

SUPPLEMENTAL MATERIAL

Supplemental Methods

Case Ascertainment: hot and cold pursuit methodology

Hot pursuit was based on the daily assessment of all patients with a possible vascular event identified by: 1) Daily searches of Emergency Department admission and symptom/diagnosis registers; 2) Daily listing from the central admissions department of all patients from our general practices admitted to hospital, and assessment of these patients in hospital; 3) Daily visits to the cardiac surgery and vascular surgery wards and review of daily lists of all patients referred to vascular surgery; 4) Daily identification via Bereavement Officers of patients dead on arrival at hospital or who died soon after; 5) Daily assessment of all patients undergoing diagnostic angiographic, angioplasty/stenting or arterial surgical procedures in any territory.

The methods of cold pursuit were: 1) Weekly review of all listed surgical procedures undertaken by vascular and cardiovascular surgery; 2) Frequent contact with general practices and monthly searches of computerised practice diagnostic codes; 3) Monthly practice-specific list of all patients with relevant diagnostic codes from the coding departments covering all acute and community hospitals (Hospital Episode Statistics – HES – data); 4) Monthly visits to the Coroner's Office to review out-of-hospital deaths; 5) Review of all death certificates and relevant clinical details in the study practices; 6) Practice-specific listings of all ICD-10 death codes from the local Department of Public Health; 7) Review of vascular surgery outpatient clinic letters to identify patients who were not admitted to hospital. For all cases not initially identified by HES data and death certification, these data sources were re-searched using NHS number and other identifiers, where possible.

Supplemental table 1: Outcome analysis of the 91 largest blood pressure lowering treatment trials

SUMMARY OF MAJOR OUTCOMES ASSESSED

	Any Stroke	Non-Fatal Stroke	Fatal Stroke	Any MI	Non-Fatal MI	Fatal MI	Peripheral Vascular Event	Coronary Revascularisation	Cardiovascular Mortality	All-cause Mortality
Total N	73	30	29	79	39	37	11	26	54	68
Total %	80.2	33.0	31.9	86.8	42.9	40.7	12.1	28.6	59.3	74.7

DETAILED ANALYSIS

STUDY DETAILS				MAJOR OUTCOMES ASSESSED										
Study	Placebo/Reference Drug	N Ref. Arm	Experimental Drug	N Exp. Arm	Any Stroke	Non-Fatal Stroke	Fatal Stroke	Any MI	Non-Fatal MI	Fatal MI	Peripheral Vascular Event	Coronary Revasc.	CVS Mortality	All-cause Mortality
AASK	Metoprolol	441	Ramipril	436	NO	NO	NO	NO	NO	NO	NO	NO	YES	YES
ABCD (H)	Enalapril	235	Nisoldipine	235	YES	NO	NO	YES	YES	YES	NO	NO	YES	YES
ACCOMPLISH	Benazepril+Am	5744	Benazepril+HCTZ	5762	YES	NO	NO	YES	NO	NO	NO	YES	YES	YES
ACTION	lodipine		Placebo	3840	YES	NO	NO	YES	NO	NO	YES	YES	YES	YES
ADVANCE	Placebo	5571	Nifedipine	3825	YES	NO	NO	YES	NO	NO	NO	NO	YES	YES
ALLHAT I	Chlortalidone	15268	Perindopril-indapamide	5569	YES	NO	NO	YES	NO	NO	NO	NO	YES	YES
ALLHAT II	Chlortalidone	15268	Doxazosin	9067	YES	NO	NO	YES	NO	NO	YES	YES	YES	YES
ANBP2	Hydrochlorothiazide	3039	Doxazosin	9067	YES	NO	NO	YES	NO	NO	YES	YES	YES	YES
ANBPS	Placebo	1706	Enalapril	3044	YES	YES	YES	YES	YES	YES	NO	NO	NO	YES
APSYS	Metoprolol	406	Chlorothiazide	1721	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
ASCOT	Metoprolol	406	Verapamil	403	YES	YES	NO	YES	YES	YES	YES	YES	YES	YES
AVER	Atenolol-based	9618	Amlodipine-based	9639	YES	NO	NO	YES	NO	NO	YES	NO	YES	YES
BBB	Amlodipine	132	Enalapril	131	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
BCAPS	Conventional treatment	1063	Intense treatment	1063	YES	NO	NO	YES	YES	YES	NO	NO	NO	NO
BENEDICT (ACEI)	Placebo	397	Metoprolol	396	YES	YES	YES	YES	YES	NO	NO	NO	NO	NO
CAMELOT (ACEI)	Placebo	300	Trandalopril	301	NO	NO	NO	YES	NO	YES	NO	NO	YES	NO
CAPPP	Placebo	655	Enalapril	673	YES	NO	NO	YES	YES	YES	YES	YES	YES	YES
CONVINCE	Diuretic or β -Blocker	5493	Captopril	5492	YES	YES	YES	YES	YES	YES	NO	NO	YES	NO
Coope	Hydrochlorothiazide or atenolol	8297	COER Verapamil	8179	YES	NO	NO	YES	NO	NO	NO	YES	YES	YES
	Control (no treatment)	465	Atenolol or bendrofluzide	419	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES

DETAIL	Enalapril	130	Telmisartan	120	NO	NO	NO	YES	YES	NO	NO	NO	YES	YES
DIABHYCAR	Placebo	2469	Ramipril	2443	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
DREAM	Placebo	2646	Ramipril	2623	YES	NO	NO	YES	NO	NO	NO	YES	YES	YES
Dutch-TIA	Placebo	741	Atenolol	732	YES	YES	YES	YES	YES	YES	NO	NO	NO	YES
E-COST	Conventional treatment	995	Candesartan	1053	YES	NO	NO	YES	NO	NO	NO	NO	NO	NO
ELSA	Atenolol	1012	Lacidipine	1023	YES	NO	NO	YES	NO	NO	NO	NO	YES	YES
ESPIRAL	Fosinopril	129	Nifedipine	112	YES	NO	NO	YES	NO	NO	NO	NO	NO	YES
EUCLID	Placebo	265	Lisinopril	265	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
EUROPA	Placebo	6108	Perindopril	6110	YES	NO	NO	YES	NO	NO	NO	NO	YES	YES
EWPHE	Placebo	424	Hydrochlorothiazide + Triamterene	416	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
FACET	Fosinopril	189	Amlodipine	191	YES	NO	NO	YES	NO	NO	NO	YES	NO	YES
FEVER	Placebo	4870	Felodipine	4841	YES	YES	YES	YES	NO	NO	NO	YES	YES	YES
FOSIDAL	Placebo	201	Fosinopril	196	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
HAPPY	Thiazide Conventional treatment	3272	β-Blocker	3297	YES	YES	YES	YES	YES	YES	NO	NO	NO	YES
HDFP	Intense treatment	5455	Intense treatment	5485	YES	NO	NO	YES	NO	NO	NO	NO	NO	YES
Himmelmann	Atenolol	129	Cilazapril	131	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
HOPE	Placebo	4652	Ramipril	4645	YES	NO	NO	YES	NO	NO	NO	YES	YES	YES
HOT	Target<90	6264	Target<85	6264	YES	NO	NO	YES	NO	NO	NO	NO	YES	YES
HSCSG	Placebo	219	Deserpidine and Methylclothiazide	233	YES	NO	NO	YES	NO	NO	NO	NO	NO	YES
HYVET	Placebo	1912	Active treatment	1933	YES	YES	YES	YES	NO	NO	NO	NO	YES	YES
IDNT (ATII)	Placebo	569	Irbesartan	579	NO	NO	NO	NO	NO	NO	NO	NO	NO	YES
INSIGHT	Co-amilozide	3164	Nifedipine	3157	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
INTACT	Placebo	131	Nifedipine	119	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
INVEST	Non-Calcium antagonist	11309	Calcium antagonist	11267	YES	YES	YES	YES	YES	NO	NO	YES	YES	YES
IPPPSH	Non-bBlocker	3172	β-Blocker	3185	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
IRMA2 (ATII150mg)	Placebo	201	Irbesartan 150mg	195	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
JMIC-B	ACE Inhibitor	822	Nifedipine	828	YES	NO	NO	YES	NO	NO	NO	YES	NO	YES
J-MIND	Nifedipine	228	Enalapril	208	YES	NO	NO	YES	NO	NO	NO	NO	NO	NO
Kondo	Baseline treatment	201	Candesartan+Baseline treatment	194	NO	NO	NO	YES	YES	YES	NO	YES	YES	YES
LAARS	Atenolol	138	Losartan	142	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
LIFE	Atenolol	4588	Losartan	4605	YES	NO	NO	YES	NO	NO	NO	YES	YES	YES
Maschio	Placebo	283	Benazepril	300	YES	NO	NO	YES	YES	YES	NO	NO	NO	NO
MIDAS	Hydrochlorothiazide	441	Isradipine	442	YES	NO	NO	YES	NO	NO	NO	YES	NO	YES
MOSES	Eposartan	681	Nitrendipine	671	YES	NO	NO	YES	NO	NO	NO	NO	NO	YES
MRC1	Placebo	8654	Bendrofluazide	4297	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
MRC2	Placebo	2213	Bendrofluazide	1081	YES	NO	YES	YES	NO	YES	NO	NO	YES	YES

NICOLE	Placebo	338	Nisoldipine	308	YES	NO	NO	YES	NO	NO	NO	YES	NO	YES
NICS	Trichlormethiazide	210	Nicardipine (SR)	204	YES	YES	YES	YES	NO	NO	NO	NO	NO	NO
NORDIL	Diuretic and/or	5471	Diltiazem (SR)	5410	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
ONTARGET (ACEI+ATII)	β -Blocker	8576	Ramipril + Telmisartan	8502.00	YES	NO	NO	YES	NO	NO	NO	NO	YES	YES
OSLO Study	Ramipril	379	Hydrochlorothiazide	406	YES	NO	NO	YES	NO	NO	NO	YES	YES	YES
PART2	Control (no treatment)	309	Ramipril	308	YES	YES	NO	YES	YES	YES	NO	NO	YES	YES
PATS	Placebo	2824	Indapamide	2841	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
PEACE	Placebo	4132	Trandolopril	4158	YES	NO	NO	YES	YES	YES	NO	YES	YES	YES
PHYLLIS	Hydrochlorothiazide	127	+Pravastatin	126	NO	NO	NO	YES	NO	NO	NO	NO	NO	NO
PREVEND IT	Combination	433	Fosinopril	431	YES	NO	NO	YES	YES	YES	YES	NO	YES	NO
PREVENT	Placebo	408	Amlodipine	417	YES	NO	NO	YES	NO	NO	NO	YES	NO	YES
PROFESS	Telmisartan	9825	Placebo	9856	YES	NO	NO	YES	NO	NO	NO	NO	YES	YES
PROGRESS	Placebo	3054	Treatment	3051	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
QUIET	Placebo	872	Quinapril	878	YES	NO	NO	YES	YES	YES	NO	YES	YES	NO
RENAAL	Placebo	762	Losartan	751	NO	NO	NO	YES	NO	NO	NO	NO	NO	YES
SCAT	Placebo	231	Enalapril	229	YES	NO	NO	YES	YES	YES	NO	YES	YES	YES
SCOPE	Placebo	2460	Candesartan	2477	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
SHELL	Chlortalidone	940	Lacidipine	942	YES	NO	NO	YES	NO	NO	NO	YES	NO	YES
SHEP	Placebo	2371	Chlortalidone	2365	YES	YES	YES	YES	YES	YES	NO	YES	YES	YES
STONE	Placebo	815	Nifedipine	817	YES	NO	NO	YES	NO	NO	NO	NO	YES	YES
STOPI	B-Blocker and/or	815	Diuretic	812	YES	NO	NO	YES	NO	NO	NO	NO	YES	YES
STOP2	Diuretic, β -Blocker or both	2213	ACE Inhibitors	2205	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
Syst-China	Placebo	1141	Nitrendipine	1253	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
Syst-Eur	Placebo	2297	Nitrendipine	2398	YES	YES	YES	YES	YES	YES	YES	NO	YES	YES
TEST	Placebo	348	Atenolol	372	YES	YES	YES	YES	YES	YES	NO	NO	YES	YES
TIBET	Atenolol	226	Nifedipine	232	NO	NO	NO	YES	YES	NO	NO	YES	NO	NO
TOMHS	Placebo	234	Acebutolol	132	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
TRANSCEND	Telmisartan	2954	Placebo	2972	YES	NO	NO	YES	NO	NO	NO	YES	NO	YES
UKPDS38	Less intense	390	Intense treatment	758	YES	NO	NO	YES	NO	NO	YES	NO	NO	YES
UKPDS39	Atenolol	358	Captopril	400	YES	YES	YES	YES	YES	YES	YES	NO	NO	YES
USPHS	Placebo	178	Chlorothiazide + Rauwolfia serpentina	175	YES	NO	NO	YES	YES	YES	NO	NO	YES	YES
VACS1	Placebo	194	Active treatment	186	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
VACS2	Placebo	186	Hydrochlorothiazide	188	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
VALUE	Valsartan	7649	Amlodipine	7596	YES	NO	NO	YES	NO	NO	NO	NO	YES	YES
VHAS	Chlortalidone	707	Verapamil (SR)	707	YES	YES	YES	YES	YES	YES	YES	NO	YES	YES
Yurenev	No β -Blocker	154	β -Blocker	150	YES	NO	NO	YES	NO	NO	NO	NO	NO	NO

Supplemental table 2: Age- and sex-specific rates per hundred thousand population (2002-2012) for incident acute peripheral arterial events for acute visceral ischaemia; acute limb ischaemia; and critical limb ischaemia

Acute Visceral Ischaemia

AGE (yrs)	<45	45-54	55-64	65-74	75-84	≥85	Total
Men							
Cases	3	1	4	3	7	10	28
Rate/100,000 (95% CI)	1 (0,3)	2 (0,9)	8 (2,20)	9 (2,25)	34 (14,70)	193 (93,355)	6 (4,9)
Women							
Cases	0	1	1	8	13	27	50
Rate/100,000 (95% CI)	--	2 (0,10)	2 (0,11)	22 (9,43)	49 (26,84)	245 (161,356)	11 (8,15)
Total							
Cases	3	2	5	11	20	37	78
Rate/100,000 (95% CI)	1 (0,2)	2 (0,6)	5 (2,11)	15 (8,28)	43 (26,66)	228 (161,315)	8 (7,11)

Acute Limb Ischaemia

AGE (yrs)	<45	45-54	55-64	65-74	75-84	≥85	Total
Men							
Cases	0	4	7	13	19	6	49
Rate/100,000 (95% CI)	--	6 (2,17)	13 (5,28)	37 (20,64)	93 (56,145)	116 (43,252)	10 (8,14)
Women							
Cases	0	1	6	8	13	16	44
Rate/100,000 (95% CI)	--	2 (0,10)	12 (4,26)	22 (9,43)	49 (26,84)	145 (83,236)	10 (7,13)
Total							
Cases	0	5	13	21	32	22	93
Rate/100,000 (95% CI)	--	4 (1,10)	13 (7,22)	29 (18,45)	68 (47,96)	136 (85,206)	10 (8,12)

Critical Limb Ischaemia

AGE (yrs)	<45	45-54	55-64	65-74	75-84	≥85	Total
Men							
Cases	0	5	22	33	33	16	109
Rate/100,000 (95% CI)	--	8 (3,19)	42 (27,64)	95 (65,133)	161 (111,226)	309 (177,502)	23 (19,28)
Women							
Cases	1	2	10	19	38	23	93
Rate/100,000 (95% CI)	0 (0,2)	3 (0,12)	20 (10,37)	52 (31,81)	143 (101,197)	209 (132,313)	21 (17,25)
Total							
Cases	1	7	32	52	71	39	202
Rate/100,000 (95% CI)	1 (0,2)	6 (2,12)	31 (21,44)	73 (54,96)	151 (118,190)	241 (171,329)	22 (19,25)

Supplemental table 3: Demographics, aetiology and risk factors for incident events in all territories by gender and type

	Acute Visceral Ischaemia			Acute Limb Ischaemia			Critical Limb Ischaemia		
	Total	Male	Female	Total	Male	Female	Total	Male	Female
N (%)	78 (100%)	28 (35.9%)	50 (64.1%)	93 (100%)	49 (52.7%)	44 (47.3%)	202 (100%)	109 (54.0%)	93 (46.0%)
Mean (SD) age, years	79.8 (14.1)	74.1 (18.4)	83.0 (9.9)	76.3 (11.9)	73.6 (11.3)	79.3 (12.0)	75.2 (10.9)	73.4 (11.2)	77.3 (10.3)
Prior symptomatic vascular disease									
Coronary Artery Disease	27 (34.6%)	9 (32.1%)	18 (36.0%)	27 (29.0%)	17 (34.6%)	10 (22.7%)	77 (38.1%)	49 (45.0%)	28 (30.1%)
Cardiac failure	26 (33.3%)	6 (21.4%)	20 (40.0%)	18 (19.4%)	5 (10.2%)	13 (29.5%)	42 (20.9%)	22 (20.4%)	20 (21.5%)
Stroke/TIA	15 (19.2%)	4 (14.3%)	11 (22.0%)	25 (26.9%)	15 (30.6%)	10 (22.7%)	43 (21.3%)	26 (23.9%)	17 (18.3%)
Peripheral arterial disease	16 (20.5%)	4 (14.3%)	12 (24.0%)	39 (41.9%)	23 (46.9%)	16 (36.4%)	143 (70.8%)	83 (76.1%)	60 (64.5%)
Any	48 (61.5%)	15 (53.6%)	33 (66.0%)	69 (74.2%)	34 (69.4%)	35 (79.5%)	171 (84.7%)	98 (89.9%)	73 (78.5%)
Risk factors									
Current smoker	13 (16.7%)	5 (17.9%)	8 (16.0%)	21 (22.6%)	10 (20.4%)	11 (25.0%)	58 (28.7%)	32 (29.4%)	26 (27.9%)
Ever smoked	53 (67.9%)	21 (75.0%)	32 (64.0%)	64 (68.8%)	37 (75.5%)	27 (61.4%)	143 (70.8%)	90 (82.6%)	53 (57.0%)
Hypertension	54 (69.2%)	14 (50.0%)	40 (80.0%)	57 (61.3%)	25 (51.0%)	32 (72.7%)	143 (70.8%)	74 (67.9%)	69 (74.2%)
Diabetes mellitus	9 (11.5%)	2 (7.1%)	7 (14.0%)	12 (12.9%)	7 (14.3%)	5 (11.4%)	89 (44.1%)	48 (44.0%)	41 (44.1%)
Hyperlipidaemia	36 (46.2%)	14 (50.0%)	22 (44.0%)	33 (35.5%)	19 (38.8%)	14 (31.8%)	112 (55.4%)	63 (57.8%)	49 (52.7%)
Atrial fibrillation	29 (37.2%)	10 (35.7%)	25 (50.0%)	36 (38.7%)	18 (36.7%)	20 (45.5%)	42 (20.8%)	26 (23.9%)	21 (22.6%)
Any	72 (92.3%)	24 (85.7%)	48 (96.0%)	92 (98.9%)	49 (100.0%)	43 (97.7%)	197 (97.5%)	107 (98.2%)	90 (96.8%)
Primary aetiology									
Embolic	43 (55.1%)	16 (57.1%)	27 (54.0%)	43 (46.2%)	19 (38.8%)	24 (54.5%)	2 (1.0%)	1 (0.9%)	1 (1.1%)
Atherosclerotic/ in-situ thrombosis	26 (33.3%)	7 (25.0%)	19 (38.0%)	22 (23.7%)	14 (28.6%)	8 (18.2%)	146 (72.3%)	77 (70.6%)	69 (74.2%)
Diabetic microvascular disease	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	15 (7.4%)	12 (11.0%)	3 (3.2%)
Multifactorial	9 (11.5%)	5 (17.9%)	4 (8.0%)	19 (20.4%)	9 (18.4%)	10 (22.7%)	38 (18.8%)	18 (16.5%)	20 (21.5%)
Occluded stent-graft/Other	0 (0%)	0 (0%)	0 (0%)	9 (9.7%)	7 (14.3%)	2 (4.5%)	1 (0.5%)	1 (0.9%)	0 (0%)
Medications									
Statin	36 (46.2%)	14 (50.0%)	22 (44.0%)	29 (31.2%)	17 (34.7%)	12 (27.3%)	101 (50.0%)	62 (56.9%)	39 (41.9%)
Antiplatelet	34 (43.6%)	11 (39.3%)	23 (46.0%)	42 (45.2%)	21 (42.9%)	21 (47.7%)	127 (62.9%)	71 (65.1%)	56 (60.2%)
Warfarin	3 (3.8%)	1 (3.6%)	2 (4.0%)	9 (9.7%)	7 (14.3%)	2 (4.5%)	17 (8.5%)	12 (11.0%)	5 (5.4%)
Antihypertensives	57 (73.1%)	15 (53.6%)	42 (84.0%)	59 (63.4%)	28 (57.1%)	31 (70.5%)	144 (71.3%)	75 (68.8%)	69 (74.2%)
Any	61 (78.2%)	19 (67.9%)	42 (84.0%)	70 (75.3%)	36 (73.5%)	34 (77.3%)	175 (86.6%)	94 (86.2%)	81 (87.1%)

Supplemental table 4: Emergency intervention within 48 hours of event

Emergency Intervention	N (%)
AVI Events	10/78 (12.8)
Laparotomy	10 (12.8)
Organ resection	6 (7.7)
Mesenteric thrombectomy	2 (2.6)
Thrombolysis	1 (1.3)
ALI Events	40/93 (43.0)
Thrombectomy	28 (15.4)
Angioplasty / Stenting	7 (23.1)
Thrombolysis	2 (2.2)
Emergency Bypass	4 (4.3)
Major Amputation	4 (4.3)
Minor Amputation	1 (1.1)
CLI Events	44/202 (21.8)
Angioplasty / Stenting	32 (23.1)
Endarterectomy	2 (0.9)
Emergency Bypass	3 (1.5)
Major Amputation	2 (0.9)
Minor Amputation	8 (4.0)

Supplemental table 5: Age-, sex-, and risk-factor specific raw numbers (2002-2012) for all incident acute peripheral arterial events

ALI	Known Hypertension			None Hypertensive			Ever Smokers			None Smokers			Diabetics			Non-diabetic		
	Men	Women	Total	Men	Women	Total	Men	Women	Total	Men	Women	Total	Men	Women	Total	Men	Women	Total
< 35	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
35-44	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
45-54	1	0	1	3	1	4	3	1	4	1	0	1	0	0	0	4	1	5
55-64	5	4	9	2	2	4	6	6	12	1	0	1	3	2	5	4	4	8
65-74	6	6	12	7	2	9	10	5	15	3	3	6	1	0	1	12	8	20
75-84	9	9	18	10	4	14	14	8	22	5	5	10	3	1	4	16	12	28
≥85	4	13	17	2	3	5	4	7	11	2	9	11	0	2	2	6	14	20
Total	25	32	57	24	12	36	37	27	64	12	17	29	7	5	12	42	39	81
AVI																		
< 35	0	0	0	2	0	2	0	0	0	2	0	2	0	0	0	2	0	2
35-44	0	0	0	1	0	1	1	0	1	0	0	0	0	0	0	1	0	1
45-54	0	0	0	1	1	2	1	1	2	0	0	0	0	0	0	1	1	2
55-64	1	0	1	3	1	4	3	1	4	1	0	1	0	0	0	4	1	5
65-74	2	8	10	1	0	1	2	7	9	1	1	2	0	1	1	3	7	10
75-84	6	10	16	1	3	4	5	11	16	2	2	4	1	0	1	6	13	19
≥85	5	22	27	5	5	10	9	12	21	1	15	16	1	6	7	9	21	30
Total	14	40	54	14	10	24	21	32	53	7	18	25	2	7	9	26	43	69
CLI																		
< 35	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
35-44	0	0	0	0	1	1	0	1	1	0	0	0	0	1	1	0	0	0
45-54	0	1	1	5	1	6	5	0	5	0	2	2	1	1	2	4	1	5
55-64	17	6	23	5	4	9	17	7	24	5	3	8	15	7	22	7	3	10
65-74	21	12	33	12	7	19	29	15	44	4	4	8	16	8	24	17	11	28
75-84	26	34	60	7	4	11	29	22	51	4	16	20	13	15	28	20	23	43
≥85	10	16	26	6	7	13	10	8	18	6	15	21	3	9	12	13	14	27
Total	74	69	143	35	24	59	90	53	143	19	40	59	48	41	89	61	52	113

Supplemental table 6: Demographics and risk factors for incident events in all territories by Aetiology

	Embolic	Atherosclerotic	Multifactorial / Other	Total
N (%)	88 (23.6%)	194 (52.0%)	91 (24.4%)	373 (100%)
Mean (SD) age, years	77.3 (14.1)	77.3 (10.8)	73.8 (12.0)	76.4 (12.0)
Male	36 (40.9%)	98 (50.5%)	52 (57.1%)	186 (49.9%)
<i>Prior symptomatic Vascular disease</i>				
Coronary Artery Disease	26 (29.5%)	72 (37.3%)	33 (36.3%)	131 (35.2%)
Cardiac failure	25 (28.4%)	40 (20.7%)	21 (23.1%)	86 (23.1%)
Stroke/TIA	19 (21.6%)	42 (21.6%)	22 (24.2%)	83 (22.3%)
Symptomatic PAD	17 (19.3%)	133 (68.6%)	49 (53.8%)	199 (53.4%)
Any	54 (61.4%)	166 (85.6%)	68 (74.7%)	288 (77.2%)
<i>Risk factors</i>				
Current smoker	18 (20.5%)	53 (27.3%)	21 (23.1%)	92 (24.7%)
Ever smoked	57 (64.8%)	140 (72.2%)	63 (69.2%)	260 (69.7%)
Hypertension	57 (64.8%)	133 (68.6%)	64 (70.3%)	254 (68.1%)
Diabetes mellitus	12 (13.6%)	48 (24.7%)	50 (54.9%)	110 (29.5%)
Hyperlipidaemia	30 (34.1%)	102 (52.6%)	49 (53.8%)	181 (48.5%)
Cardiac failure	25 (28.4%)	40 (20.7%)	21 (23.1%)	86 (23.1%)
Atrial fibrillation	48 (54.5%)	38 (19.6%)	21 (23.1%)	107 (28.7%)
Any	85 (96.5%)	185 (95.4%)	91 (100%)	361 (96.8)
<i>Medications</i>				
Statin	29 (33.0%)	91 (46.9%)	46 (50.5%)	166 (44.5%)
Antiplatelet	33 (37.5%)	115 (59.3%)	55 (60.4%)	203 (54.4%)
Warfarin	5 (5.7%)	18 (9.3%)	6 (6.6%)	29 (7.8%)
Antihypertensives	58 (65.9%)	134 (69.1%)	68 (74.7%)	260 (69.7%)
Any	65 (73.9%)	163 (84.0%)	78 (85.7%)	306 (82.0%)

Supplemental table 7: Changes in disability status for patients with incident acute events stratified by event type

Total

		6M mRS				Total
		0-2	3	4-5	6	
Pre-morbid mRS	0-2	98	55	23	54	230
	3-5	1	32	28	78	139
	Total	99	87	51	132	369

Acute Visceral Ischaemia

		6M mRS				Total
		0-2	3	4-5	6	
Pre-morbid mRS	0-2	10	3	0	31	44
	3-5	0	3	3	28	34
	Total	10	6	3	59	78

Acute Limb Ischaemia

		6M mRS				Total
		0-2	3	4-5	6	
Pre-morbid mRS	0-2	28	12	5	9	54
	3-5	0	9	5	23	37
	Total	28	21	10	32	91

Critical Limb Ischaemia

		6M mRS				Total
		0-2	3	4-5	6	
Pre-morbid mRS	0-2	60	40	18	14	132
	3-5	1	20	20	27	68
	Total	61	60	38	41	200

Disability status was not available for 4 (1.1%) cases.

Supplemental table 8: Potential risk factors for 30-day amputation/death (organ loss or death for AVI events) and 1-year mortality stratified by event type (univariate analysis)

STUDY	30 Day Amputation/ Organ loss/ Death			1-year Mortality		
	OR	95% CI	P-value	OR	95% CI	P-value
ALI (n=93)						
Age	1.04	1.00-1.09	0.04	1.08	1.04-1.14	<0.001
Male Gender	0.42	0.17-1.03	0.06	0.76	0.33-1.72	0.50
Smoking History	0.90	0.33-2.43	0.83	0.74	0.29-1.88	0.53
Diabetes	1.70	0.49-5.88	0.41	1.94	0.57-6.62	0.29
Hypertension	2.60	0.98-6.96	0.06	2.53	1.05-6.08	0.04
Hyperlipidaemia	0.94	0.37-2.36	0.89	0.74	0.31-1.76	0.50
Atrial Fibrillation	1.91	0.79-4.65	0.15	2.61	1.11-6.10	0.03
Heart Failure	2.06	0.71-5.92	0.18	4.36	1.41-13.55	0.01
Prior Coronary Artery Disease	2.26	0.88-5.78	0.09	1.52	0.62-3.74	0.37
Prior Stroke/TIA	2.18	0.84-5.68	0.11	1.55	0.62-3.89	0.35
Prior Peripheral Arterial Disease	1.46	0.60-3.53	0.41	0.81	0.35-1.86	0.61
Renal Function (CKD 1-5)*	1.53	0.89-2.61	0.12	2.96	1.58-5.55	0.001
Severity of Ischaemia on Admission [#]	7.08	2.21-22.69	0.001	4.48	1.79-11.25	0.001
AVI (n=78)						
Age	1.07	1.02-1.11	0.003	1.08	1.03-1.13	0.001
Male Gender	1.30	0.40-4.21	0.66	0.53	0.18-1.51	0.23
Smoking History	0.72	0.21-2.53	0.61	1.50	0.50-4.48	0.47
Diabetes	2.22	0.26-19.20	0.47	--	--	--
Hypertension	1.47	0.46-4.64	0.51	1.05	0.35-3.21	0.93
Hyperlipidaemia	0.82	0.27-2.48	0.73	0.94	0.33-2.64	0.90
Atrial Fibrillation	1.47	0.47-4.53	0.51	2.09	0.70-6.25	0.19
Heart Failure	4.42	0.92-21.19	0.06	13.24	1.66-105.8	0.02
Prior Coronary Artery Disease	2.74	0.71-10.61	0.15	2.40	0.71-8.12	0.16
Prior Stroke/TIA	1.04	0.26-4.24	0.96	0.86	0.24-3.10	0.82
Prior Peripheral Arterial Disease	2.23	0.46-10.97	0.32	2.90	0.60-14.04	0.19
Renal Function (CKD 1-5)*	2.70	1.37-5.31	0.004	3.61	1.73-7.53	0.001
Severity of Ischaemia on Admission [#]	20.77	2.58-167.3	0.004	7.25	1.91-27.61	0.004
CLI (n=202)						
Age	1.02	0.98-1.05	0.39	1.06	1.02-1.09	0.001
Male Gender	1.12	0.52-2.39	0.78	0.69	0.38-1.27	0.24
Smoking History	1.00	0.43-2.32	1.00	0.73	0.38-1.42	0.35
Diabetes	1.04	0.48-2.25	0.91	0.77	0.41-1.43	0.40
Hypertension	0.75	0.34-1.68	0.48	1.68	0.83-3.41	0.15
Hyperlipidaemia	0.76	0.36-1.62	0.48	0.76	0.41-1.39	0.37
Atrial Fibrillation	1.36	0.58-3.18	0.48	1.53	0.76-3.05	0.23
Heart Failure	1.70	0.72-4.03	0.23	3.76	1.85-7.65	<0.001
Prior Coronary Artery Disease	1.54	0.72-3.29	0.27	1.42	0.77-2.64	0.26
Prior Stroke/TIA	0.83	0.32-2.17	0.70	1.22	0.59-5.53	0.59
Prior Peripheral Arterial Disease	1.48	0.60-3.66	0.39	0.71	0.36-1.37	0.30
Renal Function (CKD 1-5)*	1.54	1.03-2.29	0.03	1.85	1.30-2.62	0.001
Severity of Ischaemia on Admission [#]	--	--	--	4.19	1.56-11.25	0.004

Unadjusted odds ratios provided

* CKD = Chronic Kidney disease (staging 1-5). Based on calculated eGFR. <http://www.renal.org>

[#] For AVI this is measured by the presence/absence of lactic acidosis; CLI this is tissue loss versus rest pain alone; and for ALI this is Rutherford grading I / IIA versus IIB / III

Supplemental table 9: Sex-specific incidence and outcome rates for incident peripheral arterial events by severity grading

	Men			Women			Total		
	Cases	Rate/100,000 (95% CI)	Amputation-free Survival - 30 day	Cases	Rate/100,000 (95% CI)	Amputation-free Survival - 30 day	Cases	Rate/100,000 (95% CI)	Amputation-free Survival - 30 day
Acute Limb Ischaemia									
All	49 (52.7%)	10 (8-14)	38 (77.6%)	44 (47.3%)	10 (7-13)	26 (59.1%)	93 (100%)	10 (8-12)	64 (68.8%)
Viable (Rutherford I)	19 (70.4%)	4 (2-6)	19 (100.0%)	8 (29.6%)	2 (1-3)	8 (100.0%)	27 (29.0%)	3 (2-4)	27 (100.0%)
Threatened Marginal (IIA)	8 (47.9%)	2 (1-3)	7 (87.5%)	9 (52.9%)	2 (1-4)	6 (66.7%)	17 (18.3%)	2 (1-3)	13 (76.5%)
Threatened Immediate (IIB)	13 (46.4%)	3 (1-5)	11 (84.6%)	15 (53.6%)	3 (2-5)	12 (80.0%)	28 (30.1%)	3 (2-4)	23 (82.1%)
Irreversible (III)	9 (42.9%)	2 (1-4)	1 (11.1%)	12 (57.1%)	3 (1-5)	0 (0.0%)	21 (22.6%)	2 (1-3)	1 (4.8%)
Critical Limb Ischaemia									
All	109 (54.0%)	23 (19-28)	92 (84.4%)	93 (46.0%)	21 (17-25)	79 (84.9%)	202 (100%)	22 (19-25)	171 (84.7%)
Rest Pain Only (Fontaine III/ Rutherford 4)	26 (60.5%)	6 (4-8)	26 (100.0%)	17 (39.5%)	4 (2-6)	17 (100.0%)	43 (21.3%)	5 (3-6)	43 (100.0%)
Tissue Loss minor (Fontaine IV/Rutherford 5)	78 (53.1%)	17 (13-21)	65 (83.3%)	69 (46.9%)	15 (12-20)	58 (84.1%)	147 (72.8%)	16 (14-19)	123 (83.7%)
Tissue Loss Major (Fontaine IV/Rutherford 6)	5 (41.7%)	1 (0-2)	1 (20.0%)	7 (58.3%)	2 (1-3)	4 (57.1%)	12 (5.9%)	1 (1-2)	5 (41.7%)
Acute Visceral Ischaemia									
All	28 (35.9%)	6 (4-9)	5 (17.9%)	50 (64.1%)	11 (8-15)	11 (22.0%)	78 (100%)	8 (7-11)	16 (80.5%)
No Lactic Acidosis	13 (46.4%)	3 (1-5)	4 (30.8%)	28 (56.0%)	6 (4-9)	11 (39.3%)	41 (52.6%)	4 (3-6)	15 (36.6%)
Lactic Acidosis	15 (53.6%)	3 (2-5)	1 (6.7%)	22 (44.0%)	5 (3-7)	0 (0.0%)	37 (47.4%)	4 (3-6)	1 (2.7%)

Supplemental table 10: Severity of disease and related mortality by age and event type

	< 75 yrs	75-84 yrs	≥ 85 yrs	P	Total
AVI Events	21 (26.9%)	20 (25.6%)	37 (47.4%)		78 (100%)
Lactic Acidosis*	5 (23.8%)	11 (55.0%)	21 (56.8%)	0.03	37 (47.4%)
1-year Death	11 (52.4%)	14 (70.0%)	34 (91.9%)	0.001	59 (75.6%)
ALI Events	39 (41.9%)	32 (34.4%)	22 (23.7%)		93 (100%)
Immediately threatened / non-viable*	15 (38.5%)	20 (62.5%)	14 (63.6%)	0.04	49 (52.7%)
1-year limb loss	6 (15.4%)	4 (12.5%)	0 (0.0%)	0.08	10 (10.8%)
1-year Death	9 (23.1%)	15 (46.9%)	17 (77.3%)	<0.001	41 (44.1%)
CLI Events	92 (45.5%)	71 (35.1%)	39 (19.3%)		202 (100%)
Tissue loss*	66 (71.7%)	57 (80.3%)	34 (87.2)	0.04	157 (77.7%)
1-year limb loss	19 (20.7%)	16 (22.5%)	5 (12.8%)	0.42	40 (19.8%)
1-year Death	17 (18.5%)	24 (33.8%)	18 (46.2%)	0.001	59 (29.2%)

*Indicates severity of disease on admission

Figure Legends

Supplemental figure 1. Age- and sex-specific prevalence of known hypertension, smoking history, and diabetes mellitus in the incident peripheral arterial event group and total OXVASC population (2002-2012).

Supplemental figure 2: 30-day survival for incident acute peripheral arterial events by subtype with numbers at risk tabled below.

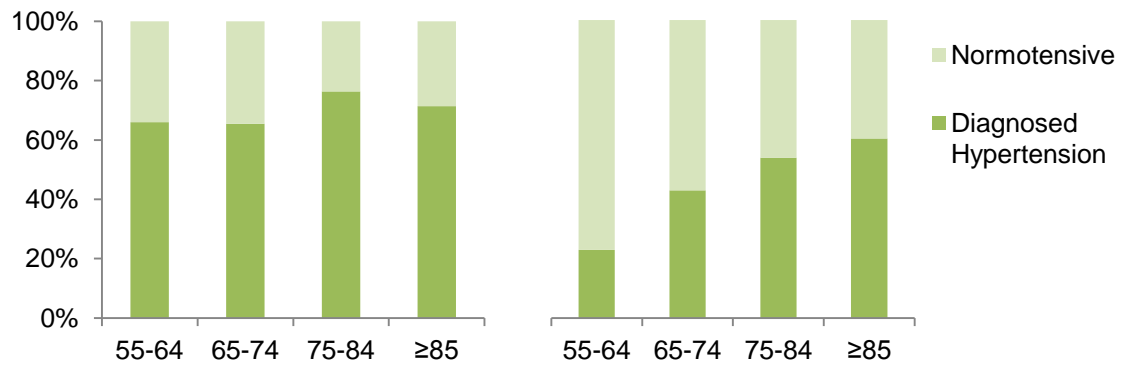
Supplemental figure 3. One-year mortality for incident acute vascular disease by subtype of acute vascular event.

Supplemental figure 1.

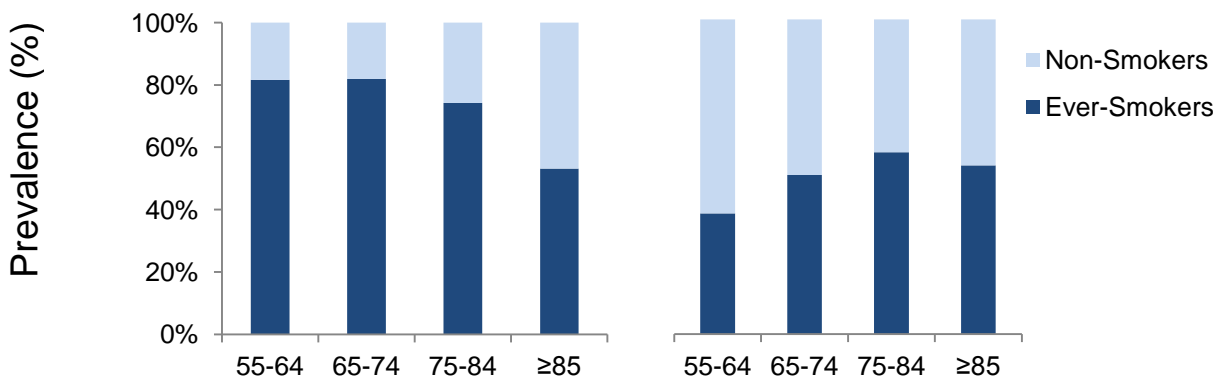
Event Group

OXVASC Population

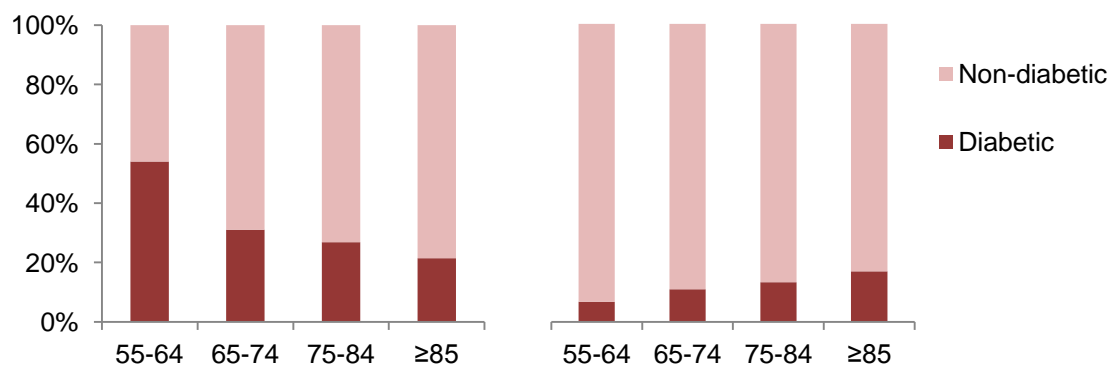
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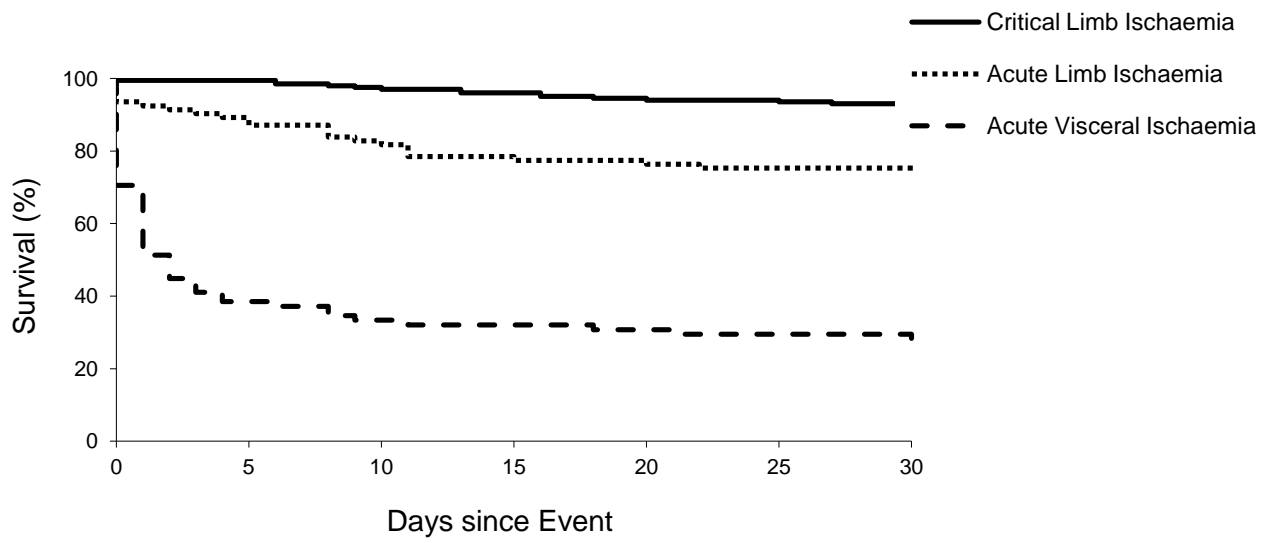
SMOKING HISTORY



DIABETES MELLITUS



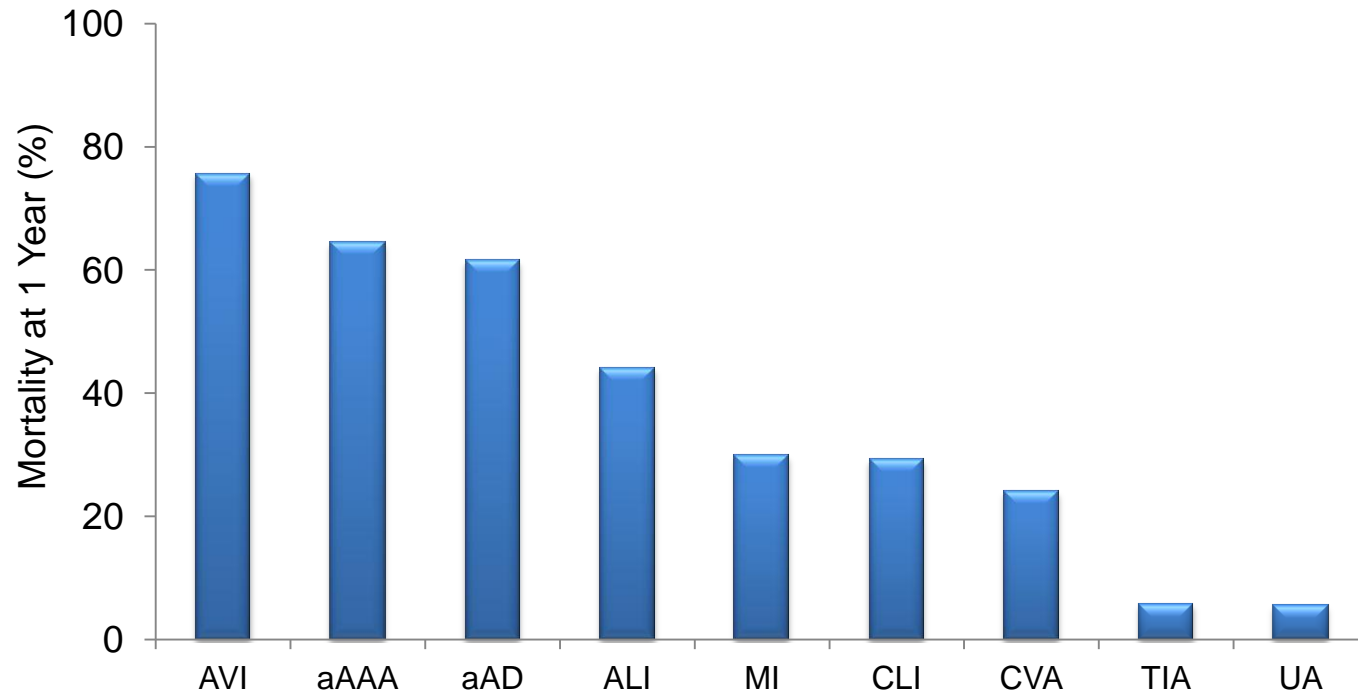
Supplemental figure 2



Numbers At Risk

CLI	202	202	198	196	191	190	189
ALI	93	84	78	73	72	71	71
AVI	78	32	27	26	25	24	24

Supplemental figure 3



AVI=acute visceral ischaemia, aAAA=acute abdominal aortic aneurysm, aAD=acute aortic dissection, ALI=acute limb ischaemia, MI= myocardial infarction, CLI=critical limb ischaemia, CVA=cerebrovascular accident (ischaemic stroke), TIA=transient ischaemic attack, UA=unstable angina