

**Supplementary Table 1.** Specific codes used for the ascertainment of the lipid and blood pressure lowering medications and cardiovascular outcomes from the relevant registries.

Lipid-lowering medication	C10
Blood pressure-lowering medication	C02, C03, C07-09
Coronary artery disease	<p>ICD-8/9 codes 410; ICD-10 codes I21–I22</p> <p>Nordic Classification of Surgical Procedure codes: TFN 40, FN1AT, FN1BT, FN1YT, FNF, FNG, FNA, FNB, FNC, FND, FNE, Before 1996: 5311-5315</p>
Any stroke	ICD-8/9 codes: 430-434; ICD-10 codes I60-I64
Peripheral artery disease	<p>ICD-10 codes S78, S88, S98</p> <p>Before 1996: 9571-75</p> <p>Nordic Classification of Surgical Procedure codes: NFQ10,20, NGQ10,20, NHQ10,20,30,40,48; PDF05, 20-22; PDH50-55, 99; PDN05, 20-22; PDW99; PEF23-25; PEH 56,57; PEN 23-25; PEW99; PGH41-47,49; PFH58-67; PDQ05, 20-22; PD1AT; PD1BT; PD1YT; PD3AT; PD3BT;PEQ23-25; PEQ99; PE1AT; PE1BT; PFQ26; PFQ99; PF1AT; PF1BT</p> <p>Before 1996: 5561-5568, 5579, 5581, 5583</p>
End-stage renal disease	ICD-10 codes: Z49, Z940, T824, Z992

	Nordic Classification of Surgical Procedure codes: KAS10, KAS20, KAS40, KAS60, KAS70, TJA30, TJA33, TJA35, TJA50, TK800, TK822, TK823, TK824, TK820, TK830, JAK10, PBL10, KA2AT before 1996: 7151,6112
Severe diabetic retinopathy (SDR)	ICD-10 codes: H3603, H3604, H3520  Nordic Classification of Surgical Procedure codes: CKC10, CKC12, CKC15, CKC50, CKD40, CKD92, CKD93  Before 1996: 3724, 3721

**Supplementary Table 2.** Baseline characteristics of the FinnDiane individuals diagnosed with type 1 diabetes in 1967 or before and either survived with diabetes for at least 50 years: the FinnDiane 50-year cohort or died before: the FinnDiane comparison cohort.

	<b>FinnDiane 50-year cohort n=729</b>	<b>FinnDiane comparison cohort n=275</b>	<b>P for difference</b>
Sex (male %)	50.6		
Age (years)	50.7 (45.7, 56.9)	48.8 (43.8, 54.1)	<0.0001
Age at diabetes diagnosis (years)	10.4 (6.1, 14.7)	12.2 (6.7, 17.5)	<0.0001
Duration of diabetes at baseline	39.3 (35.3, 45.0)	35.7 (33.6, 38.9)	<0.0001
Duration of diabetes at the end of follow-up	54.5 (51.8, 58.5)	43.8 (40.3, 46.8)	<0.0001
HbA <sub>1c</sub> , baseline value (mmol/mol)	65.0 (58.5, 72.7)	70.5 (59.6, 80.3)	<0.0001
HbA <sub>1c</sub> , baseline value (%)	8.1 (7.5, 8.8)	8.6 (7.6, 9.5)	<0.0001
Intraindividual mean of serial HbA <sub>1c</sub> (mmol/mol)	65.0 (58.5, 72.7)	70.9 (63.3, 79.8)	<0.0001
Intraindividual mean of serial HbA <sub>1c</sub> (%)	8.1 (7.5, 8.8)	8.6 (7.9, 9.5)	<0.0001
Coefficients of variation of serial HbA <sub>1c</sub> (%)	8.1 (6.4, 10.5)	11.5 (8.9, 14.3)	<0.0001
Smoking current/ex/non/missing (%)	15/27/55/3	20/33/40/7	<0.0001
Alcohol consumption (g/week) *	48 (24, 84)	48 (24, 96)	0.22
Abstainers (%)	24.5	22.5	0.46
Missing data (%)	15.0	18.8	
Socioeconomic status			0.009
Blue collar worker	56.7	56.7	
White collar worker	30.9	24.0	
Other or not known	12.4	19.3	
BMI	24.9 (22.9, 27.4)	24.6 (21.7, 27.6)	0.048

Obesity, BMI≥30 (%)	9.3	10.2	0.68
Waist-to-hip ratio	0.88 (0.82, 0.94)	0.91 (0.86, 0.97)	<0.0001
Waist-to-hip ratio, men	0.93 (0.89, 0.98)	0.96 (0.91, 1.0)	
Waist-to-hip ratio, women	0.82 (0.78, 0.87)	0.86 (0.82, 0.91)	
Systolic blood pressure (mmHg)	141 (130, 156)	150 (136, 165)	<0.0001
Diastolic blood pressure (mmHg)	76 (70, 83)	80 (73, 89)	<0.0001
S-cholesterol (mmol/l)	5.0 (4.4, 5.7)	5.20 (4.52, 5.82)	0.03
HDL-cholesterol (mmol/l)	1.35 (1.08, 1.63)	1.20 (0.94, 1.50)	<0.0001
Triglycerides (mmol/l)	1.03 (0.79, 1.37)	1.32 (1.0, 1.88)	<0.0001
LDL cholesterol (mmol/l)	3.20 (2.59, 3.76)	3.21 (2.72, 3.84)	0.33
Detectable C-peptide level (%) (available in 86.3%) †	9.5		
eGDR	5.05 (3.94, 6.38)		
Insulin dose per kg	0.56 (0.46, 0.69)	0.60 (0.47, 0.75)	0.02
eGFR (ml/min/1.73m <sup>2</sup> ) ESRD excluded	83.8 (66.3, 99.0)	64.2 (43.1, 84.6)	<0.0001
eGFR below 60 ml/min/1.73m <sup>2</sup> (%)	25.5	67.8	<0.0001
Diabetic nephropathy status			<0.0001
Normoalbuminuria	49.5	14.2	
Microalbuminuria	18.5	7.3	
Macroalbuminuria (ESRD not included)	20.4	30.3	
ESRD, kidney transplantation	7.4	33.1	
ESRD, on dialysis	1.6	12.7	
not known (%)	3.0	2.2	
SDR (%)	63.2	84.6	<0.0001
CAD (%)	11.4	20.0	<0.0001
STROKE (%)	5.6	14.2	<0.0001

PAD (%)	5.3	22.6	<0.0001
Any CVD (%)	19.1	42.9	<0.0001
hs-CRP (mg/L)	1.91 (1.1, 3.4)	2.92 (1.56, 6.64)	<0.0001
Lipid lowering therapy (%)	27.7	37.8	<0.0001
Antihypertensive medication (AHT) (%)	69.1	85.8	<0.0001

LEGEND: BMI – body mass index; AHT- antihypertensive medication (yes /no); CV-HbA<sub>1c</sub> – coefficient of variation in HbA<sub>1c</sub>; eGFR – estimated glomerular filtration rate using CKD-EPI formula; hs-CRP – high sensitive CRP; SDR – severe diabetic retinopathy; RAASi – inhibitor of the rennin-angiotensin-aldosterone system. Smoking was defined as smoking at least 1 cigarette per day for at least 1 year. \*Among those who consume alcohol; †Detectable C-peptide defined as serum concentration  $\geq 0.02$  nmol/l.

**Supplementary Table 3.** Standardized incidence ratios (SIRs) for any cardiovascular disease (CVD), coronary artery disease (CAD), peripheral artery disease (PAD) and stroke by nephropathy status in the FinnDiane 50-year cohort from the baseline visit. Data are presented as standardized incidence ratios (SIRs) with 95% confidence intervals.

	All	Normo-albuminuria	Micro-albuminuria	Macro-albuminuria	End-stage renal disease
Any CVD	7.4 (6.5-8.3)	4.9 (4.0-5.9)	8.5 (6.4-11.0)	12.1 (9.5-15.3)	28.6 (19.2-41.0)
CAD	7.2 (6.2-8.3)	5.2 (4.2-6.5)	7.1 (5.1-9.8)	10.2 (7.6-13.4)	22.3 (14.5-32.9)
PAD	20.4 (16.9-24.4)	9.0 (6.2-12.7)	31.4 (21.2-44.7)	32.3 (22.4-45.3)	98.8 (64.2-145.9)
Stroke	3.3 (2.7-4.0)	1.6 (1.0-2.2)	4.7 (3.1-6.9)	7.6 (5.3-10.8)	7.5 (4.1-12.8)

**Supplementary Table 4.** Baseline characteristics of the FinnDiane 50-year cohort in persons with normoalbuminuria compared to those with albuminuria. Data are presented as median (interquartile range) for non-normally distributed variables. (n=22 missing albuminuria status or impossible to classify)

	<b>Normoalbuminuria n=359</b>	<b>Albuminuria n=348</b>	<b>P for difference</b>
Sex (men, %)	43.5	58.1	<0.001
Age (years)	52.2 (47.4, 58.8)	49.4 (44.0, 54.6)	<0.001
Age at diabetes diagnosis (years)	11.1 (7.3, 15.7)	9.3 (4.8, 13.4)	<0.001
Duration of diabetes at baseline	39.7 (35.6, 45.6)	39.0 (35.1, 44.2)	0.14
Duration of diabetes at the end of follow-up	54.5 (52.5, 59.5)	53.5 (51.5, 57.5)	0.002
HbA <sub>1c</sub> , baseline value (mmol/mol)	63.9 (57.7, 70.5)	67.1 (58.5, 75.4)	0.002
HbA <sub>1c</sub> , baseline value (%)	8.0 (7.4, 8.6)	8.3 (7.5, 9.1)	0.002
Mean-HbA <sub>1c</sub> (mmol/mol)	65.1 (59.0, 72.3)	66.2 (58.9, 73.2)	0.15
Mean-HbA <sub>1c</sub> (%)	8.1 (7.5, 8.8)	8.2 (7.5, 8.9)	0.15
CV-HbA <sub>1c</sub> (%)	7.2 (5.8, 9.1)	9.4 (7.3, 11.9)	<0.001
Smoking current/ex/non/missing (%) *	11/23/63/3	19/32/47/3	<0.001
Alcohol consumption (g/week) †	48 (24, 84)	42 (24, 84)	0.08
Abstainers (%)	30.7	28.2	0.62
Missing data (%)	13.7	12.6	
Socioeconomic status			0.02
Blue collar worker	54.0	60.9	
White collar worker	35.9	25.6	
Other or not known	10.1	13.5	
Age of death of father	74.6 (62.0, 82.0)	70.9 (60.7, 81.3)	0.13

Age of father in 2016, if alive	84.0 (78.8, 87.5)	84.5 (82.4, 88.6)	0.48
Age of death of mother	80.4 (71.0, 86.9)	80.5 (72.6, 87.0)	0.87
Age of mother in 2016, if alive	87.7 (84.6, 93.2) §	86.2 (82.7, 88.6)	0.02
BMI	24.8 (22.9, 27.1)	25.1 (22.9, 27.7)	0.25
Obesity, BMI≥30 (%)	6.7	12.4	0.01
Waist-to-hip ratio	0.85 (0.80, 0.91)	0.90 (0.85, 0.97)	<0.001
Waist-to-hip ratio, men	0.91 (0.88, 0.96)	0.95 (0.90, 0.99)	
Waist-to-hip ratio, women	0.80 (0.77, 0.85)	0.84 (0.78, 0.89)	
Systolic blood pressure (mmHg)	138 (127, 150)	148 (134, 160)	<0.001
Diastolic blood pressure (mmHg)	75 (70, 81)	79 (71, 85)	<0.001
S-cholesterol (mmol/l)	4.88 (4.36, 5.50)	5.15 (4.53, 5.79)	0.001
HDL-cholesterol (mmol/l)	1.42 (1.16, 1.68)	1.29 (1.01, 1.59)	<0.001
Triglycerides (mmol/l)	0.90 (0.70, 1.18)	1.17 (0.90, 1.59)	<0.001
LDL cholesterol (mmol/l)	3.13 (2.53, 3.63)	3.31 (2.70, 3.86)	0.002
Detectable C-peptide level (%)**	9.9	9.0	0.70
eGDR	5.89 (4.70, 7.79)	4.40 (3.38, 5.30)	<0.001
Insulin dose per kg	0.53 (0.45, 0.65)	0.60 (0.48, 0.73)	<0.001
eGFR (ml/min/1.73m <sup>2</sup> ) ESRD excluded	90.3 (76.9, 101.4)	71.9 (50.5, 93.9)	<0.001
eGFR below 60 ml/min/1.73m <sup>2</sup> (%)	6.7	46.3	<0.001
SDR (%)	47.4	79.3	<0.001
CAD (%)	7.8	14.7	0.004
Myocardial infarction (%)	50.0	70.6	
Revascularization (%)	50.0	29.4	
STROKE (%)	4.2	6.6	0.15

PAD (%)	2.8	8.1	0.002
Major amputation (%)	10.0	39.3	
Minor amputation (%)	60.0	42.8	
Revascularization (%)	30.0	179	
Any CVD (%)	13.7	24.1	<0.001
hs-CRP (mg/L)	1.67 (1.01, 2.92)	2.26 (1.35, 4.83)	<0.001
Lipid lowering therapy (%)	22.3	33.1	0.001
Antihypertensive medication (AHT) (%)	39.6	86.2	<0.001
Type of AHT			<0.001
RAAS only (%)	12.8	26.4	
RAAS (+/- other AHT <sup>c</sup> medication) (%)	14.5	39.7	
Other AHT <sup>f</sup> medication (%)	12.3	20.1	

Legend: DKD – diabetic kidney disease, in this study defined as the presence of microalbuminuria, macroalbuminuria or ESRD; BMI – body mass index; AHT- antihypertensive medication (yes /no), eGDR – estiamted glucose disposal rate; eGFR – estimated glomerular filtration rate using CKD-EPI formula. hs-CRP – high sensitive CRP, SDR – severe diabetic retinopathy. \*Smoking was defined as smoking at least 1 cigarette per day for at least 1 year; †among those who consume alcohol; ‡ beta-blockers, calcium channel blockers, diuretics. Detectable defined as  $\geq 0.02$  nmol/l. § 23.3% alive in 2016; || 22.9% alive in 2016, p=0.91

**Supplementary Table 5.** Cause-specific hazard ratios (HR) and 95% confidence intervals for incident CAD, PAD and stroke in the FinnDiane 50-year cohort

	HR for CAD (95%CI)	P-value	HR for PAD (95%CI)	P-value	HR for stroke (95% CI)	P-value
Age (years)	<b>1.04 (1.01-1.06)</b>	0.002	<b>1.08 (1.04-1.12)</b>	0.0002	1.04 (1.00-1.09)	0.06
Duration of diabetes (years)	1.03 (1.00-1.06)	0.07	1.01 (0.98-1.04)	0.67	1.02 (0.98-1.06)	0.27
CV-HbA <sub>1c</sub> (%)	1.03 (1.00-1.06)	0.07	<b>1.05 (1.02-1.09)</b>	0.004	1.02 (0.98-1.07)	0.29
Smoking history (yes)	0.85 (0.63-1.15)	0.29	0.85 (0.58-1.26)	0.42	1.23 (0.80-1.90)	0.34
Triglycerides/HDL	<b>1.25 (1.11-1.41)</b>	0.0002	<b>1.31 (1.14-1.50)</b>	0.0002	<b>1.24 (1.01-1.51)</b>	0.04
Hypertension (yes)	1.15 (0.75-1.79)	0.52	<b>2.35 (1.03-5.37)</b>	0.04	1.00 (0.49-2.05)	0.99
DKD (yes)	<b>1.68 (1.20-2.38)</b>	0.003	<b>1.69 (1.06-2.68)</b>	0.03	<b>2.49 (1.44-4.31)</b>	0.001
Sex (male vs. female)	0.95 (0.71-1.28)	0.76	<b>2.69 (1.75-4.12)</b>	<0.0001	1.08 (0.69-1.68)	0.73

Mean-HbA <sub>1C</sub>	1.08 (0.95-1.22)	0.24	<b>1.50 (1.32-1.71)</b>	<0.0001	1.10 (0.92-1.32)	0.31
BMI	<b>0.93 (0.89-0.98)</b>	0.003	0.96 (0.91-1.02)	0.14	0.96 (0.90-1.02)	0.21
SDR (yes)	1.11 (0.81-1.75)	0.51	<b>1.95 (1.19-3.17)</b>	0.008	1.24 (0.75-2.04)	0.41
Lipid lowering medication	1.25 (0.89-1.75)	0.20	1.15 (0.76-1.75)	0.51	0.94 (0.58-1.53)	0.80

Legend: SDR – severe diabetic retinopathy; BMI – body mass index; DKD denotes microalbuminuria, macroalbuminuria or end-stage renal disease or eGFR<60. Hypertension was defined as either systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  measured at least twice or use of antihypertensive medications.

**Supplementary Table 6.** Cox regression models showing cause-specific hazard ratios (HR) for incident CVD and specifically CAD, PAD and stroke in the FinnDiane 50-year cohort in patients with normoalbuminuria.

	Hazard ratio (95% CI) for CVD in question	P-value	Hazard ratio for mortality	P-value
<b>Any cardiovascular disease (n=102)</b>				
Age (years)	1.05 (1.03-1.07)	<0.0001	1.11 (1.05-1.21)	0.0006
Serial HbA <sub>1c</sub>	1.36 (1.11-1.66)	0.003	1.13 (0.56-2.30)	0.73
CV-HbA <sub>1c</sub>	1.05 (1.01-1.08)	0.009	0.79 (0.57-1.09)	0.15
<b>Coronary artery disease (n=86)</b>				
CV-HbA <sub>1c</sub>	1.04 (1.00-1.08)	0.03	1.04 (0.98-1.10)	0.17
Triglycerides/HDL	1.46 (1.08-1.99)	0.02	1.03 (0.43-2.44)	0.95
eGFR (per 10 decrease)	1.21 (1.06-1.38)	0.004	1.40 (1.07-1.82)	0.01
<b>Peripheral artery disease (n=37)</b>				
Duration of diabetes (years)	1.12 (1.06-1.18)	<0.0001	1.14 (1.09-1.20)	<0.0001
CV-HbA <sub>1c</sub>	1.10 (1.04-1.16)	0.0007	1.04 (0.95-1.13)	0.43
Sex (men)	2.04 (1.01-4.10)	0.045	1.15 (0.60-2.20)	0.67
SDR (yes)	2.26 (1.14-4.50)	0.02	0.95 (0.47-1.90)	0.88
<b>Stroke (n=26)</b>				

eGFR (per 10 decrease)	1.43 (1.06-1.93)	0.02	1.66 (1.38-1.98)	<0.0001
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Legend: SDR – severe diabetic retinopathy; CV-HbA<sub>1c</sub> – coefficient of variation in HbA<sub>1c</sub>

**Supplementary Table 7.** Cox regression models showing hazard ratios (HR) for all-cause mortality in the FinnDiane 50-year cohort (n=729).

	Hazard ratio	95% confidence interval	p-value
Duration of diabetes (years)	1.16	1.13-1.19	<0.0001
ESRD, dialysis (yes) *	2.11	1.30-3.44	0.003
ESRD, kidney transplantation (yes) *	1.26	0.53-3.00	0.61
eGFR (ml/min/1.73m <sup>2</sup> ) (per 10 unit decrease)	1.21	1.13-1.30	<0.0001
CV-HbA <sub>1c</sub> (%)	1.06	1.03-1.09	0.0001
Prevalent PAD (yes)	2.13	1.29-3.53	0.003
hs-CRP (mg/L)	1.02	1.01-1.04	0.003
eGDR	0.83	0.76-0.91	0.0001

\* versus non-ESRD, eGDR denotes estimated glucose disposal rate (eGDR) to measure the insulin sensitivity. eGDR was calculated with an equation eGDR=24.4-12.97xWHR-3.39xHT-0.60xHbA<sub>1c</sub>, where WHR is waist-to-hip ratio and HT is hypertension (yes=1, no=0) defined as having antihypertensive treatment or blood pressure ≥140/90 mmHg; eGFR – estimated glomerular filtration rate using CKD-EPI formula; hs-CRP – high sensitive CRP

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Loimaa Health Center	A.Mäkelä, P.Eloranta
Malmi Hospital, Helsinki	H.Lanki, S.Moilanen, M.Tilly-Kiesi
Mikkeli Central Hospital	A.Gynther, R.Manninen, P.Nironen, M.Salminen, T.Vänttinen
Mänttä Regional Hospital	I.Pirttiniemi, A-M.Hänninen
North Karelian Hospital, Joensuu	U-M.Henttula, P.Kekäläinen, M.Pietarinen, A.Rissanen, M.Voutilainen
Nurmijärvi Health Center	A.Burgos, K.Urtamo
Oulaskangas Hospital, Oulainen	E.Jokelainen, P-L.Jylkkä, E.Kaarlela, J.Vuolaspuro
Oulu Health Center	L.Hiltunen, R.Häkkinen, S.Keinänen-Kiukaanniemi
Oulu University Hospital	R.Ikäheimo
Päijät-Häme Central Hospital	H.Haapamäki, A.Helanterä, S.Hämäläinen, V.Ilvesmäki, H.Miettinen
Palokka Health Center	P.Sopanen, L.Welling
Pieksämäki Hospital	V.Sevtsenko, M.Tamminen
Pietarsaari Hospital	M-L.Holmbäck, B.Isomaa, L.Sarelin
Pori City Hospital	P.Ahonen, P.Merisalo, E.Muurinen, K.Sävelä
Porvoo Hospital	M.Kallio, B.Rask, S.Rämö
Raahe Hospital	A.Holma, M.Honkala, A.Tuomivaara, R.Vainionpää

Rauma Hospital	K.Laine, K.Saarinen, T.Salminen
Riihimäki Hospital	P.Aalto, E.Immonen, L.Juurinen
Salo Hospital	A.Alanko, J.Lapinleimu, P.Rautio, M.Virtanen
Satakunta Central Hospital, Pori	M.Asola, M.Juhola, P.Kunelius, M.-L.Lahdenmäki, P.Pääkkönen, M.Rautavirta
Savonlinna Central Hospital	T.Pulli, P.Sallinen, M.Taskinen, E.Tolvanen, T.Tuominen H.Valtonen, A.Vartia, S-L.Viitanen
Seinäjoki Central Hospital	O.Antila, E.Korpi-Hyövälti, T.Latvala, E.Leijala, T.Leikkari, M.Punkari N.Rantamäki, H.Vähävuori
South Karelia Central Hospital, Lappeenranta	T.Ensala, E.Hussi, R.Härkönen, U.Nyholm, J.Toivanen
Tampere Health Center	A.Vaden, P.Alarotu, E.Kujansuu, H.Kirkkopolto-Jokinen, M.Helin, S.Gummerus, L.Calonius, T.Niskanen, T.Kaitala, T.Vatanen
Tampere University Hospital	I.Ala-Houhala, R.Kannisto, T.Kuningas, P.Lampinen, M.Määttä, H.Oksala, T.Oksanen, A.Putila, H.Saha, K.Salonen, H.Tauriainen, S.Tulokas
Tiurismaa Health Center, Hollola	T.Kivelä, L.Petlin, L.Savolainen
Turku Health Center	A.Artukka, I.Hämäläinen, L.Lehtinen, E.Pyysalo, H.Virtamo, M.Viinikala, M.Vähätilo
Turku University Central Hospital	K.Breitholz, R.Eskola, K.Metsärinne, U.Pietilä, P.Saarinen, R.Tuominen, S.Äyräpää
Vaajakoski Health Center	K.Mäkinen, P.Sopanen
Valkeakoski Regional Hospital	S.Ojanen, E.Valtonen, H.Ylönen, M.Rautiainen, T.Immonen
Vammala Regional Hospital	I.Isomäki, R.Kroneld, L.Mustaniemi, M.Tapiolinna-Mäkelä
Vasa Central Hospital	S.Bergkulla, U.Hautamäki, V-A.Myllyniemi, I.Rusk