Downloaded from http://openheart.bmj.com/ on September 16, 2016 - Published by group.bmj.com

openheart

Use of bioresorbable vascular scaffold: a meta-analysis of patients with coronary artery disease

Mohamed Farag,[1,2] Nikolaos Spinthakis,[1] Diana A Gorog,[1,2,3] Abhiram Prasad,[4] Keith Sullivan,[2] Zaki Akhtar,[1] Neville Kukreja,[1] Manivannan Srinivasan[1]

To cite: Farag M, Spinthakis N, Gorog DA, *et al*. Use of bioresorbable vascular scaffold: a meta-analysis of patients with coronary artery disease. *Open Heart* 2016;**3**:e000462. doi:10.1136/openhrt-2016-000462

► Additional material is available. To view please visit the journal (http://dx.doi.org/10.1136/openhrt-2016-000462).

MF and NS contributed equally to this manuscript.

Received 24 April 2016
Revised 4 July 2016
Accepted 24 July 2016

For numbered affiliations see end of article.

Correspondence to
Dr Manivannan Srinivasan; manivannan.srinivasan@nhs.net

ABSTRACT

Background: Differences in outcomes between bioresorbable vascular scaffold (BVS) systems and drug-eluting metal stents (DES) have not been fully evaluated. We aimed to compare clinical and angiographic outcomes in randomised studies of patients with coronary artery disease (CAD), with a secondary analysis performed among registry studies.

Methods: A meta-analysis comparing outcomes between BVS and DES in patients with CAD. Overall estimates of treatment effect were calculated with random-effects model and fixed-effects model.

Results: In 6 randomised trials (3818 patients), BVS increased the risk of subacute stent thrombosis (ST) over and above DES (OR 2.14; CI 1.01 to 4.53; p=0.05), with a trend towards an increase in the risk of myocardial infarction (MI) (125 events in those assigned to BVS and 50 to DES; OR 1.36; CI 0.97 to 1.91; p=0.07). The risk of in-device late lumen loss (LLL) was higher with BVS than DES (mean difference 0.08 mm; CI 0.03 to 0.13; p=0.004). There was no difference in the risk of death or target vessel revascularisation (TVR) between the two devices. In 6 registry studies (1845 patients), there was no difference in the risk of death, MI, TVR or subacute ST between the two stents. Final BVS dilation pressures were higher in registry than in randomised studies (18.7±4.6 vs 15.2±3.3 atm; p<0.001).

Conclusions: Patients treated with BVS had an increased risk of subacute ST and slightly higher LLL compared with those with DES, but this might be related to inadequate implantation techniques, in particular device underexpansion.

KEY QUESTIONS

What is already known about this subject?

- Recent clinical studies using the first commercially available bioresorbable vascular scaffold systems have reported promising results. However, the rate of subacute stent thrombosis was observed to be higher than expected after implantation of these devices, possibly due to suboptimal device expansion and insufficient intracoronary imaging guidance.

What does this study add?

- The aim of this study was to evaluate the efficacy and safety of bioresorbable vascular scaffold systems, compared with drug-eluting metal stents, using the data available from randomised and observational studies, with a focus on stent implantation techniques.

How might this impact on clinical practice?

- When using bioresorbable vascular scaffold systems, every effort should be made to select suitable patients, with careful lesion preparation, and with intervention guided by adequate intravascular device optimisation.

INTRODUCTION

Despite latest-generation drug-eluting metal stents (DES) demonstrating improved safety and efficacy compared with first-generation implants,[1] there remains the need for better devices for percutaneous coronary intervention (PCI). Recent clinical studies using the first commercially available bioresorbable vascular scaffold (BVS) systems have reported promising results. Unlike DES, BVS potentially allow restoration of anatomy and vascular function. This novel technology offers the promise of eliminating late stent failure related to thrombosis and neoatherosclerosis that is associated with the presence of a permanent metallic foreign body. However, in early registry studies, BVS use was associated with higher rates of stent thrombosis (ST) in the first 6 months,[2–4] possibly due to suboptimal device expansion and insufficient intracoronary imaging guidance.

The currently available data from individual randomised trials and observational studies suggest that clinical outcomes are otherwise similar between patients treated with DES or BVS,[5–16] though most studies are limited by a small sample size. The aim of this meta-analysis was to evaluate the efficacy and safety of BVS, compared with DES,

Downloaded from http://openheart.bmj.com/ on September 16, 2016 - Published by group.bmj.com

using the data available from randomised trials, with a focus on stent implantation techniques. We also performed an analysis of data from observational studies in order to determine outcomes in the 'real-world' setting.

METHODS

Study objectives and design

The outcomes of interest were death, myocardial infarction (MI), target vessel revascularisation (TVR), ST and in-device late lumen loss (LLL) at angiographic follow-up, defined according to the study protocols. We also performed a secondary analysis for death, MI, TVR and ST for registry studies. The study was designed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement and the Meta-Analysis of Observational Studies in Epidemiology (MOOSE) work groups.[17 18]

Study search strategy

Using MEDLINE, Embase, Scopus and the Cochrane Library, we performed searches of articles published until December 2015, without language restrictions. Eligible studies were identified using various combinations of the terms: absorb, bioresorbable, drug-eluting stent, percutaneous, coronary, MI, angina, angioplasty and intervention in the abstract or title. Reference lists of the retrieved articles were reviewed to identify eligible studies. Online oral presentations and expert slide presentations were also examined. Two reviewers independently reviewed all titles, or titles and abstracts from the search results to identify articles according to fulfilment of inclusion criteria. Selected trials were compared, and disagreement was resolved by team discussion and consensus. Studies were excluded from the meta-analysis if they included the use of bare-metal stent, reported duplicate or incomplete interim data, had small sample size of ≤50 patients or short follow-up of <3 months or were single-arm studies.

Data extraction

Data extraction was carried out independently and in duplicate by the study investigators. Results of data extraction were then compared, and discrepancies resolved by consensus. If results were incomplete or unclear, the study authors were contacted. Articles selected for the final review were checked to avoid inclusion of data published in duplicate. Data were collated from each study regarding baseline characteristics, including study design, device type, sample characteristics, ACC/AHA lesion classification, glycoprotein IIb/IIIa inhibitors (GPI) use, use of intracoronary imaging, predilation and postdilation pressures, duration of dual antiplatelet therapy and procedural and clinical outcomes at the end of follow-up. If TVR was not reported, we used target lesion revascularisation instead. As for ST, we pooled outcomes for any ST, including definite, probable and possible ST. All outcomes were defined according to the original study's protocol definition. ST was defined according to the Academic Research Consortium criteria[19] in all included studies. When a study reported follow-up at 1 and 2 years, outcomes for the longer time periods were abstracted.

Statistical analysis

Outcomes are presented as OR with 95% CI. Pooled OR was calculated for categorical and continuous variables using a random-effects model by the method of DerSimonian and Laird.[20] Heterogeneity was assessed using χ^2 and I^2 tests. We also used the Mantel-Haenszel fixed-effects model, when no heterogeneity was observed (ie, I^2=0%). All analyses were performed with the intention-to-treat principle. In sensitivity analysis, we included only registry studies which directly compared BVS with DES in coronary artery disease (CAD). We did meta-regression to examine the relationship between the log-transformed OR of the effect of BVS on ST risk and the log-transformed OR of the effect of BVS on mortality, in identified randomised trials. We used the unpaired two-sample mean comparison Student's t-test to compare weighted means of different populations, in particular those related to stent technical parameters (ie, BVS final dilation pressure).

Publication bias was minimised by a comprehensive and inclusive literature search. In addition, a graphical display (funnel plot) of the size of the treatment effect against the precision of the trial (1/SE) was used to investigate publication bias. All tests were two-sided, and statistical significance was fixed at 0.05 level. Analysis was carried out using Review Manager Software (RevMan V.5.3) and Stata V.11.2 (StataCorp, College Station, Texas, USA).

RESULTS

Six randomised trials involving 3818 patients were identified, which directly compared the clinical outcomes of BVS versus DES in CAD (see online supplementary figure S1).[5–10] Six registry studies[11–16] involving 1845 patients that compared clinical outcomes of BVS against DES were also included. Of these, three performed propensity score matched-sample analyses.[11 13 14] The methodological quality of included studies is described in online supplementary tables S1 and S2. The primary outcomes of included studies are listed in online supplementary tables S3 and S4. There was no evidence of publication bias having a significant effect on the results (see online supplementary figure S2).

The characteristics of randomised trials are listed in table 1. Greater than three-quarters of patients were male with a mean age of 62±4 years, 28.4% patients with diabetes and ACC/AHA lesion class was B2/C in 66.2%. All trials included patients with acute coronary syndromes (table 1). The median follow-up was 12 months. Patients randomised to receive BVS (n=2337) were treated with the Absorb everolimus-eluting scaffold

Downloaded from http://openheart.bmj.com/ on September 16, 2016 - Published by group.bmj.com

Table 1 Baseline patient and lesion characteristics of randomised trials

	ABSORB II, 2015	ABSORB III, 2015	ABSORB CHINA, 2015	ABSORB JAPAN, 2015	EVERBIO II, 2015	ABSORB STEMI TROFI II ST, 2016
Patients (n)	501	2008	480	400	238	191
BVS (n)	335	1322	241	266	78	95
DES (n)	166	686	239	134	160	96
Male (%)	77	70	72	77	79	82
Mean age (year)	61	63	57	67	65	59
Diabetes (%)	24	31	24	36	23	16
Follow-up (months)	24	12	12	12	9	6
GPI use (%)						
BVS	NR	10.1	NR	NR	NR	40
DES	NR	12.4	NR	NR	NR	38.5
DAPT duration (months)	Up to 24	12	12	12	6	12
Device type	BVS, EES	BVS, EES	BVS, EES	BVS, EES	BVS, EES, BES	BVS, EES
Intracoronary imaging used (OCT/IVUS %)						
BVS	100	11.2	0.4	100	NR	0
DES	100	10.8	0.4	100	NR	0
ACC/AHA lesion class (%)						
A	1.1	NR	9.5	3.8	24.9	NR
B1	52.1	NR	21.7	20.1	44	NR
B2	45.3	69.9*	49	53.8	15	NR
C	1.4		24.5	22	16	NR
Device predilation (%)						
BVS	100	100	99.6	100	NR	55.8
DES	99	100	98	100	NR	51
Device postdilation (%)						
BVS	61	65.5	63	82.2	34	50.5
DES	59	51.2	54.4	77.4	31	25.5
Expected maximum diameter of postdilation balloon (mm)						
BVS	3.29	3.18	3.3	3.34	NR	3.51
DES	3.35	3.12	3.2	3.31	NR	3.29
Final dilation pressure (atm)						
BVS	14.2	15.4	16.8	14.7	13.6	15.8
DES	15	15.4	16.9	15.1	14.2	18.6
Clinical presentation (%)						
STEMI	0	0	0	0	9.6	100
Non-STEMI	0	0	0	0	21	0
Unstable angina	20.9	26	64.4	12	8.4	0
Stable angina	63.8	58.4	19.5	64.5	48.3	0
Silent ischaemia	12.1	10	4.6	23.5	12.6	0

Values are means or (%).
*B2+C lesions.
BES, biolimus-eluting stent; BVS, bioresorbable vascular scaffold; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; EES, everolimus eluting stent; GPI, glycoprotein IIb/IIIa inhibitors; IVUS, intravascular ultrasound; NR, not reported; OCT, optical coherence tomography; STEMI, ST-elevation myocardial infarction.

(Abbott Vascular, Santa Clara, California, USA). BVS postdilation was performed in 64.8% of patients up to a mean maximum pressure of 15.2±3.3 atm. Intravascular imaging (OCT/IVUS) was used to guide BVS expansion in 33.2% of cases. Patients randomised to receive DES (n=1401) were treated with either an everolimus-eluting cobalt–chromium stent (Xience Prime, Xience V, or Xience Xpedition; Abbott Vascular, Santa Clara, California, USA), an everolimus-eluting platinum–chromium stent (Promus Element; Boston Scientific, Natick, Massachusetts, USA) or a biolimus-eluting stainless-steel stent (Biomatrix Flex; Biosensors, Europe, SA). Four of the clinical trials' primary end points were based on angiographic criteria.[5–8] In one trial, a 2-year interim clinical outcomes report was only available online, and these results were used.[9] All interventions were performed according to standard of care, including optimisation of stent deployment or use of intravascular imaging techniques, according to trial protocols. All patients were prescribed long-term aspirin, whereas the use of dual antiplatelet therapy varied between 6 and 12 months. All trials reported the adherence to dual

Downloaded from http://openheart.bmj.com/ on September 16, 2016 - Published by group.bmj.com

antiplatelet therapy to be >80% up to the longest follow-up period available.

In the randomised trials, there was no difference in the risk of death (OR 1.29; CI 0.43 to 3.83; I^2=23%; p=0.65) (figure 1A) or TVR (OR 1.15; CI 0.83 to 1.59; I^2=0%; p=0.40 (p=0.38 by fixed-effect model)) (figure 1B) between the two devices. Compared with DES, patients treated with BVS showed a trend towards an increase in the risk of MI (125 events in those assigned to BVS and 50 to DES; OR 1.36; CI 0.97 to 1.91; I^2=0%; p=0.07) (p=0.06 by fixed-effect model)) (figure 1C). Patients treated with BVS had a higher rate of any ST (definite, probable or possible ST; with the majority of events occurring within 30 days; n=39) compared with those treated with DES (OR 2.14; CI 1.01 to 4.53; I^2=0%; p=0.05 (p=0.03 by fixed-effect model)) (figure 2A). Definite ST occurred in 33 (0.9%) patients. There was a trend towards an increase in the risk of definite ST (27 events in those assigned to BVS and 6 to DES; OR 2.11; CI 0.92 to 4.88; I^2=0%; p=0.08) (p=0.07 by fixed-effect model)) (figure 2B). There was no correlation between the increase in ST risk with BVS and mortality among the trials reporting at least one ST and death event (p=0.66; figure 3).

In trials with angiographic surveillance, the median angiographic follow-up was 10.5 months (IQR 7.5–12.5). Coronary lesions treated with BVS had significantly higher in-device LLL at angiographic follow-up than those treated with DES (mean difference between groups 0.08 mm; CI 0.03 to 0.13; I^2=52%; p=0.004) (figure 2C).

The characteristics of registry studies are listed in table 2. Greater than three-quarters of patients enrolled were male with a mean age of 62±3 years, 18.2% patients with diabetes and ACC/AHA lesion class was B2/C in 84.7%. All studies included patients with acute coronary syndromes (table 2). The median follow-up was 8 months. Patients receiving BVS (n=785) were treated with the Absorb everolimus-eluting scaffold. BVS postdilation was performed in 60.0% of all patients up to a mean maximum pressure of 18.7±4.6 atm. Intravascular imaging (OCT/IVUS) was used to guide BVS expansion in 63.7% of cases. Patients receiving DES (n=1060) were treated with an everolimus-eluting cobalt–chromium stent (Xience Prime, Xience Pro, Xience V, or Xience Xpedition; Abbott Vascular, Santa Clara, California, USA), an everolimus-eluting platinum–chromium stent (Promus, Promus Element, Premier; Boston Scientific, Natick,

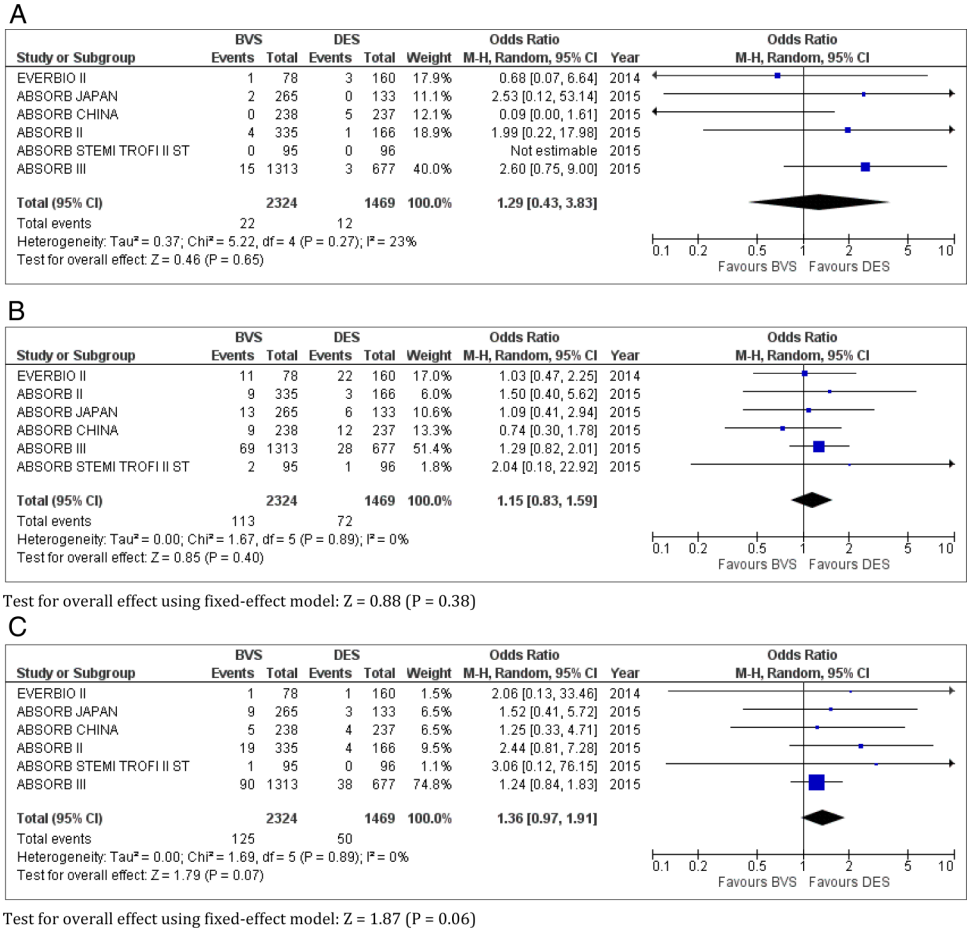


Figure 1 Death, target vessel revascularisation (TVR) and myocardial infarction (MI) with bioresorbable vascular scaffold (BVS) versus drug-eluting stent (DES) in randomised trials in coronary artery disease. (A) Death, (B) TVR and (C) MI.

Downloaded from http://openheart.bmj.com/ on September 16, 2016 - Published by group.bmj.com

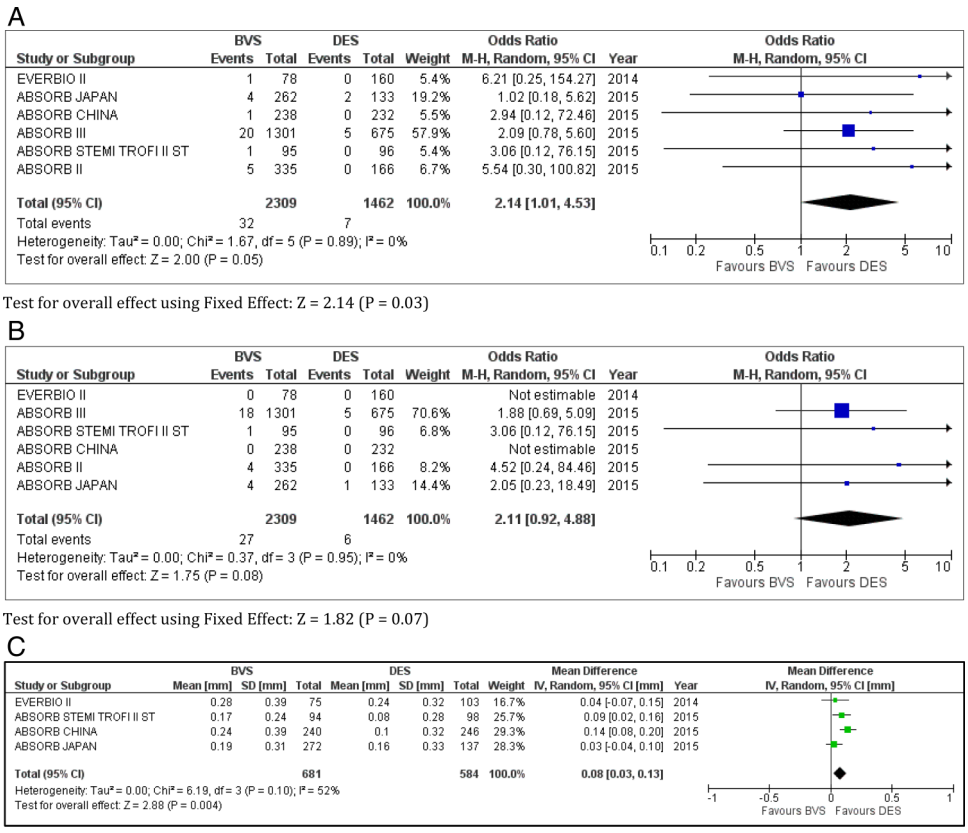


Figure 2 Any and definite stent thrombosis (ST) and in-device late lumen loss (LLL) with bioresorbable vascular scaffold (BVS) versus drug-eluting stent (DES) in randomised trials in coronary artery disease. (A) any ST, (B) definite ST and (C) in-device LLL.

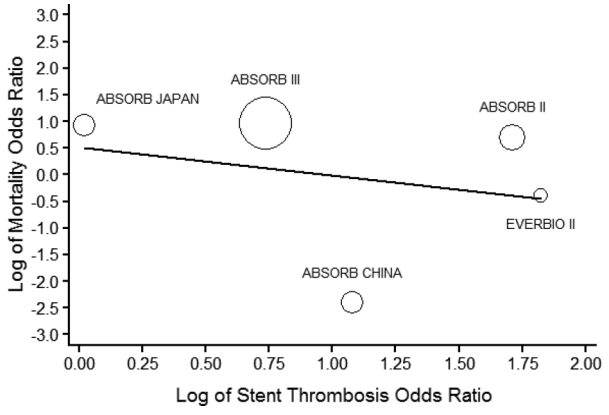


Figure 3 Relationship between stent thrombosis (ST) and mortality, restricted to trials with at least one ST and death event. Slope of the regression line −0.53, p=0.6556.

Massachusetts, USA), a biolimus-eluting stainless-steel stent (N-BES, Nobori; Terumo, Tokyo, Japan) or a zotarolimus-eluting cobalt–chromium stent (Medtronic Vascular, Santa Rosa, California, USA). All patients were prescribed long-term aspirin and dual antiplatelet therapy was given for 12 months. Only one study reported the adherence to prescribed dual antiplatelet therapy in the BVS arm up to 12 months, to be 100%.[11]

In registry studies, there was no difference in the risk of death (OR 0.64; CI 0.27 to 1.48; I^2=0%; p=0.30 (p=0.22 by fixed-effect model)) (figure 4A), TVR (OR 0.85; CI 0.49 to 1.48; I^2=0%; p=0.57 (p=0.54 by fixed-effect model)) (figure 4B), MI (OR 1.37; CI 0.77 to 2.43; I^2=0%; p=0.28) (p=0.30 by fixed-effect model)) (figure 4C), any ST (OR 1.21; CI 0.58 to 2.51; I^2=0%; p=0.61 (p=0.35 by fixed-effect model)) (figure 5A) or definite ST (OR 1.27; CI 0.58 to 2.82; I^2=0%; p=0.55) (p=0.65 by fixed-effect model)) (figure 5B) between the two devices.

The results observed in all included registry studies were also observed within the three studies that had directly compared BVS with DES (see online supplementary figure S3). Final BVS dilation pressures were higher in registries than in randomised trials (18.7±4.6 vs 15.2 ±3.3 atm; p<0.001), with a mean diameter of postdilation balloons of 3.4±0.3 vs 3.2±0.4 mm, respectively.

DISCUSSION

The major findings of this meta-analysis of six randomised trials, involving 3818 patients undergoing PCI, are that patients treated with BVS have an increased risk of subacute ST associated with a trend towards an increased risk of MI, compared with those treated with DES. There was also a greater in-device LLL with BVS. However, this was with no difference in TVR or mortality. A difference

Downloaded from http://openheart.bmj.com/ on September 16, 2016 - Published by group.bmj.com

Table 2 Baseline patient and lesion characteristics of registry studies

	Mattesini *et al*[16]	Gori *et al*[15]	Sato *et al*[11]	Cortese *et al*[12]	BVS-EXAMINATION[13]	Costopoulos *et al*[14]
Patients (n)	73	253	192	563	580	184
BVS (n)	35	150	96	122	290	92
DES (n)	38	103	96	441	290	92
Male (%)	79	72	89	78	80	87
Mean age (years)	62	62	66	59*	57	63
Diabetes (%)	31	17	23	17	13	27
Follow-up (months)	8	6	12	8*	12	6
GPI use (%)						
BVS	NR	38.7	NR	34.8	67.5	NR
DES	NR	11.7	NR	37.4	51.7	NR
DAPT duration (months)	NR	12	12	12	12	12
Device type	BVS, EES, ZES	BVS, EES	BVS, BES, EES	BVS, EES	BVS, EES	BVS, EES
Intracoronary imaging used (OCT/IVUS %)						
BVS	100	NR	91.7	4.4	NR	99.8
DES	100	NR	64.6	0.4	NR	16.8
ACC/AHA lesion class (%)						
A	0	NR	NR	NR	NR	NR
B1	0	NR	NR	NR	NR	NR
B2	31	NR	84.1†	NR	NR	80.8†
C	69	NR		NR	NR	
Device predilation (%)						
BVS	100	100	100	94.1	81	97.8
DES	100	100	72.1	60	29	75.8
Device postdilation (%)						
BVS	100	14	100	94.1	36.3	99.3
DES	100	14	86.4	37.9	15.2	77.4
Expected maximum diameter of postdilation balloon (mm)						
BVS	3.5	NR	3.2	3.5	NR	3.2
DES	3.5	NR	3.15	3.5	NR	3.1
Final dilation pressure (atm)						
BVS	21.3	15.3	21.1	10*	NR	20.9
DES	17.1	12.2	18.4	14	NR	19.0
Clinical presentation (%)			All-comers			
STEMI	0	40.7		100	100	11.4‡
Non-STEMI	0	41.8		0	0	
Unstable angina	4.1	17.3		0	0	
Stable angina	95.8	0		0	0	88.6
Silent ischaemia	0	0		0	0	0

Values are means unless otherwise specified or (%).
*Expressed as median.
†B2+C lesions.
‡Acute coronary syndrome.
BES, biolimus-eluting stent; BVS, bioresorbable vascular scaffold; DAPT, dual antiplatelet therapy; EES, everolimus-eluting stent; GPI, glycoprotein IIb/IIIa inhibitors; IVUS, intravascular ultrasound; NR, not reported; OCT, optical coherence tomography; STEMI, ST-elevation myocardial infarction; ZES, zotarolimus-eluting stent.

in ST rates was not detected among the 1845 patients from the 6 registry studies, and rates for death, TVR and MI were similar in BVS and DES treated patients.

In randomised trials, the rate of subacute ST was higher with BVS compared with DES, with an overall rate of 1.39% in 2309 patients receiving BVS and 0.49% in 1462 patients receiving DES at 12 months. Although postdilation was more frequently performed in the BVS group (table 1), the final result is considered insufficient for adequate BVS implantation as currently recommended. In randomised trials, BVS postdilation was performed in 64.8% of cases, with final dilation pressures of

Downloaded from http://openheart.bmj.com/ on September 16, 2016 - Published by group.bmj.com

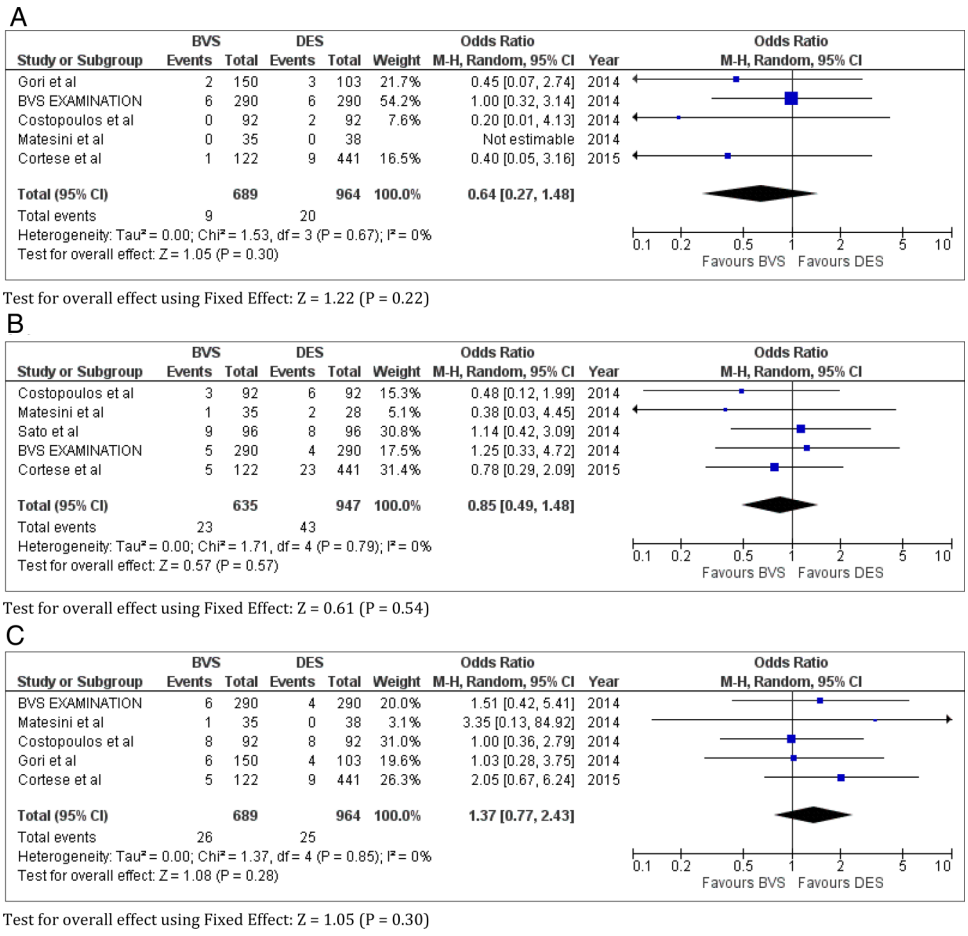


Figure 4 Death, target vessel revascularisation (TVR) and myocardial infarction (MI) with bioresorbable vascular scaffold (BVS) versus drug-eluting stent (DES) in registry studies in coronary artery disease. (A) Death, (B) TVR and (C) MI.

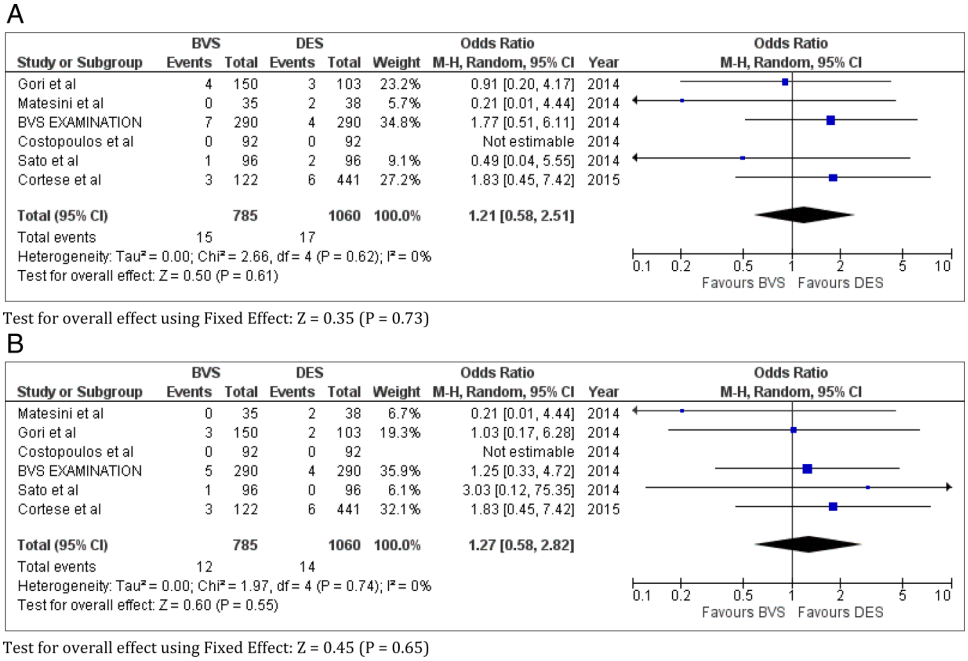


Figure 5 Any and definite stent thrombosis (ST) with bioresorbable vascular scaffold (BVS) versus drug-eluting stent (DES) in registry studies in coronary artery disease. (A) Any ST and (B) definite ST.

Downloaded from http://openheart.bmj.com/ on September 16, 2016 - Published by group.bmj.com

15.2±3.3 atm. The use of intravascular imaging (OCT/IVUS) guidance for vessel sizing and implant optimisation is recommended for BVS, but we found that this was performed in only a third of patients. In a recent multicentre study involving 1305 patients, the rate of ST with BVS was as high as 3%, but this was significantly reduced (by ~70%) when optimal implantation strategy was employed.[21] It is noteworthy that in registries that used high-pressure (≥20 atm) BVS postdilation, and routine intravascular imaging guidance, there did not appear to be an increased risk of ST,[11 14 16] and this probably shaped the findings of the meta-analysis of registry studies. Thus, a potential explanation for the observed increased risk of ST in the randomised trials may relate to suboptimal implantation techniques, rather than to the intrinsic properties of BVS. Furthermore, given the small number of patients included in this meta-analysis, it is also possible that the randomised trials were underpowered to detect a difference with respect to rare complications such as ST. Nevertheless, since ST is a rare but catastrophic complication, the available data provide cause for caution.

The Absorb BVS is a thick-strut scaffold, with the average strut thickness of 157 µm, which is almost equivalent to that of the first-generation Cipher stent (Cipher Bx Velocity 152.6 mm, Cordis Corporation, Johnson & Johnson, Warren, New Jersey, USA), and about double that of the second-generation Xience stent (Xience V 81.3 mm).[22] Indeed, the strut thickness is considered its main limitation, since it makes for a bulkier device which may prove challenging to pass across tortuous vessels or complex calcified lesions. Additionally, thick-strut, when compared with thin-strut, stents are associated with higher rates of angiographic restenosis and are considered to be thrombogenic.[23 24] Thus, there may be increased neointimal thickness and thrombogenicity with BVS indicating perhaps the need to explore the requirement for long-term adjunct antithrombotic pharmacotherapy.

Despite the apparent difference in in-device LLL at median angiographic follow-up, this was not reflected in any difference in overall revascularisation rates for BVS versus DES at 1 year. Whether the observed greater loss in BVS lumen area beyond the first year after implantation translates into worse clinical outcomes is unknown. PCI techniques continue to rapidly evolve with improvements in stent platforms and adjunctive antiplatelet and antithrombotic therapy. With longer planned follow-up, the ABSORB II,[25] ABSORB IV (NCT02173379) and AIDA[26] trials will provide valuable insight into the long-term outcomes of BVS, particularly outcomes related to late and very late ST and lumen area.

In the studies included in this meta-analysis, the majority of patients were stable and had simple *de novo* lesions. Randomised trials included a higher percentage of patients with diabetes than did registries (28.4% vs 18.2%), but of note, the lesions were less complex (ACC/AHA lesion class was B2/C in 66.2% of randomised trials vs 84.7% of registries). Despite the fact that virtually every study conducted in the era of stenting has shown higher event rates in patients with diabetes,[27] there have been no head-to-head comparisons of outcomes comparing BVS in patients with and without diabetes. Muramatsu *et al*[28] presented promising *post hoc* analyses 1 year after BVS implantation showing no difference in clinical outcomes, particularly in the incidence of subacute ST, with numerically low ST events in patients with diabetes.

Our results are in line with two previous meta-analyses by Cassese *et al*[29] and Lipinski *et al*[30] showing a higher incidence of ST and MI in the first year after BVS implantation. However, Stone *et al*[31] did not demonstrate the same pattern in a patient level, pooled meta-analysis of four randomised trials involving 3389 patients with CAD. Recently, a network meta-analysis of 147 trials showed that BVS had an increased risk of ST compared with contemporary DES.[32] Our meta-analysis of data from randomised and registry studies suggest that this might indeed be related to inadequate implantation techniques, in particular to device underexpansion.

Our meta-analysis has several limitations. First, most studies used strict selection criteria and so, high-risk patients might not have been assessed, such as those with tortuous or calcified lesions. Second, all patients receiving BVS were treated with everolimus-eluting scaffold, in contrast to patients who received DES where the vast majority were treated with everolimus-eluting stent, and small numbers were treated with either biolimus-eluting stent[7 11] or zotarolimus-eluting stent.[16] It is however important to recognise that biolimus-eluting and zotarolimus-eluting stents had similar safety and efficacy as the everolimus-eluting stent in prior studies,[33 34] and their inclusion is unlikely to confound the results of the meta-analysis. Third, three registry studies were propensity score matched-sample analyses, which did not directly compare the two devices.[11 13 14] However, a sensitivity analysis showed the same results when those studies were excluded. Fourth, data on adherence to dual antiplatelet therapy were unavailable in all but one registry. Furthermore, the studies included had some differences in design, definitions and follow-up periods. For randomised trials, the results of this meta-analysis are derived from study data and not from patient data. Availability of individual patient data could improve the reliability of the findings and permit more flexible analyses. Additionally, in one of the trials, 2-year results had been presented but not published.[9] Finally, the randomised trials included were either single-blind or open-label with a potential for high performance bias.

Whether the higher risk of subacute ST observed with BVS reflects suboptimal implantation technique, thick-strut scaffold and/or lesion selection remains to be determined. Data from large observational studies are still needed, to confirm that BVS can deliver the same results as DES with the appropriate implantation techniques. Adequately powered randomised trials of BVS

Downloaded from http://openheart.bmj.com/ on September 16, 2016 - Published by group.bmj.com

using careful lesion preparation and device optimisation are needed, with angiographic follow-up to assess clinical outcomes. Until then, caution must be exercised and when using BVS, every effort made to select suitable patients, with careful lesion preparation, with intervention guided by intravascular optimisation to embed the struts deeply in the vessel wall to avoid malapposition and to promote rapid endothelialisation.

Author affiliations
[1]Department of Cardiology, East and North Hertfordshire NHS Trust, Hertfordshire, UK
[2]Postgraduate Medical School, University of Hertfordshire, Hertfordshire, UK
[3]National Heart & Lung Institute, Imperial College, London, UK
[4]St George's, University of London, London, UK

Acknowledgements The authors thank Ashraf Nabhan, MD, and David Wellsted, PhD, for analytical support.

Contributors MF and NS did the literature search. All the authors analysed the data, interpreted the findings, drafted the manuscript and approved the manuscript submitted.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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 and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

REFERENCES

1. Iqbal J, Sumaya W, Tatman V, *et al*. Incidence and predictors of stent thrombosis: a single-centre study of 5,833 consecutive patients undergoing coronary artery stenting. *EuroIntervention* 2013;9:62–9.
2. Kraak RP, Hassell ME, Grundeken MJ, *et al*. Initial experience and clinical evaluation of the Absorb bioresorbable vascular scaffold (BVS) in real-world practice: the AMC Single Centre Real World PCI Registry. *EuroIntervention* 2015;10:1160–8.
3. Capodanno D, Gori T, Nef H, *et al*. Percutaneous coronary intervention with everolimus-eluting bioresorbable vascular scaffolds in routine clinical practice: early and midterm outcomes from the European multicentre GHOST-EU registry. *EuroIntervention* 2015;10:1144–53.
4. Kočka V, Malý M, Toušek P, *et al*. Bioresorbable vascular scaffolds in acute ST-segment elevation myocardial infarction: a prospective multicentre study 'Prague 19'. *Eur Heart J* 2014;35:787–94.
5. Sabaté M, Windecker S, Iñiguez A, *et al*. Everolimus-eluting bioresorbable stent vs. durable polymer everolimus-eluting metallic stent in patients with ST-segment elevation myocardial infarction: results of the randomized ABSORB ST-segment elevation myocardial infarction-TROFI II trial. *Eur Heart J* 2016;37:229–40.
6. Gao R, Yang Y, Han Y, *et al*. Bioresorbable vascular scaffolds versus metallic stents in patients with coronary artery disease: ABSORB China trial. *J Am Coll Cardiol* 2015;66:2298–309.
7. Puricel S, Arroyo D, Corpataux N, *et al*. Comparison of everolimus- and biolimus-eluting coronary stents with everolimus-eluting bioresorbable vascular scaffolds. *J Am Coll Cardiol* 2015;65:791–801.
8. Kimura T, Kozuma K, Tanabe K, *et al*. A randomized trial evaluating everolimus-eluting Absorb bioresorbable scaffolds vs. everolimus-eluting metallic stents in patients with coronary artery disease: ABSORB Japan. *Eur Heart J* 2015;36:3332–42.
9. Chevalier B, Serruys P. *The 2-year clinical outcomes of the ABSORB II trial: first randomized comparison between the absorb everolimus eluting bioresorbable vascular scaffold and the XIENCE everolimus eluting stent*. Transcatheter Cardiovascular Therapeutics; San Francisco, CA, USA, 2015.
10. Ellis SG, Kereiakes DJ, Metzger DC, *et al*. Everolimus-eluting bioresorbable scaffolds for coronary artery disease. *N Engl J Med* 2015;373:1905–15.
11. Sato K, Latib A, Panoulas VF, *et al*. Procedural feasibility and clinical outcomes in propensity-matched patients treated with bioresorbable scaffolds vs new-generation drug-eluting stents. *Can J Cardiol* 2015;31:328–34.
12. Cortese B, Ielasi A, Romagnoli E, *et al*. Clinical comparison with short-term follow-up of bioresorbable vascular scaffold versus everolimus-eluting stent in primary percutaneous coronary interventions. *Am J Cardiol* 2015;116:705–10.
13. Brugaletta S, Gori T, Low AF, *et al*. Absorb bioresorbable vascular scaffold versus everolimus-eluting metallic stent in ST-segment elevation myocardial infarction: 1-year results of a propensity score matching comparison: the BVS-EXAMINATION Study (bioresorbable vascular scaffold-a clinical evaluation of everolimus eluting coronary stents in the treatment of patients with ST-segment elevation myocardial infarction). *JACC Cardiovasc Interv* 2015;8(Pt B):189–97.
14. Costopoulos C, Latib A, Naganuma T, *et al*. Comparison of early clinical outcomes between ABSORB bioresorbable vascular scaffold and everolimus-eluting stent implantation in a real-world population. *Catheter Cardiovasc Interv* 2015;85:E10–15.
15. Gori T, Schulz E, Hink U, *et al*. Early outcome after implantation of Absorb bioresorbable drug-eluting scaffolds in patients with acute coronary syndromes. *EuroIntervention* 2014;9:1036–41.
16. Mattesini A, Secco GG, Dall'Ara G, *et al*. ABSORB biodegradable stents versus second-generation metal stents: a comparison study of 100 complex lesions treated under OCT guidance. *JACC Cardiovasc Interv* 2014;7:741–50.
17. Moher D, Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA Statement. *Open Med* 2009;3:e123–30.
18. Stroup DF, Berlin JA, Morton SC, *et al*. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. *JAMA* 2000;283:2008–12.
19. Cutlip DE, Windecker S, Mehran R, *et al*. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 2007;115:2344–51.
20. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177–88.
21. Puricel S, Cuculi F, Weissner M, *et al*. Bioresorbable coronary scaffold thrombosis: multicenter comprehensive analysis of clinical presentation, mechanisms, and predictors. *J Am Coll Cardiol* 2016;67:921–31.
22. Kawamoto H, Jabbour RJ, Tanaka A, *et al*. The bioresorbable scaffold: will oversizing affect outcomes? *JACC Cardiovasc Interv* 2016;9:299–300.
23. Kolandaivelu K, Swaminathan R, Gibson WJ, *et al*. Stent thrombogenicity early in high-risk interventional settings is driven by stent design and deployment and protected by polymer-drug coatings. *Circulation* 2011;123:1400–9.
24. Pache J, Kastrati A, Mehilli J, *et al*. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO-2) trial. *J Am Coll Cardiol* 2003;41:1283–8.
25. Diletti R, Serruys PW, Farooq V, *et al*. ABSORB II randomized controlled trial: a clinical evaluation to compare the safety, efficacy, and performance of the Absorb everolimus-eluting bioresorbable vascular scaffold system against the XIENCE everolimus-eluting coronary stent system in the treatment of subjects with ischemic heart disease caused by de novo native coronary artery lesions: rationale and study design. *Am Heart J* 2012;164:654–63.
26. Woudstra P, Grundeken MJ, Kraak RP, *et al*. Amsterdam Investigator-initiateD Absorb strategy all-comers trial (AIDA trial): a clinical evaluation comparing the efficacy and performance of ABSORB everolimus-eluting bioresorbable vascular scaffold strategy vs the XIENCE family (XIENCE PRIME or XIENCE Xpedition) everolimus-eluting coronary stent strategy in the treatment of coronary lesions in consecutive all-comers: rationale and study design. *Am Heart J* 2014;167:133–40.
27. Stone GW, Kedhi E, Kereiakes DJ, *et al*. Differential clinical responses to everolimus-eluting and Paclitaxel-eluting coronary stents in patients with and without diabetes mellitus. *Circulation* 2011;124:893–900.
28. Muramatsu T, Onuma Y, van Geuns RJ, *et al*. 1-year clinical outcomes of diabetic patients treated with everolimus-eluting bioresorbable vascular scaffolds: a pooled analysis of the ABSORB and the SPIRIT trials. *JACC Cardiovasc Interv* 2014;7:482–93.
29. Cassese S, Byrne RA, Ndrepepa G, *et al*. Everolimus-eluting bioresorbable vascular scaffolds versus everolimus-eluting metallic

Downloaded from http://openheart.bmj.com/ on September 16, 2016 - Published by group.bmj.com

stents: a meta-analysis of randomised controlled trials. *Lancet* 2016;387:537–44.
30. Lipinski MJ, Escarcega RO, Baker NC, *et al*. Scaffold thrombosis after percutaneous coronary intervention with ABSORB bioresorbable vascular scaffold: a systematic review and meta-analysis. *JACC Cardiovasc Interv* 2016;9:12–24.
31. Stone GW, Gao R, Kimura T, *et al*. 1-year outcomes with the Absorb bioresorbable scaffold in patients with coronary artery disease: a patient-level, pooled meta-analysis. *Lancet* 2016;387:1277–89.
32. Kang SH, Chae IH, Park JJ, *et al*. Stent thrombosis with drug-eluting stents and bioresorbable scaffolds: evidence from a network meta-analysis of 147 trials. *JACC Cardiovasc Interv* 2016;9:1203–12.
33. Iqbal J, Serruys PW, Silber S, *et al*. Comparison of zotarolimus- and everolimus-eluting coronary stents: final 5-year report of the RESOLUTE all-comers trial. *Circ Cardiovasc Interv* 2015;8:e002230.
34. 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.

Downloaded from http://openheart.bmj.com/ on September 16, 2016 - Published by group.bmj.com

Use of bioresorbable vascular scaffold: a meta-analysis of patients with coronary artery disease

Mohamed Farag, Nikolaos Spinthakis, Diana A Gorog, Abhiram Prasad, Keith Sullivan, Zaki Akhtar, Neville Kukreja and Manivannan Srinivasan

Open Heart 2016 3:
doi: 10.1136/openhrt-2016-000462

Updated information and services can be found at:
http://openheart.bmj.com/content/3/2/e000462

These include:

References This article cites 33 articles, 17 of which you can access for free at:
http://openheart.bmj.com/content/3/2/e000462#BIBL

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 and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Email alerting service Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/