

# A comparison of clinical outcomes following femoro-popliteal bypass or plain balloon angioplasty with selective bare metal stenting in the Bypass versus Angioplasty in Severe Ischaemia of the Limb (BASIL) trial

Meecham, Lewis; Bate, G; Patel, Smitaa; Bradbury, Andrew

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1 **A comparison of clinical outcomes following femoro-**  
2 **popliteal bypass or plain balloon angioplasty with selective**  
3 **bare metal stenting in the Bypass versus Angioplasty in**  
4 **Severe Ischaemia of the Limb (BASIL) trial**

5 L. Meecham<sup>1</sup>, G. Bate<sup>1</sup>, S. Patel<sup>2</sup>, A.W. Bradbury<sup>1</sup>

6 <sup>1</sup> Department of Vascular Surgery, <sup>2</sup> Birmingham Clinical Trials Unit, University of  
7 Birmingham

8 Corresponding Author: Mr Lewis Meecham

9 University Department of Vascular Surgery

10 Netherwood House

11 Solihull Hospital

12 Lode Lane

13 Solihull

14 Birmingham

15 B91 2JL

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17 WHAT THIS PAPER ADDS

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18 This by treatment received analysis of data from the publicly-funded, BASIL-1  
19 randomised controlled trial confirms the superiority of bypass over plain balloon  
20 angioplasty, with or without bare metal stenting, in patients with chronic limb  
21 threatening ischaemia (CLTI) who require femoro-popliteal intervention. Although the  
22 interventions were carried between 1999 and 2003, there are no more recently  
23 acquired randomised data that contradict the findings presented here. BASIL-1 trial  
24 data therefore remain an important and relevant standard with which to compare  
25 outcomes in current vascular and endovascular practice and the results of on-going,  
26 publicly funded, pragmatic randomised controlled trials such as BASIL-2, BASIL-3  
27 and BEST-CLI.

28

29 **ABSTRACT**

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30 Objective: To compare outcomes in patients with chronic limb threatening ischaemia  
31 (CLTI) due to femoro-popliteal (FP), with or without infra-popliteal (IP), disease who  
32 underwent FP (vein or synthetic) open surgical bypass (OSB) or plain balloon  
33 angioplasty (PBA), with or without bare metal stenting (BMS), in the Bypass versus  
34 Angioplasty in Severe Ischaemia of the Limb (BASIL-1) trial.

35 Method: Data were extracted from BASIL-1 case record forms. Outcomes reported  
36 include immediate technical success, freedom from major adverse limb events (FF-  
37 MALE) and further re-intervention (FF-R), amputation free survival (AFS), overall  
38 survival (OS), and limb salvage (LS).

39 Results: Patients underwent primary OSB (n = 128; 89 vein, 39 synthetic) or primary  
40 PBA (n = 183; 6 had BMS). Mean follow-up was 46.2 and 43.6 months respectively.  
41 Patients were well matched at baseline except that PBA +/- BMS patients were  
42 significantly more likely to be current smokers. There was no difference in overall or  
43 IP (run-off) Bollinger angiogram scores between groups. Immediate technical  
44 success was significantly higher for OSB (98% vs. 81%, p<0.0001). OSB was  
45 associated with a longer mean index hospital admission (p=0.001) but there was no  
46 difference in hospital days at 12 months. FF-MALE (HR 1.51, p=0.04) and FF-R  
47 (HR=1.68, p=0.02), but not AFS (HR 1.18, p=0.4), OS (HR 1.14, p=0.5) and LS (HR  
48 1.09, p=0.8) were significantly better following OSB.

49 Conclusion: Although AFS, OS and LS were similar in the two groups, OSB was  
50 associated with significantly fewer MALE and re-interventions. So, while PBA +/-  
51 BMS may be a less resource intensive (expensive) and morbid option in the short  
52 term, this appears unlikely to be the case in the longer term. Present data add further  
53 weight to the argument that, where possible, patients presenting with CLTI due to FP  
54 disease should be offered OSB as their primary revascularisation procedure.

55

56 **INTRODUCTION**

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57 The Bypass versus Angioplasty for Severe Ischaemia of the Leg trial, now known as  
58 the BASIL-1 trial, remains the only published randomised controlled trial (RCT) to  
59 have compared an open surgical bypass (OSB) first, with a plain balloon angioplasty,  
60 with or without bare metal stenting, (PBA +/- BMS) first revascularisation strategy for  
61 chronic limb threatening ischaemia (CLTI) due to infra-inguinal disease<sup>1,2</sup>. In BASIL-  
62 1, approximately 75% of patients had predominantly femoro-popliteal (FP) disease  
63 and intervention while in about 25% the disease and intervention were predominantly  
64 infra-popliteal (IP). A recently published BASIL-1 IP sub-group analysis showed that,  
65 when compared to PBA (no IP BMS were used), a vein bypass (VB) first strategy  
66 resulted in better overall survival (OS), amputation-free survival (AFS), and quality of  
67 revascularisation (time to wound healing and relief of ischaemic rest pain)<sup>3</sup>. Despite  
68 BASIL-1, the only currently available 'level 1' evidence, showing better long-term  
69 clinical outcomes following OSB, there has nevertheless been a non-evidence-based  
70 trend towards offering primary endovascular intervention to patients with CLTI due to  
71 FP disease. The aim of this BASIL-1 sub-group analysis, therefore, is to compare  
72 outcomes in patients who underwent FP OSB (VB and synthetic, SynB) or PBA +/-  
73 BMS as their primary revascularisation procedure.

74

75 **METHOD**

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76 *BASIL-1 trial*

77 BASIL-1 methods and ethical approvals have been published previously<sup>4</sup>. In brief,  
78 between August 1999 and June 2004, 452 patients with CLTI due to infra-inguinal  
79 disease were randomised to an OSB first or a PBA +/- BMS first revascularisation  
80 strategy. Patients were eligible for trial inclusion if the responsible clinicians felt that  
81 they required early revascularisation and were in clinical equipoise OSB and PBA +/-  
82 BMS. Patients were followed up by six dedicated research nurses at 1, 3, 6, and 12  
83 months post randomisation and then annually until death or 1 July 2007. The primary  
84 endpoint was amputation free survival (AFS) and secondary end-points included  
85 overall survival (OS), limb salvage (LS) and requirement for re-intervention. BASIL-1  
86 was a multi-centre, pragmatic, clinical effectiveness RCT that allowed participating  
87 units to continue to use their preferred post-intervention surveillance programmes.  
88 However, the majority of the re-interventions were due to persisting or recurrent  
89 symptoms and signs of CLTI.

90 *Inclusion criteria for FP subgroup analysis*

91 In order to be included in the current sub-group analysis, BASIL-1 patients had to  
92 fulfil two criteria. Firstly, they had to have atherosclerotic FP disease causing CLTI  
93 and, secondly, they only underwent intervention to the FP segment (with no IP  
94 intervention). Baseline and clinical outcome data were extracted from the original  
95 prospectively gathered BASIL-1 case record forms.

96 *Outcomes*

97 In this BASIL-1 FP sub-group analysis, we report immediate technical success (as  
98 defined by the operating surgeon or interventionalist), mean length of index hospital  
99 admission, days spent in hospital out to 12 months from randomisation, freedom  
100 from major adverse limb events (FF-MALE) and re-intervention (FF-R), AFS, OS,  
101 and LS. Major amputation was classified as amputation of the trial limb above the  
102 ankle. We have chosen not to include minor amputation as a re-intervention as we  
103 regard this as being mainly determined by the condition of the foot at presentation  
104 and not the type of primary revascularisation. Major adverse limb event (MALE)  
105 comprised any revascularisation attempt or major amputation of the trial limb during

106 follow up. Post-procedural complications are reported as 30-day mortality, morbidity  
107 (complications and re-interventions) and major adverse cardiovascular event  
108 (MACE) which comprises death, myocardial infarction or cerebrovascular event.  
109 Unplanned interventions for post-operative complications, revascularisation (OSB or  
110 PBA +/- BMS), or major amputation were collated and reported under the term  
111 surgical re-interventions if they occurred within 30-days. No patients were lost to  
112 follow up for the primary endpoint or the other secondary endpoints reported here.  
113 Patients who partially withdrew had their clinical outcome data collected via UK  
114 centralised data-bases, now known as ONS (office of national statistics) and HES  
115 (hospital episode statistics) data.

### 116 *Statistics*

117 Time to event analyses comparing all OSB (VB and SynB) with PBA +/- BMS are  
118 presented over a 7-year period using Kaplan-Meier plots and Log-Rank test for  
119 significance. Hazard ratios were used to detect statistically important differences in  
120 outcomes using 95% confidence intervals. Differences between the groups were  
121 compared using t-test,  $\chi^2$ -squared and Wilcoxon Rank Sum tests according to  
122 distribution of data using SAS v9.4.

123

## 124 RESULTS

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### 125 *Demographics*

126 There were 311 patients; 128 underwent primary OSB (89 VB, 39 SynB) and 183  
127 had primary PBA +/- BMS (6 stents). The mean follow-up was 46.2 (range 0-91) and  
128 43.6 (range 0-93) months respectively. Ipsilateral great saphenous vein (GSV) was  
129 used for 83 (93%) VB; arm vein was used for 1 (1%) and composite vein (arm and  
130 leg vein spliced) for 5 (6%). Most VB were reversed (63, 71%) with (23, 26%) being  
131 in-situ and (3, 4%) non-reversed. The two groups were very similar in terms of  
132 baseline characteristics although PBA +/- BMS patients were more likely to be  
133 current smokers, and there was a trend to more chronic obstructive pulmonary  
134 disease (COPD) in OSB patients (**Table 1**).

### 135 *Distribution of Disease*

136 There was no significant difference in the overall burden of disease between the two  
137 groups in terms of Bollinger angiographic scores ( $p = 0.2$ ) (**Table 2**). IP disease  
138 severity was also statistically similar in the two groups (Bollinger Score = 44.4 vs  
139 46.6,  $p=0.4$ ) with the peroneal artery being the least diseased run-off vessel.

### 140 *Short-term outcomes*

141 Immediate technical success was highly significantly better for OSB (98% vs. 81%,  
142  $p<0.0001$ ). Although patients undergoing OSB had a longer median (inter-quartile  
143 range, IQR) index hospital admission (16 [10-27] vs. 8 [2-19] days,  $p=0.0001$ ) by 12  
144 months patients in both groups had spent an equivalent median (range) number of  
145 days (17 [11-28] vs 17 [6-41],  $p=0.7$ ) in hospital. Statin use was low in both groups  
146 (OSB 30% vs. PBA +/- BMS 37%,  $p=0.2$ ). Antiplatelet use was significantly higher in  
147 OSB patients (66% vs. 55%  $p=0.05$ ). Although all-cause 30-day mortality was not  
148 statistically different between the two groups, OSB patients suffered more morbidity;  
149 in particular, wound infection (**Table 3**). PBA +/- BMS patients required more surgical  
150 interventions within the first 30-days (2% vs. 7%,  $p=0.06$ ).

### 151 *Long term clinical outcomes OSB vs PBA+/-BMS*

152 There was no difference in AFS (62% vs. 55%, HR 1.18, 95% CI 0.82-1.69,  $p=0.4$ )  
153 (**Figure 1**), OS (69% vs. 63%, HR 1.14, 95% CI 0.77-1.70,  $p=0.5$ ) (**Figure 2**) or LS



154 (85% vs. 85%, HR 1.09, 95% CI 0.59-2.01, p=0.8) between OSB and PBA+/-BMS.  
155 However, FF-MALE (67% vs. 56%, HR 1.51, 95% CI 1.01–2.25, p=0.04) (**Figure 3**)  
156 and FF-R (72% vs. 63%, HR=1.68, 95% CI: 1.09–2.60, p=0.02) (**Figure 4**) were  
157 significantly lower following OSB. Resolution of rest pain (85% vs 76%, HR=0.84,  
158 95%CI 0.63–1.11 p=0.2) and wound healing at 3 years (90% vs 84%, HR=0.78,  
159 95%CI 0.55-1.10 p= 0.2) (**Figure 5**) were similar in the two groups.

#### 160 *Long term clinical outcomes VB vs SynB vs PBA+/-BS*

161 There was no significant difference in AFS (67% vs. 51% vs 55%, p = 0.2), OS (72%  
162 vs. 64% vs. 63%, p=0.4) (**Figure 7**) and LS (90% vs. 72% vs 85%, p=0.3) between  
163 VB, SynB and PBA+/- BMS, although the number of SynB was small. FF-MALE  
164 (71% vs 58% vs 56%, p=0.02) was significantly better following VB.

#### 165 *Re-interventions*

166 Overall, 24 (19%) OSB, and 63 (34%) PBA +/- BMS, patients underwent re-  
167 intervention, with 38 and 85 re-interventions respectively (**Table 4**). There was no  
168 difference in the number of inflow procedures performed in each group (7 vs. 8,  
169 p=0.2). Patients in the PBA +/- BMS group underwent more secondary bypass  
170 procedures (47, 55% vs. 3, 8% p=<0.001) and more repeat angioplasties (21 ,25%,  
171 vs 5, 13%, p=0.1). OSB patients underwent more angioplasties for in-graft stenosis  
172 (13, 35% vs. 1, 1%, p=<0.001).

173

174 **DISCUSSION**

175 The main finding of this BASIL-1 FP sub-group analysis is that although major  
176 amputation rates and all-cause mortality are similar, primary OSB, especially VB,  
177 results in significantly fewer MALE and re-interventions than primary PBA+/-BMS.  
178 So, although an endovascular first revascularisation strategy may be a less resource  
179 intensive (expensive) and morbid option in the short term, in longer term, this seems  
180 unlikely to be the case. Present data add further weight to the argument that, where  
181 possible, VB should be offered as the preferred primary revascularisation procedure  
182 to most patients presenting with CLTI due to FP disease. This is especially so in  
183 standard risk patients (anticipated life expectancy >2 years) who are more likely to  
184 enjoy the long-term benefit of VB and less likely to suffer short-term peri-operative  
185 morbidity<sup>1,5-8</sup>. Present data support the previously published BASIL-1 IP sub-group  
186 outcomes indicating that the durability and quality of revascularisation are better after  
187 VB than after PBA<sup>2</sup>. In this BASIL-1 FP cohort, unlike in the IP cohort, healing of  
188 tissue loss and speed of resolution of rest pain were not significantly different  
189 between the two groups. This may be because almost a quarter (23%) of the  
190 patients who underwent primary FP PBA +/- BMS required subsequent OSB for  
191 persistent or recurrent symptoms of CLTI. Indeed, CLTI patients presenting with the  
192 most severe disease in terms of wound, ischaemia and infection<sup>9</sup>, seem to be those  
193 most likely to enjoy better outcomes following primary VB than primary endovascular  
194 intervention. This is especially so given that outcomes following secondary VB after  
195 failed primary endovascular intervention are significantly worse than those observed  
196 when VB is used as the primary revascularisation procedure<sup>10,11</sup>. The low rates of  
197 best medical therapy (antiplatelet and statin use coupled with smoking cessation)  
198 often observed in CLTI studies are worthy of discussion. In the present study, only  
199 two-thirds of patients undergoing OSB were on antiplatelet therapy at randomisation  
200 (the rate was 10% lower in PBA +/- BMS group) and only about one-third of patients  
201 in both groups were on a statin. While better medical therapy is likely to improve  
202 CLTI outcomes overall, there is no evidence this would have altered the conclusions  
203 of BASIL-1 in terms of the recommendation to offer VB first wherever possible. Thus,  
204 in a recent large case series<sup>8</sup>, although best medical therapy rates had improved to  
205 approximately 80%, the re-intervention rate was 62% for OSB and 52% for PBA at 3  
206 years. These 3 year re-intervention data are worse than those observed in BASIL-1

207 at 7 years. This is an important observation as endovascular enthusiasts often point  
208 to the fact that BASIL-1 is now a relatively old trial (patients randomised between  
209 1999 and 2004) and argue that, if BASIL-1 were to be repeated using modern  
210 endovascular techniques and technologies, the trial would show a clear advantage in  
211 favour of an endovascular first strategy for most, even perhaps all, patients. While  
212 that is possible, there is no evidence to suggest that such an outcome is likely.  
213 Indeed, the evidence we have suggests that such an outcome would be unlikely. In  
214 particular, with regard to drug coated balloons (DCB) and drug eluting stents (DES),  
215 there are no data to show that they improve clinical outcomes in patients with CLTI  
216 when compared to PBA +/-BMS<sup>12-22</sup>. While DES and DES may be associated with  
217 better anatomic outcomes, the great majority of the patients entered into the plethora  
218 of industry-funded trials had intermittent claudication, underwent treatment of short  
219 segment disease, and had short follow up with little or no reporting of clinical  
220 outcomes. Even the small minority of patents in these trials who had CLTI were very  
221 largely entered on the basis of rest pain and did not have tissue loss. Other  
222 techniques such as laser atherectomy<sup>23</sup> and covered stents<sup>24</sup> have not been widely  
223 adopted due to a lack of evidence demonstrating clinical and cost-effectiveness. At  
224 the time of writing, there are no published, publicly-funded trials comparing DCB /  
225 DES to either PBA or OSB in patients with CLTI. As a result, and given their very  
226 considerable additional cost, the UK National Institute for Health and Care  
227 Excellence (NICE) have recommended against the use of DCB and DES and are  
228 awaiting the outcome of on-going RCTs, specifically BASIL-2<sup>25</sup> and BASIL-3<sup>26</sup> in the  
229 UK and BEST-CLI trial<sup>27</sup> in the US before reconsidering the matter. The European  
230 Society of Vascular Surgery (ESVS) and European Society of Cardiology (ESC)  
231 guidelines on the diagnosis and treatment of patients with peripheral arterial disease  
232<sup>28</sup> specifically state no clinical benefit has been proven for DCB over PBA. Data  
233 reported here support the ESC/ESVS guidelines stance that vein bypass surgery for  
234 long lesions in patients with CLTI is the first choice method of revascularisation. In  
235 conclusion, this BASIL-1 FP sub-group confirms the superiority of VB as the  
236 preferred primary FP re-vascularisation procedure for most CLTI patients. However,  
237 the results of further publicly funded, pragmatic RCTs, such as BASIL-2, BASIL-3  
238 and BEST-CLI, are required to help answer the many remaining questions regarding  
239 the clinical and cost-effectiveness of alternative revascularisation strategies in  
240 different subgroups of CLTI patients.

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357 **TABLES**

358 **Table 1. Baseline characteristics in patients undergoing open surgical bypass**  
 359 **and plain balloon angioplasty +/- bare metal stent**

		OSB (n = 128)	PBA +/- BMS (n = 183)	P Value
Conduit	Vein	89 (70%)	-	
	Synthetic	39 (30%)	-	
	PBA+/-BMS	-	183 (100%)	
Gender	Male	78 (61%)	94 (51%)	0.09
Limb	Right	57 (45%)	75 (41%)	0.5
Age	Mean (SD)	71.7 (8.0)	73.1 (8.6)	0.2
Follow up (months)	Mean (SD)	46.2 (27.2)	43.6 (24.7)	0.4
Indication	Rest pain	52 (41%)	69 (38%)	0.4
	Tissue Loss	14 (11%)	14 (8%)	
	Both	62 (48%)	100 (54%)	
Creatinine	Mean (SD)	111.7 (79.4)	107.7 (60.2)	0.6
Smoker	Never	17 (13%)	36 (20%)	0.04
	Ex-Smoker	65 (51%)	67 (36%)	
	Current	46 (36%)	80 (44%)	
Diabetes Mellitus		47 (37%)	74 (40%)	0.5
Congestive Heart Failure		5 (4%)	8 (4%)	0.8
Hypertension		77 (60%)	108 (59%)	0.8
Coronary Artery Disease		35 (27%)	50 (27%)	1.0
Chronic Obstructive Airway Disease		19 (15%)	15 (8%)	0.06

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361 OSB open surgical bypass; PBA, plain balloon angioplasty; BMS, bare metal stent

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363 **Table 2. A comparison of mean (SD) Bollinger scores between open surgical**  
 364 **bypass and plain balloon angioplasty +/- bare metal stent groups**

Arterial Section	OSB (n = 128)	PBA+/-BMS (n = 183)	P Value
Profunda Femoris	1.6 (2.6)	2.1 (3.4)	0.2
Proximal Superficial Femoral	7.0 (5.9)	7.0 (5.5)	0.9
Distal Superficial Femoral	10.3 (4.9)	10.2 (5.0)	0.8
Proximal Popliteal	6.9 (5.8)	7.1 (5.7)	0.7
Distal Popliteal	1.5 (2.5)	2.7 (4.4)	0.007
Tibio-peroneal Trunk	2.5 (3.6)	2.8 (4.3)	0.6
Proximal Posterior Tibial	6.8 (5.9)	8.2 (6.6)	0.05
Distal Posterior Tibial	8.3 (6.6)	9.3 (6.5)	0.1
Proximal Peroneal	4.4 (4.8)	4.6 (5.2)	0.7
Distal Peroneal	5.8 (6.2)	4.5 (5.6)	0.1
Proximal Anterior Tibial	6.0 (6.1)	5.8 (5.7)	0.8
Distal Anterior Tibial	7.2 (6.8)	6.7 (6.6)	0.6
Plantar	6.7 (4.0)	6.5 (4.4)	0.8
Total	70.7 (24.5)	75.1 (27.3)	0.2
Total Infra-popliteal Score	44.4 (22.4)	46.6 (24.1)	0.4

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 366 OSB open surgical bypass; PBA, plain balloon angioplasty; BMS, bare metal stent  
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368 **Table 3. Morbidity and mortality (30 day) in patients undergoing open surgical**  
 369 **bypass and plain balloon angioplasty +/- bare metal stent**

	SB (n = 128)	PBA+/-BMS (n = 183)	P Value
Mortality (30 days)	7 (5%)	6 (3%)	0.3
Morbidity and mortality (30 days)	58 (45%)	59 (32%)	0.02
Myocardial infarction	5 (4%)	5 (3%)	0.6
Transient ischaemic attack	0 (-)	2 (1%)	0.2
Cerebrovascular accident	1 (1%)	3 (2%)	0.5
Haematoma (not operated)	7 (5%)	8 (4%)	0.7
Haematoma (operated)	2 (2%)	1 (1%)	0.4
Wound Infection	37 (29%)	29 (16%)	0.006
Lower respiratory tract infection	4 (3%)	5 (3%)	0.8
Urinary tract infection	2 (2%)	3 (2%)	1.0
False Aneurysm (not operated)	1 (1%)	0 (-)	0.2
False Aneurysm (operated)	0 (-)	0 (-)	-
Major Amputation	3 (2%)	9 (5%)	0.3
Surgical Intervention (30 days)	3 (2%)	13 (7%)	0.06
Major adverse cardiovascular event	10 (8%)	10 (5%)	0.4

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371 OSB open surgical bypass; PBA, plain balloon angioplasty; BMS, bare metal stent

372 \*Wound Infection includes foot infection as well as infection at the intervention site

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374 **Table 4. Re-interventions following open surgical bypass and plain balloon**  
 375 **angioplasty +/- bare metal stent**

	Re-intervention	OSB (n = 128)	PBA+/-BMS (n = 183)
Number of patients		24 (19%)	63 (34%)
Total re-interventions		38	85
Inflow	Ileo-femoral bypass	2 (5%)	1 (1%)
	Iliac PBA+/- BMS	2 (5%)	4 (5%)
	Axillo-femoral bypass	1 (3%)	0 (0%)
	Aorto-bifemoral bypass	0 (0%)	1 (1%)
	Common femoral endarterectomy	1 (3%)	2 (2%)
	Femoro-femoral crossover	1 (3%)	0 (0%)
FP Revascularisations	OSB	3 (8%)	47 (55%)
	PBA+/-BMS	5 (13%)	21 (25%)
	Graft PBA	13 (34%)	1 (1%)
	Thrombolysis	1 (3%)	1 (1%)
	Embolectomy	3 (8%)	2 (2%)
	Profundoplasty	0 (0%)	2 (2%)
	Graft patch angioplasty	1 (3%)	0 (0%)
Other	Graft explanted for infection	2 (5%)	1 (1%)
	Haemostasis	2 (5%)	0 (0%)
	Chemical Sympathectomy	1 (3%)	2 (2%)

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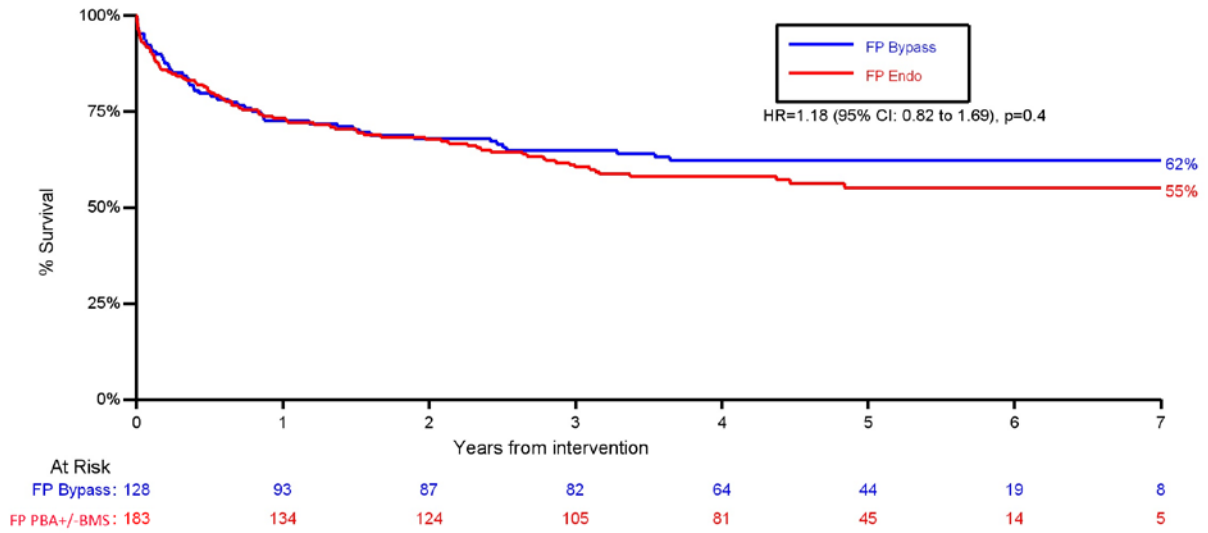
377 OSB open surgical bypass; PBA, plain balloon angioplasty; BMS, bare metal stent

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379 **FIGURES**

380 **Figure 1. Amputation free survival in patients undergoing femoro-popliteal**  
 381 **bypass and plain balloon angioplasty +/- bare metal stent in the BASIL-1 trial**

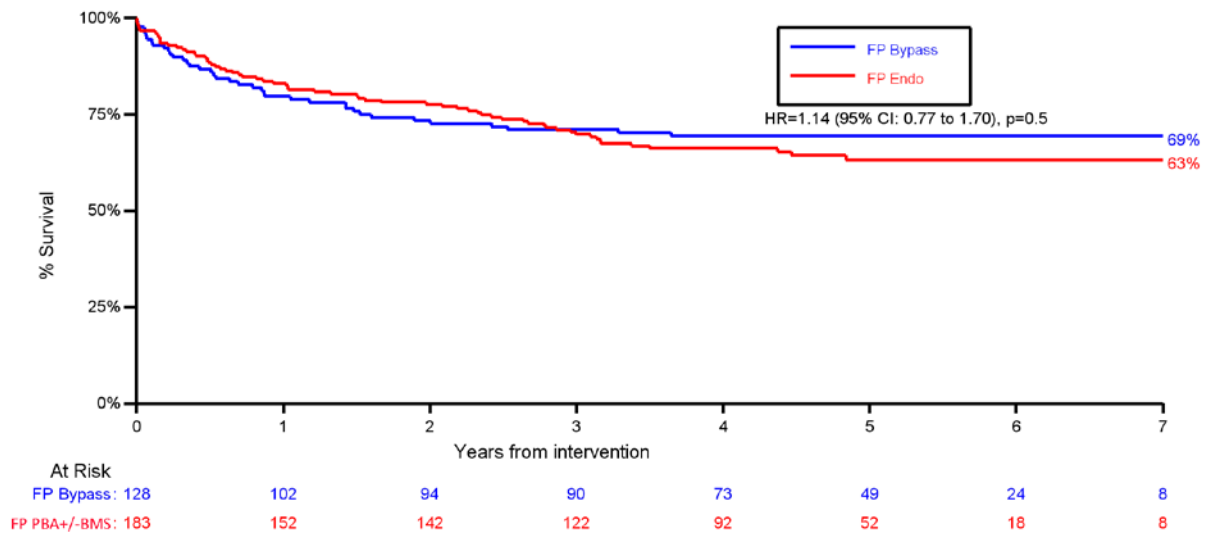
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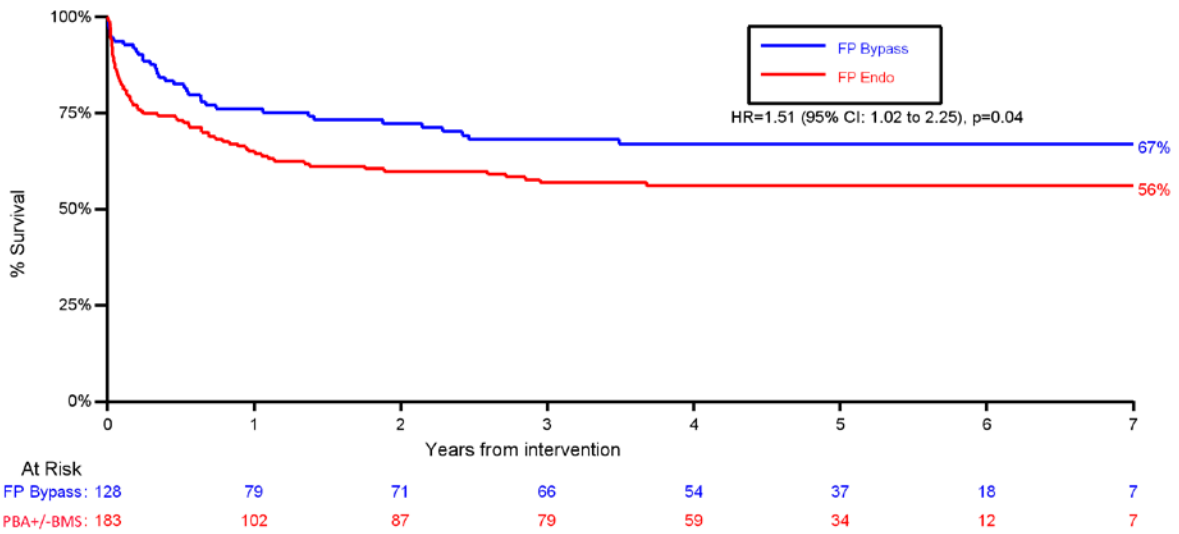
384 **Figure 2. Overall survival in patients undergoing femoro-popliteal bypass and**  
 385 **plain balloon angioplasty +/- bare metal stent in the BASIL-1 trial**

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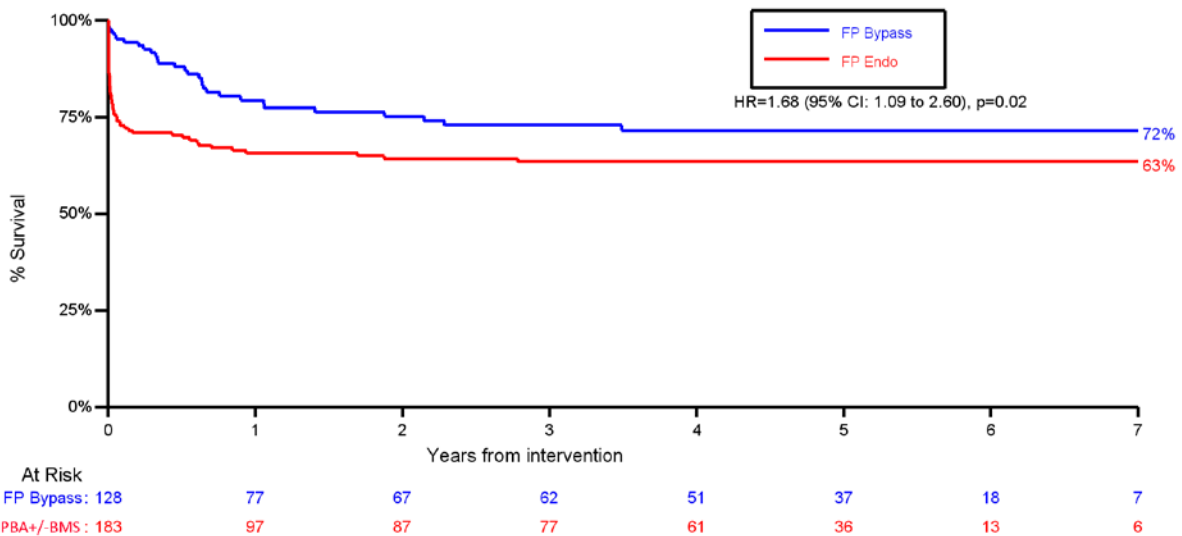
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388 **Figure 3. Freedom from major adverse limb events in patients undergoing**  
 389 **femoro-popliteal bypass and plain balloon angioplasty +/- bare metal stent in**  
 390 **the BASIL-1 trial**



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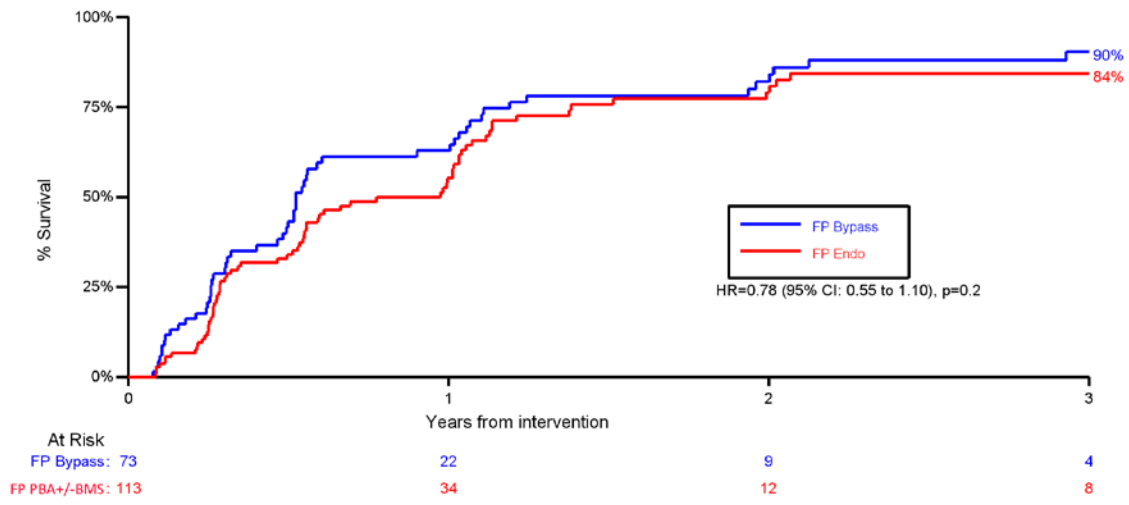
392 **Figure 4. Freedom from re-intervention in patients undergoing femoro-**  
 393 **popliteal bypass and plain balloon angioplasty +/- bare metal stent in the**  
 394 **BASIL-1 trial**



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397 **Figure 5. Wound Healing in patients undergoing femoro-popliteal bypass SB**  
398 **and plain balloon angioplasty +/- bare metal stent in the BASIL-1 trial**



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