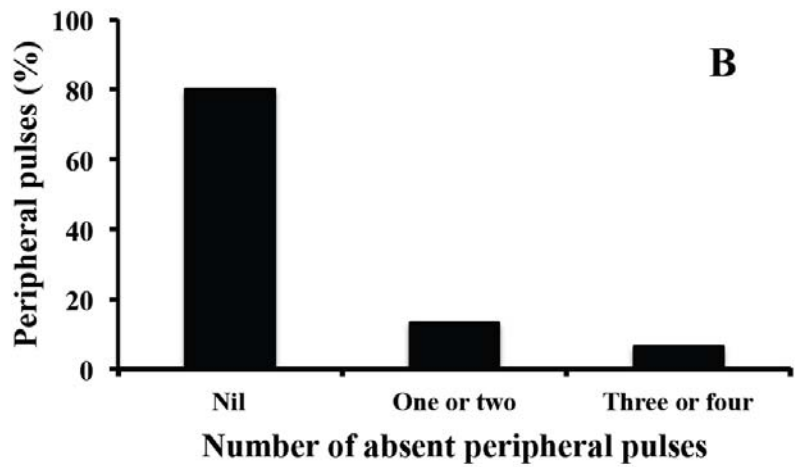
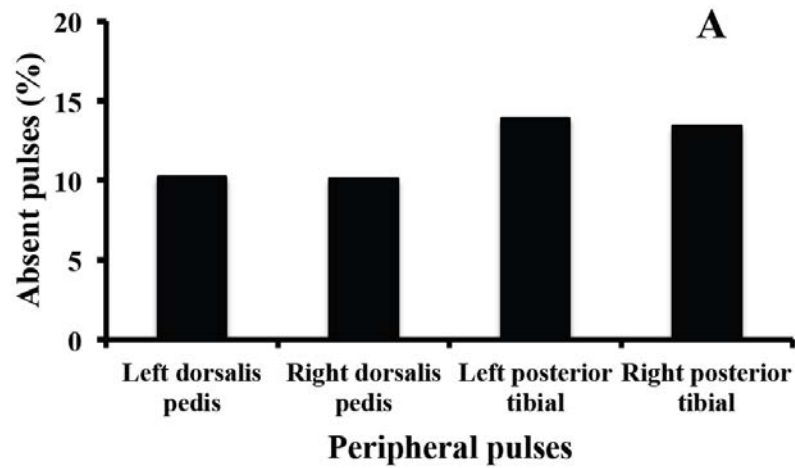


SUPPLEMENTARY DATA

**Supplementary Figure 1.**

**Panel A:** Distribution of the absence of dorsalis pedis and posterior tibial pulses (left and right) at baseline.

**Panel B:** Number of absent pulses at baseline (nil, one or two, and three or four) at baseline.



SUPPLEMENTARY DATA

**Supplementary Table 1. Hazard ratios for outcomes according to the absence of at least one dorsalis pedis or one posterior tibial pulse at baseline**

	Absent dorsalis pedis pulse at baseline				Absent posterior tibial pulse at baseline			
	No (n=9744)	Yes (n=1376)	HR (95% CI)	P	No (n=9415)	Yes (n=1705)	HR (95% CI)	P
<b>Primary end points</b>								
<b>Major macrovascular events, n (%)</b>	904 (9.3)	241 (17.5)	1.59 (1.37-1.85)	<0.0001	875 (9.3)	270 (15.8)	1.50 (1.29-1.73)	<0.0001
Nonfatal myocardial infarction, n (%)	234 (2.4)	75 (5.5)	1.49 (1.13-1.96)	0.004	221 (2.4)	88 (5.2)	1.48 (1.14-1.92)	0.004
Nonfatal stroke, n (%)	349 (3.6)	73 (5.3)	1.71 (1.30-2.23)	0.0001	340 (3.6)	82 (4.8)	1.68 (1.30-2.18)	<0.0001
Cardiovascular death, n (%)	400 (4.1)	141 (10.3)	1.83 (1.49-2.25)	<0.0001	395 (4.2)	146 (8.6)	1.54 (1.26-1.90)	<0.0001
<b>Major microvascular events, n (%)</b>	970 (9.9)	160 (11.6)	1.27 (1.07-1.51)	0.007	942 (10.0)	188 (11.0)	1.15 (0.97-1.35)	0.11
New or worsening nephropathy, n (%)	431 (4.4)	90 (6.5)	1.38 (1.09-1.76)	0.008	419 (4.5)	102 (6.0)	1.16 (0.92-1.47)	0.21
New or worsening retinopathy, n (%)	602 (6.2)	79 (5.7)	1.16 (0.91-1.48)	0.24	581 (6.2)	100 (5.9)	1.16 (0.93-1.46)	0.19
<b>Secondary end points</b>								
All-cause mortality, n (%)	782 (8.0)	245 (17.8)	1.62 (1.39-1.89)	<0.0001	766 (8.1)	261 (15.3)	1.40 (1.20-1.63)	<0.0001
Heart failure, n (%)	335 (3.4)	116 (8.4)	1.66 (1.33-2.08)	<0.0001	334 (3.6)	117 (6.9)	1.30 (1.02-1.60)	0.03
ESRD or renal death, n (%)	46 (0.5)	13 (0.9)	1.25 (0.63-2.46)	0.53	38 (0.4)	21 (1.2)	2.25 (1.20-4.22)	0.01
New or worsening peripheral neuropathy, n (%)	3961 (40.7)	693 (50.4)	1.09 (1.00-1.18)	0.04	3767 (40.0)	887 (52.0)	1.13 (1.05-1.22)	0.001
Dementia, n (%)	90 (0.9)	19 (1.4)	1.15 (0.69-1.93)	0.60	80 (0.9)	29 (1.7)	1.72 (1.09-2.71)	0.02
Cognitive decline, n (%)	1538 (15.8)	267 (19.4)	1.20 (1.05-1.38)	0.008	1484 (15.8)	321 (18.8)	1.13 (1.00-1.29)	0.06
All hospitalisations, n (%)	4081 (41.9)	790 (57.4)	1.24 (1.15-1.34)	<0.0001	3913 (41.6)	958 (56.2)	1.18 (1.10-1.27)	<0.0001

Hazards ratio (HR) computed by Cox proportional hazards survival regression analyses, adjusted as in model 2: sex, age, region of origin, duration of diabetes, body mass index, waist circumference, systolic and diastolic blood pressure with and without antihypertensive treatment, HbA1c, estimated glomerular filtration rate (eGFR), squared eGFR (except for microvascular events), urinary albumin-creatinine ratio (normoalbuminuria, microalbuminuria and macroalbuminuria), total-, and HDL-cholesterol, history of ever smoking, use of lipids lowering and antiplatelet drugs, and study treatments. P<0.05 was significant.

**Supplementary Table 2. Hazard ratios for outcomes according to each single additional absent pulse at baseline**

	HR (95% CI)	P for trend
<b>Primary end points</b>		
<b>Major macrovascular events, n (%)</b>	1.17 (1.12 – 1.23)	<0.0001
Nonfatal myocardial infarction, n (%)	1.15 (1.06 – 1.26)	0.001
Nonfatal stroke, n (%)	1.21 (1.11 – 1.31)	<0.0001
Cardiovascular death, n (%)	1.20 (1.12 – 1.27)	<0.0001
<b>Major microvascular events, n (%)</b>	1.08 (1.02 – 1.14)	0.007
New or worsening nephropathy, n (%)	1.08 (1.00 – 1.17)	0.04
New or worsening retinopathy, n (%)	1.08 (1.01 – 1.17)	0.04
<b>Secondary end points</b>		
All-cause mortality, n (%)	1.16 (1.10 – 1.21)	<0.0001
Heart failure, n (%)	1.14 (1.06 – 1.22)	0.0003
ESRD or renal death, n (%)	1.26 (1.03 – 1.53)	0.02
New or worsening peripheral neuropathy, n (%)	1.04 (1.02 – 1.07)	0.002
Dementia, n (%)	1.18 (1.02 – 1.37)	0.03
Cognitive decline, n (%)	1.07 (1.02 – 1.11)	0.004
All hospitalisations, n (%)	1.07 (1.04 – 1.10)	<0.0001

Hazards ratio (HR) computed by Cox proportional hazards survival regression analyses, adjusted as in model 2: sex, age, region of origin, duration of diabetes, body mass index, waist circumference, systolic and diastolic blood pressure with and without antihypertensive treatment, HbA1c, estimated glomerular filtration rate (eGFR), squared eGFR (except for microvascular events), urinary albumin-creatinine ratio (normoalbuminuria, microalbuminuria and macroalbuminuria), total-, and HDL-cholesterol, history of ever smoking, use of lipids lowering and antiplatelet drugs, and study treatments. P<0.05 was significant.

SUPPLEMENTARY DATA

**Supplementary Table 3. Hazard ratios for outcomes according to the absence of at least one peripheral pulse (left or right) at baseline according to study randomisation group**

	Glucose lowering treatment				Blood pressure treatment			
	Standard HR (95% CI)	P	Intensive HR (95% CI)	p	Placebo HR (95% CI)	p	Perindopril-indapamide HR (95% CI)	p
<b>Primary end points</b>								
<b>Major macrovascular events</b>	1.46 (1.20-1.77)	0.0001	1.48 (1.22-1.81)	<0.0001	1.58 (1.31-1.91)	<0.0001	1.38 (1.13-1.70)	0.002
Non-fatal myocardial infarction	1.35 (0.95-1.93)	0.09	1.56 (1.10-2.23)	0.01	1.73 (1.22-2.45)	0.002	1.23 (0.86-1.77)	0.26
Non-fatal stroke	1.99 (1.42-2.79)	<0.0001	1.26 (0.89-1.79)	0.19	1.62 (1.14-2.29)	0.007	1.60 (1.14-2.25)	0.007
Cardiovascular death	1.47 (1.12-1.93)	0.005	1.76 (1.33-2.33)	<0.0001	1.65 (1.27-2.14)	0.0002	1.59 (1.18-2.15)	0.002
<b>Major microvascular events</b>	1.21 (0.98-1.49)	0.08	1.12 (0.89-1.40)	0.34	1.16 (0.93-1.43)	0.19	1.18 (0.95-1.47)	0.14
New or worsening nephropathy	1.38 (1.03-1.84)	0.03	1.08 (0.77-1.50)	0.67	1.30 (0.96-1.76)	0.09	1.13 (0.82-1.55)	0.46
New or worsening retinopathy	1.02 (0.75-1.37)	0.92	1.23 (0.92-1.64)	0.17	1.07 (0.80-1.44)	0.65	1.19 (0.89-1.59)	0.25
<b>Secondary end points</b>								
All-cause mortality	1.45 (1.19-1.77)	0.0003	1.51 (1.23-1.85)	<0.0001	1.59 (1.31-1.93)	<0.0001	1.36 (1.10-1.69)	0.004
Heart failure	1.71 (1.27-2.30)	0.0004	1.32 (0.98-1.78)	0.07	1.51 (1.12-2.03)	0.007	1.52 (1.12-2.05)	0.007
ESRD or renal death, n (%)	3.53 (1.62-7.68)	0.002	1.06 (0.38-2.96)	0.92	2.71 (1.06-6.91)	0.04	1.47 (0.65-3.35)	0.36
New or worsening neuropathy	1.16 (1.05-1.28)	0.004	1.10 (1.00-1.22)	0.06	1.12 (1.02-1.24)	0.02	1.14 (1.03-1.26)	0.01
Dementia	1.03 (0.50-2.12)	0.93	1.78 (1.01-3.14)	0.04	1.20 (0.63-2.26)	0.58	1.66 (0.88-3.11)	0.12
Cognitive decline	1.06 (0.90-1.26)	0.50	1.15 (0.98-1.36)	0.09	1.01 (0.86-1.20)	0.87	1.23 (1.04-1.45)	0.02
All hospitalisations	1.18 (1.07-1.31)	0.0009	1.16 (1.06-1.28)	0.002	1.21 (1.10-1.34)	<0.0001	1.15 (1.04-1.26)	0.007

Hazards ratio (HR) computed by Cox proportional hazards survival regression analyses, adjusted as in model 2: sex, age, region of origin, duration of diabetes, body mass index, waist circumference, systolic and diastolic blood pressure with and without antihypertensive treatment, HbA1c, estimated glomerular filtration rate (eGFR), squared eGFR (except for microvascular events), urinary albumin-creatinine ratio (normoalbuminuria, microalbuminuria and macroalbuminuria), total-, and HDL-cholesterol, history of ever smoking, use of lipid lowering and antiplatelet drugs, glucose randomised control (analyses of blood pressure treatment groups) and blood pressure randomised treatment (analyses of glucose lowering treatment groups). P<0.05 was significant.

SUPPLEMENTARY DATA

**Supplementary Table 4. Hazard ratios for outcomes according to the absence of at least one peripheral pulse (left or right) at baseline in participants free from cardiovascular disease or major PAD at baseline**

	Subset of participants without macrovascular disease at baseline				Subset of participants without major PAD at baseline			
	Absent peripheral pulse				Absent peripheral pulse			
	No (n=6253)	Yes (n=1415)	HR (95% CI)	P	No (n=8600)	Yes (n=2014)	HR (95% CI)	P
<b>Primary end points</b>								
<b>Major macrovascular events, n (%)</b>	444 (7.1)	161 (11.4)	1.42 (1.17-1.73)	0.0004	774 (9.0)	290 (14.4)	1.45 (1.26-1.68)	<0.0001
Non-fatal myocardial infarction, n (%)	115 (1.8)	47 (3.3)	1.19 (0.83-1.70)	0.35	189 (2.2)	92 (4.6)	1.39 (1.07-1.82)	0.01
Non-fatal stroke, n (%)	170 (2.7)	59 (4.2)	1.91 (1.39-2.64)	<0.0001	315 (3.7)	88 (4.4)	1.52 (1.18-1.96)	0.001
Cardiovascular death, n (%)	187 (3.0)	80 (5.7)	1.49 (1.12-1.97)	0.006	335 (3.9)	159 (7.9)	1.67 (1.36-2.05)	<0.0001
<b>Major microvascular events, n (%)</b>	620 (9.9)	157 (11.1)	1.29 (1.07-1.56)	0.008	854 (9.9)	210 (10.4)	1.14 (0.97-1.34)	0.11
New or worsening nephropathy, n (%)	250 (4.0)	81 (5.7)	1.41 (1.07-1.85)	0.01	374 (4.4)	119 (5.9)	1.24 (0.99-1.55)	0.06
New or worsening retinopathy, n (%)	411 (6.6)	85 (6.0)	1.19 (0.93-1.52)	0.18	534 (6.2)	105 (5.2)	1.07 (0.85-1.33)	0.58
<b>Secondary end points</b>								
All-cause mortality, n (%)	423 (6.8)	169 (11.9)	1.37 (1.13-1.66)	0.001	656 (7.6)	297 (14.8)	1.52 (1.31-1.76)	<0.0001
Heart failure, n (%)	160 (2.6)	72 (5.1)	1.39 (1.03-1.87)	0.03	272 (3.2)	136 (6.8)	1.51 (1.20-1.88)	0.0003
ESRD or renal death, n (%)	24 (0.4)	15 (1.1)	2.45 (1.14-5.24)	0.02	34 (0.4)	22 (1.1)	2.05 (1.10-3.81)	0.02
New or worsening neuropathy, n (%)	2468 (39.5)	729 (51.5)	1.13 (1.03-1.23)	0.007	3374 (39.2)	1031 (51.2)	1.14 (1.06-1.23)	0.0006
Dementia, n (%)	38 (0.6)	21 (1.5)	2.28 (1.28-4.05)	0.005	75 (0.9)	31 (1.5)	1.52 (0.97-2.38)	0.07
Cognitive decline, n (%)	975 (15.6)	266 (18.8)	1.14 (0.99-1.31)	0.08	1350 (15.7)	370 (18.4)	1.11 (0.98-1.25)	0.10
All hospitalisations, n (%)	2384 (38.1)	700 (49.5)	1.12 (1.03-1.23)	0.01	3487 (40.6)	1080 (53.6)	1.15 (1.07-1.24)	0.0001

Hazards ratio (HR) computed by Cox proportional hazards survival regression analyses, adjusted as in model 2: sex, age, region of origin, duration of diabetes, body mass index, waist circumference, systolic and diastolic blood pressure with and without antihypertensive treatment, HbA1c, estimated glomerular filtration rate (eGFR), squared eGFR (except for microvascular events), urinary albumin-creatinine ratio (normoalbuminuria, microalbuminuria and macroalbuminuria), total-, and HDL-cholesterol, history of ever smoking, use of lipid lowering and antiplatelet drugs, and study treatments. P<0.05 was significant.

SUPPLEMENTARY DATA

**Supplementary Table 5. Hazard ratios for outcomes according to the absence of at least one peripheral pulse (left or right) at baseline in participants free from peripheral neuropathy at baseline**

	Absent peripheral pulse at baseline		Absent peripheral pulse vs. not		
	No (n=6893)	Yes (n=1047)	HR	95% CI	P
<b>Primary end points</b>					
<b>Major macrovascular events, n (%)</b>	615 (8.9)	148 (14.1)	1.51	1.25 – 1.83	<0.0001
Nonfatal myocardial infarction, n (%)	144 (2.1)	51 (4.9)	1.63	1.16 – 2.28	0.005
Nonfatal stroke, n (%)	258 (3.7)	44 (4.2)	1.49	1.06 – 2.10	0.02
Cardiovascular death, n (%)	266 (3.9)	76 (7.3)	1.64	1.25 – 2.16	0.0004
<b>Major microvascular events, n (%)</b>	671 (9.7)	101 (9.7)	1.17	0.94 – 1.46	0.17
New or worsening nephropathy, n (%)	295 (4.3)	63 (6.0)	1.44	1.07 – 1.94	0.02
New or worsening retinopathy, n (%)	417 (6.1)	48 (4.6)	1.05	0.77 – 1.43	0.78
<b>Secondary end points</b>					
All-cause mortality, n (%)	492 (7.1)	136 (13.0)	1.54	1.25 – 1.88	<0.0001
Heart failure, n (%)	200 (2.9)	67 (6.4)	1.74	1.29 – 2.35	0.0003
ESRD or renal death, n (%)	26 (0.4)	10 (1.0)	1.71	0.63 – 5.00	0.29
New or worsening peripheral neuropathy, n (%)	2616 (38.0)	521 (49.8)	1.09	0.99 – 1.20	0.09
Dementia, n (%)	58 (0.8)	9 (0.9)	0.74	0.36 – 1.53	0.42
Cognitive decline, n (%)	1073 (15.6)	178 (17.0)	1.00	0.85 – 1.19	0.96
All hospitalisations, n (%)	2746 (39.8)	564 (53.9)	1.21	1.10 – 1.33	<0.0001

Hazards ratio (HR) computed by Cox proportional hazards survival regression analyses, adjusted as in model 2: sex, age, region of origin, duration of diabetes, body mass index, waist circumference, systolic and diastolic blood pressure with and without antihypertensive treatment, HbA1c, estimated glomerular filtration rate (eGFR), squared eGFR (except for microvascular events), urinary albumin-creatinine ratio (normoalbuminuria, microalbuminuria and macroalbuminuria), total-, and HDL-cholesterol, history of ever smoking, use of lipid lowering and antiplatelet drugs, and study treatments. P<0.05 was significant.

SUPPLEMENTARY DATA

**Supplementary Table 6. Hazard ratios for outcomes in patients with both absent peripheral pulse and chronic ulceration at baseline compared to those without these conditions**

	Absent peripheral pulse and presence of chronic ulceration at baseline		Absent peripheral pulse and presence of chronic ulceration vs. not		
	No (n=11048)	Yes (n=72)	HR	95% CI	P
<b>Primary end points</b>					
<b>Major macrovascular events, n (%)</b>	1129 (10.2)	16 (22.2)	1.54	0.94 – 2.54	0.09
Nonfatal myocardial infarction, n (%)	303 (2.7)	6 (8.3)	2.06	0.91 – 4.65	0.08
Nonfatal stroke, n (%)	418 (3.8)	4 (5.6)	1.43	0.53 – 3.86	0.48
Cardiovascular death, n (%)	532 (4.8)	9 (12.5)	1.55	0.79 – 3.02	0.20
<b>Major microvascular events, n (%)</b>	1118 (10.1)	12 (16.7)	1.70	0.96 – 3.02	0.07
New or worsening nephropathy, n (%)	519 (4.7)	2 (2.8)	0.50	0.13 – 2.03	0.33
New or worsening retinopathy, n (%)	671 (6.1)	10 (13.9)	2.52	1.34 – 4.74	0.004
<b>Secondary end points</b>					
All-cause mortality, n (%)	1012 (9.2)	15 (20.8)	1.55	0.93 – 2.59	0.09
Heart failure, n (%)	441 (4.0)	10 (13.9)	2.34	1.24 – 4.41	0.009
ESRD or renal death, n (%)	58 (0.5)	1 (1.4)	1.28	0.17 – 9.80	0.81
New or worsening peripheral neuropathy, n (%)	4615 (41.8)	39 (54.2)	1.26	0.92 – 1.74	0.16
Dementia, n (%)	109 (1.0)	0	-	-	-
Cognitive decline, n (%)	1788 (16.2)	17 (23.6)	1.41	0.87 – 2.28	0.16
All hospitalisations, n (%)	4821 (43.6)	50 (69.4)	1.68	1.27 – 2.24	0.0003

Hazards ratio (HR) computed by Cox proportional hazards survival regression analyses, adjusted as in model 2: sex, age, region of origin, duration of diabetes, body mass index, waist circumference, systolic and diastolic blood pressure with and without antihypertensive treatment, HbA1c, estimated glomerular filtration rate (eGFR), squared eGFR (except for microvascular events), urinary albumin-creatinine ratio (normoalbuminuria, microalbuminuria and macroalbuminuria), total-, and HDL-cholesterol, history of ever smoking, use of lipid lowering and antiplatelet drugs, and study treatments. P<0.05 was significant.

SUPPLEMENTARY DATA

**Supplementary Table 7. Harrell's c-statistics for risk of outcomes according to traditional risk factors without and with absent peripheral pulses at baseline**

	C- statistics (95% CI) for traditional risk factors* alone	C- statistics (95% CI) for traditional risk factors* plus absent peripheral pulses	P
<b>Primary end points</b>			
<b>Major macrovascular events</b>	0.653 (0.632 - 0.675)	0.661 (0.639 - 0.682)	0.03
Nonfatal myocardial infarction	0.682 (0.645 - 0.720)	0.691 (0.653 - 0.729)	0.19
Nonfatal stroke	0.608 (0.572 - 0.644)	0.616 (0.580 - 0.652)	0.17
Cardiovascular death	0.733 (0.704 - 0.761)	0.741 (0.712 - 0.769)	0.07
<b>Major microvascular events</b>	0.673 (0.654 - 0.692)	0.674 (0.655 - 0.693)	0.48
New or worsening nephropathy	0.786 (0.761 - 0.811)	0.788 (0.763 - 0.813)	0.26
New or worsening retinopathy	0.638 (0.613 - 0.663)	0.640 (0.615 - 0.665)	0.43
<b>Secondary end points</b>			
All-cause mortality	0.709 (0.690 - 0.729)	0.714 (0.695 - 0.734)	0.04
Heart failure	0.725 (0.693 - 0.757)	0.735 (0.704 - 0.766)	0.03
ESRD or renal death	0.906 (0.857 - 0.954)	0.911 (0.862 - 0.959)	0.29
New or worsening peripheral neuropathy	0.625 (0.616 - 0.635)	0.629 (0.620 - 0.638)	0.001
Dementia	0.781 (0.726 - 0.837)	0.787 (0.732 - 0.842)	0.28
Cognitive decline	0.594 (0.578 - 0.610)	0.596 (0.580 - 0.612)	0.15
All hospitalisations	0.593 (0.583 - 0.602)	0.598 (0.588 - 0.607)	<0.0001

\*Sex, age, systolic blood pressure, antihypertensive treatment, estimated glomerular filtration rate (eGFR), urinary albumin-creatinine ratio, HbA1C, total-, and HDL-cholesterol, history of ever smoking, and study treatments. Patients with baseline history of myocardial infarction, stroke, or macroalbuminuria (n=2522) were excluded from these analyses. P<0.05 was significant.