Am J Cardiovasc Dis 2024;14(5):267-280
www.AJCD.us /ISSN:2160-200X/AJCD0159006

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

Farah Yasmin[1], Syeda Farwa Zaidi[2], Abdul Moeed[2], Muneeba Khan[3], Eman Ali[2], Muhammad Sohaib Asghar[4], Waqas Ullah[5], Michael P Savage[5], Alec Vishnevsky[5], Nicholas J Ruggiero[5], David L Fischman[5]

[1]Yale School of Medicine, New Haven, CT 06511, USA; [2]Dow Medical College, Karachi 74200, Pakistan; [3]Jinnah Sindh Medical University, Karachi 75510, Pakistan; [4]Advent Health, FLorida, USA; [5]Thomas Jefferson University Hospitals, Philadelphia, PA 19107, USA

Received July 5, 2024; Accepted September 23, 2024; Epub October 15, 2024; Published October 30, 2024

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 queried 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 2nd 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, 1st 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 1st generation DES [3]. To overcome these issues, 2nd generation 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].

https://doi.org/10.62347/UCLC9729

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 DES-induced 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 (≤ 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 ≤ 70 μm were defined as ultrathin whereas those > 70 μm were classified under thin-strut 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 I^2 value was used to evaluate heterogeneity. A value of I^2=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,

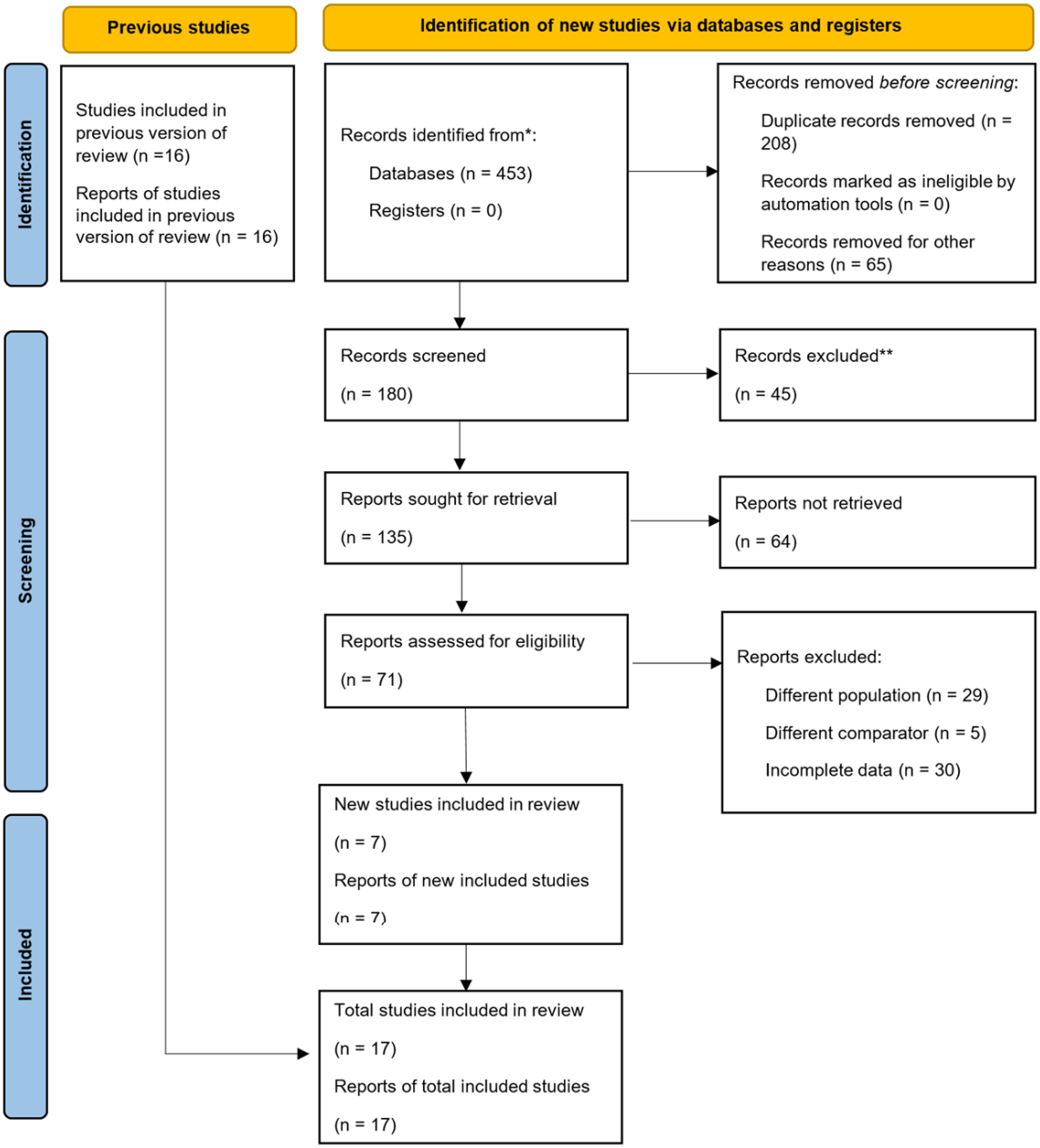

Figure 1. PRISMA flow diagram for new systematic reviews which included searches of databases and additional records.

95% CI 0.72-0.95, P=0.008, I^2=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, I^2=0%), all cause MI (RR 0.98, 95% CI 0.87-1.10, P=0.74, I^2=0%) and definite or probable ST (RR 0.92, 95% CI 0.76-1.13, P=0.44, I^2=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, I^2=0%), non-cardiac (RR 1.09, 95% CI 0.91-1.30, P=0.35, I^2=18%) and all-cause death (RR 1.07, 95% CI 0.96-1.19, P=0.22, I^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.

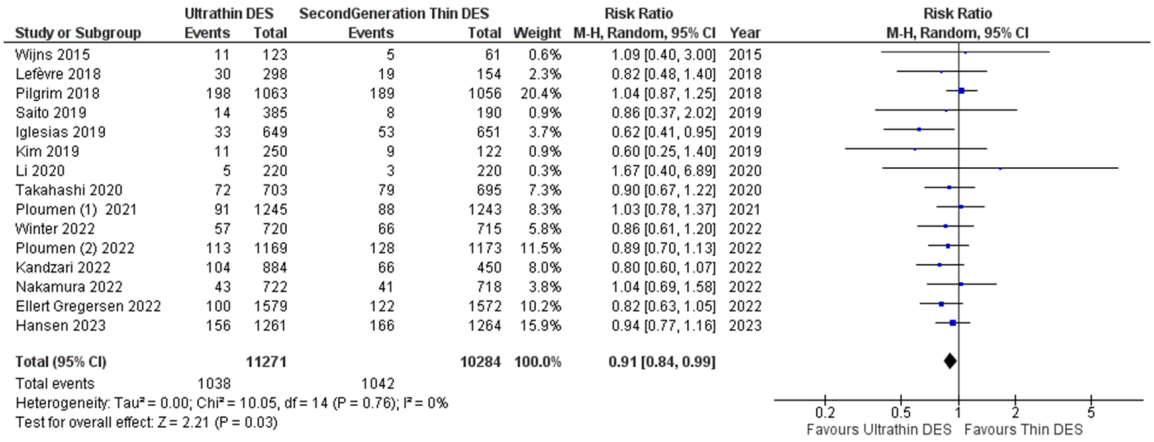

Figure 2. Forest plot for the outcome of target lesion failure (TLF).

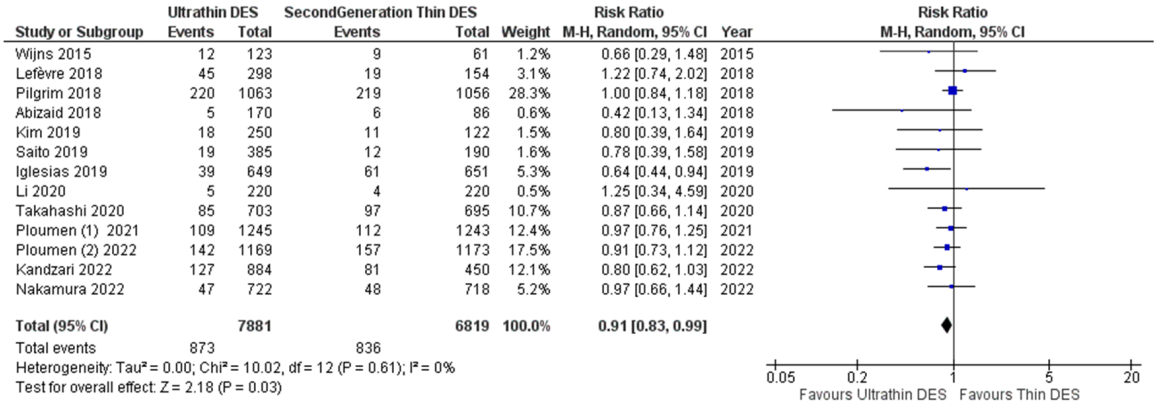

Figure 3. Forest plot for the outcome of target vessel failure (TVF).

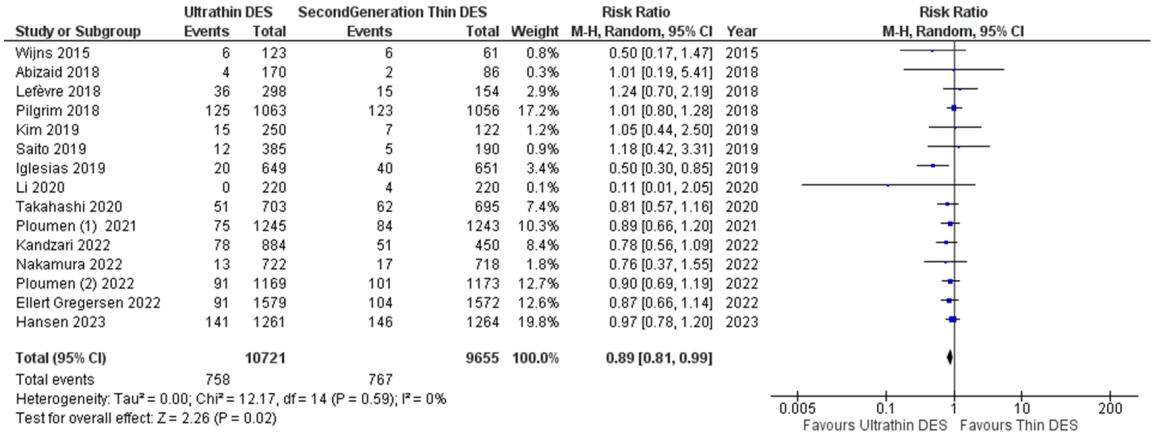

Figure 4. Forest plot for the outcome of clinically driven target-vessel revascularization (CD-TVR).

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

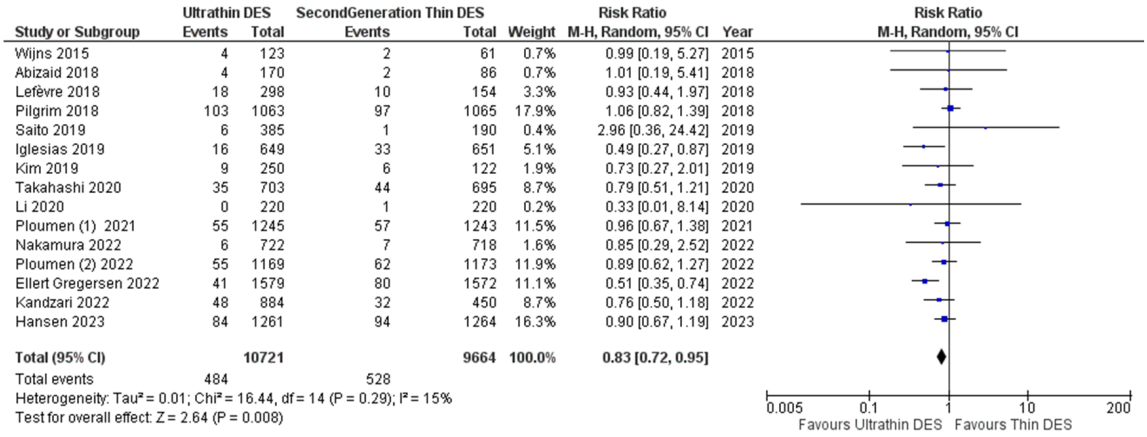

Figure 5. Forest plot for the outcome of clinically driven target-lesion revascularization (CD-TLR).

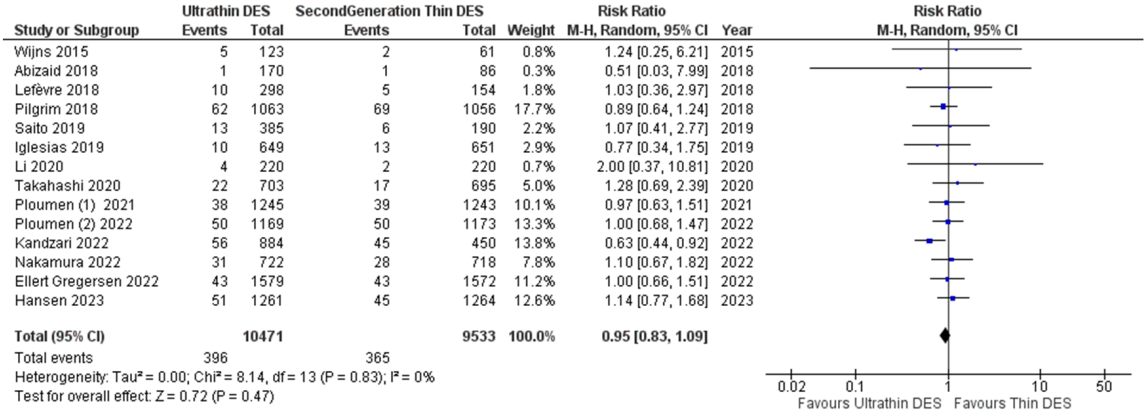

Figure 6. Forest plot for the outcome of target vessel myocardial infarction (TV-MI).

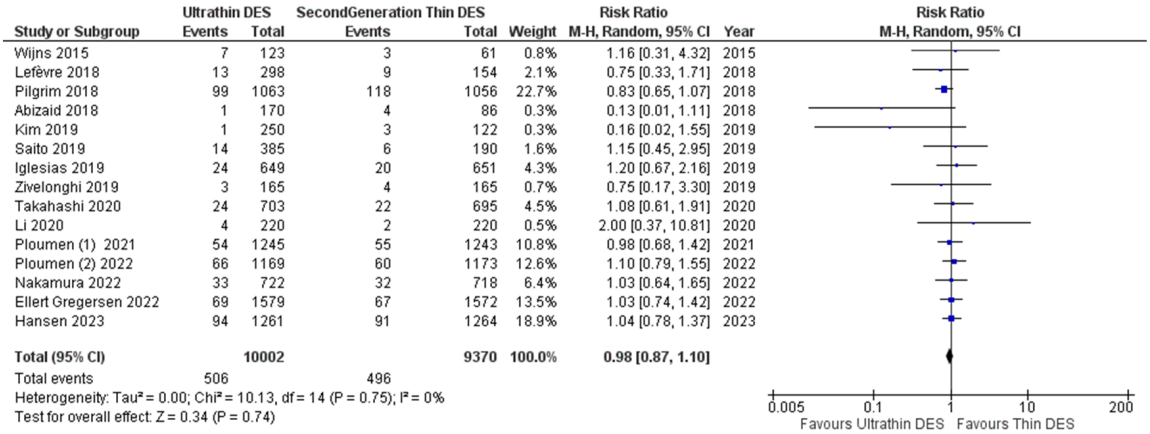

Figure 7. Forest plot for the outcome of all-cause myocardial infarction (MI).

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

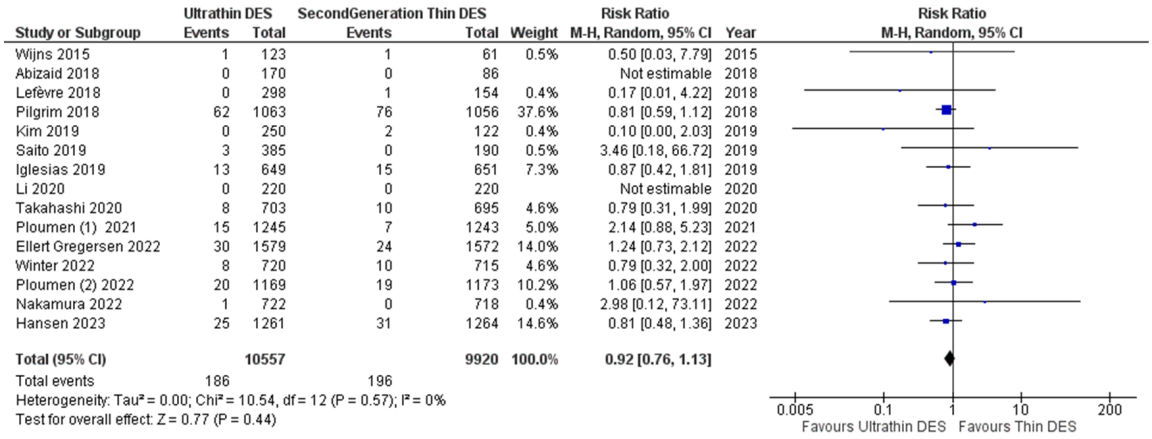

Figure 8. Forest plot for the outcome of probable or definite stent thrombosis (ST).

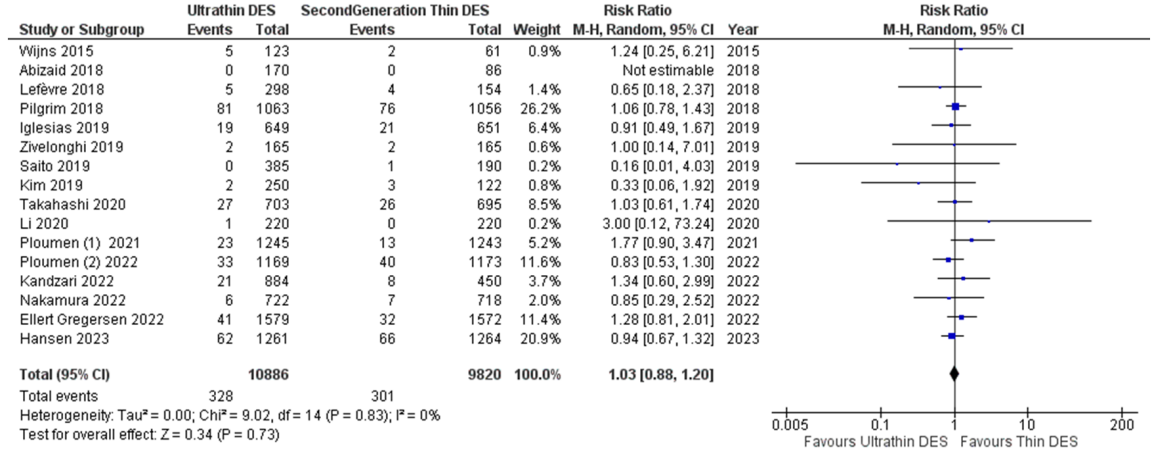

Figure 9. Forest plot for the outcome of cardiac death.

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, I^2=0%), sirolimus DES vs zotarolimus DES (RR 0.99, 95% CI 0.76-1.28, P=0.91, I^2=0%) and sirolimus DES vs biolimus DES (RR 0.89, 95% CI 0.76-1.04, P=0.15, I^2=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, I^2=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, I^2=0%), whereas no significant differ-

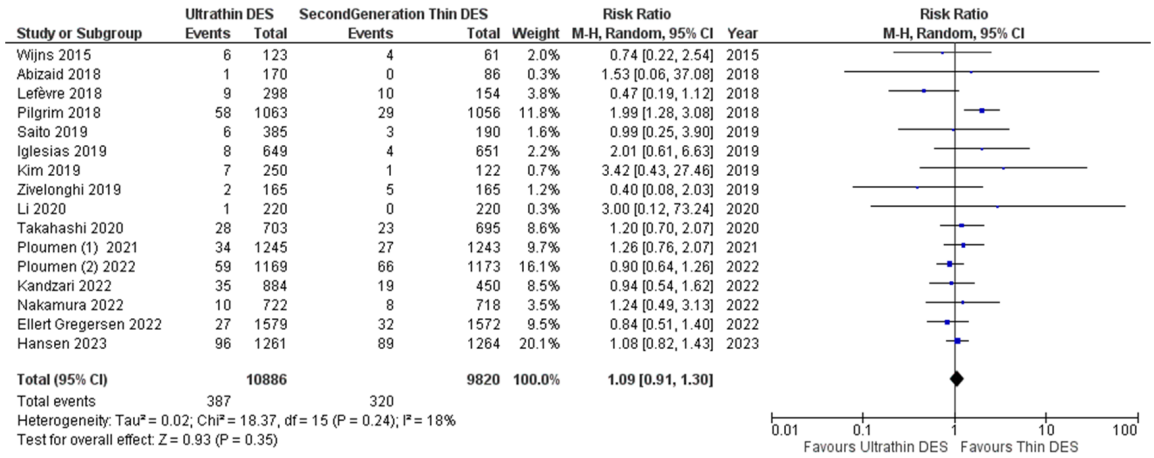

Figure 10. Forest plot for the outcome of non-cardiac death.

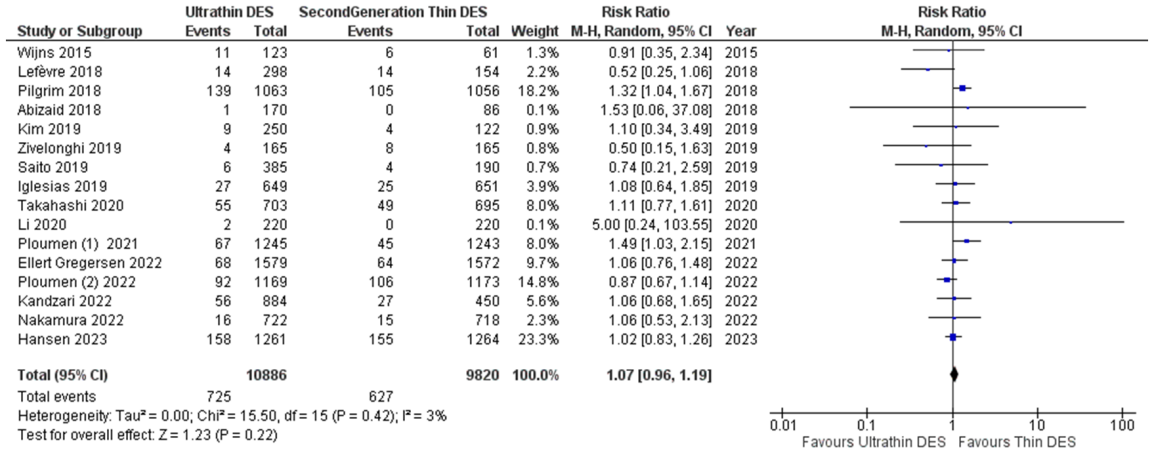

Figure 11. Forest plot for the outcome of all-cause death.

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, I^2=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, I^2=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, I^2=16%), as shown in Figure S27. 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 (Figures S28, S29, S30, S31, S32, S33, S34, S35, S36).

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 ≤ 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 meta-analysis 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 meta-analyses 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 longest-term impact of ultrathin vs thin strut DES on clinical outcomes following PCI. The results provide further confirmation that the risk of long-term 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.

Address correspondence to: Eman Ali, Dow Medical College, Karachi 74200, Pakistan. E-mail: eeman.ali2001@gmail.com

References

[1] Stone GW, Rizvi A, Newman W, Mastali K, Wang JC, Caputo R, Doostzadeh J, Cao S, Simonton CA, Sudhir K, Lansky AJ, Cutlip DE and Kereiakes DJ; SPIRIT IV Investigators.

Everolimus-eluting versus paclitaxel-eluting stents in coronary artery disease. N Engl J Med 2010; 362: 1663-74.
[2] Levine GN, Bates ER, Bittl JA, Brindis RG, Fihn SD, Fleisher LA, Granger CB, Lange RA, Mack MJ, Mauri L, Mehran R, Mukherjee D, Newby LK, O'Gara PT, Sabatine MS, Smith PK and Smith SC Jr. 2016 ACC/AHA Guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. Circulation 2016; 134: 123-55.
[3] Navarese EP, Kowalewski M, Kandzari D, Lansky A, Górny B, Kołtowski Ł, Waksman R, Berti S, Musumeci G, Limbruno U, van der Schaaf RJ, Kelm M, Kubica J and Suryapranata H. First-generation versus second-generation drug-eluting stents in current clinical practice: updated evidence from a comprehensive meta-analysis of randomised clinical trials comprising 31379 patients. Open Heart 2014; 1: e000064.
[4] Serruys PW, Ruygrok P, Neuzner J, Piek JJ, Seth A, Schofer JJ, Richardt G, Wiemer M, Carrié D, Thuesen L, Boone E, Miquel-Herbert K and Daemen J. A randomised comparison of an everolimus-eluting coronary stent with a paclitaxel-eluting coronary stent:the SPIRIT II trial. EuroIntervention 2006; 2: 286-94.
[5] Stone GW, Moses JW, Ellis SG, Schofer J, Dawkins KD, Morice MC, Colombo A, Schampaert E, Grube E, Kirtane AJ, Cutlip DE, Fahy M, Pocock SJ, Mehran R and Leon MB. Safety and efficacy of sirolimus- and paclitaxel-eluting coronary stents. N Engl J Med 2007; 356: 998-1008.
[6] Spaulding C, Daemen J, Boersma E, Cutlip DE and Serruys PW. A pooled analysis of data comparing sirolimus-eluting stents with bare-metal stents. N Engl J Med 2007; 356: 989-97.
[7] Jensen LO, Tilsted HH, Thayssen P, Kaltoft A, Maeng M, Lassen JF, Hansen KN, Madsen M, Ravkilde J, Johnsen SP, Sørensen HT and Thuesen L. Paclitaxel and sirolimus eluting stents versus bare metal stents: long-term risk of stent thrombosis and other outcomes. From the western denmark heart registry. EuroIntervention 2010; 5: 898-905.
[8] Yuan H, Wu Z, Lu T, Wei T, Zeng Y, Liu Y and Huang C. Comparison of biodegradable and durable polymer drug-eluting stents in acute coronary syndrome: a meta-analysis. BMJ Open 2022; 12: e058075.
[9] Räber L, Magro M, Stefanini GG, Kalesan B, van Domburg RT, Onuma Y, Wenaweser P, Daemen J, Meier B, Jüni P, Serruys PW and Windecker S. Very late coronary stent thrombosis of a newer-generation everolimus-eluting stent compared with early-generation drug-eluting stents: a prospective cohort study. Circulation 2012; 125: 1110-21.
[10] Stefanini GG, Byrne RA, Windecker S and Kastrati A. State of the art: coronary artery stents - past, present and future. EuroIntervention 2017; 13: 706-16.
[11] Joner M, Nakazawa G, Finn AV, Quee SC, Coleman L, Acampado E, Wilson PS, Skorija K, Cheng Q, Xu X, Gold HK, Kolodgie FD and Virmani R. Endothelial cell recovery between comparator polymer-based drug-eluting stents. J Am Coll Cardiol 2008; 52: 333-42.
[12] Madhavan MV, Kirtane AJ, Redfors B, Généreux P, Ben-Yehuda O, Palmerini T, Benedetto U, Biondi-Zoccai G, Smits PC, von Birgelen C, Mehran R, McAndrew T, Serruys PW, Leon MB, Pocock SJ and Stone GW. Stent-related adverse events >1 year after percutaneous coronary intervention. J Am Coll Cardiol 2020; 75: 590-604.
[13] Kastrati A, Mehilli J, Dirschinger J, Dotzer F, Schühlen H, Neumann FJ, Fleckenstein M, Pfafferott C, Seyfarth M and Schömig A. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO) trial. Circulation 2001; 103: 2816-21.
[14] Madhavan MV, Howard JP, Naqvi A, Ben-Yehuda O, Redfors B, Prasad M, Shahim B, Leon MB, Bangalore S, Stone GW and Ahmad Y. Long-term follow-up after ultrathin vs. conventional 2nd-generation drug-eluting stents: a systematic review and meta-analysis of randomized controlled trials. Eur Heart J 2021; 42: 2643-54.
[15] Nakamura M, Kadota K, Nakagawa Y, Tanabe K, Ito Y, Amano T, Maekawa Y, Takahashi A, Shiode N, Otsuka Y, Kawasaki T, Hikichi Y, Shite J, Kozuma K, Iijima R and Murakami Y; CASTLE Investigators. Ultrathin, biodegradable-polymer sirolimus-eluting stent vs thin, durable-polymer everolimus-eluting stent. JACC Cardiovasc Interv 2022; 15: 1324-34.
[16] Saito S, Toelg R, Witzenbichler B, Haude M, Masotti M, Salmeron R, Witkowski A, Uematsu M, Takahashi A, Waksman R and Slagboom T. BIOFLOW-IV, a randomised, intercontinental, multicentre study to assess the safety and effectiveness of the Orsiro sirolimus-eluting stent in the treatment of subjects with de novo coronary artery lesions: primary outcome target vessel failure at 12 months. EuroIntervention 2019; 15: 1006-13.
[17] Lefèvre T, Haude M, Neumann FJ, Stangl K, Skurk C, Slagboom T, Sabaté M, Goicolea J, Barragan P, Cook S, Macia JC and Windecker S. Comparison of a novel biodegradable poly-

mer sirolimus-eluting stent with a durable polymer everolimus-eluting stent: 5-year outcomes of the randomized BIOFLOW-II trial. JACC Cardiovasc Interv 2018; 11: 995-1002.

[18] Pilgrim T, Piccolo R, Heg D, Roffi M, Tüller D, Muller O, Moarof I, Siontis GCM, Cook S, Weilenmann D, Kaiser C, Cuculi F, Hunziker L, Eberli FR, Jüni P and Windecker S. Ultrathin-strut, biodegradable-polymer, sirolimus-eluting stents versus thin-strut, durable-polymer, everolimus-eluting stents for percutaneous coronary revascularisation: 5-year outcomes of the BIOSCIENCE randomised trial. Lancet 2018; 392: 737-46.

[19] Takahashi K, Serruys PW, Kogame N, Buszman P, Lurz P, Jessurun GAJ, Koch KT, Troquay RPT, Hamer BJB, Oude Ophuis T, Milewski KP, Hofma SH, Wykrzykowska JJ, Onuma Y, de Winter RJ and Wijns W. Final 3-year outcomes of mistent biodegradable polymer crystalline sirolimus-eluting stent versus xience permanent polymer everolimus-eluting stent: insights from the DESSOLVE III all-comers randomized trial. Circ Cardiovasc Interv 2020; 13: e008737.

[20] Kim SH, Kang SH, Lee JM, Chung WY, Park JJ, Yoon CH, Suh JW, Cho YS, Doh JH, Cho JM, Bae JW, Youn TJ and Chae IH. Three-year clinical outcome of biodegradable hybrid polymer Orsiro sirolimus-eluting stent and the durable biocompatible polymer Resolute Integrity zotarolimus-eluting stent: a randomized controlled trial. Catheter Cardiovasc Interv 2020; 96: 1399-406.

[21] Zivelonghi C, Agostoni P, Teeuwen K, van der Schaaf RJ, Henriques JPS, Vermeersch PHMJ, Bosschaert MAR, Kelder JC, Tijssen JGP and Suttorp MJ. 3-year clinical outcomes of the PRISON-IV trial: ultrathin struts versus conventional drug-eluting stents in total coronary occlusions. JACC Cardiovasc Interv 2019; 12: 1747-9.

[22] Abizaid A, Kedev S, Kedhi E, Talwar S, Erglis A, Hlinomaz O, Masotti M, Fath-Ordoubadi F, Lemos PA, Milewski K, Botelho R, Costa R and Bangalore S. Randomised comparison of a biodegradable polymer ultra-thin sirolimus-eluting stent versus a durable polymer everolimus-eluting stent in patients with de novo native coronary artery lesions: the meriT-V trial. EuroIntervention 2018; 14: 1207-14.

[23] Li C, Yang Y, Han Y, Song D, Xu J, Guan C, Gao R, Garcia-Garcia HM, Waksman R and Xu B; BIOFLOW VI Trial Investigators. Comparison of the ultrathin strut, biodegradable polymer sirolimus-eluting stent with a durable polymer everolimus-eluting stent in a chinese population: the randomized BIOFLOW VI trial. Clin Ther 2020; 42: 649-660.

[24] Iglesias JF, Muller O, Heg D, Roffi M, Kurz DJ, Moarof I, Weilenmann D, Kaiser C, Tapponnier M, Stortecky S, Losdat S, Eeckhout E, Valgimigli M, Odutayo A, Zwahlen M, Jüni P, Windecker S and Pilgrim T. Biodegradable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents in patients with ST-segment elevation myocardial infarction (BIOSTEMI): a single-blind, prospective, randomised superiority trial. Lancet 2019; 394: 1243-53.

[25] Wijns W, Vrolix M, Verheye S, Schoors D, Slagboom T, Gosselink M, Benit E, Donohoe D, Knape C, Attizzani GF, Lansky AJ and Ormiston J; DESSOLVE II Investigators. Randomised study of a bioabsorbable polymer-coated sirolimus-eluting stent: results of the DESSOLVE II trial. EuroIntervention 2015; 10: 1383-90.

[26] Ellert-Gregersen J, Jensen LO, Jakobsen L, Freeman PM, Eftekhari A, Maeng M, Raungaard B, Engstroem T, Kahlert J, Hansen HS and Christiansen EH. Polymer-free biolimus-coated stents versus ultrathin-strut biodegradable polymer sirolimus-eluting stents: two-year outcomes of the randomised SORT OUT IX trial. EuroIntervention 2022; 18: e124-31.

[27] Ploumen EH, Pinxterhuis TH, Buiten RA, Zocca P, Danse PW, Schotborgh CE, Scholte M, Gin RMTJ, Somi S, van Houwelingen KG, Stoel MG, de Man HAF, Hartmann M, Linssen GCM, van der Heijden LC, Kok MM, Doggen CJM and von Birgelen C. Final 5-year report of the randomized BIO-RESORT trial comparing 3 contemporary drug-eluting stents in all-comers. J Am Heart Assoc 2022; 11: e026041.

[28] Ploumen EH, Buiten RA, Zocca P, Doggen CJ, Aminian A, Schotborgh CE, Jessurun GA, Roguin A, Danse PW, Benit E and von Birgelen C. First report of 3-year clinical outcome after treatment with novel resolute onyx stents in the randomized BIONYX trial. Circ J 2021; 85: 1983-1990.

[29] Hansen KN, Jensen LO, Maeng M, Christensen MK, Noori M, Kahlert J, Jakobsen L, Junker A, Freeman P, Ellert-Gregersen J, Raungaard B, Terkelsen CJ, Veien KT and Christiansen EH. Five-year clinical outcome of the biodegradable polymer ultrathin strut sirolimus-eluting stent compared to the biodegradable polymer biolimus-eluting stent in patients treated with percutaneous coronary intervention: from the SORT OUT VII trial. Circ Cardiovasc Interv 2023; 16: e012332.

[30] Kandzari DE, Koolen JJ, Doros G, Garcia-Garcia HM, Bennett J, Roguin A, Gharib EG, Cutlip DE and Waksman R; BIOFLOW V Investigators. Ultrathin bioresorbable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents: BIOFLOW V final 5-year out-

comes. JACC Cardiovasc Interv 2022; 15: 1852-60.
[31] de Winter RJ, Zaman A, Hara H, Gao C, Ono M, Garg S, Smits PC, Tonino PAL, Hofma SH, Moreno R, Choudhury A, Petrov I, Cequier A, Colombo A, Kaul U, Onuma Y and Serruys PW. Sirolimus-eluting stents with ultrathin struts versus everolimus-eluting stents for patients undergoing percutaneous coronary intervention: final three-year results of the TALENT trial. EuroIntervention 2022; 18: 492-502.
[32] PRISMA [Internet]. Prisma-statement.org. 2022 [cited August 31, 2022]. Available at: https://prisma-statement.org/.
[33] McKenzie JE, Salanti G, Lewis SC and Altman DG. Meta-analysis and The Cochrane Collaboration: 20 years of the Cochrane statistical methods group. Syst Rev 2013; 2: 80.
[34] Cutlip DE, Windecker S, Mehran R, Boam A, Cohen DJ, van Es GA, Steg PG, Morel MA, Mauri L, Vranckx P, McFadden E, Lansky A, Hamon M, Krucoff MW and Serruys PW; Academic Research Consortium. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation 2007; 115: 2344-51.
[35] Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng HY, Corbett MS, Eldridge SM, Emberson JR, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF and Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. BMJ 2019; 366: l4898.
[36] Garg S, Serruys P, Onuma Y, Dorange C, Veldhof S, Miquel-Hébert K, Sudhir K, Boland J, Huber K, Garcia E and te Riele JA; SPIRIT II Investigators. 3-year clinical follow-up of the XIENCE V everolimus-eluting coronary stent system in the treatment of patients with de novo coronary artery lesions: the SPIRIT II trial (Clinical Evaluation of the Xience V Everolimus Eluting Coronary Stent System in the Treatment of Patients with de novo Native Coronary Artery Lesions). JACC Cardiovasc Interv 2009; 2: 1190-8.
[37] Stone GW, Midei M, Newman W, Sanz M, Hermiller JB, Williams J, Farhat N, Mahaffey KW, Cutlip DE, Fitzgerald PJ, Sood P, Su X and Lansky AJ; SPIRIT III Investigators. Comparison of an everolimus-eluting stent and a paclitaxel-eluting stent in patients with coronary artery disease: a randomized trial. JAMA 2008; 299: 1903-13.
[38] Stone GW, Rizvi A, Newman W, Mastali K, Wang JC, Caputo R, Doostzadeh J, Cao S, Simonton CA, Sudhir K, Lansky AJ, Cutlip DE and Kereiakes DJ; SPIRIT IV Investigators. Everolimus-eluting versus paclitaxel-eluting stents in coronary artery disease. N Engl J Med 2010; 362: 1663-74.
[39] Palmerini T, Biondi-Zoccai G, Della Riva D, Mariani A, Sabaté M, Smits PC, Kaiser C, D'Ascenzo F, Frati G, Mancone M, Genereux P and Stone GW. Clinical outcomes with bioabsorbable polymer-versus durable polymer-based drug-eluting and bare-metal stents: evidence from a comprehensive network meta-analysis. J Am Coll Cardiol 2014; 63: 299-307.
[40] Nogic J, Thein P, Mirzaee S, Comella A, Soon K, Cameron JD, West NEJ and Brown AJ. Biodegradable-polymer versus polymer-free drug-eluting stents for the treatment of coronary artery disease. Cardiovasc Revasc Med 2019; 20: 865-70.
[41] Stone GW, Kimura T, Gao R, Kereiakes DJ, Ellis SG, Onuma Y, Chevalier B, Simonton C, Dressler O, Crowley A, Ali ZA and Serruys PW. Time-varying outcomes with the absorb bioresorbable vascular scaffold during 5-year follow-up: a systematic meta-analysis and individual patient data pooled study. JAMA Cardiol 2019; 4: 1261-1269.
[42] Grundeken MJ and Beijk MA. A narrative review of ultrathin-strut drug-eluting stents: the thinner the better? Heart Int 2021; 15: 84-93.
[43] Bangalore S, Toklu B, Patel N, Feit F and Stone GW. Newer-generation ultrathin strut drug-eluting stents versus older second-generation thicker strut drug-eluting stents for coronary artery disease. Circulation 2018; 138: 2216-26.
[44] Taglieri N, Bruno AG, Ghetti G, Marrozzini C, Saia F, Galié N and Palmerini T. Target lesion failure with current drug-eluting stents. JACC Cardiovasc Interv 2020; 13: 2868-78.
[45] Waksman R, Lipinski MJ, Acampado E, Cheng Q, Adams L, Torii S, Gai J, Torguson R, Hellinga DM, Westman PC, Joner M, Zumstein P, Kolodgie FD and Virmani R. Comparison of acute thrombogenicity for metallic and polymeric bioabsorbable scaffolds: magmaris versus absorb in a porcine arteriovenous shunt model. Circ Cardiovasc Interv 2017; 10: e004762.
[46] Garasic JM, Edelman ER, Squire JC, Seifert P, Williams MS and Rogers C. Stent and artery geometry determine intimal thickening independent of arterial injury. Circulation 2000; 101: 812-8.
[47] Pache J, Kastrati A, Mehilli J, Schühlen H, Dotzer F, Hausleiter J, Fleckenstein M, Neumann FJ, Sattelberger U, Schmitt C, Müller M, Dirschinger J and Schömig A. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO-2) trial. J Am Coll Cardiol 2003; 41: 1283-8.

[48] Kastrati A, Mehilli J, Dirschinger J, Dotzer F, Schühlen H, Neumann FJ, Fleckenstein M, Pfafferott C, Seyfarth M and Schömig A. Intracoronary stenting and angiographic results. Circulation 2001; 103: 2816-21.

[49] Palmerini T, Della Riva D, Biondi-Zoccai G, Leon MB, Serruys PW, Smits PC, von Birgelen C, Ben-Yehuda O, Généreux P, Bruno AG, Jenkins P and Stone GW. Mortality following nonemergent, uncomplicated target lesion revascularization after percutaneous coronary intervention. JACC Cardiovasc Interv 2018; 11: 892-902.

[50] Brener SJ, Tarantini G, Leon MB, Serruys PW, Smits PC, von Birgelen C, Crowley A, Ben-Yehuda O and Stone GW. Cardiovascular and noncardiovascular death after percutaneous coronary intervention: insights from 32 882 patients enrolled in 21 randomized trials. Circ Cardiovasc Interv 2018; 11: e006488.

[51] Giustino G, Serruys PW, Sabik JF 3rd, Mehran R, Maehara A, Puskas JD, Simonton CA, Lembo NJ, Kandzari DE, Morice MC, Taggart DP, Gershlick AH, Ragosta M 3rd, Kron IL, Liu Y, Zhang Z, McAndrew T, Dressler O, Généreux P, Ben-Yehuda O, Pocock SJ, Kappetein AP and Stone GW. Mortality after repeat revascularization following PCI or CABG for left main disease: the EXCEL trial. JACC Cardiovasc Interv 2020; 13: 375-87.

Table S1. Detailed literature search of each database

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 S2. Study characteristics of the included trials

Author’s Name	Study Name	Year	N	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 vessels, 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 occlusions (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 artery 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 lesion 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, reference 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% diameter 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, saphenous 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 angina 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 estimate of diameter between 2.5 mm and 3.5 mm. This stenosis was suitable for coverage 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 outcome 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

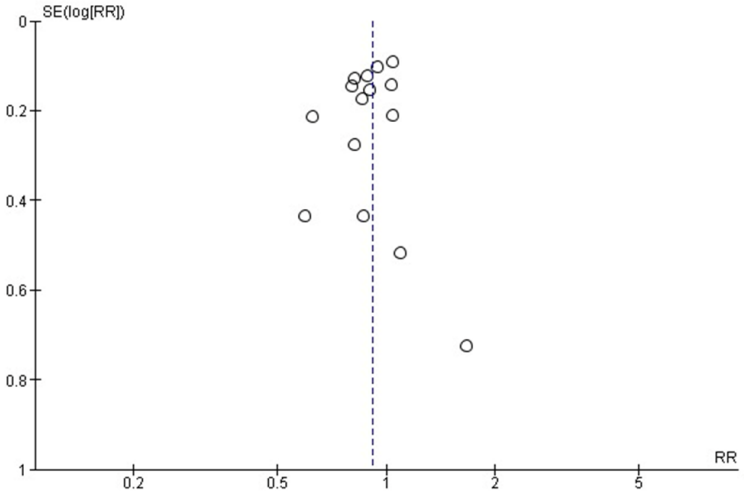

Figure S1. Funnel plot for the outcome of TLF.

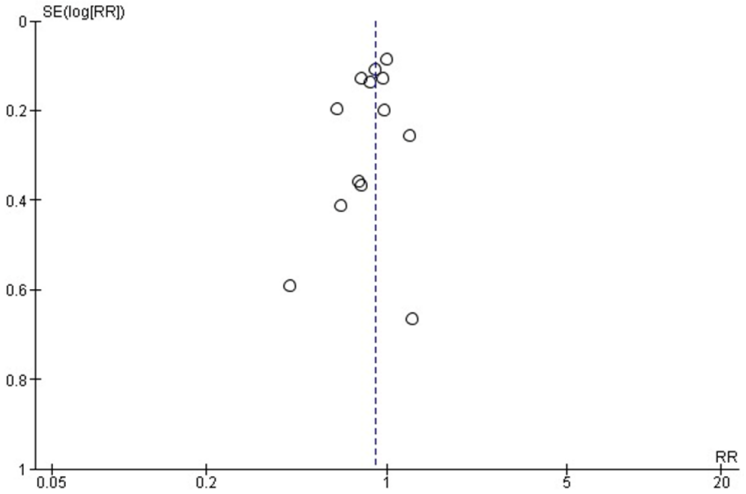

Figure S2. Funnel plot for the outcome of TVF.

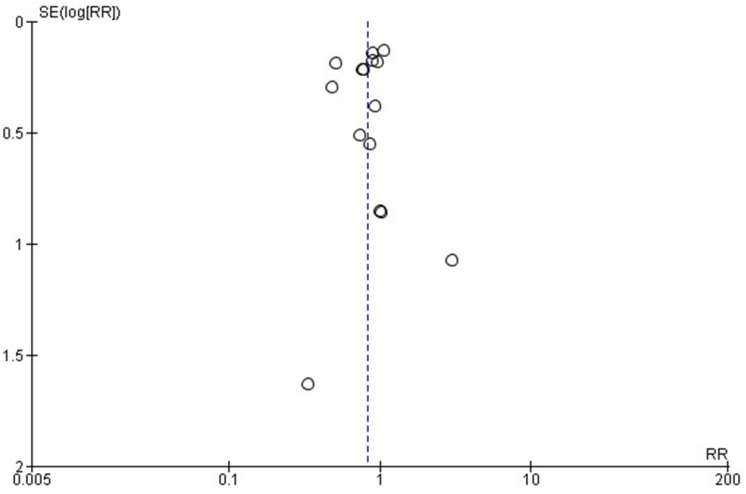

Figure S3. Funnel plot for the outcome of CD-TLR.

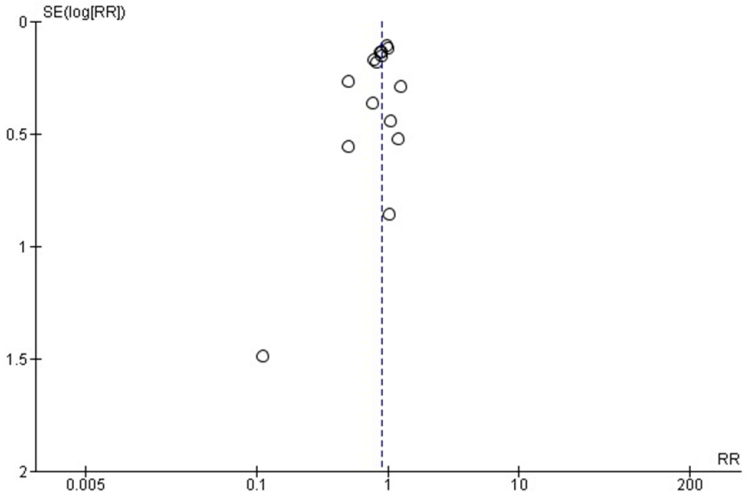

Figure S4. Funnel plot for the outcome of CD-TVR.

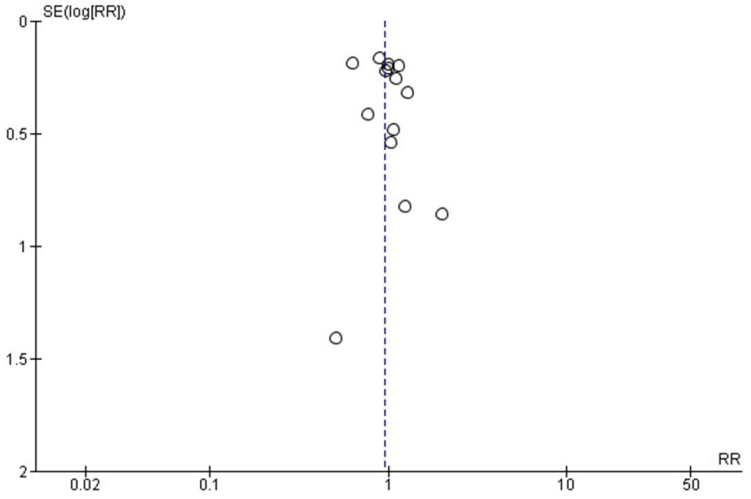

Figure S5. Funnel plot for the outcome of TV-MI.

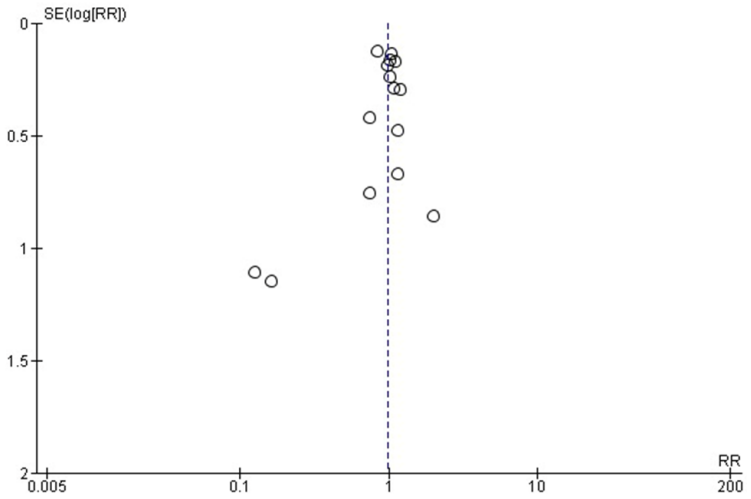

Figure S6. Funnel plot for the outcome of all cause MI.

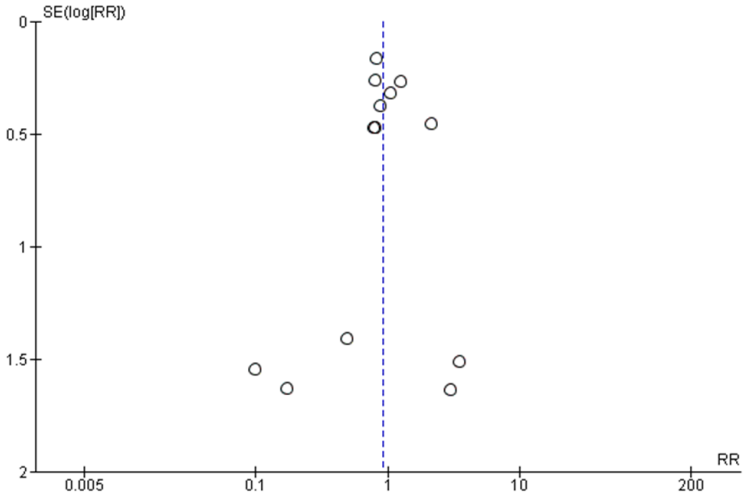

Figure S7. Funnel plot for the outcome of definite or probable ST.

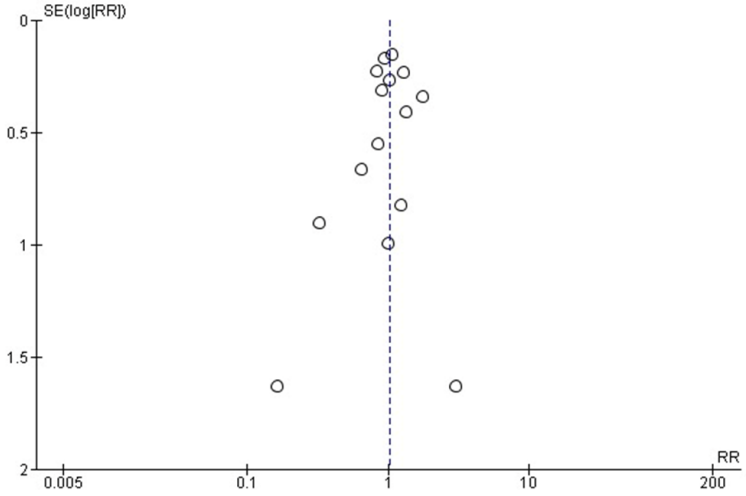

Figure S8. Funnel plot for the outcome of cardiac death.

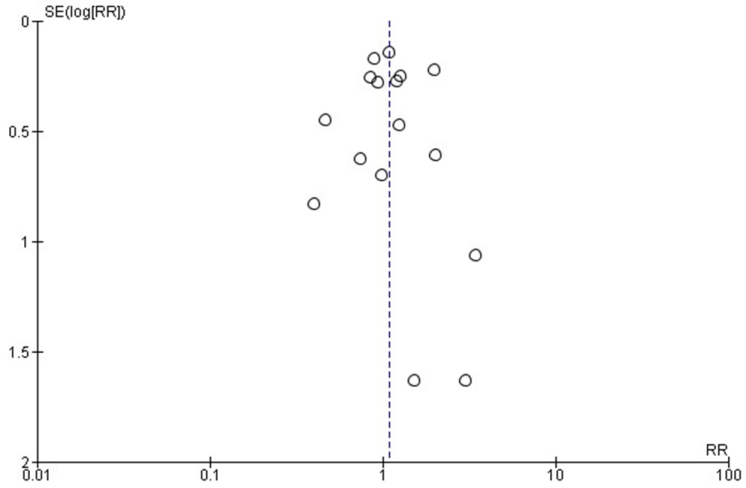

Figure S9. Funnel plot for the outcome of non-cardiac death.

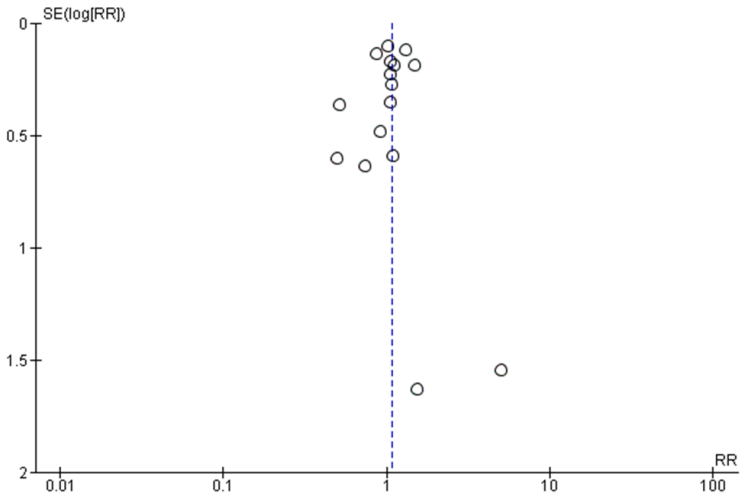

Figure S10. Funnel plot for the outcome of all-cause death.

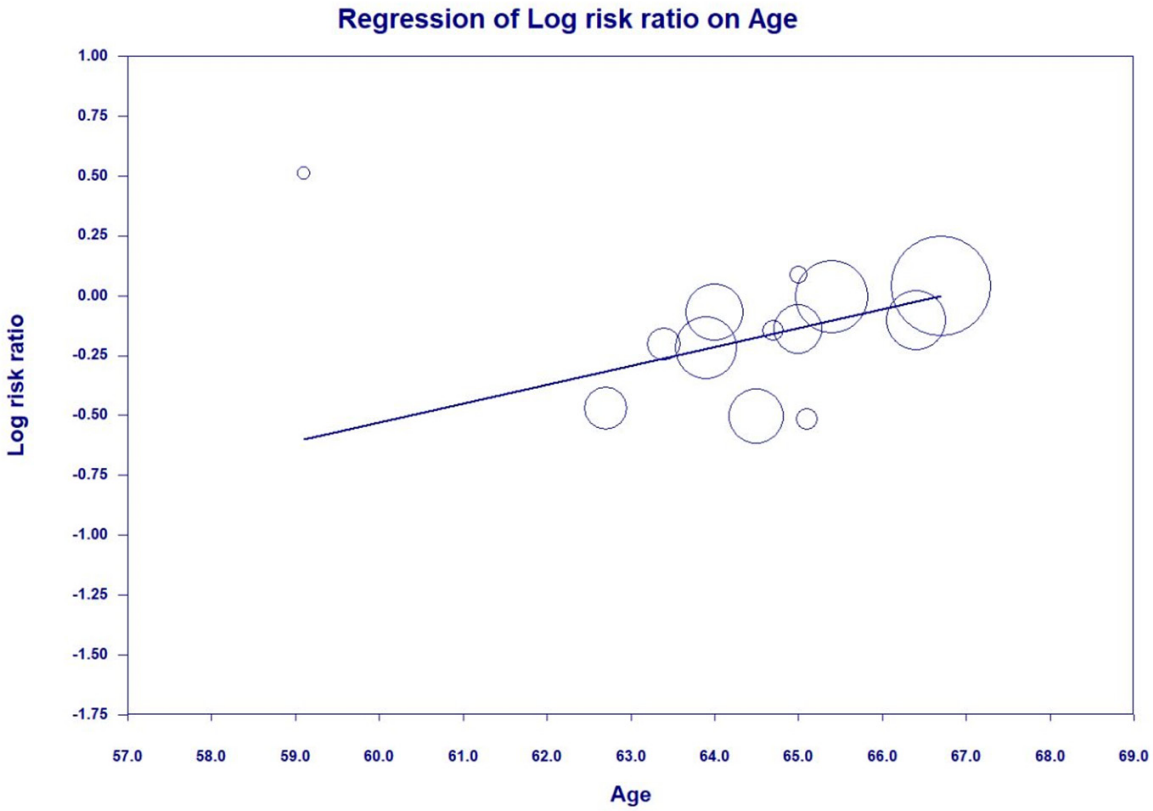

Figure S11. Regression of Log risk ratio on age.

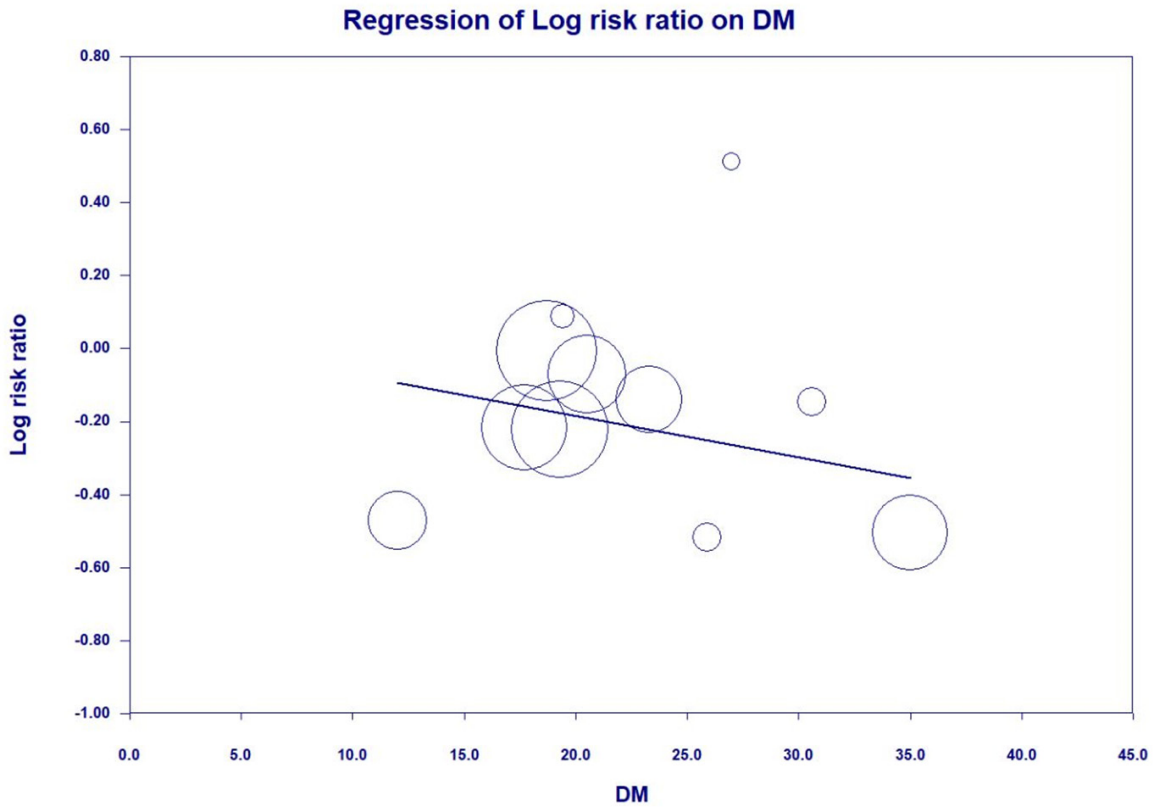

Figure S12. Regression of log risk ratio on diabetes mellitus.

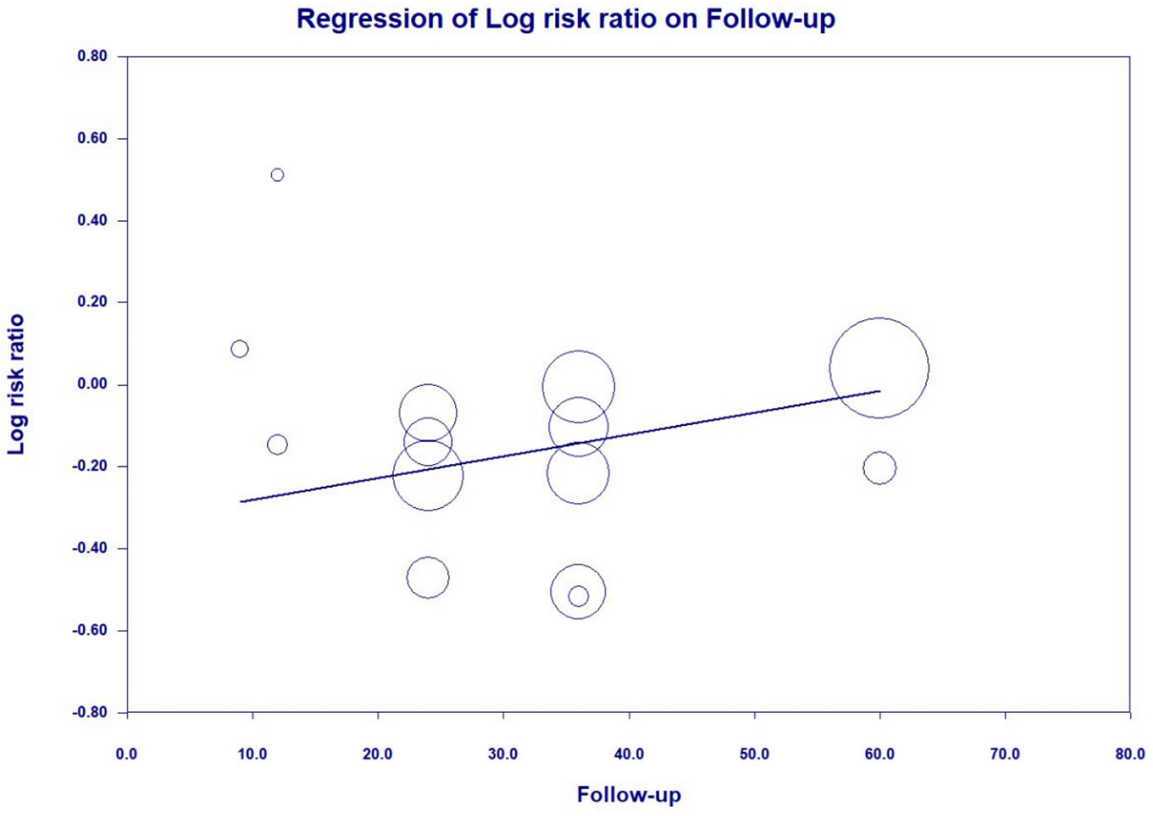

Figure S13. Regression of log risk ratio on follow-up duration.

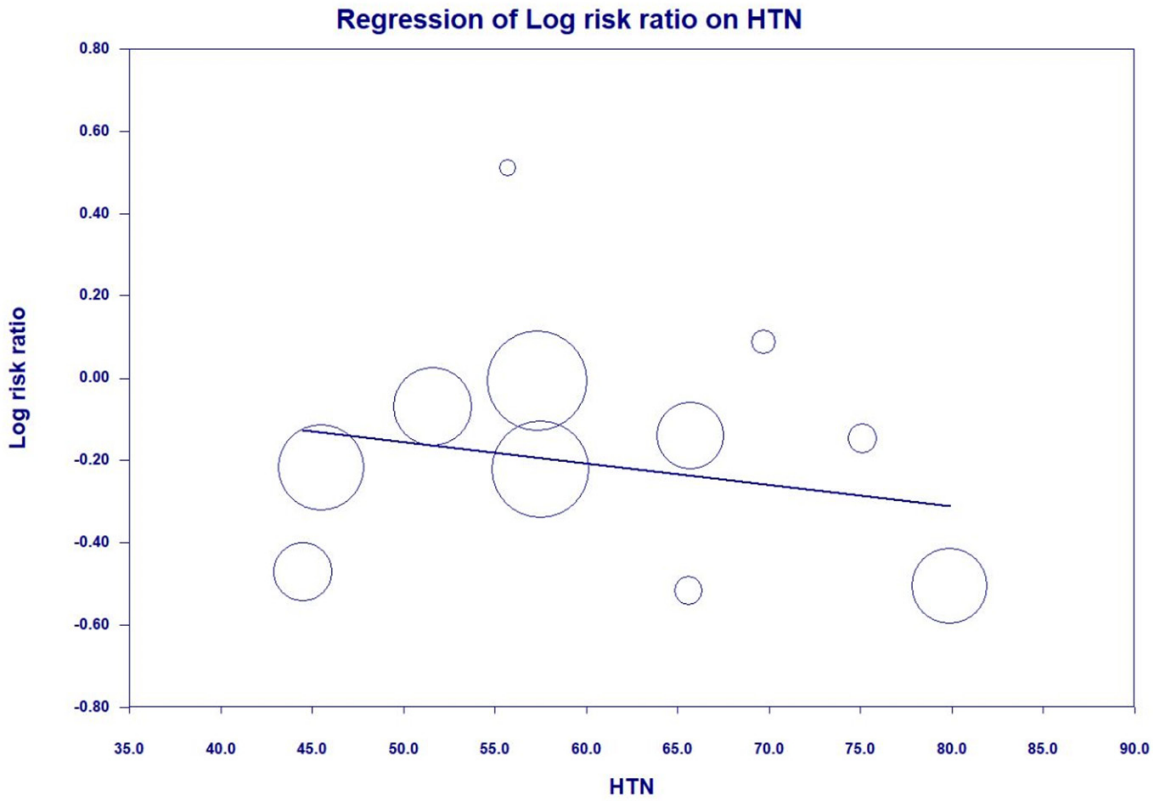

Figure S14. Regression of log risk ratio on hypertension.

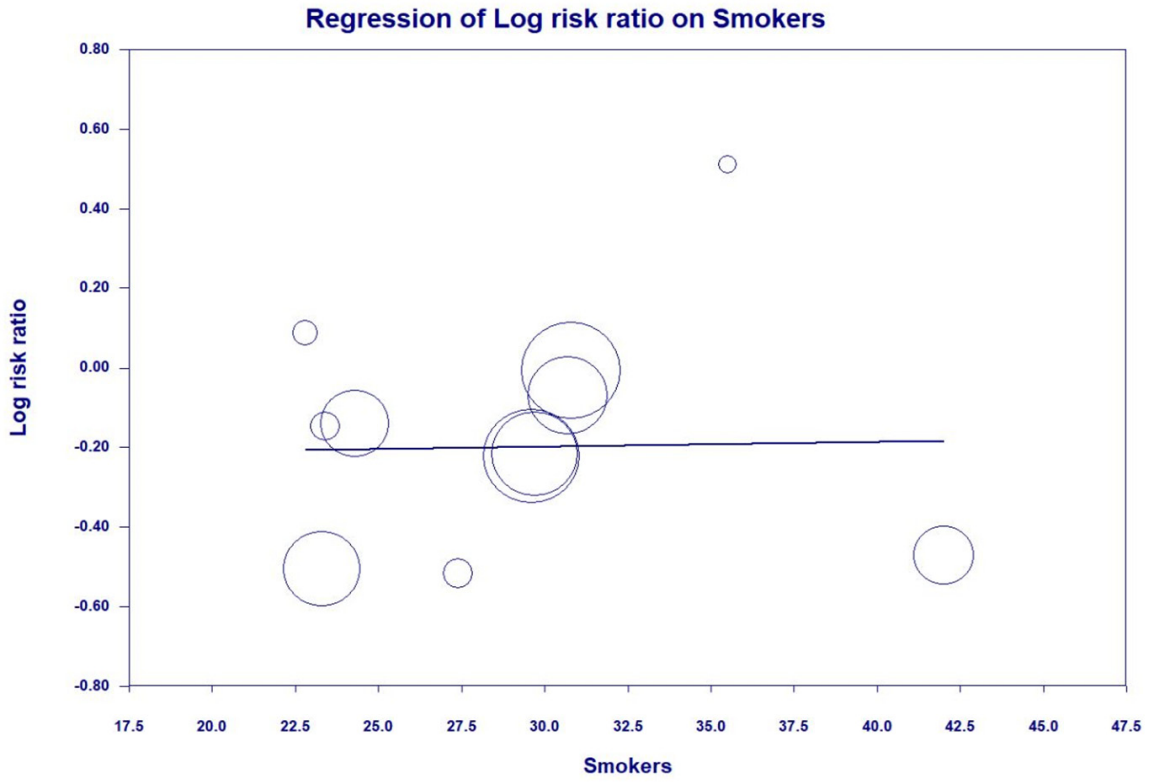

Figure S15. Regression of log risk ratio on smokers.

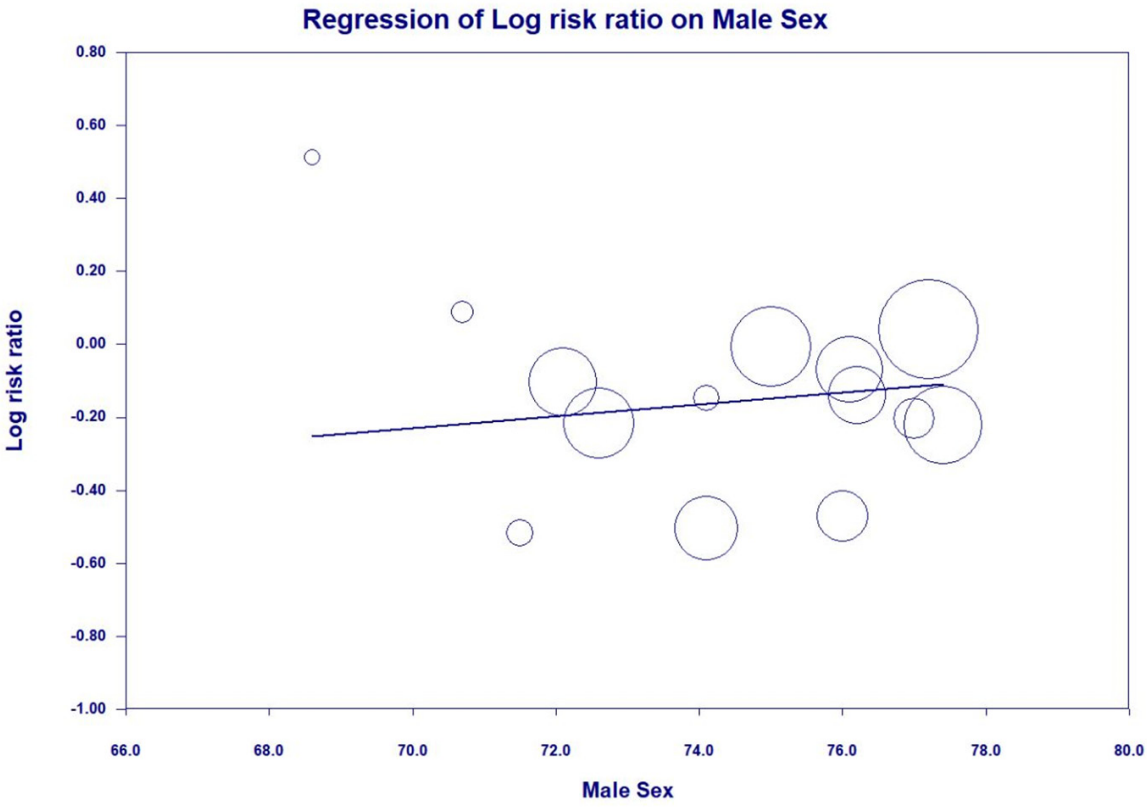

Figure S16. Regression of log risk ratio on male sex.

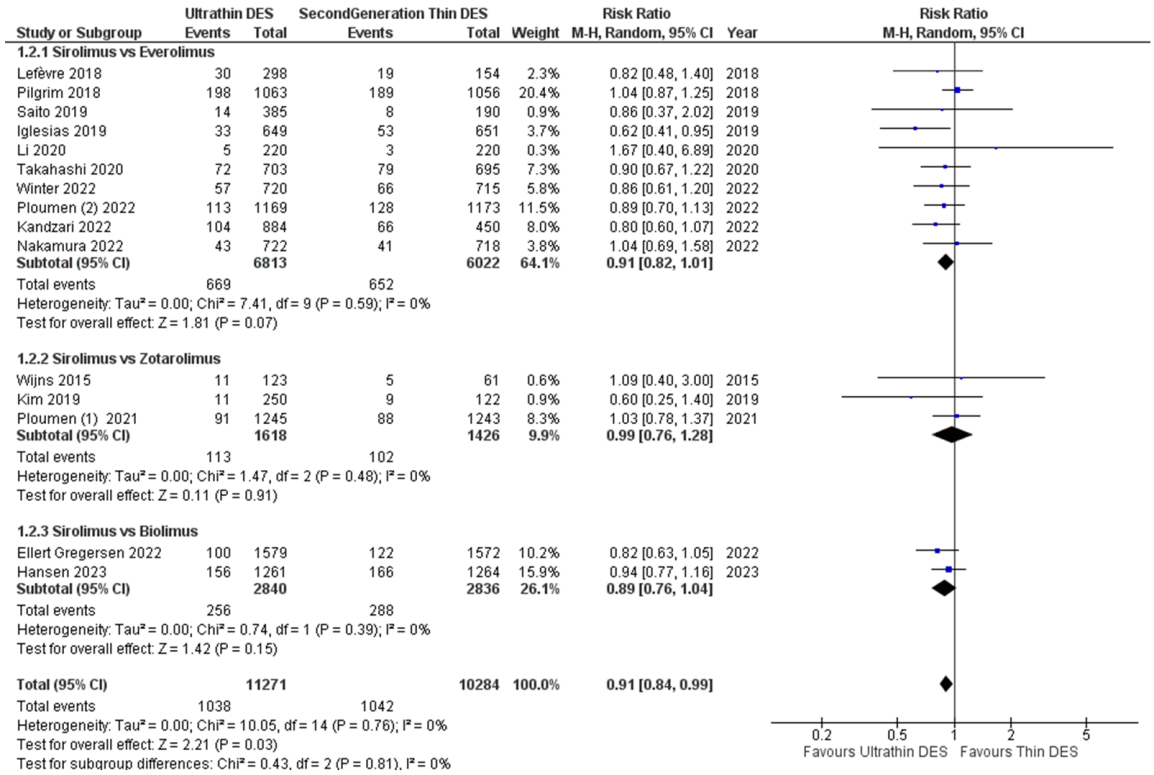

Figure S17. Effect of anti-proliferative drug on TLF.

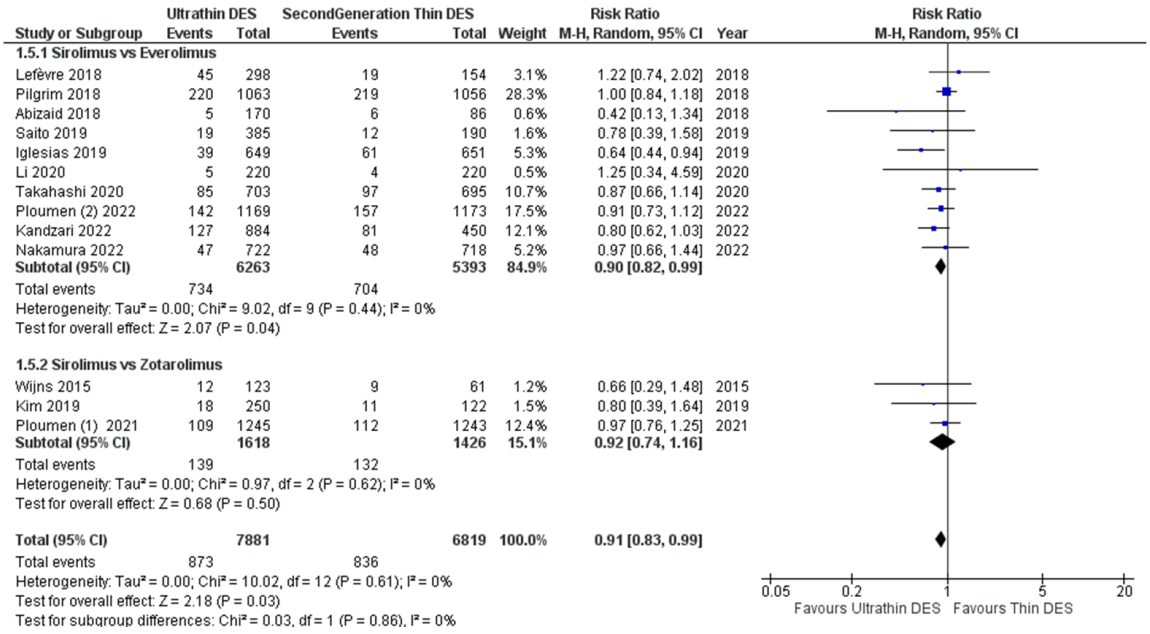

Figure S18. Effect of anti-proliferative drug on TVF.

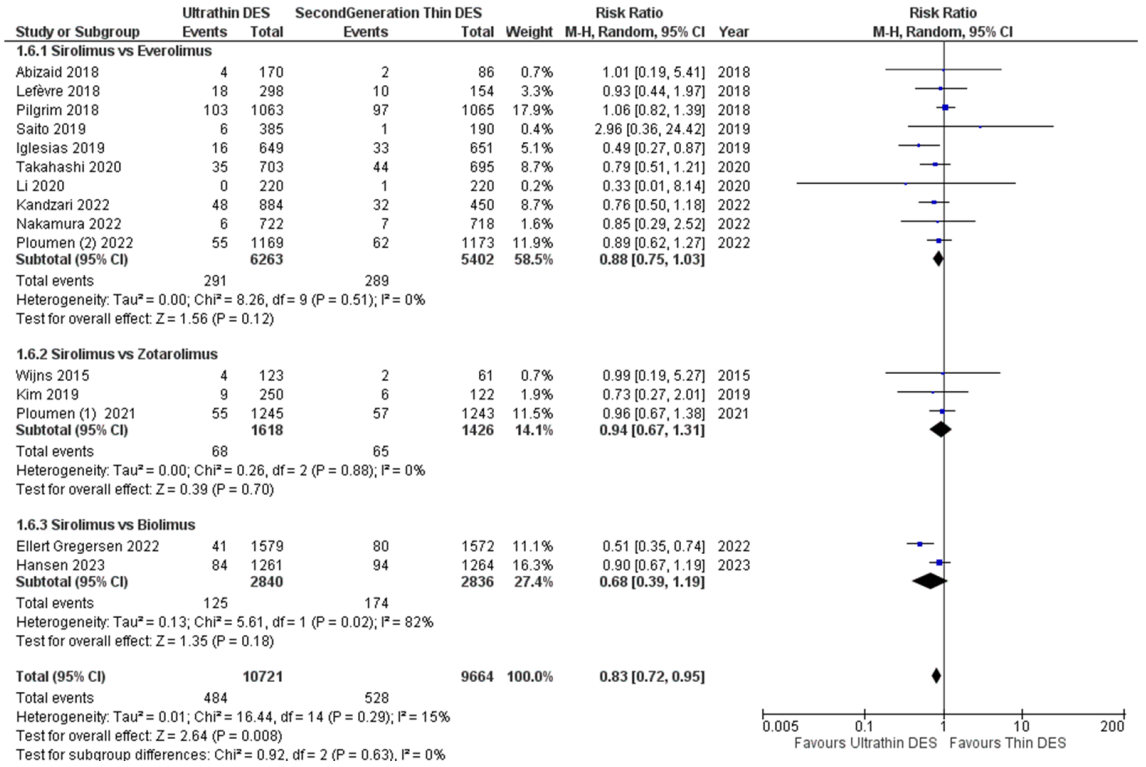

Figure S19. Effect of anti-proliferative drug on CD-TLR.

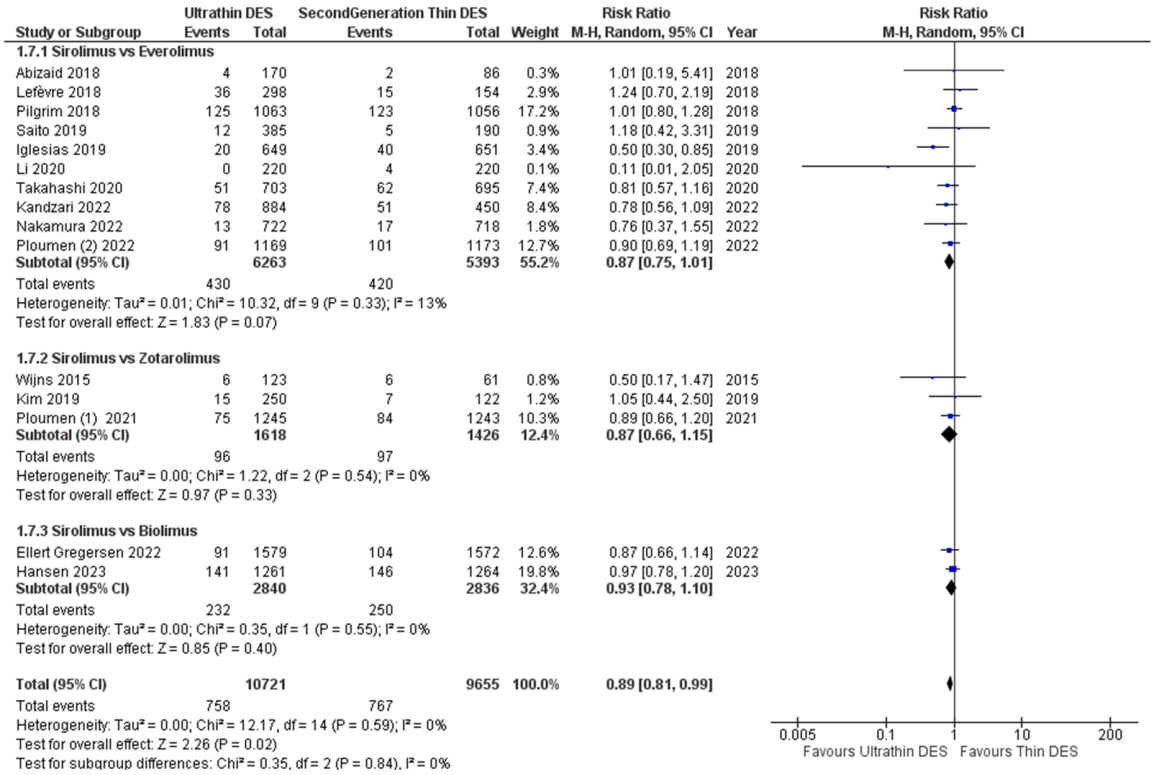

Figure S20. Effect of anti-proliferative drug on CD-TVR.

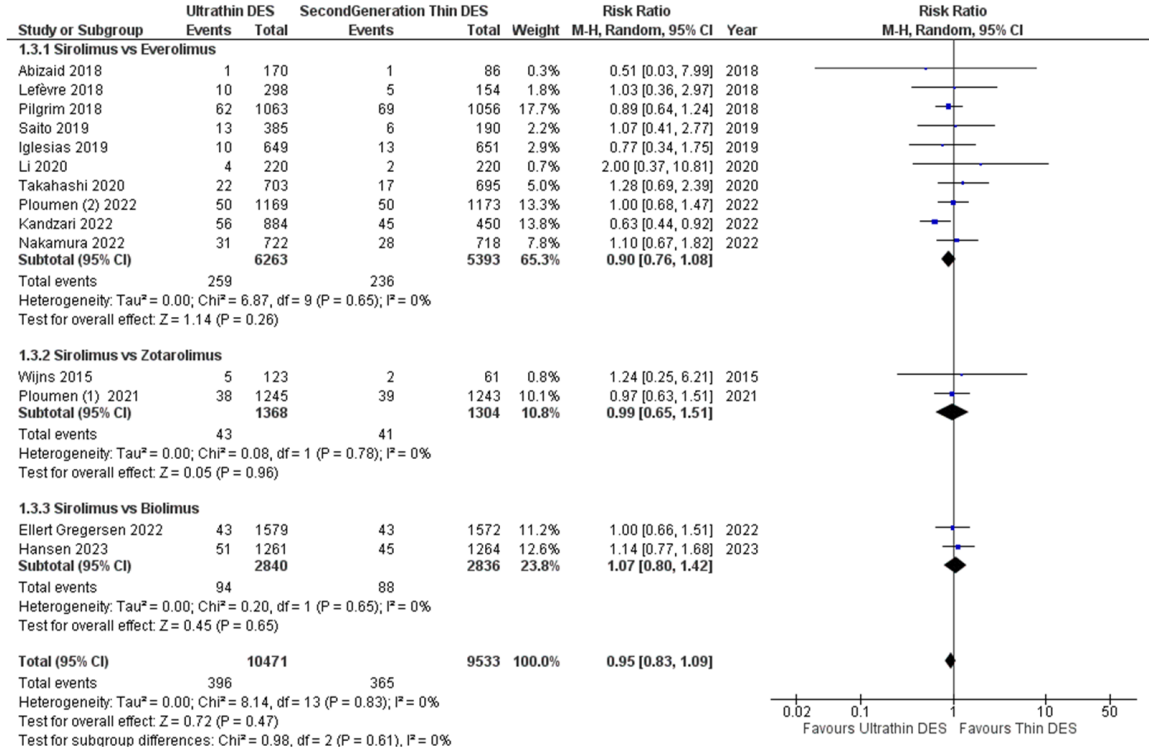

Figure S21. Effect of anti-proliferative drug on TV-MI.

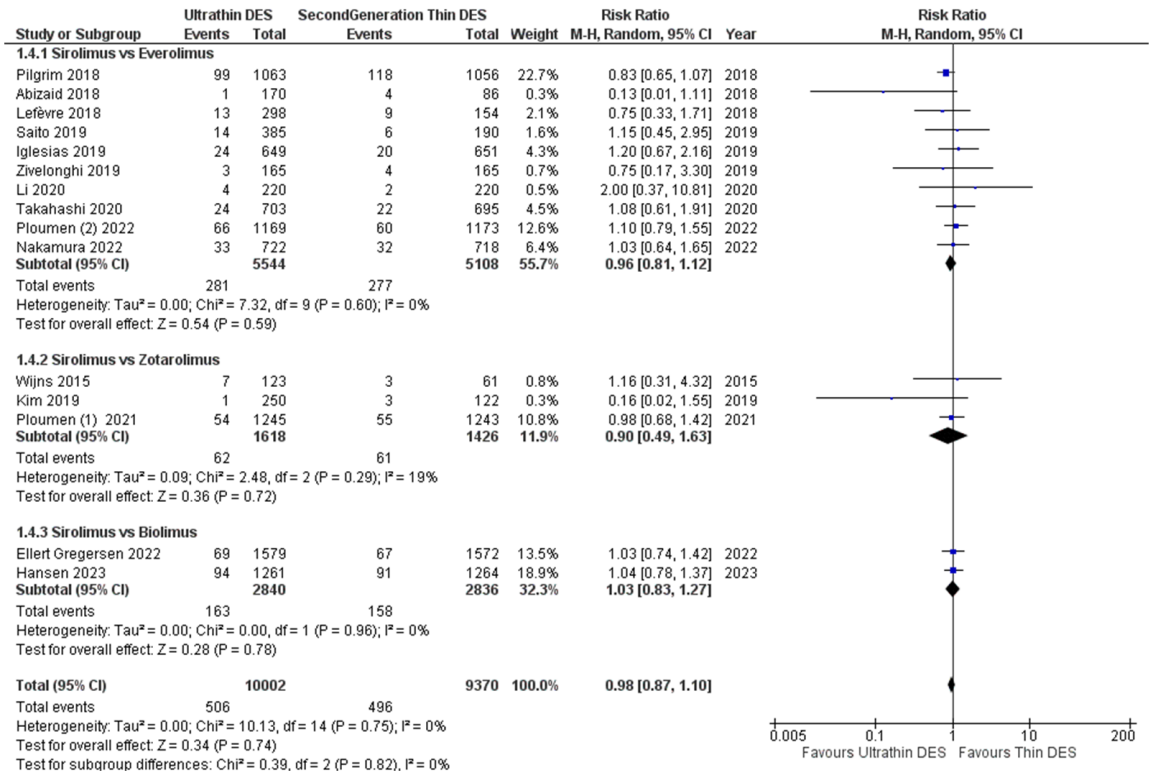

Figure S22. Effect of anti-proliferative drug on all-cause MI.

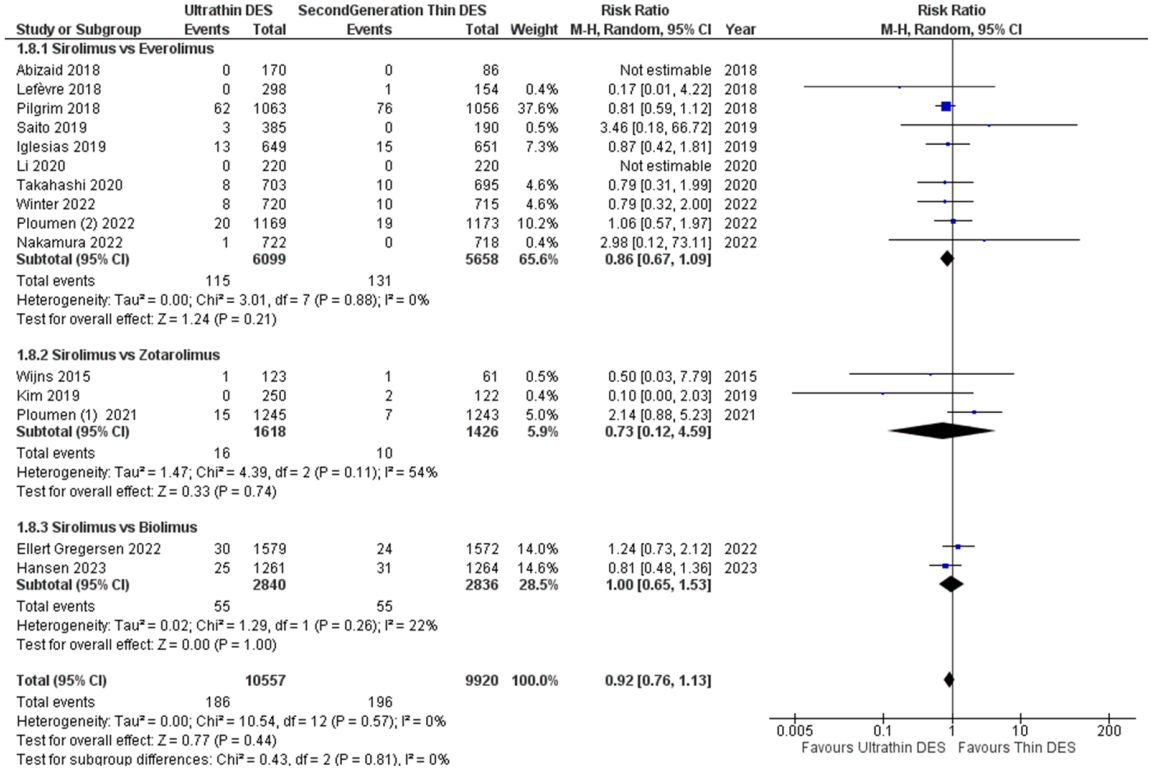

Figure S23. Effect of anti-proliferative drug on definite or probable ST.

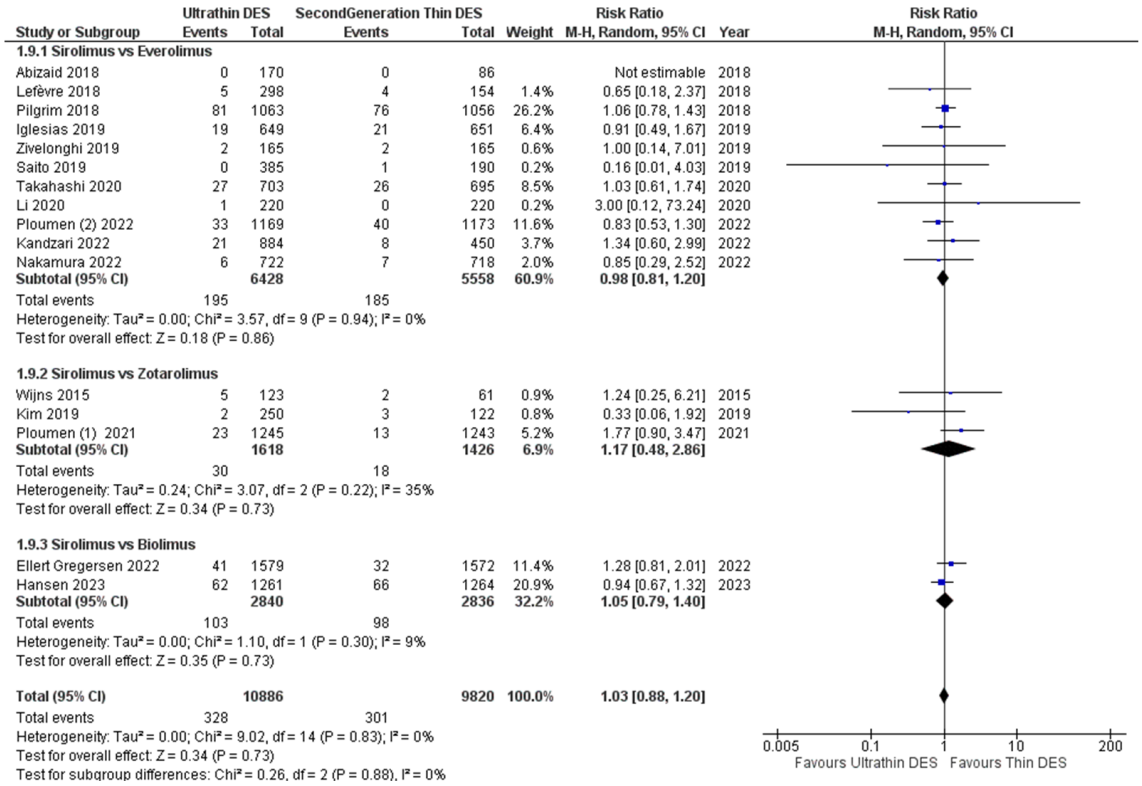

Figure S24. Effect of anti-proliferative drug on cardiac death.

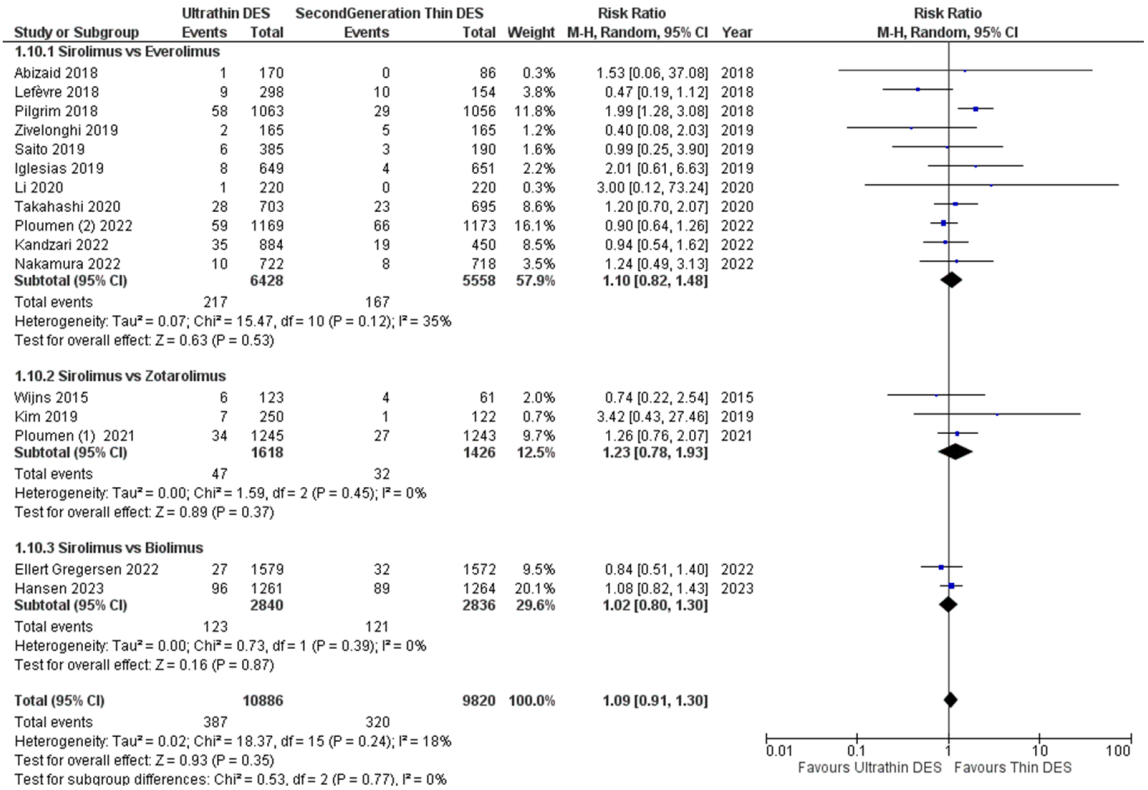

Figure S25. Effect of anti-proliferative drug on non-cardiac death.

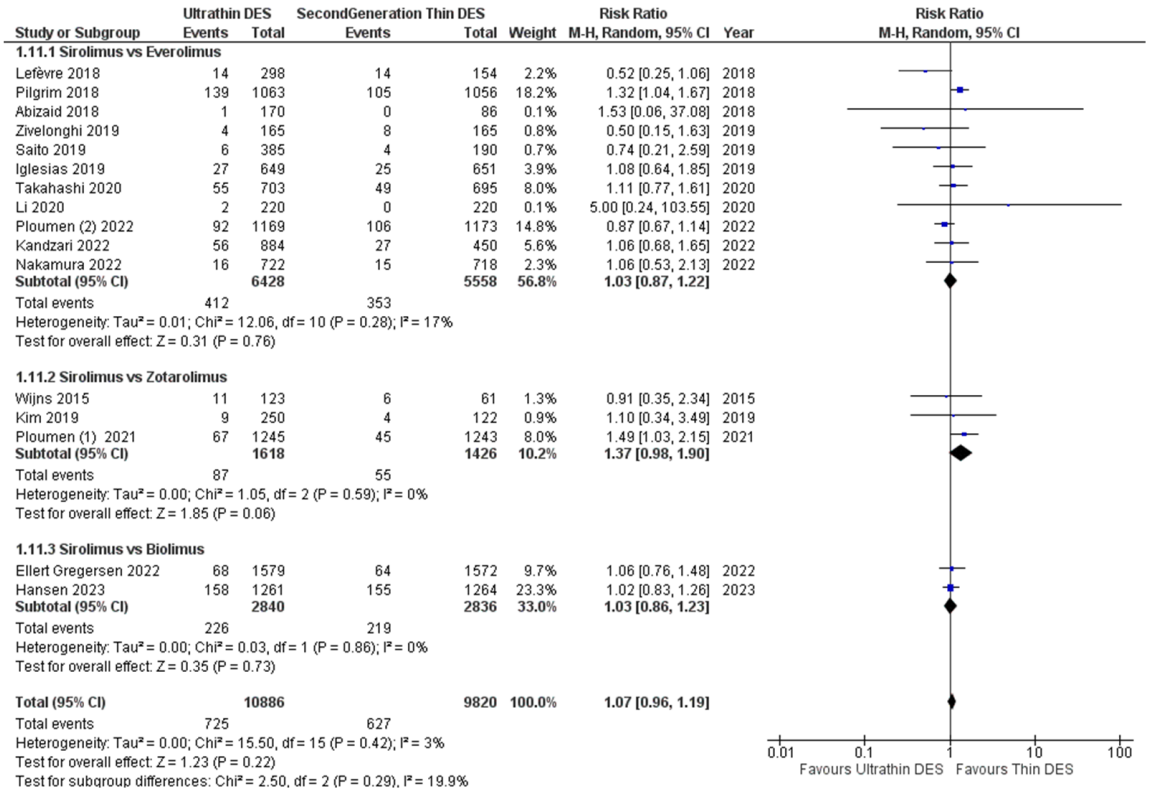

Figure S26. Effect of anti-proliferative drug on all-cause death.

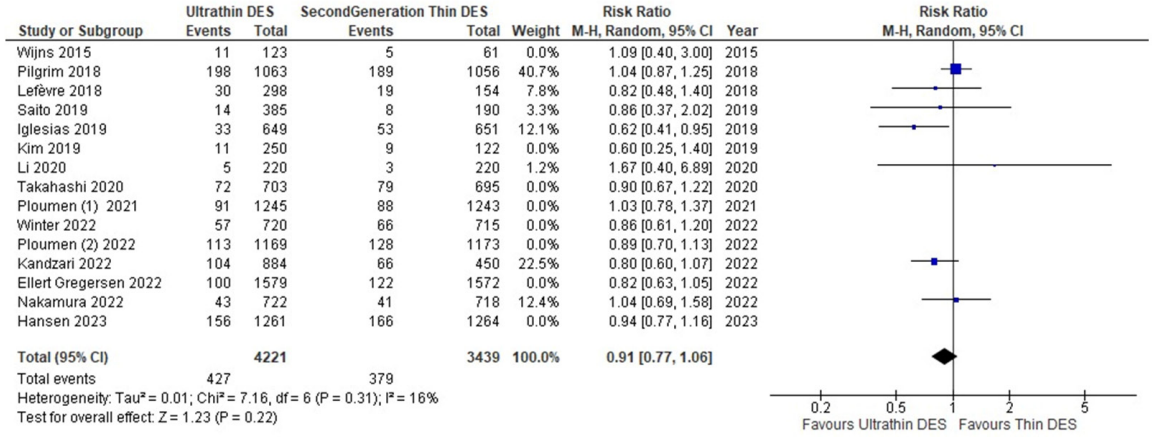

Figure S27. Sensitivity analysis based on stent type for TLF.

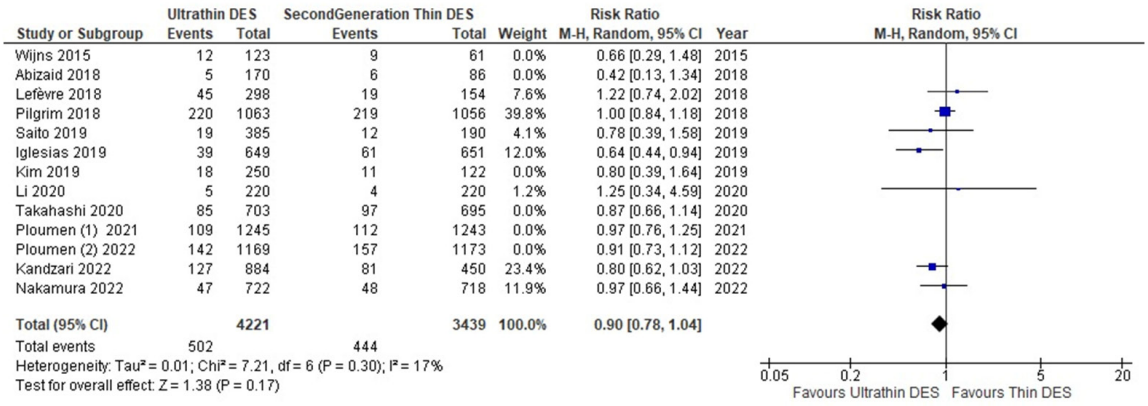

Figure S28. Sensitivity analysis based on stent type for TVF.

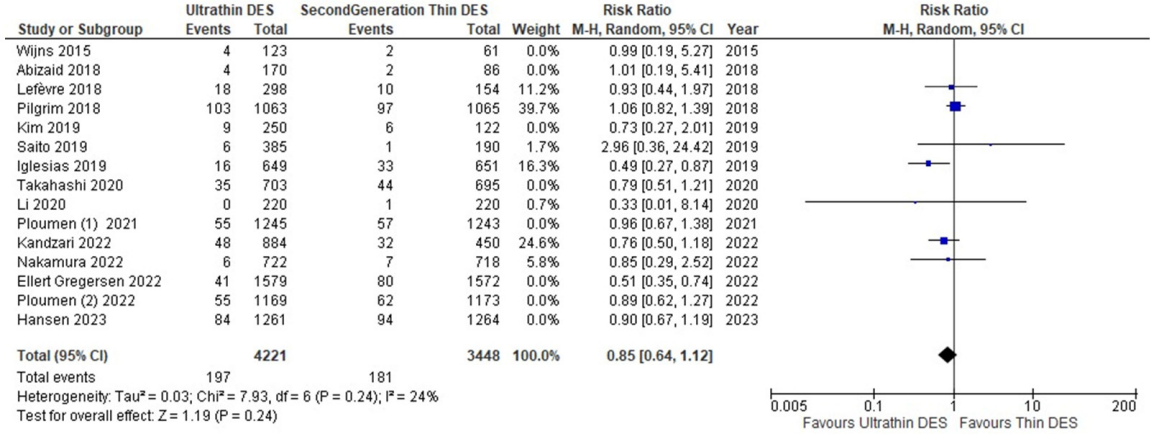

Figure S29. Sensitivity analysis based on stent type for CD-TLR.

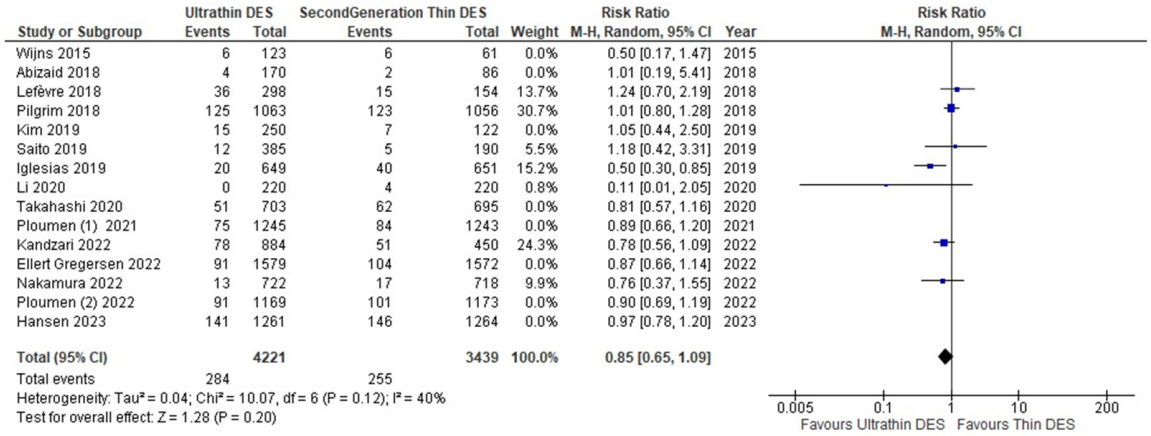

Figure S30. Sensitivity analysis based on stent type for CD-TVR.

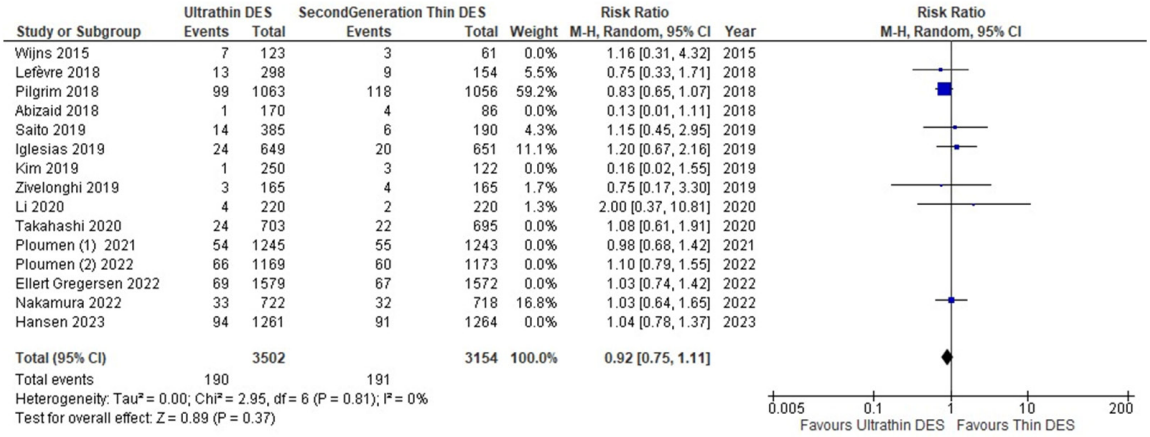

Figure S31. Sensitivity analysis based on stent type for all-cause MI.

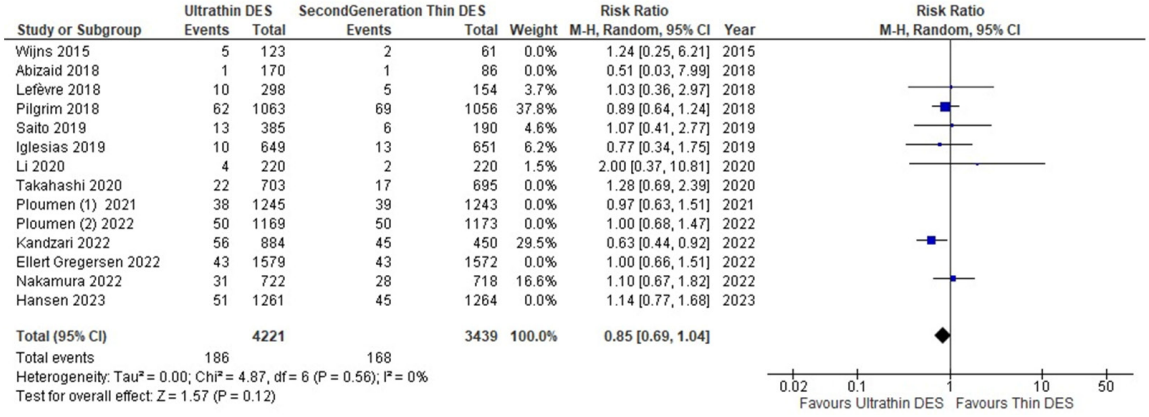

Figure S32. Sensitivity analysis based on stent type for TV-MI.

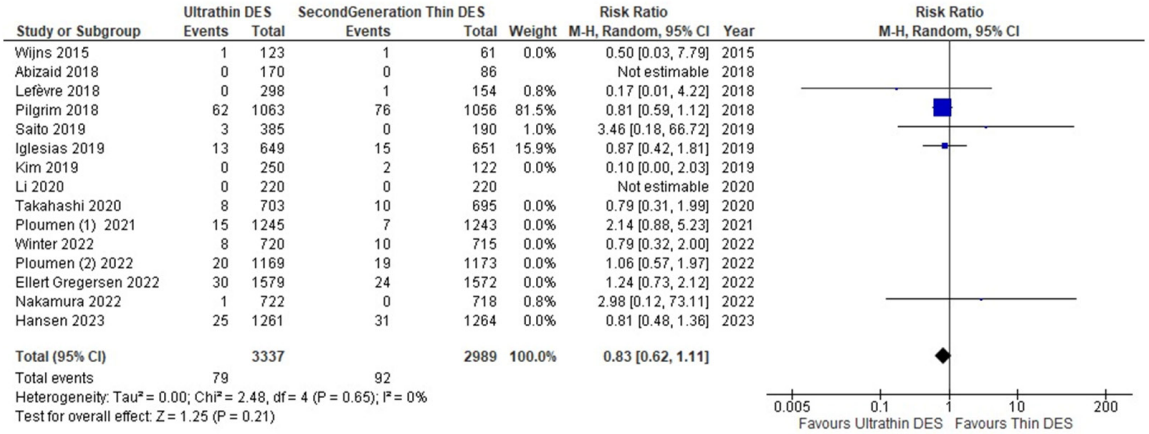

Figure S33. Sensitivity analysis based on stent type for definite or probable ST.

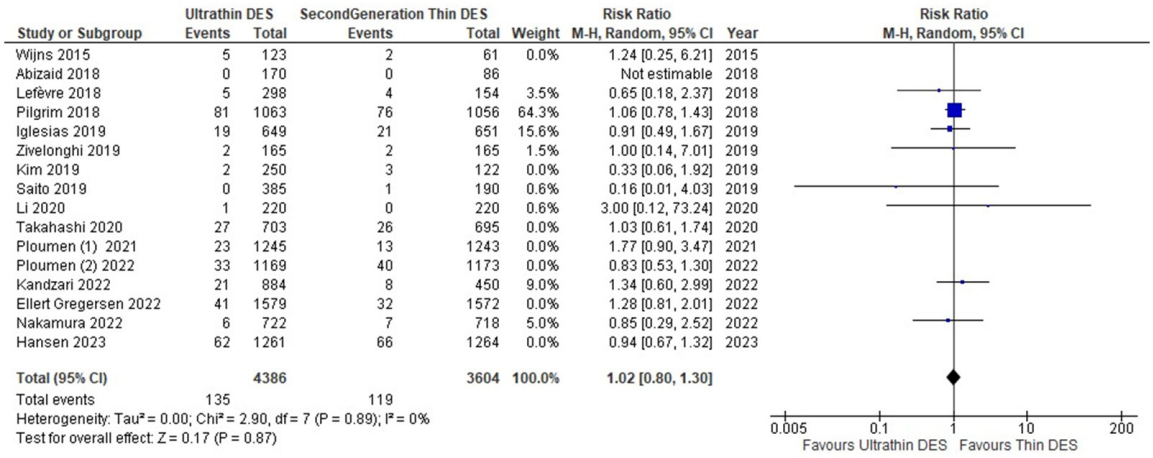

Figure S34. Sensitivity analysis based on stent type for cardiac death.

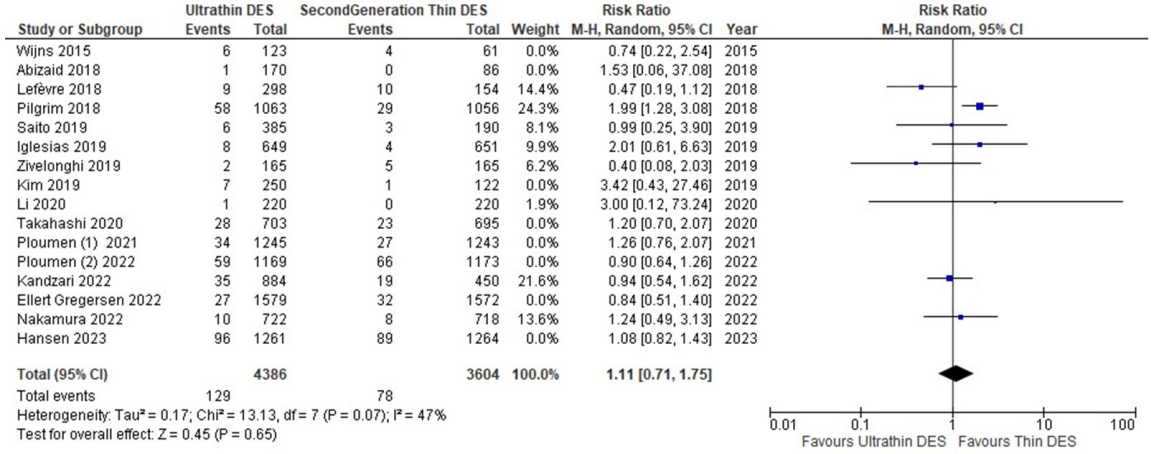

Figure S35. Sensitivity analysis based on stent type for non-cardiac death.

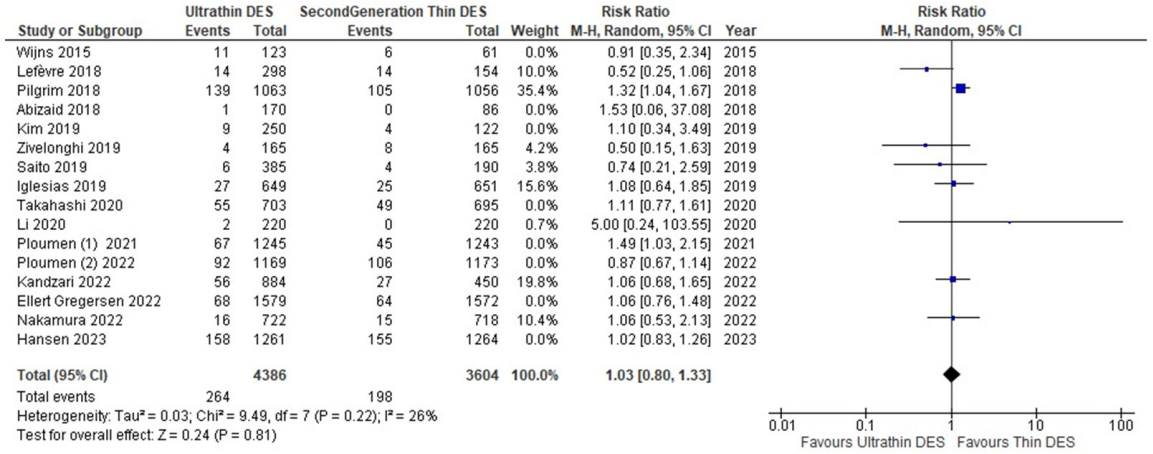

Figure S36. Sensitivity analysis based on stent type for all-cause death.