

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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## Supplementary Appendix 1

### Time to Primary Event

Primary Event	Treatment	# of Events	6-Year Event-free Rate	p-value (Log rank)	Hazard Ratio	Lower CL	Upper CL
<b>First Primary Event</b>	Standard	264	0.66	0.14	0.88	0.74	1.05
	Intensive	235	0.70				
<b>MI</b>	Standard	78	0.90	0.24	0.82	0.59	1.14
	Intensive	64	0.91				
<b>CHF</b>	Standard	82	0.89	0.57	0.91	0.67	1.25
	Intensive	76	0.90				
<b>Stroke</b>	Standard	36	0.95	0.32	0.78	0.48	1.28
	Intensive	28	0.96				
<b>Coronary Revascularization</b>	Standard	127	0.83	0.19	0.84	0.65	1.09
	Intensive	107	0.86				
<b>Peripheral Revascularization</b>	Standard	23	0.97	0.66	0.87	0.48	1.59
	Intensive	20	0.97				
<b>Cerebro-revascularization</b>	Standard	15	0.98	0.86	0.94	0.45	1.94
	Intensive	14	0.98				
<b>Amputation</b>	Standard	17	0.98	0.26	0.65	0.31	1.39
	Intensive	11	0.98				
<b>Inoperable CAD</b>	Standard	8	0.98	0.35	1.52	0.62	3.72
	Intensive	12	0.98				
<b>CV Death</b>	Standard	29	0.96	0.26	1.32	0.81	2.14
	Intensive	38	0.95				

Results of analysis of composite primary endpoint and each component of the composite.

**Supplementary Appendix 2**

**Time to Secondary Cardiovascular Events and Total Mortality**

Secondary Event	Treatment	# of Events	6-Year Event-free Rate	p-value (Log rank)	Hazard Ratio	Lower CL	Upper CL
Angina	Standard	139	0.82	0.11	1.20	0.96	1.51
	Intensive	163	0.79				
CLI*	Standard	19	0.97	0.51	0.80	0.40	1.56
	Intensive	15	0.98				
IC**	Standard	17	0.98	0.49	0.78	0.38	1.60
	Intensive	13	0.98				
TIA***	Standard	13	0.98	0.28	1.48	0.73	2.99
	Intensive	19	0.97				
All Cause Mortality	Standard	95	0.88	0.62	1.07	0.81	1.42
	Intensive	102	0.87				

Abbreviations: \* CLI= critical limb ischemia, \*\* IC=intermittent Claudication,  
\*\*\*TIA= transient ischemic attacks

**Results of Secondary Macrovascular Events with Treatment**

### Supplementary Appendix 3

#### Cause of Cardiovascular Death

	Treatment				Total	
	Standard		Intensive		Total	
	N	%	N	%	N	%
<b>Myocardial infarction</b>	12	1.3	13	1.5	25	1.4
<b>Congestive heart failure</b>	9	1.0	8	0.9	17	0.9
<b>Coronary Revascularization</b>	0	0	1	0.1	1	0.1
<b>Stroke</b>	4	0.4	6	0.7	10	0.6
<b>Cerebrovascularization</b>	1	0.1	0	0	1	0.1
<b>Complications of Occlusions</b>	1	0.1	0	0	1	0.1
<b>Peripheral Revascularization</b>	1	0.1	1	0.1	2	0.1
<b>Sudden Death (p=0.07)</b>	4	0.4	11	1.2	15	0.8
<b>Pulmonary Embolism</b>	1	0.1	0	0	1	0.1
<b>Total Cardiovascular death (p=0.29)</b>	33	3.7	40	4.5	73	4.1

Total Cardiovascular Deaths and Individual Causes. All results are non-significant.

## Supplementary Appendix 4A

### Cause of Death: Neoplasm (Non-cardiovascular)

	Treatment				Total	
	Standard		Intensive			
	N	%	N	%	N	%
<b>Neoplasm</b>	2	0.2	3	0.3	5	0.3
<b>Lung cancer</b>	7	0.8	6	0.7	13	0.7
<b>Liver cancer</b>	2	0.2	1	0.1	3	0.2
<b>Renal cancer</b>	1	0.1	3	0.3	4	0.2
<b>Colon cancer</b>	2	0.2	4	0.4	6	0.3
<b>Bile duct cancer</b>	0	0	1	0.1	1	0.1
<b>Prostate cancer</b>	0	0	1	0.1	1	0.1
<b>Pancreatic cancer</b>	1	0.1	4	0.4	5	0.3
<b>Lymphatic cancer</b>	2	0.2	0	0	2	0.1
<b>Other</b>	4	0.4	1	0.1	5	0.3
<b>Total Neoplasm</b>	21	2.3	24	2.7	45	2.5

All results are non-significant

**Supplementary Appendix 4B**

**Other Causes of Death (Non-cardiovascular)**

	Treatment				Total	
	Standard		Intensive			
	N	%	N	%	N	%
<b>Infection</b>	3	0.3	3	0.3	6	0.3
<b>Unknown</b>	14	1.6	6	0.7	20	1.1
<b>Suicide</b>	3	0.3	3	0.3	6	0.3
<b>Pancreatitis and complications</b>	1	0.1	2	0.2	3	0.2
<b>Acute morphine and temazepam intoxication</b>	1	0.1	1	0.1	2	0.1
<b>Renal failure</b>	3	0.3	2	0.2	5	0.3
<b>Respiratory failure</b>	5	0.6	7	0.8	12	0.7
<b>Other</b>	11	1.2	14	1.6	25	1.4
<b>Total non-CV, non-neoplastic deaths</b>	<b>41</b>	<b>4.6</b>	<b>38</b>	<b>4.3</b>	<b>79</b>	<b>4.4</b>

Non cardiovascular and non-neoplastic causes of death. All non-significant.

**Supplementary Appendix 5**

### Reporting of Confirmed SAE at least once during follow-up\*

Number of patients reporting Serious Adverse Events	Standard		Intensive		P-value
	N	%	N	%	
<b>ALL</b>	899	100.0	892	100.0	
<b>never reported</b>	741	82.4	677	75.9	0.001
<b>dyspnea SAE</b>	65	7.2	98	11.0	0.006
<b>hypoglycemia SAE</b>	28	3.1	76	8.5	0.000
<b>edema SAE</b>	46	5.1	58	6.5	0.210
<b>altered consciousness (not associated with hypoglycemia) SAE</b>	27	3.0	28	3.1	0.868
<b>weakness/numbness of limb(s) SAE</b>	17	1.9	25	2.8	0.202
<b>nausea SAE</b>	18	2.0	22	2.5	0.506
<b>vomiting SAE</b>	15	1.7	20	2.2	0.381
<b>upper respiratory infection SAE</b>	13	1.4	19	2.1	0.275
<b>vertigo SAE</b>	11	1.2	14	1.6	0.533
<b>diarrhea SAE</b>	6	0.7	13	1.5	0.103
<b>blurred or double vision SAE</b>	7	0.8	13	1.5	0.172
<b>hyperglycemia SAE</b>	15	1.7	11	1.2	0.441
<b>newly appearing or worsening headaches SAE</b>	9	1.0	11	1.2	0.640
<b>neuropathic ulcer SAE</b>	9	1.0	6	0.7	0.446
<b>dysphasia SAE</b>	5	0.6	5	0.6	1.000
<b>ataxia SAE</b>	8	0.9	4	0.4	0.252
<b>dysarthria SAE</b>	4	0.4	4	0.4	1.000
<b>pruritus SAE</b>	0	0	2	0.2	0.248
<b>skin ulcers (other than extremity ulcers) SAE</b>	5	0.6	2	0.2	0.452
<b>erectile/sexual dysfunction SAE</b>	1	0.1	1	0.1	1.000
<b>jaundice SAE</b>	2	0.2	1	0.1	1.000
<b>rash SAE</b>	1	0.1	1	0.1	1.000
<b>nystagmus SAE</b>	1	0.1	0	0	1.000

\*SAE: Life threatening, death, hospitalization, disability or incapacity, cancer or other important event requiring medical intervention/treatment.