Bioresorbable vascular scaffolds versus conventional drug-eluting stents across time: a meta-analysis of randomised controlled trials

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ABSTRACT
Background Bioresorbable vascular scaffolds (BVS) were designed to reduce the rate of late adverse events observed in conventional drug-eluting stents (DES) by dissolving once they have restored lasting patency.

Objectives Compare the safety and efficacy of BVS versus DES in patients receiving percutaneous coronary intervention for coronary artery disease across a complete range of randomised controlled trial (RCT) follow-up intervals.

Methods A systematic review and meta-analysis was performed using Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. MEDLINE, EMBASE and Web of Science were searched from inception through 5 January 2022 for RCTs comparing the clinical outcomes of BVS versus DES. The primary safety outcome was stent/scaffold thrombosis (ST), and the primary efficacy outcome was target lesion failure (TLF: composite of cardiac death, target vessel myocardial infarction (TVMI) and ischaemia-driven target lesion revascularisation (ID-TLR)). Secondary outcomes were patient-oriented composite endpoint (combining all-death, all-MI and all-revascularisation), its individual components and those of TLF. Studies were appraised using Cochrane’s Risk of Bias tool and meta-analysis was performed using RevMan V.5.4.

Results 11919 patients were randomised to receive either BVS (n=6438) or DES (n=5481) across 17 trials (differing follow-up intervals from 3 months to 5 years). BVS demonstrated increased risk of ST across all timepoints (peaking at 2 years with risk ratio (RR): 3.47; 95% CI 1.80 to 6.70; p=0.0002). Similarly, they showed increased risk of TLF (peaking at 3 years, RR: 1.35; 95% CI 1.07 to 1.70; p=0.01) resulting from high rates of TVMI and ID-TLR. Though improvements were observed after device dissolution (5-year follow-up), these were non-significant. All other outcomes were statistically equivalent. Applicability to all BVS is limited by 91% of the BVS group receiving Abbott’s Absorb.

Conclusion This meta-analysis demonstrates that current BVS are inferior to contemporary DES throughout the first 5 years at minimum.

INTRODUCTION
Drug-eluting stents (DES) replaced bare-metal stents (BMS) as the convention for percutaneous coronary intervention (PCI). DES use polymeric coatings to deliver an immunosuppressant (e.g., everolimus) that inhibits neointimal hyperplasia and subsequently reduces restenosis.1 Clinically, this reduces the rate of repeat myocardial infarction (MI) and the need for revascularisation.2 DES development appears to have reached maturity, with the competing designs (using permanent or bioabsorbable coatings) achieving equivalence in large-scale, long-term clinical trials.3,4 However, even the contemporary DES have their problems. The permanently retained metallic stent and its polymeric coating cause persistent inflammation—driving neoatherosclerosis, restenosis and late stent thrombosis—while eliminating local vasomotor function.5 Subsequently, stent-related events (i.e., thrombosis, MI and...
A potential solution to this lies with bioresorbable vascular scaffolds (BVS). The premise being that these devices provide adequate structural support to the target artery while it remodels, before completely dissolving to return normal vascular function and negate the late adverse events described above. Abbott Vascular’s Absorb BVS was the first device of this kind to gain regulatory approval and is currently the most extensively studied. As detailed in table 3, Absorb is an all polymer, everolimus-eluting BVS with an indicated time to total dissolution of around 2 years. Despite its early promise, the GHOST-EU registry and BVS-EXAMINATION study soon demonstrated an increased risk of early stent/scaffold thrombosis (ST) in the Absorb BVS groups. A review of seven randomised controlled trials (RCTs) comparing the midterm clinical outcomes of Absorb BVS versus DES by Cassese et al went on to confirm that the BVS carried a significantly increased risk of adverse safety and efficacy outcomes over the first 2 years (namely ST and target lesion failure (TLF)—discussed ahead). Similar reviews comparing BVS to DES have been published, all citing similar limitations: (1) a limited number of published studies and (2) a focus on a single BVS type (Absorb). Ni et al indicated that the observed failure may change as new BVS come to the fore with ‘smaller footprints, less thrombogenicity (eg, magnesium), faster reabsorption and advanced mechanical properties’. As such, this review aims to incorporate recent developments and identify the more current consensus on the safety and efficacy of BVS versus DES with respect to clinical outcomes. Further, given that BVS are a transient intervention this study looks to evaluate how this safety and efficacy profile changes with time, with particular interest to the pre- and post-bioabsorption window.

Objective

Compare the safety and efficacy of BVS versus conventional DES in the treatment of coronary artery disease by PCI across all available timepoints, using published data on clinical outcomes from RCTs.

METHODS

This review was designed in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (presented in online supplemental appendix C). The protocol is registered with PROSPERO, accessible at: www.crd.york.ac.uk/ with

### Table 1 Full inclusion and exclusion criteria for the systematic review

| Inclusion criteria | Exclusion criteria |
|--------------------|--------------------|
| Participants | Individuals receiving PCI for coronary artery disease (CAD) | Non-human (animal models or in vitro) |
| Intervention | BVS (entirely bioabsorbable scaffold) | Conventional permanent DES or BMS |
| Comparator | DES (permanent stent) | BMS |
| Outcomes | Reporting at least one of: the primary safety and/or efficacy outcomes (definite/probable ST and TLF) | Non-clinical outcomes (histological, imaging, economic) |
| Study design | Prospective RCT | Non-RCT (single-arm, registries) |
| Publications | Published full-text articles | Reviews, conference abstracts, posters, letters, case reports |
| Language | English | Other languages |

BVS, bioresorbable vascular scaffolds; DES, drug-eluting stents; PCI, percutaneous coronary intervention; RCT, randomised controlled trial; ST, stent/scaffold thrombosis; TLF, target lesion failure.
Coronary artery disease

Coronary artery disease registration number: CRD42022301449. There was no patient or public involvement in this study.

Eligibility criteria
For a study to be included in the meta-analysis, the outcomes of interest must be extractable as incidence rates on an intention-to-treat (ITT) basis (table 1).

Study outcomes
The primary safety outcome is definite/probable ST (ST). The primary efficacy outcome is TLF, this is the device-oriented composite endpoint of cardiac death, target vessel MI (TVMI) and ischaemia-driven target lesion revascularisation (ID-TLR). Secondary outcomes include: the patient-oriented composite endpoint (POCE; a composite of all-cause mortality, all-MI and all-revascularisation), its individual components, cardiac death, TVMI and ID-TLR. These standardised outcomes have previously been defined by the Academic Research Consortium on coronary device trials. All outcomes are assessed on an ITT basis.

Search and screening strategy
A keyword search was performed across MEDLINE, EMBASE and Web of Science from inception to 5 January 2022, as summarised below (detailed in online supplemental appendix A):

- Coronary Disease OR Myocardial Infarction OR Percutaneous Coronary Intervention
- AND: Bioresorbable Vascular Scaffold OR Bioresorbable Vascular Stent OR Third-Generation Stent
- AND: Drug Eluting Stent OR Everolimus Eluting Stent OR Second-Generation Stent

Duplicates were removed and publications were screened by title and abstract; a second investigator (SZ) independently screened a sample of the publications to ensure agreement. Subsequently, full text articles were retrieved and assessed for eligibility. The reference lists of the included articles were searched for appropriate trials to include. Details of this process are summarised in a PRISMA flowchart (figure 1).

Data collection and analysis
A data extraction table was developed using Cochrane guidance. Two reviewers piloted the data extraction method on a sample of papers in parallel, consensus was established, and the remaining studies were analysed by the main reviewer.

All statistical analysis was completed using RevMan V.5.4 software. The summary statistic used for this study is

Table 2 Salient characteristics of the included studies

| Study                  | Trial ID          | Centres, n | Patients, n | Stent/scaffold type | Available outcome data (Y/N) | Follow-up durations (months) | Year |
|------------------------|-------------------|------------|-------------|---------------------|-----------------------------|-----------------------------|------|
| ABSORB CHINA           | NCT01923740       | 24         | 241         | 239                 | ABSORB BVS                 | 12, 36                      | 2018 |
| ABSORB II              | NCT01425281       | 46         | 335         | 166                 | ABSORB BVS                 | 12, 24, 36, 48, 60          | 2020 |
| ABSORB III             | NCT01751906       | 193        | 1322        | 686                 | ABSORB BVS                 | 12, 36, 60                  | 2019 |
| ABSORB IV              | NCT02173739       | 147        | 1296        | 1308                | ABSORB BVS                 | 12                          | 2018 |
| ABSORB JAPAN           | NCT01844284       | 38         | 266         | 134                 | ABSORB BVS                 | 12, 24, 60                  | 2020 |
| AIDA                   | NCT01858077       | 5          | 924         | 921                 | ABSORB BVS                 | 12, 24, 60                  | 2021 |
| COMPARE-ABSORB         | NCT02486068       | 45         | 848         | 822                 | ABSORB BVS                 | 12                          | 2020 |
| COVER-AMI              | NCT02890589       | 1          | 10          | 12                  | ABSORB BVS                 | N                           | 2019 |
| EVERBIO                | NCT01711931       | 1          | 80          | 160                 | ABSORB BVS                 | Y                           | 9    |
| Hernandez et al        | –                 | 1          | 100         | 100                 | ABSORB BVS                 | 12                          | 2016 |
| ISAR-ABSORB            | NCT01942070       | 5          | 173         | 89                  | ABSORB BVS                 | Y                           | 12   |
| MAGSTEMI               | NCT03234348       | 11         | 74          | 76                  | Magmaris                    | Y                           | 12   |
| NeoVas                 | NCT02305485       | 32         | 278         | 282                 | NeoVas                      | Y                           | 12   |
| PRAGUE-22              | ISRCTN89434356    | 2          | 25          | 25                  | Magmaris                    | Y                           | 12   |
| Seo et al              | NCT02796157       | Multi-     | 171         | 170                 | ABSORB BVS                 | Y                           | 12   |
| TROFI-II               | NCT01986903       | 8          | 95          | 96                  | ABSORB BVS                 | Y                           | 12, 36 |
| XINSORB                | ChiCTR1800014966  | 17         | 200         | 195                 | XINSORB SES                | Y                           | 12   |

All prospective, non-inferiority, RCTs in adult patients. Published follow-up durations are given with year of latest publication.

BVS, bioresorbable vascular scaffolds; DES, drug-eluting stents; EES, everolimus-eluting stent; RCT, randomised controlled trial; SES, sirolimus-eluting stent; ST, stent/scaffold thrombosis; TLF, target lesion failure.
risk ratio (RR) with 95% CIs, given its proven consistency for dichotomous outcomes and ease of interpretation compared with other methods, for example, OR. In view of the variation in population and procedural characteristics across the included studies, for example, differing clinical indications (stable angina vs STEMI), devices, and preinflation/postinflation protocols, a Mantel-Haenszel random-effects model was used. Model-based sensitivity analysis comparing the consistency of results using fixed-effect models was performed to verify this decision.

Outcomes were evaluated at all available follow-up durations. Grouped analysis of follow-up intervals of ≤12 months and 2, 3 and 5 years was also performed to investigate the relationship between adverse event accrual and the BVS resorption window. Statistical significance is interpreted using p<0.05 and non-overlap of 95% CIs. Heterogeneity among trials is estimated using Cochran’s Q test and the I²-statistic (where <25%, 25–50% and >50% represent low, moderate and high heterogeneity, respectively).

Study-based sensitivity analysis was performed by individually omitting each study from the meta-analysis and assessing changes in outcome (in terms of direction of change and change in magnitude and significance). Small study effects and publication bias was evaluated by visual inspection of funnel plots. Risk of bias in the included studies is evaluated using the Cochrane Risk of Bias Tool (RoB 2).

RESULTS

Study selection and characteristics

A PRISMA flow diagram describing the search strategy is presented in figure 1. The search identified 680 publications for screening; 173 duplicates were removed and a further 407 were excluded at title and abstract review. One hundred full-text articles were reviewed for eligibility, of which, 70 were excluded (reasons given in figure 1). The 30 remaining articles meeting the inclusion criteria report different follow-up durations of 17 individual RCTs—enrolling a total of 11,919 patients for PCI with either BVS (n=6438) or DES (n=5481).

The main characteristics of the 17 included studies are presented in table 2. Salient characteristics of the included studies. The most studied stents were Abbott Vascular’s ABSORB BVS (n=5861) and XIENCE DES (n=4631). Details of all included stents are given in table 3. The most common follow-up duration presented is 12 months (14 independent studies), with 5 studies going out to 5 years. Only one follow-up at 48 months was identified (ABSORB II); given the lack of comparators at this interval and that these data are incorporated in to ABSORB II’s 6-month follow-up, it was excluded from meta-analysis. Patient and procedural characteristics are presented in online supplemental appendix table 1.

Study quality assessment

Quality assessment of the included RCTs using Cochrane’s Risk of Bias (RoB 2) tool is summarised in table 4. Most of the studies were assessed as having a low risk of bias, with four exceptions. Briefly, prepublished protocols/plans for result reporting could not be found for COVER-AMI, PRAGUE-22, Hernandez et al and XINSORB, while Hernandez et al also did not provide adequate information on their randomisation procedure. It was decided that these concerns alone were not sufficient to exclude these studies from the analysis.

Funnel plots for the primary safety and efficacy outcomes are presented in figure 2; they show no
Table 4  Quality assessment of studies included for meta-analysis (using Cochrane’s RoB2 tool)

| Study               | Randomisation process | Deviations from intended interventions | Missing outcome data | Measurement of the outcome | Selection of the reported result | Overall bias |
|---------------------|-----------------------|----------------------------------------|----------------------|---------------------------|----------------------------------|--------------|
| ABSORB CHINA        | +                     | +                                      | +                    | +                         | +                                | +            |
| ABSORB II           | +                     | +                                      | +                    | +                         | +                                | +            |
| ABSORB III          | +                     | +                                      | +                    | +                         | +                                | +            |
| ABSORB IV           | +                     | +                                      | +                    | +                         | +                                | +            |
| ABSORB JAPAN        | +                     | +                                      | +                    | +                         | +                                | +            |
| AIDA                | +                     | +                                      | +                    | +                         | +                                | +            |
| COMPARE-ABSORB      | +                     | +                                      | +                    | +                         | +                                | +            |
| COVER-AMI           | +                     | +                                      | +                    | +                         | -                                | -            |
| EVERBIO II          | +                     | +                                      | +                    | +                         | +                                | +            |
| Hernandez et al     | -                     | +                                      | +                    | +                         | -                                | -            |
| ISAR-ABSORB         | +                     | +                                      | +                    | +                         | -                                | -            |
| MAGSTEMI            | +                     | +                                      | +                    | +                         | +                                | +            |
| NeoVas              | +                     | +                                      | +                    | +                         | +                                | +            |
| PRAGUE-22           | +                     | +                                      | +                    | +                         | -                                | -            |
| Seo et al           | +                     | +                                      | +                    | +                         | +                                | +            |
| TROFI-II            | +                     | +                                      | +                    | +                         | +                                | +            |
| XINSORB             | +                     | +                                      | +                    | +                         | -                                | -            |

[Diagram of data showing funnel plots for A] Primary safety outcome - ST 
[Diagram of data showing funnel plots for B] Primary efficacy outcome - TLF

Figure 2  Funnel plot analysis for (A) the primary safety outcome (stent/scaffold thrombosis, ST) and (B) the primary efficacy outcome (target lesion failure, TLF) at latest follow-up. Diagonal lines show pseudo-95% CIs. RR, risk ratio.

Jackson-Smith E, et al. Open Heart 2022;9:e002107. doi:10.1136/openhrt-2022-002107
significant interference from small-study effects and the relative symmetry suggests limited publication bias.

There was no evidence of significant heterogeneity in the included studies across the outcomes of interest. Sensitivity analysis across each outcome did not demonstrate significant deviation due to any one included study—including the four with identified bias concerns. Results remain consistent when checked using a fixed-effects model.

Study outcomes

Primary safety outcome: ST
Excluding COVER-AMI, all studies reported the primary safety outcome of definite/probable ST. As demonstrated in figure 3, patient enrolled to the BVS group have a statistically significantly increased risk of ST across all time-points. This appears to peak with a relative risk of 3.47 (95% CI 1.80 to 6.70; p=0.0002; I²=0%) at 24-month follow-up and decrease over the proceeding intervals to 2.99 at 60-months (95% CI 1.90 to 4.71; p≤0.0001; I²=0%), however, this is not statistically significant. At latest follow-up (online supplemental appendix figure 2), this outcome occurred in 2.05% of BVS versus 0.69% of DES patients (RR: 2.56; 95% CI 1.79 to 3.66; p≤0.00001; I²=0%).

Subgroup analysis of early (0–30 days), late (31 days to 1 year) and very late ST (VLST; 1 year onwards) was performed exclusively on studies that provided extractable data for all three of these time points. BVS exhibit an increased risk of ST across the described intervals, the relative risk appears to peak in the late phase (31 days to 1 year), though there is no significant difference between the intervals (figure 4).

Primary efficacy outcome: TLF
Excluding Hernandez et al and Seo et al, all other studies report the primary efficacy outcome of TLF. As demonstrated in figure 5, patients with BVS have a significantly increased risk of TLF at all time-points. While remaining inferior throughout, the extent of inferiority (in terms of RR) appears to decrease between 36-month and 60-month follow-up (from RR=1.33 to RR=1.18), though this drop is not statistically significant (overlapping 95% CIs 1.07 to 1.70 and 95% CI 1.02 to 1.37, respectively).

Figure 3  Forest plot for the primary safety outcome of stent thrombosis (ST)—grouped by follow-up duration. Diamonds indicate point estimates and extremes of 95% CIs. See online supplemental appendix B figure 3 for corresponding funnel plot. BVS, bioresorbable vascular scaffolds; DES, drug-eluting stents.
Coronary artery disease

At latest follow-up (online supplemental figure 4), TLF occurred in 9.73% of BVS versus 7.45% of DES patients (RR: 1.21; 95% CI 1.07 to 1.37; p=0.002; I²=0%).

Secondary outcomes

Patient-oriented composite endpoint

All studies excluding Hernandez et al and Seo et al reported POCE or provided adequate information to reliably calculate it. While RR's favoured DES at all time points, overlapping CIs failed to grant this true significance. At latest available follow-up for all studies, POCE occurred in 17.64% of BVS versus 14.78% of DES patients (RR: 1.10; 95% CI 1.01 to 1.19; p=0.03; I²=0%; see online supplemental appendix B, figure 6).

All death

All studies excluding Hernandez et al and Seo et al provided mortality outcomes. Mortality rates were lower for BVS versus DES across 24-month, 36-month and 60-month follow-ups, but higher in the 12-month and under group. None of which reached statistical significance. See online supplemental figure 8.

Cardiac death

All studies provided incidence of cardiac death. The same relationship described for all-death above was observed for the outcome of cardiac death. See online supplemental figure 9.

All MI

All studies provided incidence of MI. Significantly increased rates of MI occurred in BVS versus DES groups across all follow-up durations (10.49% vs 7.26% at 60 month follow-up; RR: 1.39; 95% CI 1.15 to 1.67; p=0.0007), with no significant difference in rate between each group. See online supplemental figure 10.

Target vessel MI

Excluding Hernandez et al, Seo et al, MAGSTEMI and ABSORB II at 48 and 60 months, incidence of TVMI was reported for all other studies. The BVS group showed increased rates of TVMI across all follow-up durations compared with DES, this reached significance in the ≤12, 24 and 60-month groups (for the latter: 8.49% vs 5.26%; RR: 1.48; 95% CI 1.18 to 1.86; p=0.0008). See online supplemental figure 11.

All revascularisation

All studies but Seo et al reported incidence of revascularisation. This was similar between BVS and DES at all follow-up durations. See online supplemental figure 12.
Ischaemia-driven target lesion reintervention

All studies but Hernandez et al and ISAR-ABSORB provided incidence of ID-TLR. The BS group showed increased rates of ID-TLR at each follow-up duration, but this only reached significance at 24 and 60 months (for the latter: 9.09% vs 7.11%; RR: 1.36; 95% CI 1.11 to 1.65; p=0.003). online supplemental figure 13.

Summarising the significant findings, BS was found to be inferior to DES in terms of ST, TLF, ID-TLR, TVMI and all-MI, but not POCE, all-death, cardiac death or all-revascularisation. Table 5 provides a summary of all finding.

| Study or Subgroup | Events | Total | Risk Ratio | Risk Ratio |
|-------------------|--------|-------|------------|------------|
|                    | BS     | DES   | M-H, Random, 95% CI | M-H, Random, 95% CI |
| BS vs DES         |        |       | BS vs DES | BS vs DES  |
| BS vs DES         |        |       | BS vs DES | BS vs DES  |
| BS vs DES         |        |       | BS vs DES | BS vs DES  |
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| BS vs DES         |        |       | BS vs DES | BS vs DES  |
| BS vs DES         |        |       | BS vs DES | BS vs DES  |
| BS vs DES         |        |       | BS vs DES | BS vs DES  |

Figure 5  Forest plot for the primary efficacy outcome of target lesion failure (TLF)—grouped by follow-up duration. See Figure 5, Appendix B for corresponding funnel plot. BS, bioresorbable vascular scaffolds; DES, drug-eluting stents.

**DISCUSSION**

The main findings of this meta-analysis of 17 RCTs comparing BS with DES across all available follow-up durations (grouped to ≤12 months and 2, 3, and 5 years) are as follow: First, BS are inferior to DES at all timepoints with respect to the primary safety (ST) and efficacy outcomes (TLF). Second, the increased risk of ST is significant (5.47-fold greater at 2years), starts early (the first 30 days) and remains durable throughout 5 years of follow-up (2.99-fold greater risk at 5years). Third, the increased risk of TLF (1.18-fold higher at 5 years) appears to be driven primarily by elevated rates of TVMI and ID-TLR. Finally, the more generalised secondary outcomes (POCE, all-death, cardiac death and all-revascularisation) are statistically equivalent between groups across all time points—confirming that it is local, device-specific failings driving the inferiority of BS.

It is important to note that while there is an increased relative risk of ST in BS versus DES, the incidence of this complication is low (2.05% and 0.69% at latest follow-up, respectively), and its overall clinical relevance is ultimately limited, with equivocal all-cause mortality and revascularisation rates observed across all time points.
The low heterogeneity demonstrated throughout this meta-analysis supports conclusions that the elevated adverse outcome rates are attributed directly to the use of BVS versus DES, rather than any inter-study differences. Our findings are in agreement with previous reviews of outcomes at early and interim follow-up durations. For example, in their exclusive analysis of Absorb BVS trials at 2-year follow-up, Cassese et al demonstrated a similar threelfold increased risk of ST accompanied by an increased risk of TLF due to high relative TVMI and ID-TLR rates—as depicted above. Thus, confirming that BVS are at least inferior to DES as solid stents—prior to their complete bio-absorption at around 2 years.

But conceptually, the value of BVS is their promise of a reduction in the late events that plague conventional DES by disappearing once they have fulfilled their purpose of restoring patency to the target artery. To a limited extent, this review supports this premise. Here, both primary outcomes demonstrate a relative plateau in event accumulation for BVS after their dissolution window—with drops in the relative risk between 3-year and 5-year follow-ups, although non-significant with overlapping 95% CIs. However, even if this relationship were to achieve significance at later intervals—which is not unreasonable to suggest, given the adverse event accrual rate of 2% per year for permanent metallic stents—the high initial adverse event rates could continue to render BVS both clinically and economically unfavourable.

Given the particularly high relative risk of ST, and the fact that it can mechanistically drive TLF via TVMI and ID-TLR, it presents as the obvious target for investigation. Cuculi and colleagues studied the causes of ST in BVS using quantitative coronary angiography and optical coherence tomography. They describe a biphasic model, where early ST results from inadequate antithrombotic therapy and poor implantation technique (scaffold undersizing and underexpansion); and late/VLST is associated with peri-strut low-intensity areas (indicative of...

| Study or Subgroup | BVS Events Total | DES Events Total | Risk Ratio M-H, Random, 95% CI | Risk Ratio M-H, Random, 95% CI |
|-------------------|------------------|------------------|------------------------------|------------------------------|
| 3.2.1 ≤12-month follow-up | | | | |
| ABSORB CHINA (1x2mo) | 19 241 22 339 4.7% | 0.82 [0.46, 1.46] | | |
| ABSORB II (1x2mo) | 24 335 15 166 4.2% | 0.79 [0.43, 1.47] | | |
| ABSORB III (1x2mo) | 225 1322 96 686 32.8% | 1.22 [0.98, 1.52] | | |
| ABSORB IV (1x2mo) | 67 1296 53 1308 12.8% | 1.28 [0.90, 1.81] | | |
| ABSORB JAPAN (1x2mo) | 26 266 11 134 3.5% | 1.19 [0.61, 2.34] | | |
| COMPARE-ABSORB (1x2mo) | 99 848 85 822 21.3% | 1.13 [0.86, 1.48] | | |
| COVER-AMI (3mo) | 3 10 1 12 0.4% | 3.60 [0.44, 29.45] | | |
| EVERBIO II (3mo) | 21 80 41 160 7.8% | 1.02 [0.65, 1.61] | | |
| ISAAN-ABSORB (1x2mo) | 26 173 13 89 4.2% | 1.03 [0.56, 1.90] | | |
| MACSTEMI (1x2mo) | 17 74 11 76 3.4% | 1.59 [0.80, 3.16] | | |
| NeoVas (1x2mo) | 3 278 3 282 0.6% | 1.01 [0.21, 4.98] | | |
| PRAGUE-22 (1x2mo) | 4 25 1 25 0.4% | 4.00 [0.48, 33.33] | | |
| TROFI II (6mo) | 7 95 6 96 1.4% | 1.18 [0.41, 3.38] | | |
| XINSORB (1x2mo) | 10 200 14 195 2.6% | 0.70 [0.32, 1.53] | | |
| Subtotal (95% CI) | 5243 4290 100.0% | 1.14 [1.00, 1.29] | | |

Total events | 551 | 373 | | |

Heterogeneity: Tau² = 0.00; Chi² = 8.56, df = 13 (P = 0.81); I² = 0%
Test for overall effect: Z = 2.01 (P = 0.04)

| 3.2.2 24-month follow-up | | | | |
|---------------------------|------------------|------------------|------------------------------|------------------------------|
| ABSORB II (2x4mo) | 39 335 21 166 10.8% | 0.92 [0.56, 1.51] | | |
| ABSORB JAPAN (2x4mo) | 52 266 16 134 9.9% | 1.04 [0.97, 2.76] | | |
| ADA (2x4mo) | 155 924 140 921 60.9% | 1.10 [0.89, 1.36] | | |
| EVERBIO II (2x4mo) | 27 80 51 160 18.4% | 1.06 [0.72, 1.55] | | |
| Subtotal (95% CI) | 1605 | 1381 100.0% | 1.12 [0.95, 1.31] | | |

Total events | 273 | 228 | | |

Heterogeneity: Tau² = 0.00; Chi² = 2.75, df = 3 (P = 0.43); I² = 0%
Test for overall effect: Z = 1.32 (P = 0.19)

| 3.2.3 36-month follow-up | | | | |
|---------------------------|------------------|------------------|------------------------------|------------------------------|
| ABSORB CHINA (3x6mo) | 28 241 28 239 16.0% | 0.90 [0.61, 1.62] | | |
| ABSORB II (3x6mo) | 68 335 39 166 27.1% | 0.80 [0.61, 1.22] | | |
| ABSORB JAPAN (3x6mo) | 296 1322 120 688 51.5% | 1.28 [1.06, 1.55] | | |
| TROFI II (3x6mo) | 9 95 8 96 5.4% | 1.14 [0.46, 2.82] | | |
| Subtotal (95% CI) | 1993 | 1187 100.0% | 1.10 [0.88, 1.37] | | |

Total events | 401 | 195 | | |

Heterogeneity: Tau² = 0.01; Chi² = 4.17, df = 3 (P = 0.24); I² = 28%
Test for overall effect: Z = 0.83 (P = 0.40)

| 3.2.4 60-month follow-up | | | | |
|---------------------------|------------------|------------------|------------------------------|------------------------------|
| ABSORB II (6x0mo) | 80 335 41 166 8.3% | 0.97 [0.70, 1.34] | | |
| ABSORB III (6x0mo) | 378 1322 168 688 36.4% | 1.17 [1.00, 1.37] | | |
| ABSORB JAPAN (6x0mo) | 74 266 34 134 7.3% | 1.10 [0.77, 1.55] | | |
| ADA (6x0mo) | 259 924 241 921 39.7% | 1.07 [0.92, 1.24] | | |
| EVERBIO II (6x0mo) | 31 80 69 160 8.3% | 0.90 [0.65, 1.25] | | |
| Subtotal (95% CI) | 2927 | 2067 100.0% | 1.08 [0.98, 1.19] | | |

Total events | 822 | 553 | | |

Heterogeneity: Tau² = 0.00; Chi² = 2.62, df = 4 (P = 0.62); I² = 0%
Test for overall effect: Z = 1.63 (P = 0.10)

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Figure 6 Forest plot for the patient-oriented composite endpoint—grouped by follow-up. See Appendix B, Figure 7 for corresponding funnel plot. BVS, bioresorbable vascular scaffolds; DES, drug-eluting stents.
Possible underlying causes of the above observations have previously been discussed and may be grouped as device and operator driven. Device-related failings include their thicker strut profile—Table 3 shows this to be around double that of DES across the included studies. This is required to achieve adequate radial strength from the dissolvable material, a factor which would decrease non-linearly as stents dissolve. Strut thickness is known to increase rates of ST clinically, where the increased surface area and changes to haemodynamics at the micro-level are widely discussed to be thrombogenic. Novel metallic BVS with thinner struts and reduced thrombogenicity may address this going forwards, though they present mixed results in the Prague-22 and MAGSTEMI23 trials evaluated in this study. Operator related failings include specific implantation strategy (involving specific sizing and predilation and postdilation parameters) that effectively reduced ST rates from 3.3% to 1% at 1 year. Clearly there are numerous opportunities for improving outcomes.

Key limitations

Conclusions regarding BVS versus DES are limited in general applicability, given that 91% of the BVS population studied received Abbott’s Absorb. Further, a lack of access to the raw data meant it was not possible to statistically analyse the effect that important patient, lesion and procedural characteristics had on the observed outcome.

CONCLUSIONS

This meta-analysis demonstrates that current BVS are inferior to contemporary DES throughout the first 5 years at minimum, increasing patients’ risk of serious adverse events (ST and MI) and the need for reintervention of the target lesion during this time. This appears to be applicable to the use of PCI for silent ischaemia through to full STEMI. However, this may change with the implementation of improved implantation strategies, better antiplatelet therapies, progressions in scaffold design and the availability of later follow-up data from more recent trials. These remain important areas for future research, remembering that BVS are compared with contemporary DES like Abbott’s Xience, whose gold-standard safety and efficacy profiles follow extensive iterative development.

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Contributors EJ-S was responsible for the planning, conduct and reporting of this study. SZ assisted with screening articles, trialling data extraction methods and report editing. PB guided and critically reviewed the work and is the guarantor of this work.

| Table 5 | Summary of meta-analysis findings relating to key clinical outcomes (grouped by follow-up duration) |
|---------|---------------------------------------------------------------------------------------------------|
| Outcome | Follow-up duration | ≤12 months | 24 months | 36 months | 60 months |
|---------|-------------------|-----------|-----------|-----------|-----------|
| Primary safety: definite/probable-ST | | x | | | |
| Primary efficacy: TLF | | | x | | |
| POCE | | | | x | |
| All-death | | | | | x |
| Cardiac death | | | | | |
| All-MI | | x | x | x | |
| TVMI | | x | x | | |
| All-revascularisation | | | | | |
| ID-TLR | | | | x | |
| | Based on risk ratio and significance interpreted using 95% CIs and p<0.05. | |
| | BVS superior to DES. | |
| | Equivalent. | |
| | BVS inferior to DES. | |

BVS, bioresorbable vascular scaffolds; DES, drug-eluting stents; ID-TLR, ischaemia-driven target lesion revascularisation; MI, myocardial infarction; POCE, patient-oriented composite endpoint; TLF, target lesion failure; TVMI, target vessel myocardial infarction.
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