


BMJ Open Comparison of biodegradable and durable polymer drug-eluting stents in acute coronary syndrome: a meta-analysis

Haoyong Yuan,^{1,2} Zhongshi Wu,^{1,2} Ting Lu,^{1,2} Tingting Wei,³ Yifan Zeng,¹ Yalin Liu,^{1,2} Can Huang ^{1,2}

To cite: Yuan H, Wu Z, Lu T, *et al.* Comparison of biodegradable and durable polymer drug-eluting stents in acute coronary syndrome: a meta-analysis. *BMJ Open* 2022;**12**:e058075. doi:10.1136/bmjopen-2021-058075

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2021-058075>).

Received 07 October 2021
Accepted 09 May 2022



© Author(s) (or their employer(s)) 2022. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

¹Department of Cardiovascular Surgery, The second xiangya hospital of Central South University, Changsha, Hunan, China

²Engineering Laboratory of Hunan Province for Cardiovascular Biomaterials, Changsha, Hunan, China

³Department of Paediatrics, Hunan Provincial Maternal and Child Health Care Hospital, Changsha, Hunan, China

Correspondence to

Dr Can Huang;
huangcan413@csu.edu.cn

ABSTRACT

Objective To compare the safety and effectiveness between biodegradable polymer drug-eluting stents (BP-DES) and durable polymer drug-eluting stents (DP-DES) in patients with acute coronary syndrome (ACS).

Design Meta-analysis of randomised controlled trials (RCTs).

Primary and secondary outcome measures Major adverse cardiovascular events (MACEs) were considered the primary endpoint. Efficacy endpoints included target vessel revascularisation (TVR) and target lesion revascularisation (TLR). Safety endpoints included all-cause death, cardiac death, target vessel myocardial infarction and stent thrombosis (ST).

Methods We searched PubMed, Medline, Embase and the Cochrane Controlled Register of Trials for comparative studies of BP-DES and DP-DES in patients with ACS from January 2000 to July 2021. Statistical pooling was performed to estimate incidence using a random-effects model with generic inverse-variance weighting. Risk estimates were computed with 95% CIs.

Results Eight articles with seven RCTs that compared BP-DES and DP-DES in patients with ACS were identified and included in the qualitative and quantitative analyses. There was no difference in the baseline characteristics, except for the number of smoking patients (OR: 1.13, 95% CI 1.03 to 1.24; $p=0.008$, $I^2=29\%$), which was significantly lower in the BP-DES group. The meta-analysis demonstrated that MACEs, efficacy endpoints and safety endpoints were similar between the groups at 1 year. However, the incidence of total ST was significantly different between the BP-DES and DP-DES groups in the follow-up period ($p=0.0001$). Further analysis showed a statistically significant difference in MACEs (OR: 0.71, 95% CI 0.57 to 0.88; $p=0.002$, $I^2=0\%$), TLR (OR: 0.71, 95% CI 0.51 to 1.01; $p=0.05$, $I^2=0\%$), TVR (OR: 0.70, 95% CI 0.52 to 0.94; $p=0.002$, $I^2=15\%$), total ST incidence (OR: 0.59, 95% CI 0.46 to 0.77; $p=0.0001$, $I^2=48\%$) and ST incidence (OR: 0.63, 95% CI 0.47 to 0.85; $p=0.002$, $I^2=0\%$) over 2 years.

Conclusion This meta-analysis revealed that both stent types demonstrated excellent safety and efficacy profiles at 12 months. However, a slight increase in MACEs, TLR, TVR and ST incidence was observed in the DP-DES group over the 2-year follow-up period, suggesting that BP-DES may be more favourable when treating patients with ACS.

Trial registration number NCT00389220.

STRENGTHS AND LIMITATIONS OF THIS STUDY

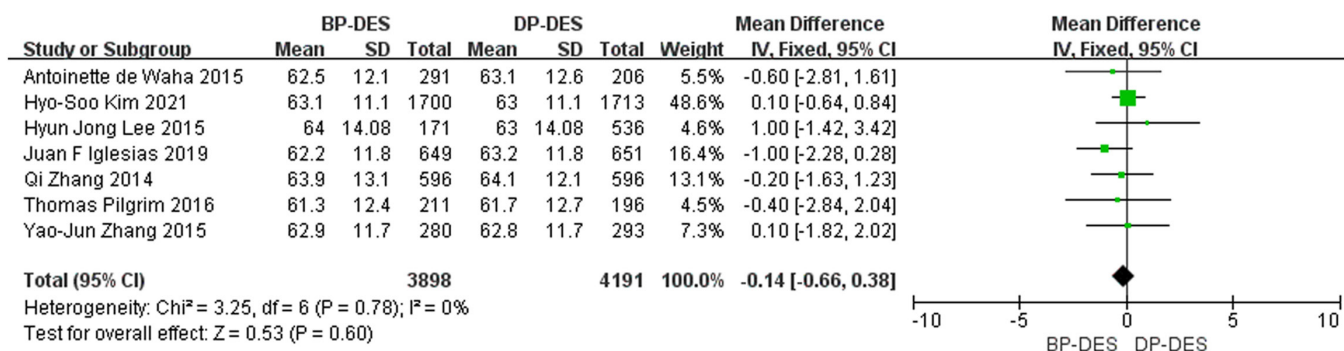
- ⇒ This meta-analysis included randomised controlled trials with long-term follow-ups.
- ⇒ The large sample size ensures adequate statistical power to detect even a small effect of interest.
- ⇒ Heterogeneity among the biodegradable polymer drug-eluting stents may distort the reported results.
- ⇒ The differences in the duration of dual antiplatelet therapy may influence clinical outcomes.

INTRODUCTION

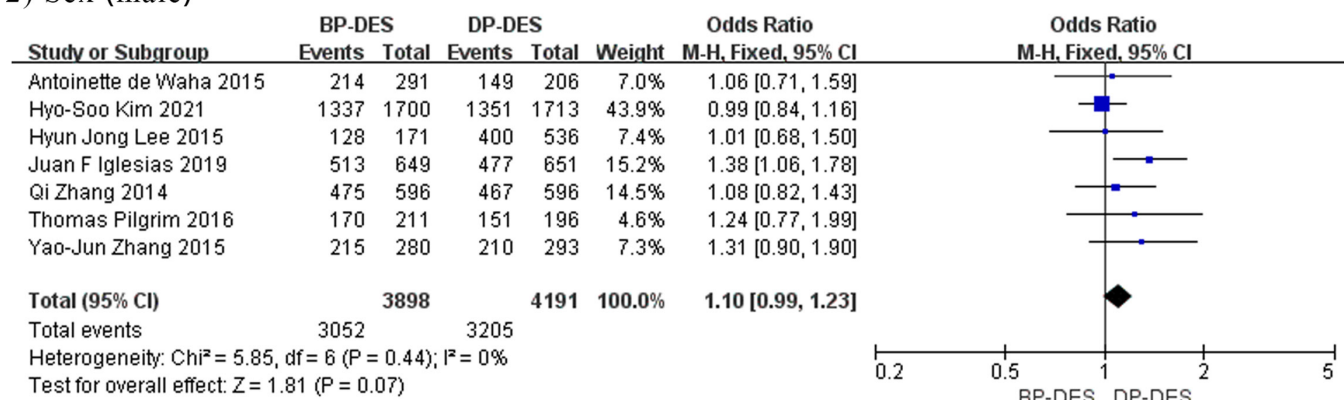
Percutaneous coronary intervention (PCI) is the current standard of care for patients with coronary artery disease, particularly acute coronary syndrome (ACS).^{1 2} Unlike bare-metal stents (BMS), drug-eluting stents (DES) use antiproliferative agents embedded in a polymer coating on the stent's surface, which inhibit neointimal hyperplasia to reduce the risk of restenosis.³ DES have substantially improved clinical outcomes; however, the first-generation durable polymer DES (DP-DES) were known to release sirolimus or paclitaxel, and were associated with similar risks of death and myocardial infarction compared with those of BMS beyond 1 year after implantation.⁴ Later, the second-generation DP-DES were confirmed to have lower restenosis rates than the first-generation devices and demonstrated reduced rates of stent thrombosis (ST).⁵ Recently, very late ST and neoatherosclerosis, with adverse clinical outcomes, have been observed with the second-generation DP-DES, which has improved the biocompatibility of the polymer.⁶ Late stent failure has been attributed to delayed endothelial healing secondary to a hypersensitivity reaction due to the DP.⁷

To address this potential limitation of DP-DES, biodegradable polymer DES (BP-DES) have been developed. Theoretically, BP-DES would lead to a reduction in vascular inflammation and a decreased risk of late

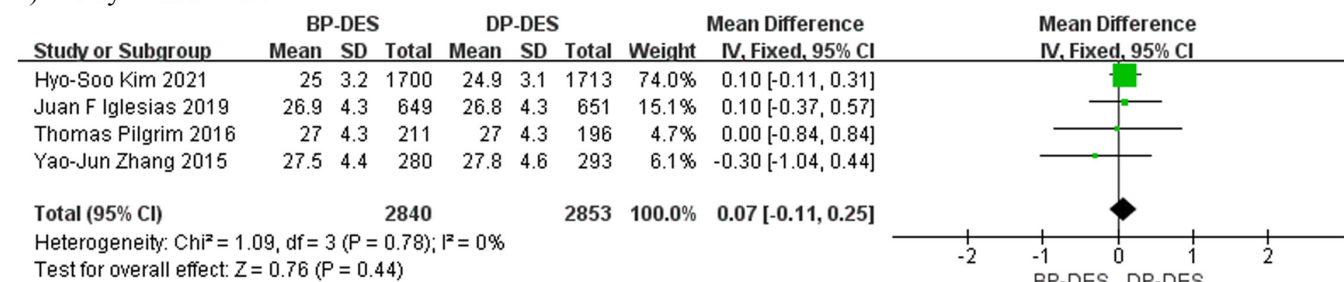
1) Age



2) Sex (male)



3) Body mass index



4) Hypertension

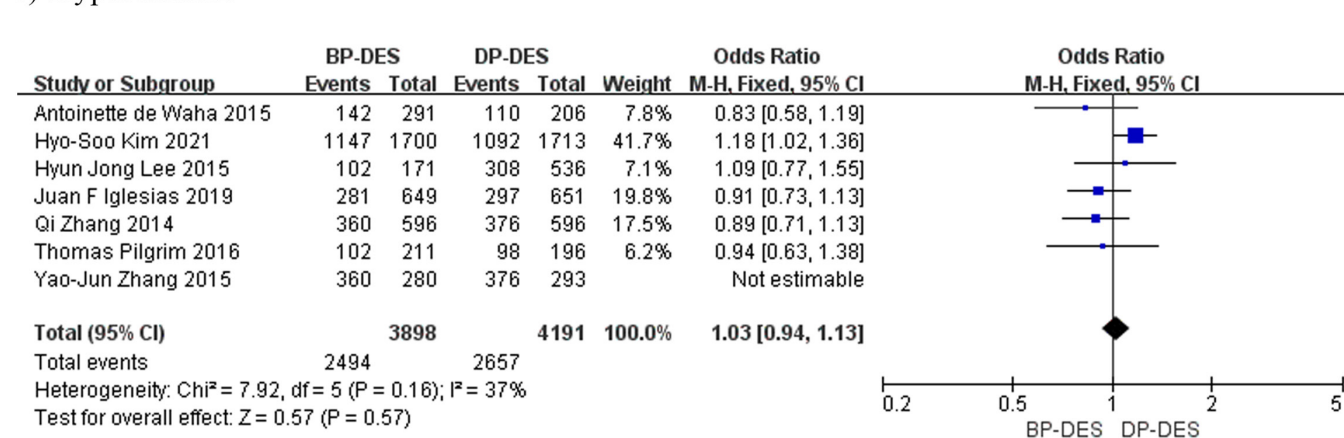
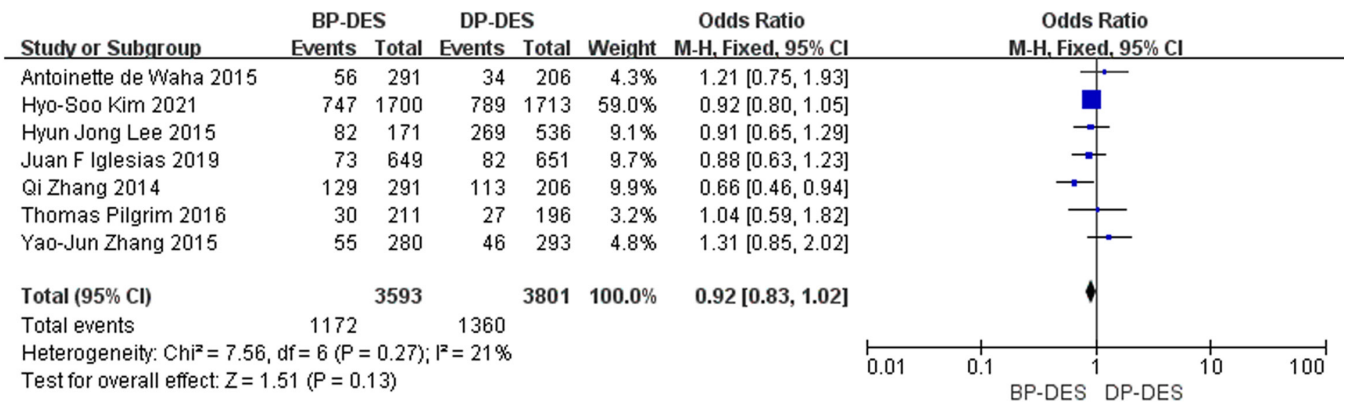
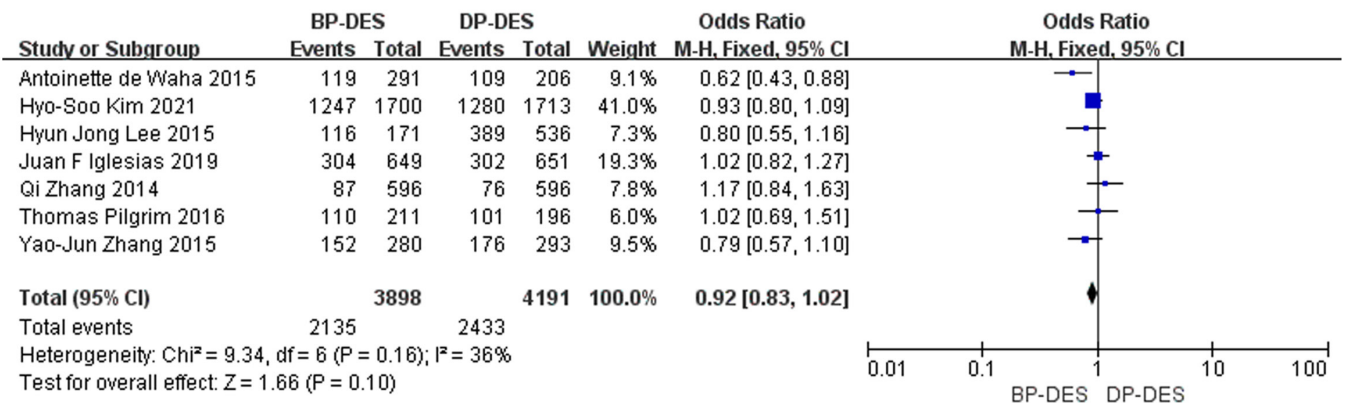


Figure 1 Baseline characteristics and stent information of patients with acute coronary syndrome (ACS). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

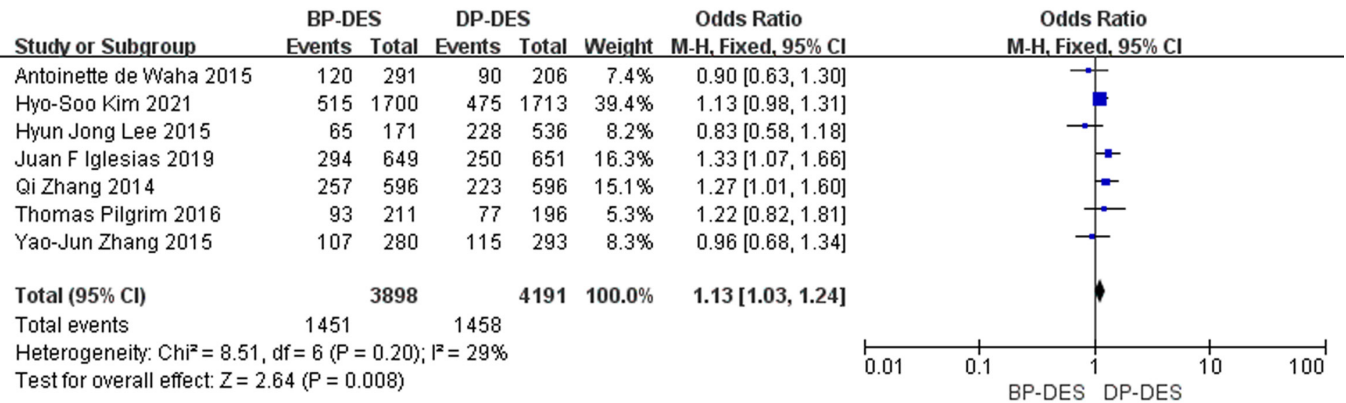
5) Diabetes



6) Dyslipidemia



7) Smoking



8) LVEF

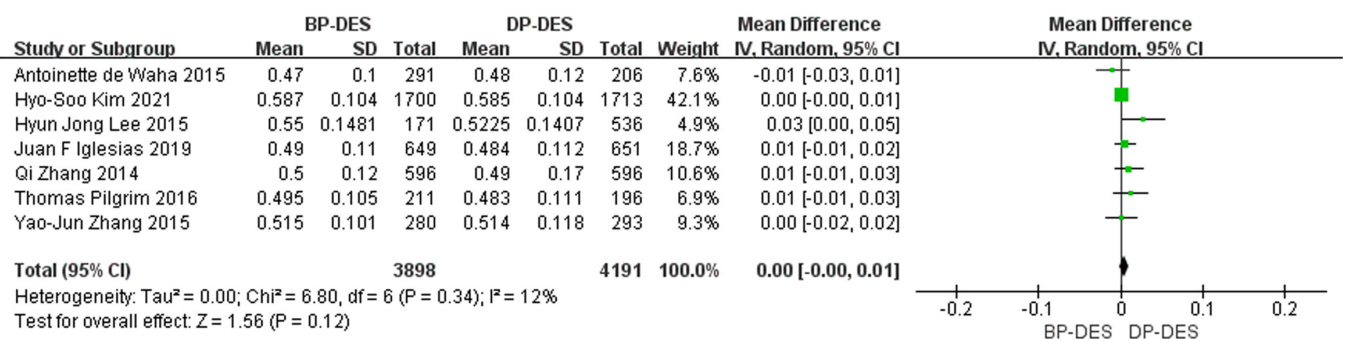
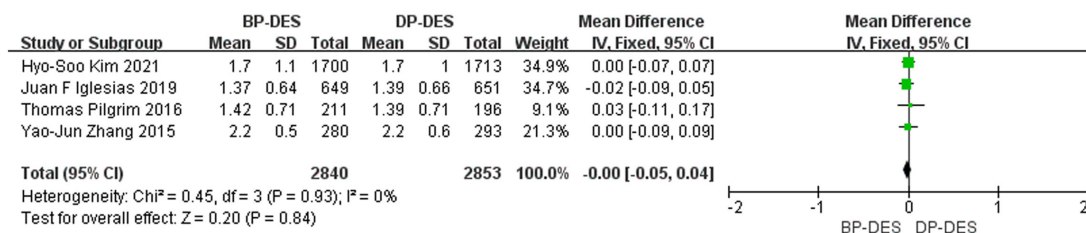


Figure 2 Baseline characteristics and stent information of patients with acute coronary syndrome (ACS). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents; LVEF, left ventricular ejection fraction.

9) Stent number per person



10) Total stent length

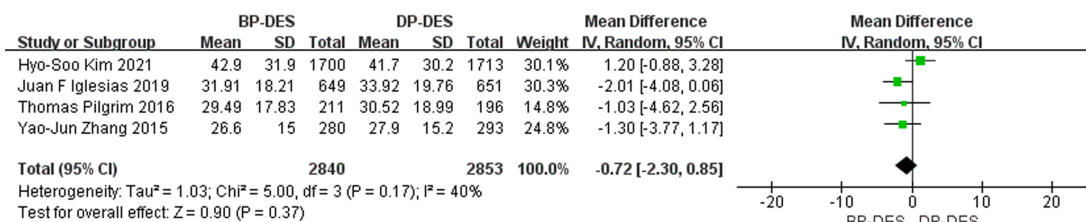


Figure 3 Baseline characteristics and stent information of patients with acute coronary syndrome (ACS). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents

stent-related complications due to the advantage of leaving the BMS only after complete drug elution and polymer degradation. BP-DES have been observed to reduce the rate of major adverse cardiac events (MACEs) compared with BMS⁸ and first-generation DP-DES.⁹ Studies of patients who underwent PCI revealed that the device-related outcomes were comparable between BP-DES and second-generation DP-DES.^{10–13} Thus, BP-DES would be expected to reduce the risk of ST-related MACEs beyond the first year compared with that of DP-DES. However, previous studies enrolled a significant proportion of stable angina patients. ACS confers an increased risk of adverse outcomes due to plaque characteristics, including culprit lesions, thrombus burden and persistent inflammation, compared with stable coronary artery diseases. ACS also increases the risk of delayed arterial healing and vessel remodelling,¹⁴ reflected by higher rates of incomplete stent strut coverage^{15 16} and malpositioning.¹⁷

Recently, many randomised trials have been performed to compare the efficacy and safety of DP-DES and BP-DES in patients with ACS who underwent PCI. In this meta-analysis, we aimed to summarise the studies comparing the two polymer technologies in patients with ACS and analyse the safety and effectiveness of these therapeutic options.

METHODS

Search strategy and registration

This study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was approved by the institutional review board of the Second Xiangya Hospital, Central South University. The protocol was registered with PROSPERO (CRD42021253412).

Based on the PRISMA statement, PubMed, Medline, Embase and the Cochrane Controlled Register of Trials databases were searched for comparative studies of

BP-DES and DP-DES that were used in the treatment of patients with ACS who underwent PCI. The following search terms were used: “BP-DES,” “biodegradable,” “bioabsorbable,” “bioabsorbable polymer drug-eluting stent,” “biodegradable polymer drug-eluting stent,” “DP-DES,” “durable polymer,” “durable polymer drug-eluting stent,” “acute coronary syndrome,” “ACS,” “AMI,” “Acute myocardial infarction,” “Non ST segment elevation myocardial infarction,” “ST segment elevation myocardial infarction,” “NSTEMI,” and “STEMI.” We also reviewed prior meta-analyses and the reference lists of the original trials and reviewed articles to identify further studies. Only English language articles published in peer-reviewed journals from January 2000 to July 2021 were selected. Analyses were conducted by two independent reviewers.

Eligibility criteria

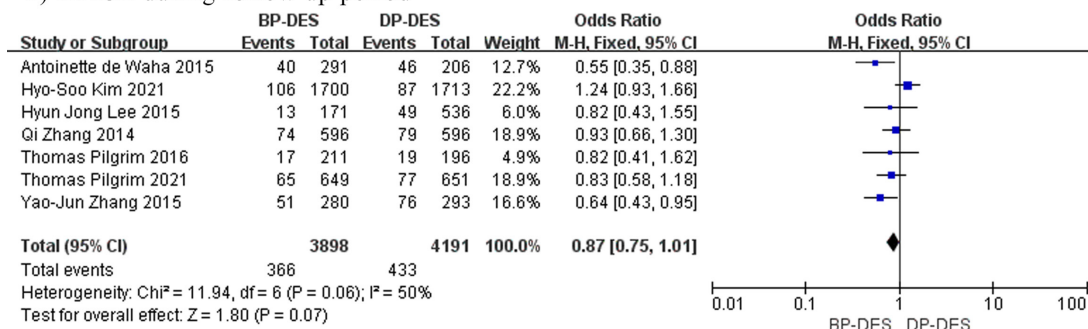
The inclusion criteria for this meta-analysis were as follows: (1) randomised controlled trials (RCTs) comparing BP-DES and DP-DES in the treatment of patients with ACS who underwent PCI; (2) data reporting patients’ baseline characteristics, follow-up durations, outcomes at the primary, safety and efficacy endpoints; (3) mean follow-up time over 12 months; and (4) full-text articles.

The exclusion criteria for the meta-analysis were as follows: (1) duplications of samples and reports (evaluated by two independent reviewers); (2) case reports/series; and (3) studies involving data from a national database.

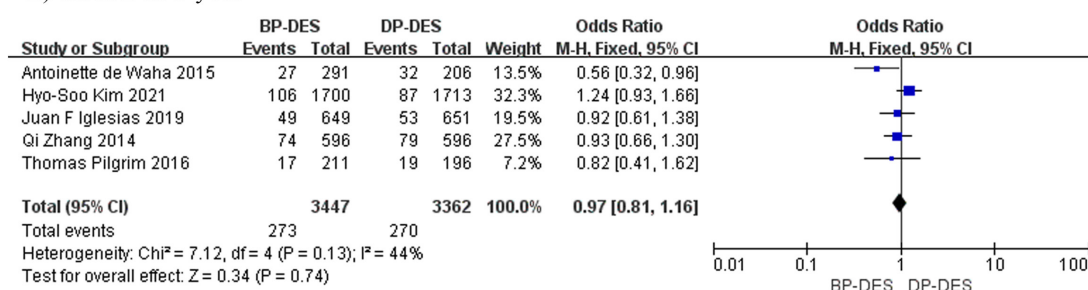
Data extraction and outcome measurement

Two authors (HY and TW) systematically screened the titles and abstracts of publications retrieved using the search strategy to select studies that met the above inclusion criteria. Any disagreement regarding the eligibility of particular studies was resolved through discussion and involvement of a third author (ZW), when necessary. First, baseline characteristics, including the name

1) MACE during follow up period



2) MACE at 1 year



3) MACE over 2 years

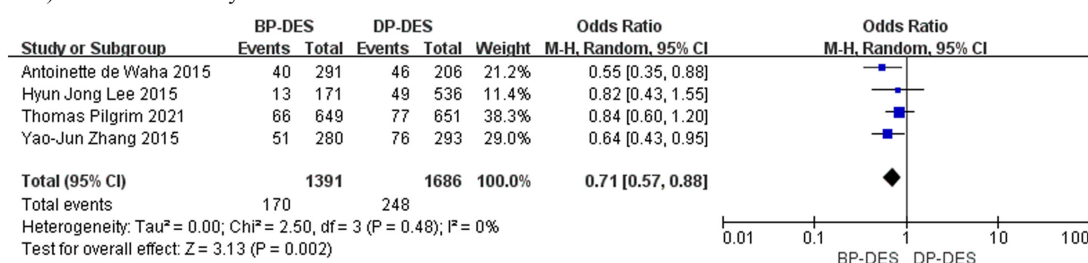


Figure 4 Primary endpoint: major adverse cardiac events (MACEs). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

of the first author, year of publication, study design, country of origin, number of patients, mean age of participants and mean duration of follow-up, were gathered from each included article. In addition, data on sex; body mass index; the presence of hypertension, diabetes, dyslipidaemia, chronic kidney disease, peripheral vessel disease or smoking; left ventricular ejection fraction (LVEF); number of stents per person; and total stent length were collected for evaluation of procedure-related risks. MACEs were considered the primary endpoint. The efficacy endpoints included target vessel revascularisation (TVR) and target lesion revascularisation (TLR). In addition, all-cause death, cardiac death, target vessel myocardial infarction (TVMI), and ST were used as endpoints to evaluate the safety of BP-DES and DP-DES.

The Risk of Bias 2 tool was used to assess the quality of RCTs based on sequence generation; randomised group allocation; concealment; blinding of participants, personnel and outcome assessors; incomplete data; selectivity; outcome reporting; and other sources of bias (online supplementary material 1).¹⁸

Data analysis and synthesis

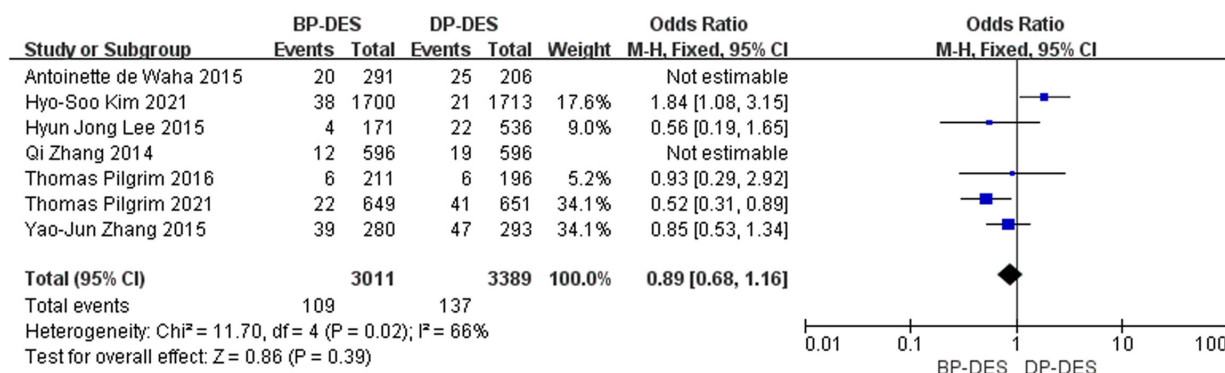
Continuous variables were reported as the mean (SD), and categorical variables were expressed as numbers. Statistical pooling was performed to estimate incidence, according to a random-effects model with generic inverse-variance weighting. We computed risk estimates with 95% CIs, using RevMan V.5.3 (The Cochrane Collaboration, The NordicCochrane Centre, Copenhagen, Denmark). Hypothesis testing for superiority was set at the two-tailed 0.05 level. Hypothesis testing for statistical homogeneity was set at the two-tailed 0.10 level and was based on the Cochran Q test, with I² values of 25%, 50% and 75% representing mild, moderate and severe heterogeneity, respectively.

RESULTS

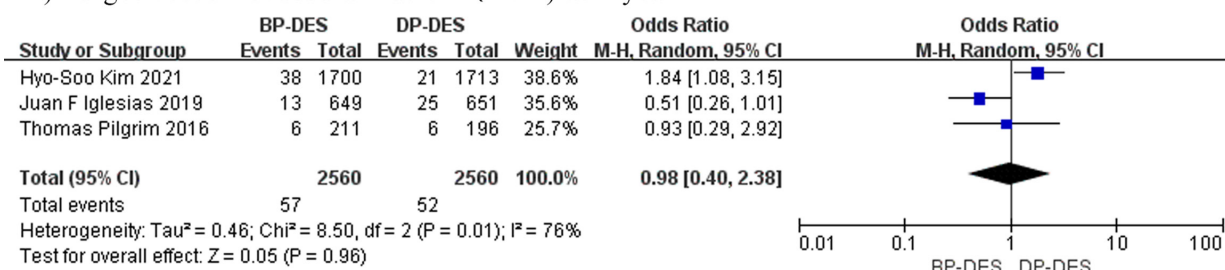
Search results

A total of 895 articles, written in English, were identified through the literature search. After an initial screening of the titles and abstracts, 803 articles were eliminated, as they were not related to the topic of this study. Following

1) Target vessel revascularization (TVR) during follow up period



2) Target vessel revascularization (TVR) at 1 year



3) Target vessel revascularization (TVR) over 2 years



Figure 5 Target vessel revascularisation (TVR). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

the removal of these articles, 92 clinical studies and RCTs of the 2 polymers remained. After reading the full texts, 28 articles about ACS remained, with 20 articles including chronic and ACS. Finally, 8 articles, with 7 RCTs, comparing BP-DES and DP-DES in patients with ACS were identified and included in the qualitative and quantitative analyses.^{19–26} The follow-up duration ranged from 1 year to 5 years (online supplementary table 1 and online supplementary material 2).

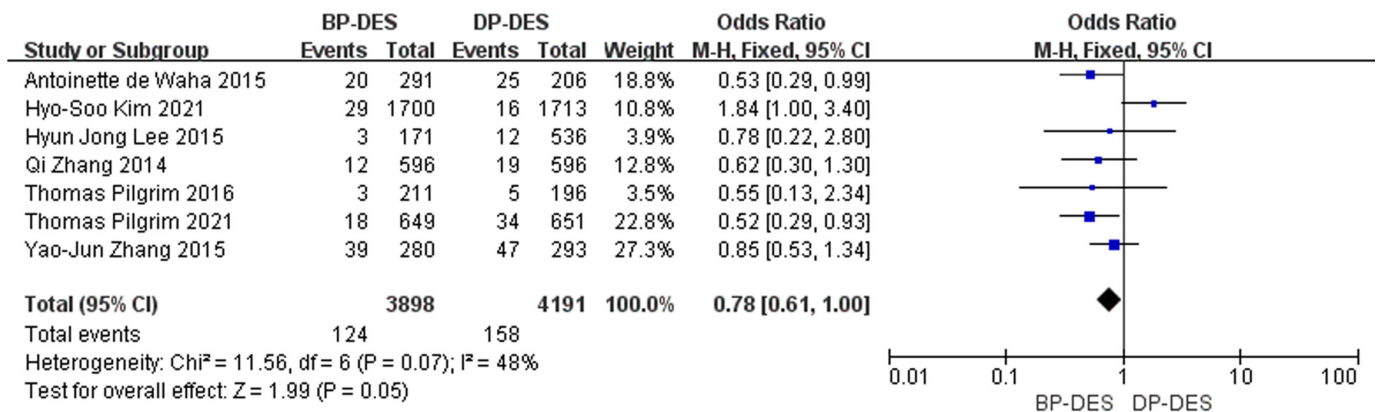
General features of the trials

A total number of 8089 patients (3898 patients who were treated with BP-DES and 4191 patients who were treated with DP-DES) were included in this analysis. Further details about the quality of RCTs; total number of patients retrieved from each trial; publication years; countries of origin of the publications; centres in which the trials were performed; follow-up durations; risk factors; and primary, efficacy, and safety endpoints are listed in online supplementary table 2 and online supplementary material 2.

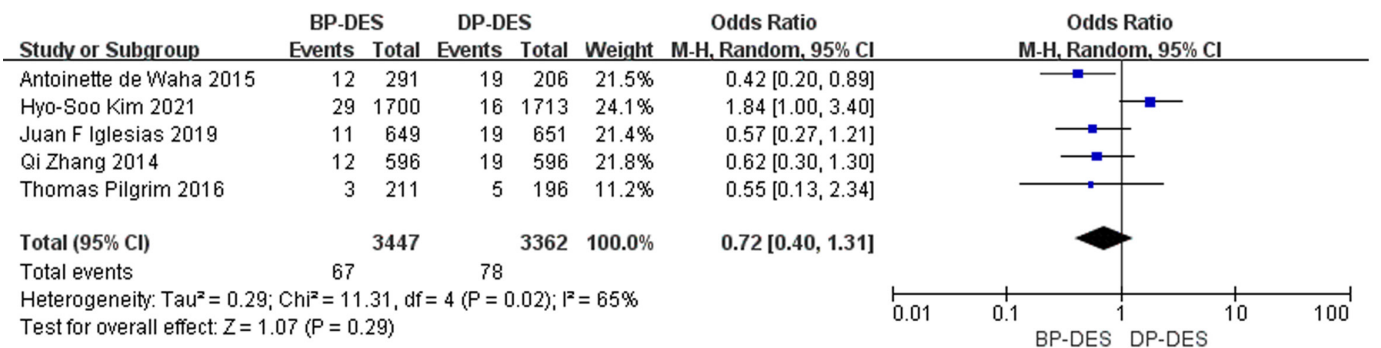
Patient characteristics

The baseline features of the patients are summarised in online supplemental table 2. The mean age of the patients who were treated by BP-DES ranged from 61.3 to 64 years, whereas the mean age of the patients who were treated by DP-DES ranged from 61.7 to 64.1 years. The proportions of male patients were above 70% in all included trials. There was no difference in age (mean difference (MD): 0.14, 95% CI –0.66 to 0.38; p=0.60, I²=0%), sex (male) (OR: 1.10, 95% CI 0.99 to 1.23; p=0.07, I²=0%), hypertension (OR: 1.03, 95% CI 0.94 to 1.13; p=0.57, I²=37%), dyslipidaemia (OR: 0.92, 95% CI 0.83 to 1.02; p=0.10, I²=36%), LVEF (MD: 0.00, 95% CI 0.00 to 0.01; p=0.12, I²=12%), body mass index (MD: 0.07, 95% CI –0.11 to 0.25; p=0.44, I²=0%), diabetes (OR: 0.92, 95% CI 0.83 to 1.02; p=0.13, I²=21%), total stent length (MD: –0.72, 95% CI –2.30 to –0.85; p=0.37, I²=40%) and in the number of stents per person (MD: –0.00, 95% CI –0.05 to 0.04; p=0.84, I²=0%) among patients who were

1) Target lesion revascularization(TLR) during follow up period



2)Target lesion revascularization(TLR) at 1 year



3) Target lesion revascularization(TLR) over 2 years

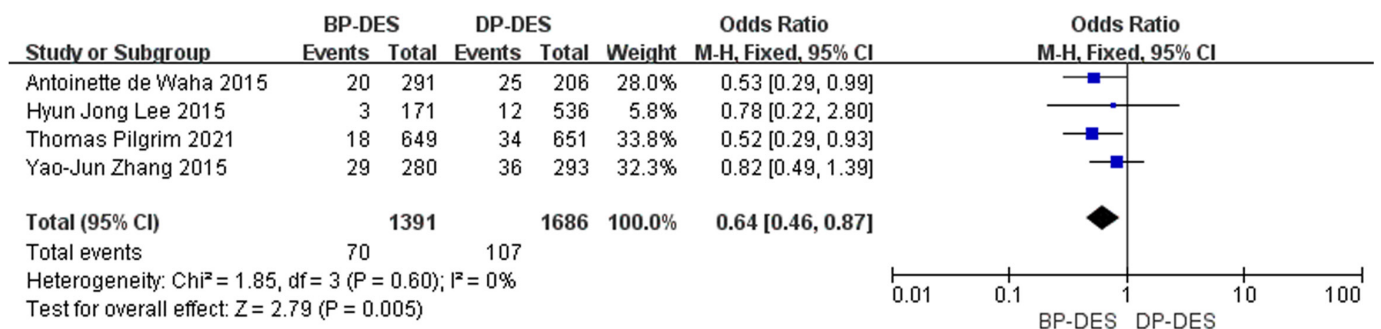


Figure 6 Target lesion revascularisation (TLR). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

implanted with BP-DES or DP-DES. The meta-analysis demonstrated that the number of smoking patients (OR: 1.13, 95% CI 1.03 to 1.24; $p=0.008$, $I^2=29\%$) was significantly lower in the BP-DES group than that in the DP-DES group (figures 1–3).

Primary endpoint: MACEs reported during follow-up periods of 1–5 years, 1 year and over 2 years

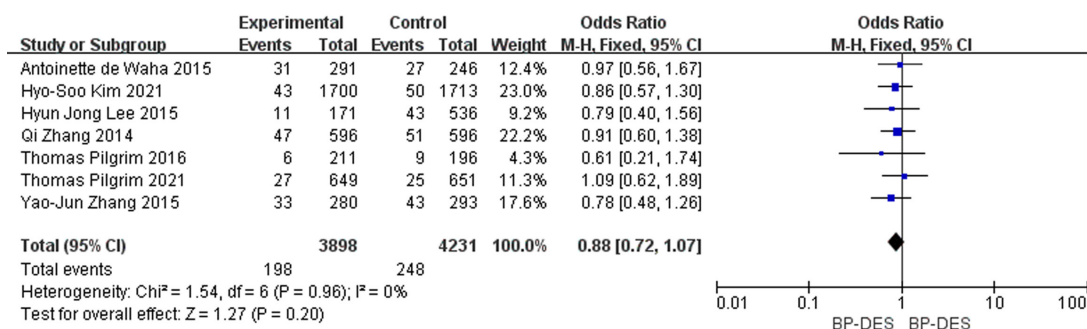
MACEs, including all-cause death, recurrent myocardial infarction (MI), or any coronary repeat revascularisation involving TLR, TVR and non-TVR, were considered to be the primary endpoint of the trials. A meta-analysis indicated no statistically significant difference in the MACEs in a follow-up period ranging from 1 to 5 years between the two groups (OR: 0.87, 95% CI 0.75 to 1.01; $p=0.07$, $I^2=50\%$). Of the five studies that published

1-year outcomes, MACEs were not significantly different between the BP-DES and DP-DES groups (OR: 0.97, 95% CI 0.81 to 1.16; $p=0.74$, $I^2=44\%$). However, MACEs with follow-up periods of over 2 years were significantly lower in the BP-DES group (OR: 0.71, 95% CI 0.57 to 0.88; $p=0.002$, $I^2=0\%$) (figure 4).

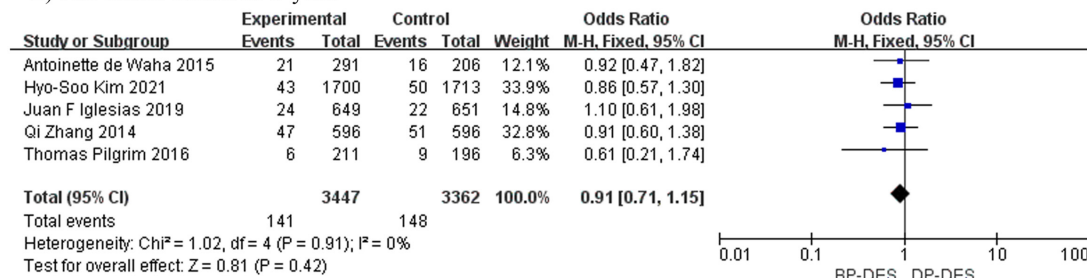
Efficacy endpoint: TVR and TLR reported during follow-up periods of 1–5 years, 1 year and over 2 years

TLR and TVR were considered the efficacy endpoints of the trials. The meta-analysis indicated no statistically significant difference in TLR in the follow-up periods ranging from 1 to 5 years between the two groups (OR: 0.78, 95% CI 0.61 to 1.00; $p=0.05$, $I^2=48\%$). Among the five studies that published 1-year data, TLR was not significantly different between the BP-DES and DP-DES groups (OR:

1) All cause death during follow up period



2) All cause death at 1 year



3) All cause death over 2 years

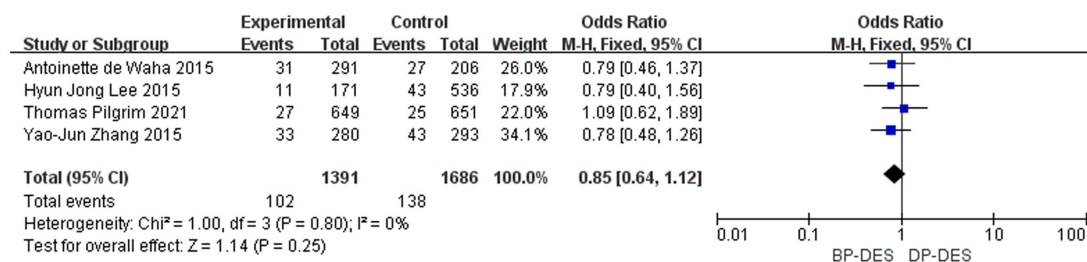


Figure 7 All-cause death. BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

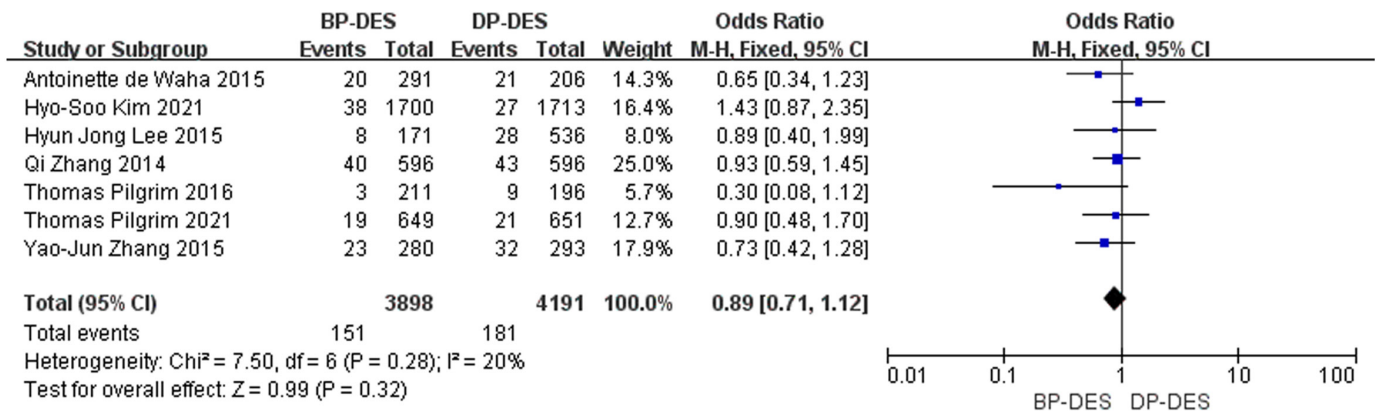
0.72, 95% CI 0.40 to 1.31; $p=0.29$, $I^2=65\%$). The meta-analysis indicated no statistically significant difference in TVR in the follow-up periods ranging from 1 to 5 years (OR: 1.01, 95% CI 0.79 to 1.28; $p=0.96$, $I^2=46\%$) or in the three publications with 1-year follow-up periods (OR: 0.98, 95% CI 0.40 to 2.38; $p=0.96$, $I^2=76\%$). However, the difference in TLR was statistically significant in four RCT studies with follow-up periods of over 2 years (OR: 0.71, 95% CI 0.51 to 1.01; $p=0.05$, $I^2=0\%$), and the difference in TVR was also statistically significant in three RCT studies with follow-up periods of over 2 years (OR: 0.70, 95% CI 0.52 to 0.94; $p=0.002$, $I^2=15\%$), with values much lower in the BP-DES group (figures 5 and 6).

Safety endpoint: all-cause death, cardiac-related death, TVMI and ST over follow-up periods of 1–5 years, 1 year and over 2 years

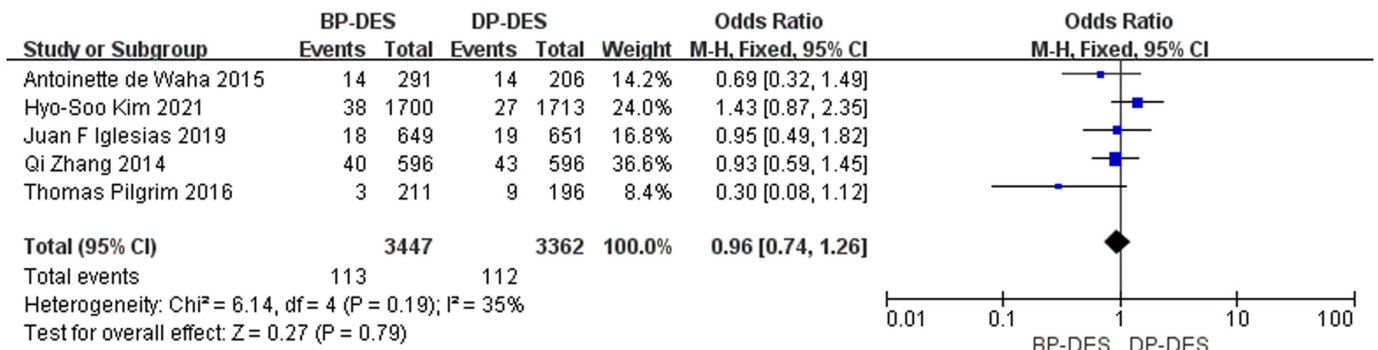
All-cause death, cardiac-related death, TVMI and ST were considered the efficacy endpoints. The meta-analysis indicated no statistically significant difference between the two groups in all-cause death (OR: 0.88, 95% CI 0.72 to 1.07; $p=0.20$, $I^2=0\%$), cardiac-related death (OR: 0.89, 95% CI 0.71 to 1.12; $p=0.32$, $I^2=20\%$) and TVMI (OR: 0.73, 95% CI 0.53 to 1.01; $p=0.05$, $I^2=0\%$) over a follow-up

period ranging from 1 to 5 years. Of the five studies that published 1-year data, all-cause death, cardiac-related death and TVMI were also not significantly different between the BP-DES and DP-DES groups ((all-cause death, OR: 0.91, 95% CI 0.71 to 1.15; $p=0.42$, $I^2=0\%$), (cardiac-related death, OR: 0.96, 95% CI 0.74 to 1.26; $p=0.79$, $I^2=35\%$) and (TVMI, OR: 0.73, 95% CI 0.53 to 1.01; $p=0.05$, $I^2=0\%$)). In the five studies with follow-up periods of over 2 years, similar findings were observed for the all-cause cardiac death, cardiac-related death and TVMI ((all-cause death, OR: 0.85, 95% CI 0.64 to 1.12; $p=0.25$, $I^2=0\%$), (cardiac-related death, OR: 0.77, 95% CI 0.56 to 1.17; $p=0.12$, $I^2=0\%$) and (TVMI, OR: 0.79, 95% CI 0.51 to 1.22; $p=0.28$, $I^2=0\%$)) (figures 7–9). However, the total ST incidence, including the definite ST, probable ST and definite or probable ST incidence, was significantly different between the BP-DES and DP-DES groups during the follow-up period (OR: 0.59, 95% CI 0.46 to 0.77; $p=0.0001$, $I^2=48\%$). Further analysis revealed no difference in total ST for the 1-year follow-up (OR: 0.61, 95% CI 0.32 to 1.15; $p=0.13$, $I^2=72\%$), while the meta-analysis indicated a statistically significant difference in the total ST for the follow-up

1) cardiac death during follow up period



2) cardiac death at 1 year



3) cardiac death over 2 years

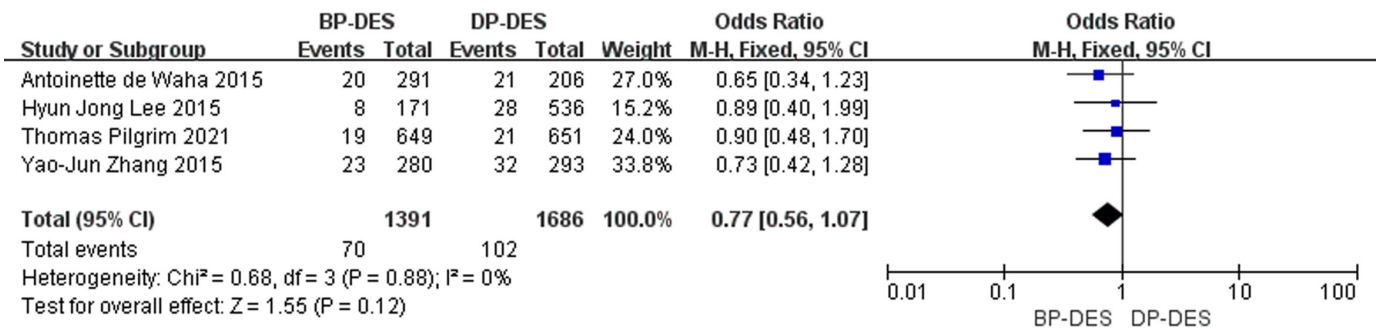


Figure 8 Cardiac-related death. BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

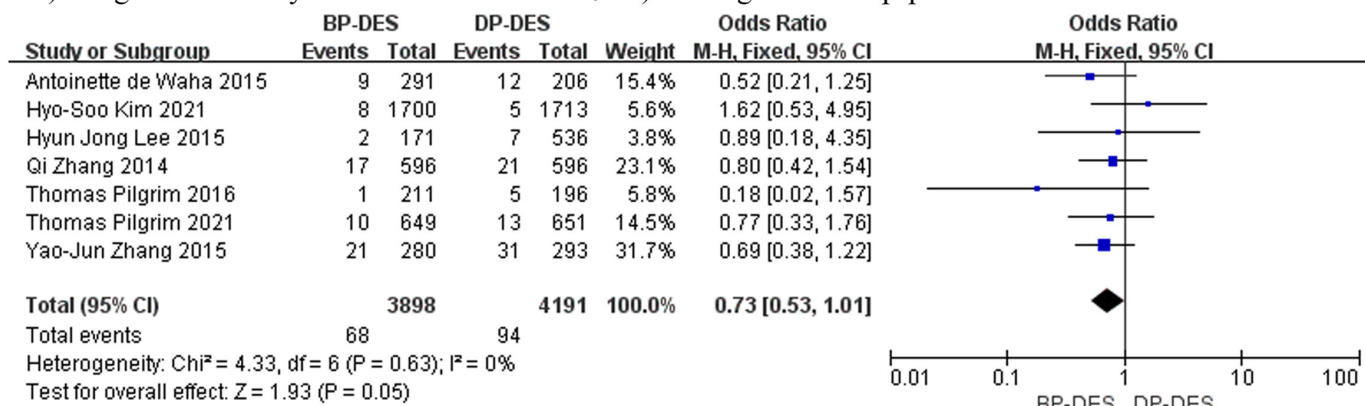
periods of over 2 years (OR: 0.63, 95% CI 0.47 to 0.85; p=0.002, I²=0%) (figure 10).

DISCUSSION

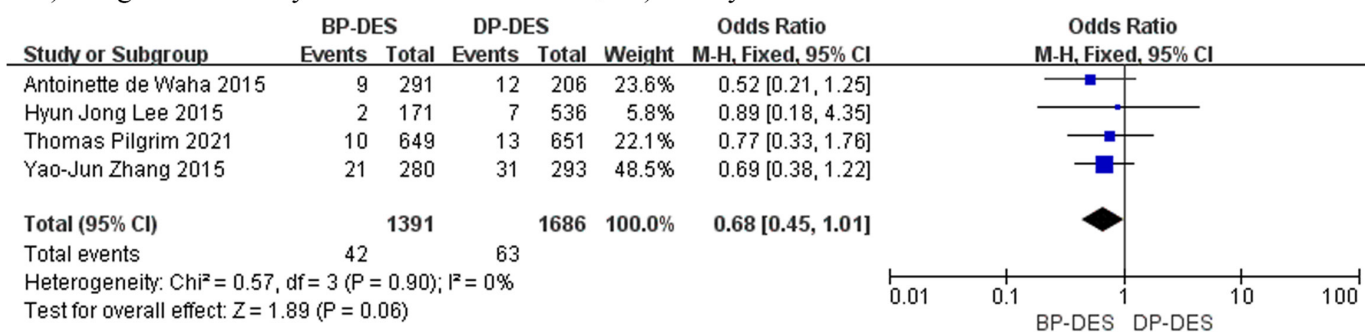
The choice of stent in patients undergoing PCI for ACS is debated. Coronary intervention with second-generation DP-DES generally reduces the need for revascularisation and improves mortality compared with BMS and first-generation DP-DES. Furthermore, the risk of late ST with DP-DES tends to off-set these benefits, as seen in registries and clinical trials comparing DP-DES to BMS.^{15 27} BP-DES was designed to leave only the BMS behind once the polymer completely bio-degraded after drug elution

and may represent an attractive solution for patients with ACS.²⁸ Prior meta-analyses have compared the clinical outcomes among BMS, DP-DES and BP-DES in patients with stable coronary artery disease, but no previous meta-analysis of RCTs and prospective trials directly compared clinical outcomes between BP-DES and DP-DES for the treatment of ACS. To our knowledge, this meta-analysis exclusively compared BP-DES to DP-DES. It included 7 trials representing 8089 patients with relatively long follow-up durations, ranging from 1 year to 5 years. BP-DES have been hypothesised to offer improved outcomes, mainly in the long term; however, several prior meta-analyses have demonstrated different outcomes with

1) Target vessel myocardial infarction (MI) during follow up period



2) Target vessel myocardial infarction (MI) at 1 year



3) Target vessel myocardial infarction (MI) over 2 year

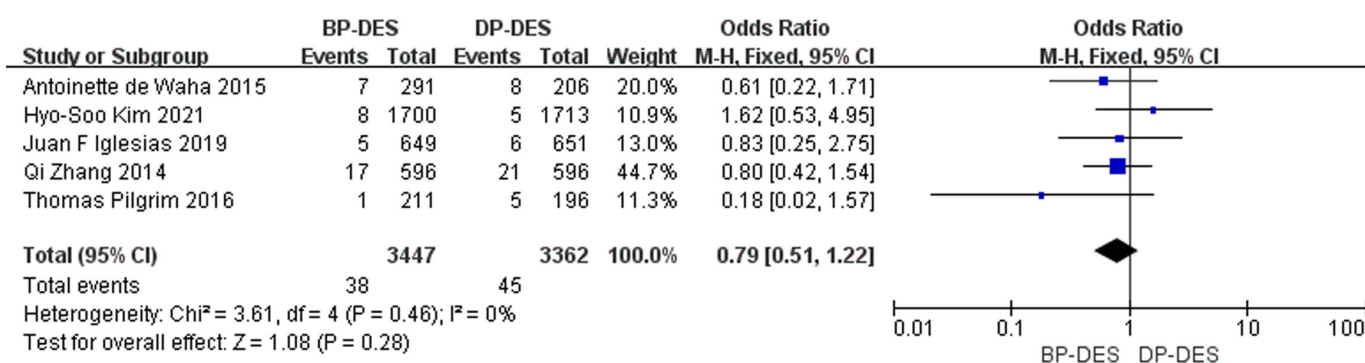


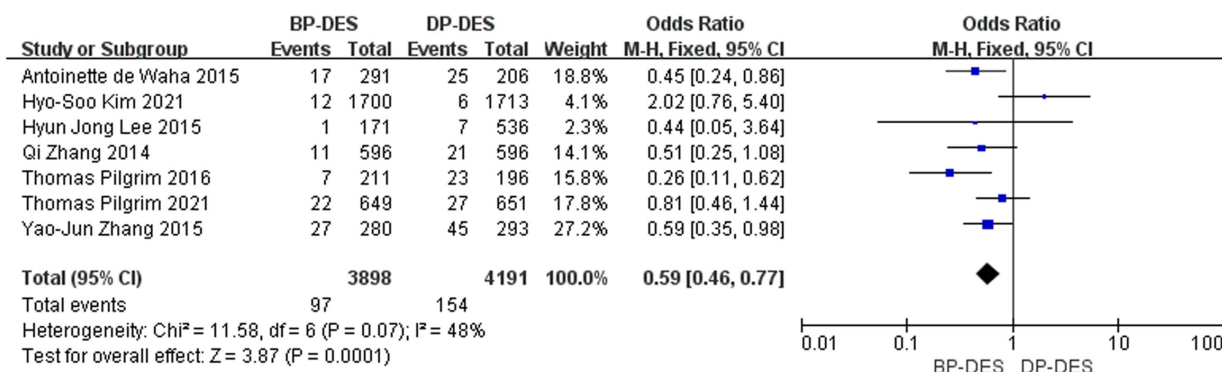
Figure 9 Target vessel myocardial infarction (MI). BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

BP-DES compared with DP-DES in patients undergoing PCI. Bangalore *et al* observed that BP-DES were associated with higher mortality than DP-DES beyond 1 year of follow-up.²⁹ El-Hayek *et al* demonstrated no significant difference in mortality between these stent types.⁶ In our study, there were no significant differences in MACEs, all-cause death, cardiac-related death, TVMI, TVR or TLR at a follow-up period of 1 year and no significant differences in all-cause death, cardiac death or TVMI at a follow-up period of over 2 years. However, at a follow-up of over 2 years, MACEs, TVR and TLR were significantly lower in the BP group than those in the DP group. Pilgrim *et al* observed higher all-cause mortality among patients treated with BP-DES than with DP-DES in the BIOSCIENCE trial; they also observed comparable all-cause

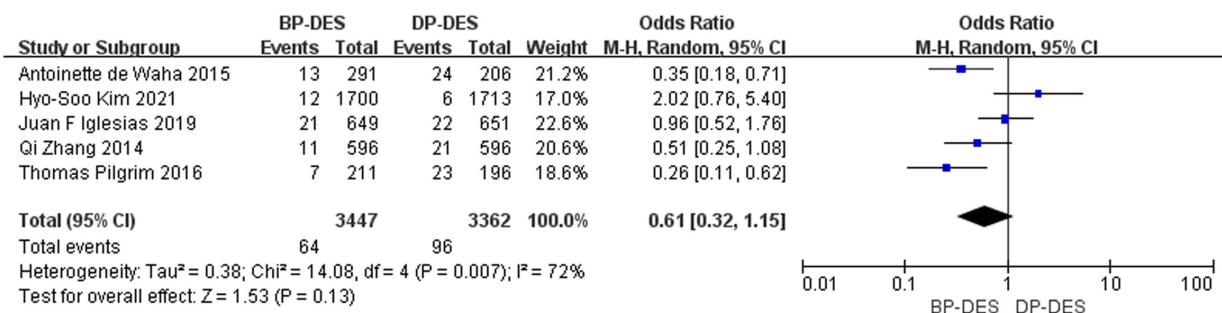
mortality rates among patients treated with BP-DES and DP-DES in the BIOSSTEMI trial with a 2-year follow-up.⁶ Iannaccone *et al* observed that BP-DES might decrease the risk of ischaemic events in selected high-risk subgroups of patients, although the two DES stents share the same safety factors for patients in high-anatomical-risk settings like left main disease.³⁰ Together, these findings suggest that BP-DES share similar outcomes in terms of MACEs (all-cause death, cardiac-related death, TVMI, TVR and TLR) during a 1-year follow-up and might show significantly improved clinical outcomes over a 2-year follow-up.

ST is defined as a thrombotic occlusion of a coronary stent³¹ and is a major complication. The risk of ST, particularly late ST (occurring beyond 30 days), remains one of the major concerns limiting the use of DES in

1) Stent thrombosis during follow up period



2) Stent thrombosis at 1 year



3) Stent thrombosis over 2 years



Figure 10 Stent thrombosis. BP-DES, biodegradable polymer drug-eluting stents; DP-DES, durable polymer drug-eluting stents.

the treatment of ACS.³² Early-generation DP-DES were associated with increased rates of very late (>1 year) ST compared with BMS. It was hypothesised that the mechanism underlying late ST with first DP-DES in ACS was related to adverse reactions with the DP,³³ and the use of more biocompatible polymers has been associated with a reduction in ST in high-risk patients.⁹ In the LEADERS trial, the rate of very late ST was lower with the use of the BP-DES than that with DP-DES.³⁴ Our data demonstrated that both BP-DES and DP-DES have similar risks of ST beyond 1 year. However, BP-DES are associated with a significantly reduced risk of ST at a follow-up of over 2 years compared with DP-DES (OR: 0.64, 95% CI 0.46 to 0.88; $p=0.006$, $I^2=0\%$). In contrast, Kim *et al* observed that the incidence of ST by groups demonstrated numerically lower rates in the DP-DES group (0.1%) than those in the BP-DES group and that all late ST cases occurred in those receiving thick-strut BP-DES stents. They proposed that no meaningful differences in terms of ST could be identified

between the different polymer technologies by intravascular imaging and that the association of polymer technology and the risk of the ST was difficult to prove.^{20 35 36} Therefore, it may be hypothesised that BP-DES result in improved arterial healing, which not only minimises the risk of ST, but also improves the long-term durability of the antirestenotic efficacy in the long term, although the two groups have a similar risk of ST beyond 1 year.

Limitations

The present study had several limitations. First, this study included RCTs and shares the limitations of original studies. Second, BP-DES are a heterogeneous group of stents, differing in stent platform thickness, time to complete degradation of the polymer and drug-elution kinetics. DP-DES are equally heterogeneous groups. Innaccone *et al* observed that lower strut thickness would have a positive clinical outcome, thereby reducing ST and TLRs.³⁷ We were unable to match the stents with regards

to the strut thickness. Consequently, the reported results may not be generalisable to all stents from the respective group. Third, over 6 months of dual antiplatelet therapy (DAPT) was provided to the patients in our study, including those in RCTs. D'Ascenzo *et al* observed a similar rate of MACEs between durable and BPs, irrespective of DAPT length, and the DAPT duration seems to partially impact the risk of adverse events of different types of stents during follow-up.³⁸ Thus, we remain concerned that the duration differences of DAPT may influence the clinical outcomes.

CONCLUSION

In this meta-analysis comparing BP-DES to DP-DES in patients with ACS who underwent PCI, the data indicated that both polymer types demonstrated excellent safety and efficacy profiles at 1 year. There was a slightly increased incidence of MACEs, TLR, TVR and ST in the DP-DES group in the follow-up period of over 2 years, suggesting that BP-DES may be more favourable for treating patients with ACS. These findings should be confirmed by long-term follow-ups in RCT trials.

Data availability statement

No additional data is available.

Patient and public involvement

We did not require patient and public involvement, as this is a meta-analysis, and no new patients were enrolled in the study.

Contributors CH, ZW and HY developed the idea of the study, participated in its design and coordination and helped draft the manuscript. TL and TW contributed to the acquisition and interpretation of data. YZ and YL provided a critical review and substantially revised the manuscript. All authors read and approved the final manuscript.

Funding This work was supported by the Hunan Provincial Natural Science Foundation of China (grant number 2020JJ4787).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

Supplemental material This content has been supplied by the author(s). It has not been vetted by BMJ Publishing Group Limited (BMJ) and may not have been peer-reviewed. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by BMJ. BMJ disclaims all liability and responsibility arising from any reliance placed on the content. Where the content includes any translated material, BMJ does not warrant the accuracy and reliability of the translations (including but not limited to local regulations, clinical guidelines, terminology, drug names and drug dosages), and is not responsible for any error and/or omissions arising from translation and adaptation or otherwise.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

ORCID iD

Can Huang <http://orcid.org/0000-0002-8659-9178>

REFERENCES

- Mehta SR, Cannon CP, Fox KAA, *et al*. Routine vs selective invasive strategies in patients with acute coronary syndromes: a collaborative meta-analysis of randomized trials. *JAMA* 2005;293:2908–17.
- Fox KAA, Clayton TC, Damman P, *et al*. Long-Term outcome of a routine versus selective invasive strategy in patients with non-ST-segment elevation acute coronary syndrome a meta-analysis of individual patient data. *J Am Coll Cardiol* 2010;55:2435–45.
- Torii S, Jinnouchi H, Sakamoto A, *et al*. Drug-Eluting coronary stents: insights from preclinical and pathology studies. *Nat Rev Cardiol* 2020;17:37–51.
- Valgimigli M, Campo G, Percoco G, *et al*. Comparison of angioplasty with infusion of tirofiban or abciximab and with implantation of sirolimus-eluting or uncoated stents for acute myocardial infarction: the MULTISTRATEGY randomized trial. *JAMA* 2008;299:1788–99.
- Räber L, Magro M, Stefanini GG, *et al*. 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.
- El-Hayek G, Bangalore S, Casso Dominguez A, Casso DA, *et al*. Meta-Analysis of randomized clinical trials comparing biodegradable polymer drug-eluting stent to second-generation durable polymer drug-eluting stents. *JACC Cardiovasc Interv* 2017;10:462–73.
- Finn AV, Nakazawa G, Kolodgie FD, *et al*. Temporal course of neointimal formation after drug-eluting stent placement: is our understanding of restenosis changing? *JACC Cardiovasc Interv* 2009;2:300–2.
- Räber L, Kelbæk H, Ostojic M, *et al*. Effect of biolimus-eluting stents with biodegradable polymer vs bare-metal stents on cardiovascular events among patients with acute myocardial infarction: the comfortable AMI randomized trial. *JAMA* 2012;308:777–87.
- Sabate M, Cequier A, Iñiguez A, *et al*. Everolimus-Eluting stent versus bare-metal stent in ST-segment elevation myocardial infarction (examination): 1 year results of a randomised controlled trial. *Lancet* 2012;380:1482–90.
- von Birgelen C, Kok MM, van der Heijden LC, *et al*. Very thin strut biodegradable polymer everolimus-eluting and sirolimus-eluting stents versus durable polymer zotarolimus-eluting stents in allcomers with coronary artery disease (BIO-RESORT): a three-arm, randomised, non-inferiority trial. *Lancet* 2016;388:2607–17.
- Pilgrim T, Heg D, Roffi M, *et al*. Ultrathin strut biodegradable polymer sirolimus-eluting stent versus durable polymer everolimus-eluting stent for percutaneous coronary revascularisation (bioscience): a randomised, single-blind, non-inferiority trial. *Lancet* 2014;384:2111–22.
- Smits PC, Hofma S, Togni M, *et al*. Abluminal biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent (compare II): a randomised, controlled, non-inferiority trial. *Lancet* 2013;381:651–60.
- Natsuaki M, Kozuma K, Morimoto T, *et al*. Biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent: a randomized, controlled, noninferiority trial. *J Am Coll Cardiol* 2013;62:181–90.
- Pilgrim T, Piccolo R, Heg D, *et al*. Biodegradable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents for primary percutaneous coronary revascularisation of acute myocardial infarction. *EuroIntervention* 2016;12:e1343–54.
- Gonzalo N, Barlis P, Serruys PW, *et al*. Incomplete stent apposition and delayed tissue coverage are more frequent in drug-eluting stents implanted during primary percutaneous coronary intervention for ST-segment elevation myocardial infarction than in drug-eluting stents implanted for stable/unstable angina: insights from optical coherence tomography. *JACC Cardiovasc Interv* 2009;2:445–52.
- Räber L, Baumgartner S, Garcia-Garcia HM, *et al*. Long-Term vascular healing in response to sirolimus- and paclitaxel-eluting stents: an optical coherence tomography study. *JACC Cardiovasc Interv* 2012;5:946–57.
- Cook S, Ladich E, Nakazawa G, *et al*. Correlation of intravascular ultrasound findings with histopathological analysis of thrombus aspirates in patients with very late drug-eluting stent thrombosis. *Circulation* 2009;120:391–9.
- Sterne JA, Hernán MA, Reeves BC, *et al*. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ* 2016;355:i4919.
- de Waha A, King LA, Stefanini GG, *et al*. Long-Term outcomes of biodegradable versus durable polymer drug-eluting stents in patients

- with acute ST-segment elevation myocardial infarction: a pooled analysis of individual patient data from three randomised trials. *EuroIntervention* 2015;10:1425–31.
- 20 Kim H-S, Kang J, Hwang D, *et al.* Durable polymer versus biodegradable polymer drug-eluting stents after percutaneous coronary intervention in patients with acute coronary syndrome: the HOST-REDUCE-POLYTECH-ACS trial. *Circulation* 2021;143:1081–91.
 - 21 Lee HJ, Park TK, Song YB, *et al.* Biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent in patients with acute myocardial infarction. *Int J Cardiol* 2015;183:190–7.
 - 22 Iglesias JF, Muller O, Heg D, *et al.* 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.
 - 23 Zhang Q, Qiu JP, Kirtane AJ, *et al.* Comparison of biodegradable polymer versus durable polymer sirolimus-eluting stenting in patients with acute ST-elevation myocardial infarction undergoing primary percutaneous coronary intervention: results of the resolve study. *J Interv Cardiol* 2014;27:131–41.
 - 24 Pilgrim T, Piccolo R, Heg D, *et al.* Biodegradable polymer sirolimus-eluting stents versus durable polymer everolimus-eluting stents for primary percutaneous coronary revascularisation of acute myocardial infarction. *EuroIntervention* 2016;12:e1343–54.
 - 25 Zhang Y-J, Iqbal J, Windecker S, *et al.* Biolimus-eluting stent with biodegradable polymer improves clinical outcomes in patients with acute myocardial infarction. *Heart* 2015;101:271–8.
 - 26 Pilgrim T, Muller O, Heg D, *et al.* Biodegradable- Versus Durable-Polymer Drug-Eluting Stents for STEMI: Final 2-Year Outcomes of the BIOSTEMI Trial. *JACC Cardiovasc Interv* 2021;14:639–48.
 - 27 Guagliumi G, Costa MA, Sirbu V, *et al.* Strut coverage and late malapposition with paclitaxel-eluting stents compared with bare metal stents in acute myocardial infarction: optical coherence tomography substudy of the Harmonizing outcomes with revascularization and stents in acute myocardial infarction (HORIZONS-AMI) trial. *Circulation* 2011;123:274–81.
 - 28 Torii S, Jinnouchi H, Sakamoto A, *et al.* Drug-Eluting coronary stents: insights from preclinical and pathology studies. *Nat Rev Cardiol* 2020;17:37–51.
 - 29 Bangalore S, Toklu B, Amoroso N, *et al.* Bare metal stents, durable polymer drug eluting stents, and biodegradable polymer drug eluting stents for coronary artery disease: mixed treatment comparison meta-analysis. *BMJ* 2013;347:f6625.
 - 30 Iannaccone M, Barbero U, De Benedictis M, *et al.* Comparison of bioresorbable vs durable polymer drug-eluting stents in unprotected left main (from the RAIN-CARDIOGROUP VII study). *BMC Cardiovasc Disord* 2020;20:225.
 - 31 Modi K, Soos MP, Mahajan K. *Stent thrombosis*, 2022.
 - 32 Daemen J, Wenaweser P, Tsuchida K, *et al.* Early and late coronary stent thrombosis of sirolimus-eluting and paclitaxel-eluting stents in routine clinical practice: data from a large two-institutional cohort study. *Lancet* 2007;369:667–78.
 - 33 Siqueira DA, Abizaid AA, Costa JdeR, *et al.* Late incomplete apposition after drug-eluting stent implantation: incidence and potential for adverse clinical outcomes. *Eur Heart J* 2007;28:1304–9.
 - 34 Stefanini GG, Byrne RA, Serruys PW, *et al.* Biodegradable polymer drug-eluting stents reduce the risk of stent thrombosis at 4 years in patients undergoing percutaneous coronary intervention: a pooled analysis of individual patient data from the ISAR-TEST 3, ISAR-TEST 4, and leaders randomized trials. *Eur Heart J* 2012;33:1214–22.
 - 35 Guagliumi G, Shimamura K, Sirbu V, *et al.* Temporal course of vascular healing and neoatherosclerosis after implantation of durable- or biodegradable-polymer drug-eluting stents. *Eur Heart J* 2018;39:2448–56.
 - 36 Kuramitsu S, Kazuno Y, Sonoda S, *et al.* Vascular response to bioresorbable polymer sirolimus-eluting stent vs. permanent polymer everolimus-eluting stent at 9-month follow-up: an optical coherence tomography sub-study from the century II trial. *Eur Heart J Cardiovasc Imaging* 2016;17:34–40.
 - 37 Iannaccone M, Gatti P, Barbero U, *et al.* Impact of strut thickness and number of crown and connectors on clinical outcomes on patients treated with second-generation drug eluting stent. *Catheter Cardiovasc Interv* 2020;96:1417–22.
 - 38 D'Ascenzo F, Iannaccone M, Saint-Hilary G, *et al.* Impact of design of coronary stents and length of dual antiplatelet therapies on ischaemic and bleeding events: a network meta-analysis of 64 randomized controlled trials and 102 735 patients. *Eur Heart J* 2017;38:3160–72.

Supplementary Material 2: search strategie and PRISMA flow chart for included studies**A. Search strategie****1. Pubmed (N=688)**

Search date: from January 2000 to July 2021

Search terms:

1#. ("BP-DES"[MeSH Terms] OR "BP-DES"[All Fields] OR "biodegradable "[All Fields] OR "bioabsorbable "[All Fields] OR "bioabsorbable polymer drug-eluting stent"[All Fields] OR "biodegradable polymer drug-eluting stent"[All Fields]) AND ("acute coronary syndrome"[All Fields] OR "ACS"[All Fields] OR "AMI"[All Fields] OR "Acute myocardial infarction"[All Fields] OR "Non ST segment elevation myocardial infarction"[All Fields] OR "ST segment elevation myocardial infarction"[All Fields] OR "NSTEMI"[All Fields] OR "STEMI"[All Fields])

2#. ("DP-DES"[All Fields] OR "DP-DES"[MeSH Terms] OR "durable polymer"[All Fields] OR "durable polymer drug-eluting stent"[All Fields]) AND ("acute coronary syndrome"[All Fields] OR "ACS"[All Fields] OR "AMI"[All Fields] OR "Acute myocardial infarction"[All Fields] OR "Non ST segment elevation myocardial infarction"[All Fields] OR "ST segment elevation myocardial infarction"[All Fields] OR "NSTEMI"[All Fields] OR "STEMI"[All Fields])

3#. ("BP-DES"[MeSH Terms] OR "BP-DES"[All Fields] OR "biodegradable "[All Fields] OR "bioabsorbable "[All Fields] OR "bioabsorbable polymer drug-eluting stent"[All Fields] OR "biodegradable polymer drug-eluting stent"[All Fields]) and ("DP-DES"[All Fields] OR "DP-DES"[MeSH Terms] OR "durable polymer"[All Fields] OR "durable polymer drug-eluting stent"[All Fields]) AND ("acute coronary syndrome"[All Fields] OR "ACS"[All Fields] OR "AMI"[All Fields] OR "Acute myocardial infarction"[All Fields] OR "Non ST segment elevation myocardial infarction"[All Fields] OR "ST segment elevation myocardial infarction"[All Fields] OR "NSTEMI"[All Fields] OR "STEMI"[All Fields])

2. OVID (N=207, EMBS=134, MEDLINE=54, Controlled Register of Trials=19)

Search date: from January 2000 to July 2021

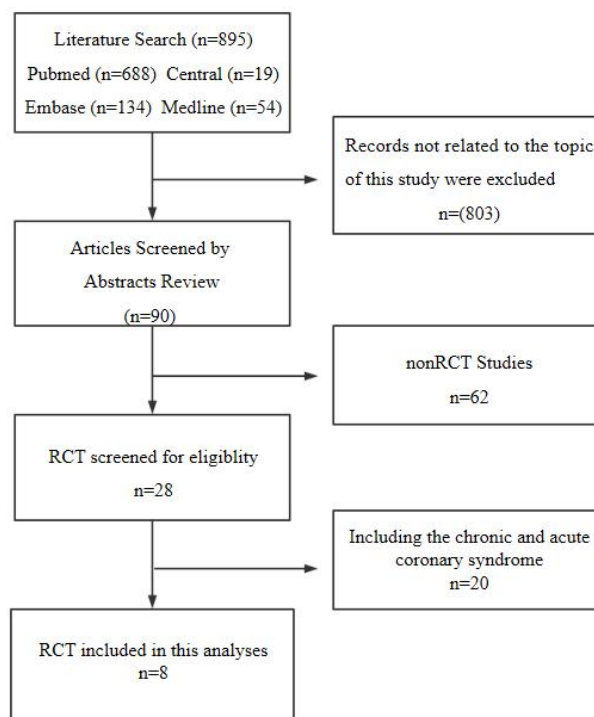
Search terms:

1#.("BP-DES" OR "bioabsorbable polymer drug-eluting stent" OR "biodegradable polymer drug-eluting stent") and ("acute coronary syndrome" OR "ACS" OR "AMI" OR "Acute myocardial infarction" OR "Non ST segment elevation myocardial infarction" OR "ST segment elevation myocardial infarction" OR "NSTEMI" OR "STEMI")

2#.("DP-DES" OR "durable polymer drug-eluting stent") and ("acute coronary syndrome" OR "ACS" OR "AMI" OR "Acute myocardial infarction" OR "Non ST segment elevation myocardial infarction" OR "ST segment elevation myocardial infarction" OR "NSTEMI" OR "STEMI")

3#.("BP-DES" OR "bioabsorbable polymer drug-eluting stent" OR "biodegradable polymer drug-eluting stent") and ("DP-DES" OR "durable polymer drug-eluting stent") and ("acute coronary syndrome" OR "ACS" OR "AMI" OR "Acute myocardial infarction" OR "Non ST segment elevation myocardial infarction" OR "ST segment elevation myocardial infarction" OR "NSTEMI" OR "STEMI")

B. PRISMA flow chart for studies included in the meta-analysis



Supplementary Material 2. Risk-of-bias summary for included trials

A.

Unique ID	Study ID	D1	D2	D3	D4	D5	Overall	
meta1	Hyo-Soo Kim	+	+	+	+	+	+	+
meta2	Thomas Pilgrim	+	+	+	+	+	+	+
meta3	Juan F Iglesias	!	+	+	+	+	+	!
meta4	Thomas Pilgrim	+	+	+	+	+	+	+
meta5	Yao-Jun Zhang	+	+	+	+	!	+	!
meta6	Hyun Jong Lee	+	+	+	+	+	+	+
meta7	Antoinette de Waha	+	!	+	+	!	+	!
meta8	QI ZHANG	!	!	+	+	!	+	!

+	Low risk
!	Some concerns
-	High risk
D1	Randomisation process
D2	Deviations from the intended interventions
D3	Missing outcome data
D4	Measurement of the outcome
D5	Selection of the reported result

B.

As percentage (intention-to-treat)

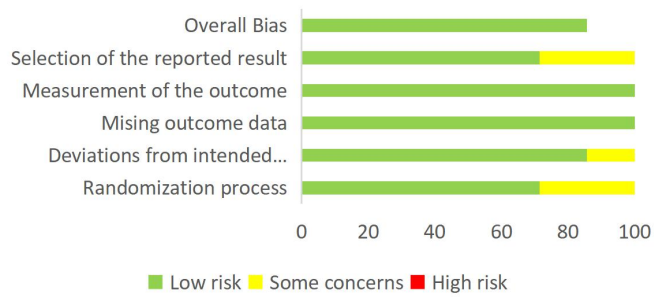


Table 1. The characteristics of the included trails

Authors	Years	Journal	Study	Center	Country	Follow up	NO.patients	
							BP-DES	DP-DES
<u>Hyo-Soo Kim</u>	<u>2021</u>	<u>Circulation</u>	<u>RCT</u>	<u>multicentre</u>	<u>Korea</u>	<u>12 month</u>	<u>1700</u>	<u>1713</u>
<u>Thomas Pilgrim</u>	<u>2021</u>	<u>JACC</u>	<u>RCT</u>	<u>multicentre</u>	<u>Switzerland</u>	<u>24month</u>	<u>649</u>	<u>651</u>
<u>Juan F Iglesias</u>	<u>2019</u>	<u>The Lancet</u>	<u>RCT</u>	<u>multicentre</u>	<u>Switzerland</u>	<u>12 month</u>	<u>649</u>	<u>651</u>
<u>Thomas Pilgrim</u>	<u>2016</u>	<u>EuroIntervention</u>	<u>RCT</u>	<u>multicentre</u>	<u>Switzerland</u>	<u>12 month</u>	<u>211</u>	<u>196</u>
<u>Yao-Jun Zhang</u>	<u>2015</u>	<u>Heart</u>	<u>RCT</u>	<u>multicentre</u>	<u>Netherlands</u>	<u>60month</u>	<u>280</u>	<u>293</u>
<u>Hyun Jong Lee</u>	<u>2015</u>	<u>International journal of cardiology</u>	<u>RCT</u>	<u>multicentre</u>	<u>Korea</u>	<u>24month</u>	<u>171</u>	<u>536</u>
<u>Antoinette de Waha</u>	<u>2015</u>	<u>EuroIntervention</u>	<u>RCT</u>	<u>multicentre</u>	<u>multicentre</u>	<u>48month</u>	<u>291</u>	<u>206</u>
<u>Qi Zhang</u>	<u>2014</u>	<u>Journal of Interventional Cardiology</u>	<u>RCT</u>	<u>multicentre</u>	<u>China</u>	<u>12 month</u>	<u>596</u>	<u>596</u>

Table 2. The baseline features of the patients

Authors	basic characters									
	Age		SEX(MALE)		Body mass index		Hypertension		Diabetes	
	BP-DES	DP-DES	BP-DES	DP-DES	BP-DES	DP-DES	BP-DES	DP-DES	BP-DES	DP-DES
Hyo-Soo Kim	63.1±11.1	63.0±11.1	1337	1351	25.0±3.2	24.9±3.1	1147	1092	747	789
Juan F Iglesias	62.2±11.8	63.2±11.8	513	477	26.9± 4.3	26.8± 4.3	281	297	73	82
Thomas Pilgrim	61.3±12.4	61.7±12.7	170	151	27.0±4.3	27.0±4.3	102	98	30	27
Yao-Jun Zhang	62.9±11.7	62.8±11.7	215	210	27.5±4.4	27.8±4.6	181	198	55	46
Hyun Jong Lee	64±14.08	63±14.08	128	400	/	/	102	308	82	269
Antoinette de Waha	62.5±12.1	63.1±12.6	214	149	/	/	142	110	56	34
Qi Zhang	63.9±13.1	64.1±12.1	475	467	/	/	360	376	129	113

Table 2. The baseline features of the patients

Authors	basic characters									
	Dyslipidemia		smoking		LVEF, %		Stent number per person		Total stent length, mm	
	BP-DES	DP-DES	BP-DES	DP-DES	BP-DES	DP-DES	BP-DES	DP-DES	BP-DES	DP-DES
Hyo-Soo Kim	1,247	1,280	515	475	58.7±10.4	58.5±10.4	1.7±1.1	1.7±1.0	42.9±31.9	41.7±30.2
Juan F Iglesias	304	302	294	250	49.0 ± 11.0	48.4 ± 11.2	1.37 ± 0.64	1.39 ± 0.66	31.91± 18.21	33.92± 19.76
Thomas Pilgrim	110	101	93	77	49.5±10.9	48.3±11.1	1.42±0.71	1.39±0.71	29.49±17.83	30.52±18.99
Yao-Jun Zhang	152	176	107	115	51.5±10.1	51.4±11.8	2.2±0.5	2.2±0.6	26.6±15	27.9±15.2
Hyun Jong Lee	116	389	65	228	55 (45–65)	52 (43–62)	/	/	/	/
Antoinette de Waha	119	109	120	90	47±10	48±12	/	/	25.9±12.6	27.7±14.2
Qi Zhang	87	76	257	223	50±12	49.0 ± 17.0	/	/	/	/