plot for the outcome of CD-TLR.

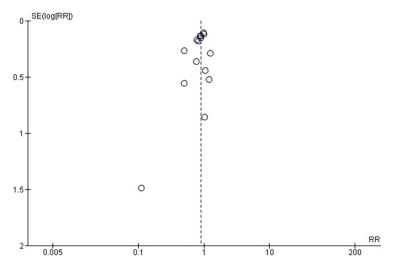


Figure S4. Funnel plot for the outcome of CD-TVR.

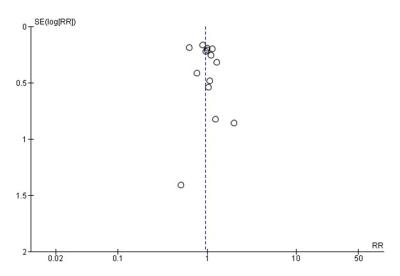


Figure S5. Funnel plot for the outcome of TV-MI.

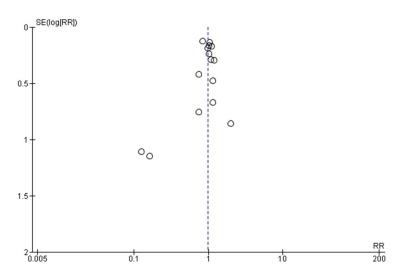


Figure S6. Funnel plot for the outcome of all cause MI.

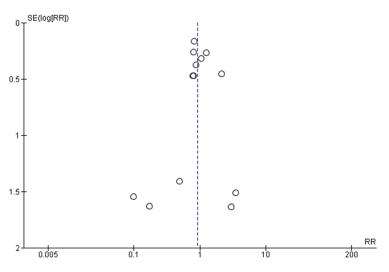


Figure S7. Funnel plot for the outcome of definite or probable ST.

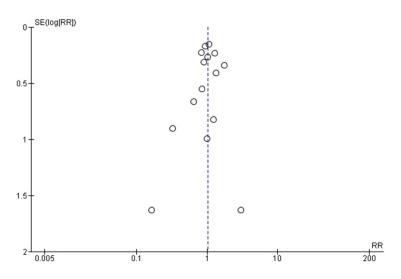


Figure S8. Funnel plot for the outcome of cardiac death.

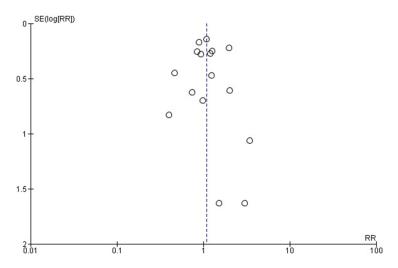


Figure S9. Funnel plot for the outcome of non-cardiac death.

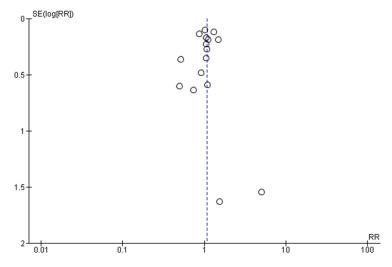
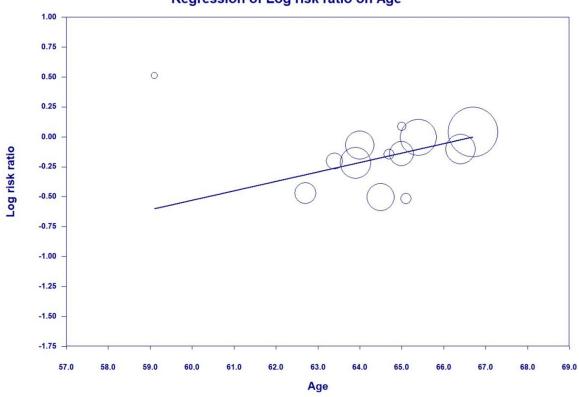


Figure S10. Funnel plot for the outcome of all-cause death.



Regression of Log risk ratio on Age

Figure S11. Regression of Log risk ratio on age.

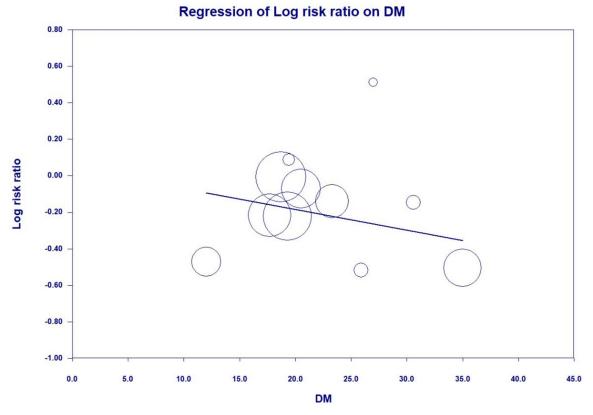


Figure S12. Regression of log risk ratio on diabetes mellitus.

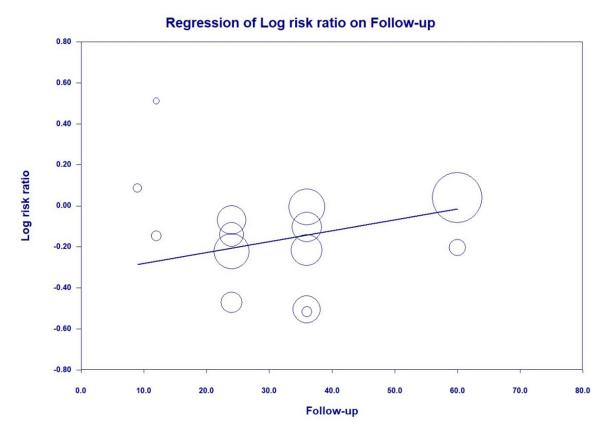


Figure S13. Regression of log risk ratio on follow-up duration.

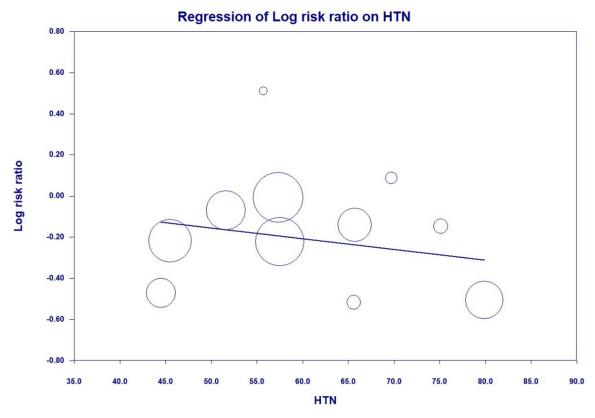


Figure S14. Regression of log risk ratio on hypertension.

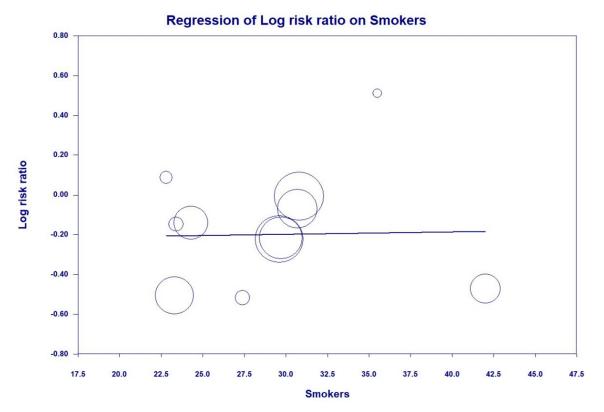


Figure S15. Regression of log risk ratio on smokers.

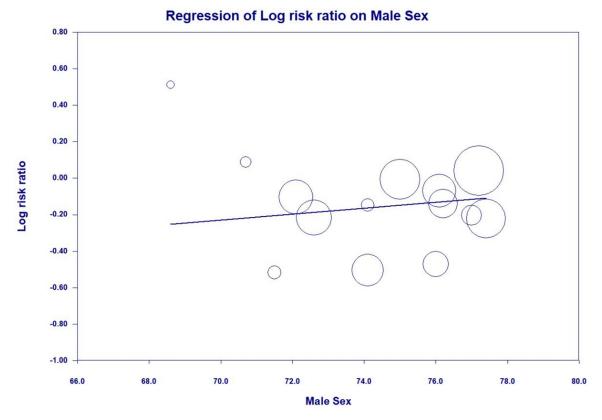


Figure S16. Regression of log risk ratio on male sex.

	Ultrathir	DEC	SecondGeneration Thi			Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events		Weight	M-H, Random, 95% Cl	Voar	M-H. Random, 95% Cl
1.2.1 Sirolimus vs Ever		Total	Lycino	Total	weight	m-n, random, 55% cr	rear	
Lefèvre 2018	30	298	19	154	2.3%	0.82 [0.48, 1.40]	2018	
Pilgrim 2018	198	1063	189	1056	20.4%	1.04 [0.87, 1.25]		
Saito 2019	14	385	8	190	0.9%	0.86 [0.37, 2.02]		
Iglesias 2019	33	649	53	651	3.7%	0.62 [0.41, 0.95]		
Li 2020	5	220	3	220	0.3%	1.67 [0.40, 6.89]		
Takahashi 2020	72	703	79	695	7.3%	0.90 [0.67, 1.22]	2020	
Winter 2022	57	720	66	715	5.8%	0.86 [0.61, 1.20]	2022	
Ploumen (2) 2022	113	1169	128	1173	11.5%	0.89 [0.70, 1.13]	2022	
Kandzari 2022	104	884	66	450	8.0%	0.80 [0.60, 1.07]	2022	
Nakamura 2022	43	722	41	718	3.8%	1.04 [0.69, 1.58]	2022	
Subtotal (95% CI)		6813		6022	64.1%	0.91 [0.82, 1.01]		•
Total events	669		652					
Heterogeneity: Tau ² = 0			= 9 (P = 0.59); I ² = 0%					
Test for overall effect: Z	= 1.81 (P =	0.07)						
1.2.2 Sirolimus vs Zota								
Wijns 2015	11	123	5	61	0.6%	1.09 [0.40, 3.00]		
Kim 2019	11	250	9	122	0.9%	0.60 [0.25, 1.40]		
Ploumen (1) 2021	91	1245 1618	88	1243 1426	8.3% 9.9 %	1.03 [0.78, 1.37] 0.99 [0.76, 1.28]	2021	
Subtotal (95% CI)		1018		1420	9.9%	0.99 [0.76, 1.28]		
Total events	113		102					
Heterogeneity: Tau ² = 0			= 2 (P = 0.48); P = 0%					
Test for overall effect: Z	= 0.11 (P =	0.91)						
1.2.3 Sirolimus vs Bioli	mus							
Ellert Gregersen 2022	100	1579	122	1572	10.2%	0.82 [0.63, 1.05]	2022	
Hansen 2023	156	1261	166	1264	15.9%	0.94 [0.77, 1.16]		
Subtotal (95% CI)		2840		2836		0.89 [0.76, 1.04]		◆
Total events	256		288					
Heterogeneity: Tau ² = 0	.00; Chi ² =	0.74, df	= 1 (P = 0.39); I ² = 0%					
Test for overall effect: Z	= 1.42 (P =	0.15)						
T-1-1 (0.5%) ON					100.00			
Total (95% CI)		11271		10284	100.0%	0.91 [0.84, 0.99]		▼
Total events	1038		1042					
			f=14 (P=0.76); I ² =0%				-	0.2 0.5 1 2 5
Test for overall effect: Z								Favours Ultrathin DES Favours Thin DES
l est for subgroup differ	rences: Chi	*= U.43.	df = 2 (P = 0.81), I ² = 0%					

Figure S17. Effect of anti-proliferative drug on TLF.

	Ultrathin	DES	SecondGeneration Th	in DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
1.5.1 Sirolimus vs Ev	erolimus							
Lefèvre 2018	45	298	19	154	3.1%	1.22 [0.74, 2.02]	2018	_ -
Pilgrim 2018	220	1063	219	1056	28.3%	1.00 [0.84, 1.18]	2018	+
Abizaid 2018	5	170	6	86	0.6%	0.42 [0.13, 1.34]	2018	
Saito 2019	19	385	12	190	1.6%	0.78 [0.39, 1.58]	2019	
Iglesias 2019	39	649	61	651	5.3%	0.64 [0.44, 0.94]	2019	_ _
Li 2020	5	220	4	220	0.5%	1.25 [0.34, 4.59]	2020	
Takahashi 2020	85	703	97	695	10.7%	0.87 [0.66, 1.14]	2020	
Ploumen (2) 2022	142	1169	157	1173	17.5%	0.91 [0.73, 1.12]	2022	
Kandzari 2022	127	884	81	450	12.1%	0.80 [0.62, 1.03]	2022	
Nakamura 2022	47	722	48	718	5.2%	0.97 [0.66, 1.44]	2022	
Subtotal (95% CI)		6263		5393	84.9%	0.90 [0.82, 0.99]		•
Total events	734		704					
Heterogeneity: Tau ² =	0.00; Chi	² = 9.02,	df = 9 (P = 0.44); I ² = 09	6				
Test for overall effect:	Z= 2.07 (P = 0.04)					
1.5.2 Sirolimus vs Zo	tarolimus							
Wijns 2015	12	123	9	61	1.2%	0.66 [0.29, 1.48]	2015	
Kim 2019	18	250	11	122	1.5%	0.80 [0.39, 1.64]	2019	
Ploumen (1) 2021	109	1245	112	1243	12.4%	0.97 [0.76, 1.25]	2021	+
Subtotal (95% CI)		1618		1426	15.1%	0.92 [0.74, 1.16]		
Total events	139		132					
Heterogeneity: Tau ² =	0.00; Chi	² = 0.97,	$df = 2 (P = 0.62); I^2 = 0.9$	6				
Test for overall effect:	Z=0.68 (P = 0.50)					
Total (95% CI)		7881		6819	100.0%	0.91 [0.83, 0.99]		•
Total events	873		836					
		² = 10.02	2, df = 12 (P = 0.61); I ² =	0%				
Test for overall effect:								
			, 03. df = 1 (P = 0.86), I ² =	0%				Favours Ultrathin DES Favours Thin DES

Figure S18. Effect of anti-proliferative drug on TVF.

	Ultrathin		SecondGeneration Thin			Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
1.6.1 Sirolimus vs Ever								
Abizaid 2018	4	170	2	86	0.7%			
Lefèvre 2018	18	298	10	154	3.3%	0.93 [0.44, 1.97]		
Pilgrim 2018	103	1063	97	1065		1.06 [0.82, 1.39]		T
Saito 2019	6	385	1	190		2.96 [0.36, 24.42]		
Iglesias 2019	16	649	33	651	5.1%	0.49 [0.27, 0.87]		
Takahashi 2020	35	703	44	695	8.7%	0.79 [0.51, 1.21]		
Li 2020	0	220	1	220	0.2%			
Kandzari 2022	48	884	32	450	8.7%	0.76 [0.50, 1.18]		
Nakamura 2022	6	722	7	718	1.6%			
Ploumen (2) 2022 Subtotal (95% Cl)	55	1169 6263	62	1173 5402		0.89 [0.62, 1.27] 0.88 [0.75, 1.03]	2022	•
Total events	291		289					
Heterogeneity: Tau ² = 0			= 9 (P = 0.51); I ² = 0%					
Test for overall effect: Z		0.12)						
1.6.2 Sirolimus vs Zota	rolimus							
Wijns 2015	4	123	2	61	0.7%	0.99 [0.19, 5.27]	2015	
Kim 2019	9	250	6	122	1.9%	0.73 [0.27, 2.01]	2019	
Ploumen (1) 2021 Subtotal (95% Cl)	55	1245 1618	57	1243 1426			2021	↓
Total events	68		65					
Heterogeneity: Tau ² = 0	.00; Chi ² =	0.26, df	= 2 (P = 0.88); I ² = 0%					
Test for overall effect: Z	= 0.39 (P =	0.70)						
1.6.3 Sirolimus vs Bioli	mus							
Ellert Gregersen 2022	41	1579	80	1572	11.1%	0.51 [0.35, 0.74]	2022	
Hansen 2023 Subtotal (95% CI)	84	1261 2840	94	1264 2836		0.90 [0.67, 1.19] 0.68 [0.39, 1.19]	2023	▲
Total events	125		174					-
Heterogeneity: Tau ² = 0		5.61. df						
Test for overall effect: Z								
Total (95% CI)		10721		9664	100.0%	0.83 [0.72, 0.95]		•
Total events	484		528					
Heterogeneity: Tau ² = 0	.01; Chi ² =	16.44. d	f = 14 (P = 0.29); I ² = 15%					
Test for overall effect: Z								0.005 0.1 1 10 200 Favours Ultrathin DES Favours Thin DES
			df = 2 (P = 0.63), I ² = 0%					Favours Oltrathin DES Favours Thin DES

Figure S19. Effect of anti-proliferative drug on CD-TLR.

	Ultrathin		SecondGeneration Thin			Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
1.7.1 Sirolimus vs Ever	olimus							
Abizaid 2018	4	170	2	86	0.3%	1.01 [0.19, 5.41]		
Lefèvre 2018	36	298	15	154	2.9%	1.24 [0.70, 2.19]		
Pilgrim 2018	125	1063	123	1056	17.2%	1.01 [0.80, 1.28]	2018	+
Saito 2019	12	385	5	190	0.9%	1.18 [0.42, 3.31]	2019	
Iglesias 2019	20	649	40	651	3.4%	0.50 [0.30, 0.85]	2019	
Li 2020	0	220	4	220	0.1%	0.11 [0.01, 2.05]		
Takahashi 2020	51	703	62	695	7.4%	0.81 [0.57, 1.16]	2020	
Kandzari 2022	78	884	51	450	8.4%	0.78 [0.56, 1.09]	2022	
Nakamura 2022	13	722	17	718	1.8%	0.76 [0.37, 1.55]	2022	
Ploumen (2) 2022	91	1169	101	1173	12.7%	0.90 [0.69, 1.19]	2022	-
Subtotal (95% CI)		6263		5393	55.2%	0.87 [0.75, 1.01]		•
Total events	430		420					
Heterogeneity: Tau ² = 0	.01; Chi ² =	10.32, d	f= 9 (P = 0.33); I ² = 13%					
Test for overall effect: Z	= 1.83 (P =	0.07)						
1.7.2 Sirolimus vs Zota	rolimus							
/Vijns 2015	6	123	6	61	0.8%	0.50 [0.17, 1.47]	2015	
<im 2019<="" td=""><td>15</td><td>250</td><td>7</td><td>122</td><td>1.2%</td><td>1.05 [0.44, 2.50]</td><td>2019</td><td></td></im>	15	250	7	122	1.2%	1.05 [0.44, 2.50]	2019	
Ploumen (1) 2021	75	1245	84	1243	10.3%	0.89 [0.66, 1.20]	2021	-
Subtotal (95% CI)		1618		1426	12.4%	0.87 [0.66, 1.15]		•
Total events	96		97					
Heterogeneity: Tau ² = 0	.00; Chi ² =	1.22, df	= 2 (P = 0.54); I ² = 0%					
Test for overall effect: Z	= 0.97 (P =	0.33)						
1.7.3 Sirolimus vs Bioli	mus							
Ellert Gregersen 2022	91	1579	104	1572	12.6%	0.87 [0.66, 1.14]	2022	
Hansen 2023	141	1261	146	1264	19.8%	0.97 [0.78, 1.20]	2023	+
Subtotal (95% CI)		2840		2836	32.4%	0.93 [0.78, 1.10]		•
Total events	232		250					
Heterogeneity: Tau² = 0	.00; Chi ² =	0.35, df:	= 1 (P = 0.55); I ² = 0%					
Test for overall effect: Z	= 0.85 (P =	0.40)						
fotal (95% CI)		10721		9655	100.0%	0.89 [0.81, 0.99]		•
Total events	758		767					
	.00: Chi ² =	12.17. d	f=14 (P=0.59); I ² =0%					
Test for overall effect: Z								0.005 0.1 1 10 20
			df = 2 (P = 0.84), I ² = 0%					Favours Ultrathin DES Favours Thin DES

Figure S20. Effect of anti-proliferative drug on CD-TVR.

	Ultrathin		SecondGeneration Thin			Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
1.3.1 Sirolimus vs Ever	olimus							
Abizaid 2018	1	170	1	86	0.3%	0.51 [0.03, 7.99]	2018	
Lefèvre 2018	10	298	5	154	1.8%	1.03 [0.36, 2.97]	2018	
Pilgrim 2018	62	1063	69	1056	17.7%	0.89 [0.64, 1.24]	2018	
Saito 2019	13	385	6	190	2.2%	1.07 [0.41, 2.77]	2019	
Iglesias 2019	10	649	13	651	2.9%	0.77 [0.34, 1.75]	2019	
Li 2020	4	220	2	220	0.7%	2.00 [0.37, 10.81]	2020	
Takahashi 2020	22	703	17	695	5.0%	1.28 [0.69, 2.39]	2020	- +
Ploumen (2) 2022	50	1169	50	1173	13.3%	1.00 [0.68, 1.47]	2022	+
Kandzari 2022	56	884	45	450	13.8%	0.63 [0.44, 0.92]	2022	
Nakamura 2022	31	722	28	718	7.8%	1.10 [0.67, 1.82]	2022	_ - _
Subtotal (95% CI)		6263		5393	65.3%	0.90 [0.76, 1.08]		•
Total events	259		236					
Heterogeneity: Tau ² = 0	.00; Chi ² = I	6.87, df:	= 9 (P = 0.65); I ² = 0%					
Test for overall effect: Z			- (,					
1.3.2 Sirolimus vs Zota	rolimus							
Wijns 2015	5	123	2	61	0.8%	1.24 [0.25, 6.21]	2015	
Ploumen (1) 2021	38	1245	39	1243	10.1%	0.97 [0.63, 1.51]	2021	-
Subtotal (95% CI)		1368		1304	10.8%	0.99 [0.65, 1.51]		◆
Total events	43		41					
Heterogeneity: Tau ² = 0	.00; Chi ² =	0.08, df:	= 1 (P = 0.78); I ² = 0%					
Test for overall effect: Z								
1.3.3 Sirolimus vs Bioli	imus							
Ellert Gregersen 2022	43	1579	43	1572	11.2%	1.00 [0.66, 1.51]	2022	
Hansen 2023	51	1261	45	1264	12.6%	1.14 [0.77, 1.68]		
Subtotal (95% CI)		2840		2836	23.8%	1.07 [0.80, 1.42]		
Total events	94		88			. , .		[
Heterogeneity: Tau ² = 0		0.20. df:						
Test for overall effect: Z								
	2.14 (/ -	,						
Total (95% CI)		10471		9533	100.0%	0.95 [0.83, 1.09]		•
Total events	396		365					1
		8 1 4 df	= 13 (P = 0.83); I ² = 0%					
			- 10 (1 = 0.00),1 = 0.0					0.02 0.1 1 10 50
Test for overall effect: Z								Favours Ultrathin DES Favours Thin DES

Figure S21. Effect of anti-proliferative drug on TV-MI.

	Ultrathin		SecondGeneration Thin			Risk Ratio		Risk Ratio
Study or Subgroup 1.4.1 Sirolimus vs Evero	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
		1063	110	1050	22.70	0.00/0.05 4.071	204.0	
Pilgrim 2018	99		118	1056	22.7%	0.83 [0.65, 1.07]		
Abizaid 2018	1	170	4	86	0.3%	0.13 [0.01, 1.11]		
Lefèvre 2018	13	298	9	154	2.1%	0.75 [0.33, 1.71]		
Saito 2019	14	385	6	190	1.6%	1.15 [0.45, 2.95]		
Iglesias 2019 Zhalanaki 2010	24	649	20	651	4.3%	1.20 [0.67, 2.16]		
Zivelonghi 2019	3	165	4	165	0.7%	0.75 [0.17, 3.30]		
Li 2020	4	220	2	220	0.5%	2.00 [0.37, 10.81]		
Takahashi 2020	24	703	22	695	4.5%	1.08 [0.61, 1.91]		
Ploumen (2) 2022	66	1169	60	1173	12.6%	1.10 [0.79, 1.55]		
Nakamura 2022 Subtotal (95% CI)	33	722 5544	32	718 5108	6.4% 55.7%	1.03 [0.64, 1.65] 0.96 [0.81, 1.12]	2022	T
Total events	281	5544	277	5108	55.770	0.90 [0.01, 1.12]		T
Heterogeneity: Tau ² = 0.1		7 22 46						
Heterogeneity: Tau-= 0. Test for overall effect: Z =			= 9 (P = 0.60); F = 0%					
restion overall ellect. Z -	- 0.04 (F -	0.55)						
1.4.2 Sirolimus vs Zotar	olimus							
Wijns 2015	7	123	3	61	0.8%	1.16 [0.31, 4.32]	2015	
Kim 2019	1	250	3	122	0.3%	0.16 [0.02, 1.55]	2019	
Ploumen (1) 2021	54	1245	55	1243	10.8%	0.98 [0.68, 1.42]	2021	+
Subtotal (95% CI)		1618		1426	11.9%	0.90 [0.49, 1.63]		•
Total events	62		61					
Heterogeneity: Tau² = 0.			= 2 (P = 0.29); I ² = 19%					
Test for overall effect: Z =	= 0.36 (P =	0.72)						
1.4.3 Sirolimus vs Biolir	nus							
Ellert Gregersen 2022	69	1579	67	1572	13.5%	1.03 [0.74, 1.42]	2022	+
Hansen 2023	94	1261	91	1264	18.9%	1.04 [0.78, 1.37]	2023	+
Subtotal (95% CI)		2840		2836	32.3%	1.03 [0.83, 1.27]		♦
Total events	163		158					
Heterogeneity: Tau ² = 0.1	00; Chi ² = I	0.00, df:	= 1 (P = 0.96); I ² = 0%					
Test for overall effect: Z =	= 0.28 (P =	0.78)						
Total (95% CI)		10002		9370	100.0%	0.98 [0.87, 1.10]		4
Total events	506		496]
Heterogeneity: Tau ² = 0.1		10.13 d						+ + + +
Test for overall effect: Z =								0.005 0.1 1 10 2
reactor overall ellect. Z -			df = 2 (P = 0.82), I ² = 0%					Favours Ultrathin DES Favours Thin DES

Figure S22. Effect of anti-proliferative drug on all-cause MI.

	Ultrathin		SecondGeneration Thin			Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
1.8.1 Sirolimus vs Ever	olimus							
Abizaid 2018	0	170	0	86		Not estimable		
Lefèvre 2018	0	298	1	154	0.4%	0.17 [0.01, 4.22]		
Pilgrim 2018	62	1063	76	1056	37.6%	0.81 [0.59, 1.12]		
Saito 2019	3	385	0	190	0.5%	3.46 [0.18, 66.72]		
Iglesias 2019	13	649	15	651	7.3%	0.87 [0.42, 1.81]		
Li 2020	0	220	0	220		Not estimable		
Takahashi 2020	8	703	10	695	4.6%	0.79 [0.31, 1.99]		
/Vinter 2022	8	720	10	715	4.6%	0.79 [0.32, 2.00]	2022	
Ploumen (2) 2022	20	1169	19	1173	10.2%	1.06 [0.57, 1.97]	2022	_ + _
Nakamura 2022	1	722	0	718	0.4%	2.98 [0.12, 73.11]	2022	
Subtotal (95% CI)		6099		5658	65.6%	0.86 [0.67, 1.09]		•
Total events	115		131					
Heterogeneity: Tau ² = 0.	00; Chi ² = 3	3.01, df	= 7 (P = 0.88); I ² = 0%					
Test for overall effect: Z	= 1.24 (P =	0.21)						
1.8.2 Sirolimus vs Zota	rolimus							
Niins 2015	1	123	1	61	0.5%	0.50 [0.03, 7.79]	2015	
<im 2019<="" td=""><td>0</td><td>250</td><td>2</td><td>122</td><td>0.4%</td><td>0.10 [0.00, 2.03]</td><td></td><td></td></im>	0	250	2	122	0.4%	0.10 [0.00, 2.03]		
Ploumen (1) 2021	15	1245	7	1243	5.0%	2.14 [0.88, 5.23]		
Subtotal (95% CI)		1618		1426	5.9%	0.73 [0.12, 4.59]	2021	
Total events	16		10					
Heterogeneity: Tau ² = 1.	47; Chi ² = 4	4.39, df	= 2 (P = 0.11); I ² = 54%					
Test for overall effect: Z	= 0.33 (P =	0.74)						
1.8.3 Sirolimus vs Bioli	nus							
Ellert Gregersen 2022	30	1579	24	1572	14.0%	1.24 [0.73, 2.12]	2022	
Hansen 2023	25	1261	31	1264	14.6%	0.81 [0.48, 1.36]		
Subtotal (95% CI)		2840		2836	28.5%	1.00 [0.65, 1.53]		•
Fotal events	55		55					
Heterogeneity: Tau ² = 0.	02; Chi ² = '	1.29, df	= 1 (P = 0.26); I ² = 22%					
Test for overall effect: Z	= 0.00 (P =	1.00)	. //					
fotal (95% CI)		10557		9920	100.0%	0.92 [0.76, 1.13]		4
Total events	186		196			. , .		
		10.54 d	f = 12 (P = 0.57); I ² = 0%					
Fest for overall effect: Z								0.005 0.1 1 10 200
			df = 2 (P = 0.81), I ² = 0%					Favours Ultrathin DES Favours Thin DES

Figure S23. Effect of anti-proliferative drug on definite or probable ST.

	Ultrathin		SecondGeneration Thin			Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
1.9.1 Sirolimus vs Ever	limus							
Abizaid 2018	0	170	0	86		Not estimable	2018	
Lefèvre 2018	5	298	4	154	1.4%	0.65 [0.18, 2.37]	2018	
Pilgrim 2018	81	1063	76	1056	26.2%	1.06 [0.78, 1.43]	2018	+
Iglesias 2019	19	649	21	651	6.4%	0.91 [0.49, 1.67]	2019	
Zivelonghi 2019	2	165	2	165	0.6%	1.00 [0.14, 7.01]	2019	
Saito 2019	0	385	1	190	0.2%	0.16 [0.01, 4.03]	2019	
Takahashi 2020	27	703	26	695	8.5%	1.03 [0.61, 1.74]	2020	+
Li 2020	1	220	0	220	0.2%	3.00 [0.12, 73.24]	2020	
Ploumen (2) 2022	33	1169	40	1173	11.6%	0.83 [0.53, 1.30]	2022	
Kandzari 2022	21	884	8	450	3.7%	1.34 [0.60, 2.99]	2022	- -
Nakamura 2022	6	722	7	718	2.0%	0.85 [0.29, 2.52]	2022	
Subtotal (95% CI)		6428		5558	60.9 %	0.98 [0.81, 1.20]		♦
Total events	195		185					
Heterogeneity: Tau ² = 0.	00; Chi ² = 1	3.57, df:	= 9 (P = 0.94); I ² = 0%					
Test for overall effect: Z =	= 0.18 (P =	0.86)						
1.9.2 Sirolimus vs Zotar								
Nijns 2015	5	123	2	61	0.9%	1.24 [0.25, 6.21]		
Kim 2019	2	250	3	122	0.8%	0.33 [0.06, 1.92]		
Ploumen (1) 2021	23	1245	13	1243	5.2%	1.77 [0.90, 3.47]	2021	
Subtotal (95% CI)		1618		1426	6.9%	1.17 [0.48, 2.86]		
Fotal events	30		18					
Heterogeneity: Tau² = 0.	24; Chi² = 1	3.07, df:	= 2 (P = 0.22); I ² = 35%					
Test for overall effect: Z =	= 0.34 (P =	0.73)						
1.9.3 Sirolimus vs Biolir	nus							
Ellert Gregersen 2022	41	1579	32	1572	11.4%	1.28 [0.81, 2.01]	2022	
Hansen 2023	62	1261	66	1264	20.9%	0.94 [0.67, 1.32]		+
Subtotal (95% CI)		2840		2836	32.2%	1.05 [0.79, 1.40]	2020	
Total events	103		98					Ť
Heterogeneity: Tau ² = 0.		1 10 df:						
Test for overall effect: Z =								
		,						
Total (95% CI)		10886		9820	100.0%	1.03 [0.88, 1.20]		♦
Total events	328		301					
Heterogeneity: Tau ² = 0.	00; Chi ² =	9.02, df:	= 14 (P = 0.83); I ² = 0%					0.005 0.1 1 10 20
	0.24 /0 -	0 7 2						
Test for overall effect: Z =	- U.34 (F =	0.73)						Favours Ultrathin DES Favours Thin DES

Figure S24. Effect of anti-proliferative drug on cardiac death.

	Ultrathin		SecondGeneration Thin			Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
1.10.1 Sirolimus vs Ev								
Abizaid 2018	1	170	0	86	0.3%	1.53 [0.06, 37.08]		
Lefèvre 2018	9	298	10	154	3.8%	0.47 [0.19, 1.12]		
Pilgrim 2018	58	1063	29	1056	11.8%	1.99 [1.28, 3.08]		
Zivelonghi 2019	2	165	5	165	1.2%	0.40 [0.08, 2.03]		
Saito 2019	6	385	3	190	1.6%	0.99 [0.25, 3.90]		
glesias 2019	8	649	4	651	2.2%	2.01 [0.61, 6.63]	2019	
Li 2020	1	220	0	220	0.3%	3.00 [0.12, 73.24]	2020	
Takahashi 2020	28	703	23	695	8.6%	1.20 [0.70, 2.07]	2020	
Ploumen (2) 2022	59	1169	66	1173	16.1%	0.90 [0.64, 1.26]	2022	
Kandzari 2022	35	884	19	450	8.5%	0.94 [0.54, 1.62]	2022	
Nakamura 2022	10	722	8	718	3.5%	1.24 [0.49, 3.13]	2022	
Subtotal (95% CI)		6428		5558	57.9%	1.10 [0.82, 1.48]		•
Total events	217		167					
Heterogeneity: Tau ² = 0	1.07; Chi ² =	15.47, d	f = 10 (P = 0.12); I ² = 35%					
Test for overall effect: Z	= 0.63 (P =	0.53)						
1.10.2 Sirolimus vs Zo	tarolimus							
/Vijns 2015	6	123	4	61	2.0%	0.74 [0.22, 2.54]		
Kim 2019	7	250	1	122	0.7%	3.42 [0.43, 27.46]		
Ploumen (1) 2021	34	1245	27	1243	9.7%	1.26 [0.76, 2.07]	2021	
Subtotal (95% CI)		1618		1426	12.5%	1.23 [0.78, 1.93]		•
Total events	47		32					
Heterogeneity: Tau² = 0			= 2 (P = 0.45); I ² = 0%					
Test for overall effect: Z	= 0.89 (P =	0.37)						
1.10.3 Sirolimus vs Bio	limus							
Ellert Gregersen 2022	27	1579	32	1572	9.5%	0.84 [0.51, 1.40]	2022	
Hansen 2023	96	1261	89	1264	20.1%	1.08 [0.82, 1.43]		-
Subtotal (95% CI)	50	2840	03	2836	20.1%	1.02 [0.80, 1.30]	2023	▲
Total events	123	2010	121	2000	Lolon	102 [0100, 1100]		Ť
Heterogeneity: Tau² = 0		0 73 df						
Test for overall effect: Z			- 1 (1 - 0.00), 1 - 0.00					
Confort overall ellett. Z	- 5.10 (* -	0.077						
Fotal (95% CI)		10886		9820	100.0%	1.09 [0.91, 1.30]		•
Total events	387		320					[
		18 37 d	f= 15 (P = 0.24); I ² = 18%					· · · · · · · · · · · · · · · · · · ·
Test for overall effect: Z			- 10 0 - 0.24),1 - 10 0					0.01 0.1 i 10 1
			df = 2 (P = 0.77), I ² = 0%					Favours Ultrathin DES Favours Thin DES

Figure S25. Effect of anti-proliferative drug on non-cardiac death.

Ct	Ultrathir		SecondGeneration Thi		144-1-1-4	Risk Ratio		Risk Ratio
Study or Subgroup 1.11.1 Sirolimus vs Eve	Events	Total	Events	Total	weight	M-H, Random, 95% Cl	rear	M-H, Random, 95% Cl
Lefèvre 2018	14	298	14	154	2.2%	0.50.00.05.4.001	2010	
	14	1063	14	1056	2.2%	0.52 [0.25, 1.06]		
Pilgrim 2018 Abizaid 2018	139	1003	0	1056	0.1%	1.32 [1.04, 1.67]		
	4		8		0.1%	1.53 [0.06, 37.08]		
Zivelonghi 2019		165		165		0.50 [0.15, 1.63]		
Saito 2019	6	385	4	190	0.7%	0.74 [0.21, 2.59]		
lglesias 2019 Tababa abi 2000	27	649	25	651	3.9%	1.08 [0.64, 1.85]		
Takahashi 2020	55	703	49	695	8.0%	1.11 [0.77, 1.61]		
Li 2020	2	220	0	220	0.1%	5.00 [0.24, 103.55]		
Ploumen (2) 2022	92	1169	106	1173	14.8%	0.87 [0.67, 1.14]		-
Kandzari 2022	56	884	27	450	5.6%	1.06 [0.68, 1.65]		
Nakamura 2022 Subtotal (95% CI)	16	722 6428	15	718 5558	2.3% 56.8%	1.06 [0.53, 2.13] 1.03 [0.87, 1.22]	2022	•
Total events	412		353					
Heterogeneity: Tau ² = 0.	01; Chi ² =	12.06, d	f = 10 (P = 0.28); I ² = 17%	5				
Test for overall effect: Z =	= 0.31 (P =	0.76)						
1.11.2 Sirolimus vs Zota	arolimus							
Wijns 2015	11	123	6	61	1.3%	0.91 [0.35, 2.34]	2015	
Kim 2019	9	250	4	122	0.9%	1.10 [0.34, 3.49]	2019	
Ploumen (1) 2021 Subtotal (95% Cl)	67	1245 1618	45	1243 1426	8.0% 10.2 %	1.49 [1.03, 2.15] 1.37 [0.98, 1.90]	2021	◆
Total events	87		55					
Heterogeneity: Tau ² = 0.	00: Chi ² =	1.05. df	= 2 (P = 0.59); I ² = 0%					
Test for overall effect: Z =								
1.11.3 Sirolimus vs Biol	limus							
Ellert Gregersen 2022	68	1579	64	1572	9.7%	1.06 [0.76, 1.48]	2022	+
Hansen 2023	158	1261	155	1264	23.3%	1.02 [0.83, 1.26]		+
Subtotal (95% CI)		2840		2836	33.0%	1.03 [0.86, 1.23]		♦
Total events	226		219					
Heterogeneity: Tau ² = 0.		0.03, df						
Test for overall effect: Z =								
Total (95% CI)		10886		9820	100.0%	1.07 [0.96, 1.19]		•
Total events	725		627					
		15.50. d	f= 15 (P = 0.42); I ² = 3%				-	
Test for overall effect: Z =							1	0.01 0.1 1 10 1
			$df = 2 (P = 0.29), I^2 = 19.1$					Favours Ultrathin DES Favours Thin DES

Figure S26. Effect of anti-proliferative drug on all-cause death.

	Ultrathin	DES	SecondGeneration Thi	n DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Wijns 2015	11	123	5	61	0.0%	1.09 [0.40, 3.00]	2015	
Pilgrim 2018	198	1063	189	1056	40.7%	1.04 [0.87, 1.25]	2018	-
Lefèvre 2018	30	298	19	154	7.8%	0.82 [0.48, 1.40]	2018	
Saito 2019	14	385	8	190	3.3%	0.86 [0.37, 2.02]	2019	
Iglesias 2019	33	649	53	651	12.1%	0.62 [0.41, 0.95]	2019	
Kim 2019	11	250	9	122	0.0%	0.60 [0.25, 1.40]	2019	
Li 2020	5	220	3	220	1.2%	1.67 [0.40, 6.89]	2020	
Takahashi 2020	72	703	79	695	0.0%	0.90 [0.67, 1.22]	2020	
Ploumen (1) 2021	91	1245	88	1243	0.0%	1.03 [0.78, 1.37]	2021	
Winter 2022	57	720	66	715	0.0%	0.86 [0.61, 1.20]	2022	
Ploumen (2) 2022	113	1169	128	1173	0.0%	0.89 [0.70, 1.13]	2022	
Kandzari 2022	104	884	66	450	22.5%	0.80 [0.60, 1.07]	2022	
Ellert Gregersen 2022	100	1579	122	1572	0.0%	0.82 [0.63, 1.05]	2022	
Nakamura 2022	43	722	41	718	12.4%	1.04 [0.69, 1.58]	2022	
Hansen 2023	156	1261	166	1264	0.0%	0.94 [0.77, 1.16]	2023	
Total (95% CI)		4221		3439	100.0%	0.91 [0.77, 1.06]		•
Total events	427		379					
Heterogeneity: Tau ² = 0.	01; Chi ² = 1	7.16, df	= 6 (P = 0.31); I ² = 16%				-	
Test for overall effect: Z:	= 1.23 (P =	0.22)						0.2 0.5 1 2 5 Favours Ultrathin DES Favours Thin DES

Figure S27. Sensitivity analysis based on stent type for TLF.

	Ultrathin	DES	SecondGeneration Thin	DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Wijns 2015	12	123	9	61	0.0%	0.66 [0.29, 1.48]	2015	
Abizaid 2018	5	170	6	86	0.0%	0.42 [0.13, 1.34]	2018	
Lefèvre 2018	45	298	19	154	7.6%	1.22 [0.74, 2.02]	2018	
Pilgrim 2018	220	1063	219	1056	39.8%	1.00 [0.84, 1.18]	2018	+
Saito 2019	19	385	12	190	4.1%	0.78 [0.39, 1.58]	2019	
Iglesias 2019	39	649	61	651	12.0%	0.64 [0.44, 0.94]	2019	
Kim 2019	18	250	11	122	0.0%	0.80 [0.39, 1.64]	2019	
Li 2020	5	220	4	220	1.2%	1.25 [0.34, 4.59]	2020	
Takahashi 2020	85	703	97	695	0.0%	0.87 [0.66, 1.14]	2020	
Ploumen (1) 2021	109	1245	112	1243	0.0%	0.97 [0.76, 1.25]	2021	
Ploumen (2) 2022	142	1169	157	1173	0.0%	0.91 [0.73, 1.12]	2022	
Kandzari 2022	127	884	81	450	23.4%	0.80 [0.62, 1.03]	2022	
Nakamura 2022	47	722	48	718	11.9%	0.97 [0.66, 1.44]	2022	-+-
Total (95% CI)		4221		3439	100.0%	0.90 [0.78, 1.04]		•
Total events	502		444					
Heterogeneity: Tau ² =	0.01; Chi ^a	= 7.21,	df = 6 (P = 0.30); I ² = 17%					0.05 0.2 1 5 20
Test for overall effect:	Z=1.38 (F	P = 0.17)					0.05 0.2 1 5 20 Favours Ultrathin DES Favours Thin DES

Figure S28.	Sensitivity	analysis based	on stent type for TVF.
	e e nonci neg		

	Ultrathin	DES	SecondGeneration This	n DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Wijns 2015	4	123	2	61	0.0%	0.99 [0.19, 5.27]	2015	
Abizaid 2018	4	170	2	86	0.0%	1.01 [0.19, 5.41]	2018	
Lefèvre 2018	18	298	10	154	11.2%	0.93 [0.44, 1.97]	2018	
Pilgrim 2018	103	1063	97	1065	39.7%	1.06 [0.82, 1.39]	2018	+
Kim 2019	9	250	6	122	0.0%	0.73 [0.27, 2.01]	2019	
Saito 2019	6	385	1	190	1.7%	2.96 [0.36, 24.42]	2019	
Iglesias 2019	16	649	33	651	16.3%	0.49 [0.27, 0.87]	2019	
Takahashi 2020	35	703	44	695	0.0%	0.79 [0.51, 1.21]	2020	
Li 2020	0	220	1	220	0.7%	0.33 [0.01, 8.14]	2020	
Ploumen (1) 2021	55	1245	57	1243	0.0%	0.96 [0.67, 1.38]	2021	
Kandzari 2022	48	884	32	450	24.6%	0.76 [0.50, 1.18]	2022	
Nakamura 2022	6	722	7	718	5.8%	0.85 [0.29, 2.52]	2022	
Ellert Gregersen 2022	41	1579	80	1572	0.0%	0.51 [0.35, 0.74]	2022	
Ploumen (2) 2022	55	1169	62	1173	0.0%	0.89 [0.62, 1.27]	2022	
Hansen 2023	84	1261	94	1264	0.0%	0.90 [0.67, 1.19]	2023	
Total (95% CI)		4221		3448	100.0%	0.85 [0.64, 1.12]		•
Total events	197		181					
Heterogeneity: Tau ² = 0.	.03; Chi ² = 1	7.93, df	= 6 (P = 0.24); I ² = 24%					
Test for overall effect: Z								0.005 0.1 1 10 200 Favours Ultrathin DES Favours Thin DES

Figure S29.	Sensitivity	analvsis	based on	stent type	for	CD-TLR.
	••••••••	0.1.10.1.9 0.10				

	Ultrathin	DES	SecondGeneration Thin	DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% CI
Wijns 2015	6	123	6	61	0.0%	0.50 [0.17, 1.47]	2015	
Abizaid 2018	4	170	2	86	0.0%	1.01 [0.19, 5.41]	2018	
Lefèvre 2018	36	298	15	154	13.7%	1.24 [0.70, 2.19]	2018	
Pilgrim 2018	125	1063	123	1056	30.7%	1.01 [0.80, 1.28]	2018	+
Kim 2019	15	250	7	122	0.0%	1.05 [0.44, 2.50]	2019	
Saito 2019	12	385	5	190	5.5%	1.18 [0.42, 3.31]	2019	
Iglesias 2019	20	649	40	651	15.2%	0.50 [0.30, 0.85]	2019	
Li 2020	0	220	4	220	0.8%	0.11 [0.01, 2.05]	2020	
Takahashi 2020	51	703	62	695	0.0%	0.81 [0.57, 1.16]	2020	
Ploumen (1) 2021	75	1245	84	1243	0.0%	0.89 [0.66, 1.20]	2021	
Kandzari 2022	78	884	51	450	24.3%	0.78 [0.56, 1.09]	2022	
Ellert Gregersen 2022	91	1579	104	1572	0.0%	0.87 [0.66, 1.14]	2022	
Nakamura 2022	13	722	17	718	9.9%	0.76 [0.37, 1.55]	2022	
Ploumen (2) 2022	91	1169	101	1173	0.0%	0.90 [0.69, 1.19]	2022	
Hansen 2023	141	1261	146	1264	0.0%	0.97 [0.78, 1.20]	2023	
Total (95% CI)		4221		3439	100.0%	0.85 [0.65, 1.09]		•
Total events	284		255					
Heterogeneity: Tau ² = 0.	.04; Chi ² =	10.07, d	f= 6 (P = 0.12); I ² = 40%					
Test for overall effect: Z								0.005 0.1 1 10 200 Favours Ultrathin DES Favours Thin DES

Figure S30. Sensitivity analysis based on stent type for CD-TVR.

	Ultrathin	DES	SecondGeneration Thi	in DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Wijns 2015	7	123	3	61	0.0%	1.16 [0.31, 4.32]	2015	
Lefèvre 2018	13	298	9	154	5.5%	0.75 [0.33, 1.71]	2018	
Pilgrim 2018	99	1063	118	1056	59.2%	0.83 [0.65, 1.07]	2018	
Abizaid 2018	1	170	4	86	0.0%	0.13 [0.01, 1.11]	2018	
Saito 2019	14	385	6	190	4.3%	1.15 [0.45, 2.95]	2019	
Iglesias 2019	24	649	20	651	11.1%	1.20 [0.67, 2.16]	2019	
Kim 2019	1	250	3	122	0.0%	0.16 [0.02, 1.55]	2019	
Zivelonghi 2019	3	165	4	165	1.7%	0.75 [0.17, 3.30]	2019	
Li 2020	4	220	2	220	1.3%	2.00 [0.37, 10.81]	2020	
Takahashi 2020	24	703	22	695	0.0%	1.08 [0.61, 1.91]	2020	
Ploumen (1) 2021	54	1245	55	1243	0.0%	0.98 [0.68, 1.42]	2021	
Ploumen (2) 2022	66	1169	60	1173	0.0%	1.10 [0.79, 1.55]	2022	
Ellert Gregersen 2022	69	1579	67	1572	0.0%	1.03 [0.74, 1.42]	2022	
Nakamura 2022	33	722	32	718	16.8%	1.03 [0.64, 1.65]	2022	+
Hansen 2023	94	1261	91	1264	0.0%	1.04 [0.78, 1.37]	2023	
Total (95% CI)		3502		3154	100.0%	0.92 [0.75, 1.11]		•
Total events	190		191					
Heterogeneity: Tau ² = 0.	.00; Chi ² =	2.95, df	= 6 (P = 0.81); I ² = 0%					0.005 0.1 1 10 200
Test for overall effect: Z	= 0.89 (P =	0.37)						0.005 0.1 1 10 200 Favours Ultrathin DES Favours Thin DES

Figure S31. Sensitivity analysis based on stent type for all-cause MI.

	Ultrathin	DES	SecondGeneration Thi	in DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% Cl
Wijns 2015	5	123	2	61	0.0%	1.24 [0.25, 6.21]	2015	
Abizaid 2018	1	170	1	86	0.0%	0.51 [0.03, 7.99]	2018	
Lefèvre 2018	10	298	5	154	3.7%	1.03 [0.36, 2.97]	2018	
Pilgrim 2018	62	1063	69	1056	37.8%	0.89 [0.64, 1.24]	2018	-
Saito 2019	13	385	6	190	4.6%	1.07 [0.41, 2.77]	2019	
Iglesias 2019	10	649	13	651	6.2%	0.77 [0.34, 1.75]	2019	
Li 2020	4	220	2	220	1.5%	2.00 [0.37, 10.81]	2020	
Takahashi 2020	22	703	17	695	0.0%	1.28 [0.69, 2.39]	2020	
Ploumen (1) 2021	38	1245	39	1243	0.0%	0.97 [0.63, 1.51]	2021	
Ploumen (2) 2022	50	1169	50	1173	0.0%	1.00 [0.68, 1.47]	2022	
Kandzari 2022	56	884	45	450	29.5%	0.63 [0.44, 0.92]	2022	
Ellert Gregersen 2022	43	1579	43	1572	0.0%	1.00 [0.66, 1.51]	2022	
Nakamura 2022	31	722	28	718	16.6%	1.10 [0.67, 1.82]	2022	-
Hansen 2023	51	1261	45	1264	0.0%	1.14 [0.77, 1.68]	2023	
Total (95% CI)		4221		3439	100.0%	0.85 [0.69, 1.04]		•
Total events	186		168					
Heterogeneity: Tau ² = 0.	.00; Chi ² =	4.87, df	= 6 (P = 0.56); I ² = 0%					
Test for overall effect: Z	= 1.57 (P =	0.12)						0.02 0.1 1 10 50 Favours Ultrathin DES Favours Thin DES

	Ultrathin	DES	SecondGeneration Thi	n DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Vijns 2015	1	123	1	61	0.0%	0.50 [0.03, 7.79]	2015	
Abizaid 2018	0	170	0	86		Not estimable	2018	
_efèvre 2018	0	298	1	154	0.8%	0.17 [0.01, 4.22]	2018	
Pilgrim 2018	62	1063	76	1056	81.5%	0.81 [0.59, 1.12]	2018	
Saito 2019	3	385	0	190	1.0%	3.46 [0.18, 66.72]	2019	
glesias 2019	13	649	15	651	15.9%	0.87 [0.42, 1.81]	2019	
Kim 2019	0	250	2	122	0.0%	0.10 [0.00, 2.03]	2019	
Li 2020	0	220	0	220		Not estimable	2020	
Fakahashi 2020	8	703	10	695	0.0%	0.79 [0.31, 1.99]	2020	
Ploumen (1) 2021	15	1245	7	1243	0.0%	2.14 [0.88, 5.23]	2021	
Vinter 2022	8	720	10	715	0.0%	0.79 [0.32, 2.00]	2022	
Ploumen (2) 2022	20	1169	19	1173	0.0%	1.06 [0.57, 1.97]	2022	
Ellert Gregersen 2022	30	1579	24	1572	0.0%	1.24 [0.73, 2.12]	2022	
Nakamura 2022	1	722	0	718	0.8%	2.98 [0.12, 73.11]	2022	
Hansen 2023	25	1261	31	1264	0.0%	0.81 [0.48, 1.36]	2023	
Fotal (95% CI)		3337		2989	100.0%	0.83 [0.62, 1.11]		•
Total events	79		92					
Heterogeneity: Tau ² = 0.	.00; Chi ² = :	2.48, df	= 4 (P = 0.65); I ² = 0%					
fest for overall effect: Z	= 1.25 (P =	0.21)						0.005 0.1 1 10 200 Favours Ultrathin DES Favours Thin DES

Figure S33. Sensitivity analysis based on stent type for definite or probable ST.

	Ultrathin	DES	SecondGeneration Thi	in DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Wijns 2015	5	123	2	61	0.0%	1.24 [0.25, 6.21]	2015	
Abizaid 2018	0	170	0	86		Not estimable	2018	
Lefèvre 2018	5	298	4	154	3.5%	0.65 [0.18, 2.37]	2018	
Pilgrim 2018	81	1063	76	1056	64.3%	1.06 [0.78, 1.43]	2018	#
Iglesias 2019	19	649	21	651	15.6%	0.91 [0.49, 1.67]	2019	
Zivelonghi 2019	2	165	2	165	1.5%	1.00 [0.14, 7.01]	2019	
Kim 2019	2	250	3	122	0.0%	0.33 [0.06, 1.92]	2019	
Saito 2019	0	385	1	190	0.6%	0.16 [0.01, 4.03]	2019	
Li 2020	1	220	0	220	0.6%	3.00 [0.12, 73.24]	2020	
Takahashi 2020	27	703	26	695	0.0%	1.03 [0.61, 1.74]	2020	
Ploumen (1) 2021	23	1245	13	1243	0.0%	1.77 [0.90, 3.47]	2021	
Ploumen (2) 2022	33	1169	40	1173	0.0%	0.83 [0.53, 1.30]	2022	
Kandzari 2022	21	884	8	450	9.0%	1.34 [0.60, 2.99]	2022	
Ellert Gregersen 2022	41	1579	32	1572	0.0%	1.28 [0.81, 2.01]	2022	
Nakamura 2022	6	722	7	718	5.0%	0.85 [0.29, 2.52]	2022	
Hansen 2023	62	1261	66	1264	0.0%	0.94 [0.67, 1.32]	2023	
Total (95% CI)		4386		3604	100.0%	1.02 [0.80, 1.30]		•
Total events	135		119					
Heterogeneity: Tau ² = 0.	00: Chi ² = 3	2.90. df:	= 7 (P = 0.89); I ² = 0%					the state of the state
Test for overall effect: Z								0.005 0.1 1 10 20 Favours Ultrathin DES Favours Thin DES

Figure S34. Sensitivity analysis based on stent type for cardiac death.

	Ultrathin	DES	SecondGeneration Thin	DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Wijns 2015	6	123	4	61	0.0%	0.74 [0.22, 2.54]	2015	
Abizaid 2018	1	170	0	86	0.0%	1.53 [0.06, 37.08]	2018	
Lefèvre 2018	9	298	10	154	14.4%	0.47 [0.19, 1.12]	2018	
Pilgrim 2018	58	1063	29	1056	24.3%	1.99 [1.28, 3.08]	2018	
Saito 2019	6	385	3	190	8.1%	0.99 [0.25, 3.90]	2019	
Iglesias 2019	8	649	4	651	9.9%	2.01 [0.61, 6.63]	2019	
Zivelonghi 2019	2	165	5	165	6.2%	0.40 [0.08, 2.03]	2019	
Kim 2019	7	250	1	122	0.0%	3.42 [0.43, 27.46]	2019	
Li 2020	1	220	0	220	1.9%	3.00 [0.12, 73.24]	2020	
Takahashi 2020	28	703	23	695	0.0%	1.20 [0.70, 2.07]	2020	
Ploumen (1) 2021	34	1245	27	1243	0.0%	1.26 [0.76, 2.07]	2021	
Ploumen (2) 2022	59	1169	66	1173	0.0%	0.90 [0.64, 1.26]	2022	
Kandzari 2022	35	884	19	450	21.6%	0.94 [0.54, 1.62]	2022	
Ellert Gregersen 2022	27	1579	32	1572	0.0%	0.84 [0.51, 1.40]	2022	
Nakamura 2022	10	722	8	718	13.6%	1.24 [0.49, 3.13]	2022	
Hansen 2023	96	1261	89	1264	0.0%	1.08 [0.82, 1.43]	2023	
Total (95% CI)		4386		3604	100.0%	1.11 [0.71, 1.75]		+
Total events	129		78					
Heterogeneity: Tau ² = 0.	17; Chi ² =	13.13, d	f = 7 (P = 0.07); I ² = 47%					
Test for overall effect: Z								0.01 0.1 1 10 100 Favours Ultrathin DES Favours Thin DES

Figure S35. Sens	itivity analysis base	ed on stent type for non-cardiac death.	

	Ultrathin	DES	SecondGeneration This	n DES		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	Year	M-H, Random, 95% CI
Wijns 2015	11	123	6	61	0.0%	0.91 [0.35, 2.34]	2015	
Lefèvre 2018	14	298	14	154	10.0%	0.52 [0.25, 1.06]	2018	
Pilgrim 2018	139	1063	105	1056	35.4%	1.32 [1.04, 1.67]	2018	-
Abizaid 2018	1	170	0	86	0.0%	1.53 [0.06, 37.08]	2018	
Kim 2019	9	250	4	122	0.0%	1.10 [0.34, 3.49]	2019	
Zivelonghi 2019	4	165	8	165	4.2%	0.50 [0.15, 1.63]	2019	
Saito 2019	6	385	4	190	3.8%	0.74 [0.21, 2.59]	2019	
Iglesias 2019	27	649	25	651	15.6%	1.08 [0.64, 1.85]	2019	-
Takahashi 2020	55	703	49	695	0.0%	1.11 [0.77, 1.61]	2020	
Li 2020	2	220	0	220	0.7%	5.00 [0.24, 103.55]	2020	
Ploumen (1) 2021	67	1245	45	1243	0.0%	1.49 [1.03, 2.15]	2021	
Ploumen (2) 2022	92	1169	106	1173	0.0%	0.87 [0.67, 1.14]	2022	
Kandzari 2022	56	884	27	450	19.8%	1.06 [0.68, 1.65]	2022	-+-
Ellert Gregersen 2022	68	1579	64	1572	0.0%	1.06 [0.76, 1.48]	2022	
Nakamura 2022	16	722	15	718	10.4%	1.06 [0.53, 2.13]	2022	
Hansen 2023	158	1261	155	1264	0.0%	1.02 [0.83, 1.26]	2023	
Total (95% CI)		4386		3604	100.0%	1.03 [0.80, 1.33]		•
Total events	264		198					
Heterogeneity: Tau ² = 0.	03; Chi ² =	9.49, df	= 7 (P = 0.22); I ² = 26%					0.01 0.1 1 10 10
Test for overall effect: Z								0.01 0.1 1 10 10 Favours Ultrathin DES Favours Thin DES

Figure S36. Sensitivity analysis based on stent type for all-cause death.