

Electronic Supplemental Material

ESM Tab. 1. Main characteristics of included versus excluded individuals in both cohorts. As participants were excluded from the analysis because of missing data, a formal comparison was not possible and only key characteristics are shown for a qualitative evaluation of generalizability.

	Cohort 1		Cohort 2	
	Included	Excluded	Included	Excluded
Number	1934	2036	13,277	36,803
Age, years	62.7 (11.7)	62.8 (12.8)	61.6 (12.7)	65.7 (13.3)
Male sex, %	57.3	58.9	58.9	58.5
Diabetes duration, years	0.8 (1.8)	0.3 (1.6)	1.0 (1.3)	1.3 (1.4)
Body mass index, kg/m²	29.5 (5.2)	29.2 (5.3)	30.1 (5.7)	30.0 (5.8)
HbA_{1c}, mmol/mol	64 (17)	69 (19)	57 (13)	54 (11)
%	8.0 (2.1)	8.5 (2.3)	7.4 (1.7)	7.1 (1.5)
Total cholesterol, mg/dl	206.8 (48.3)	209.3 (54.6)	189.1 (43.3)	182.2 (44.9)
mmol/l	5.3 (1.7)	5.4 (1.9)	4.8 (1.5)	4.7 (1.5)
Triglycerides, mg/dl	150.0 (77.0)	156.6 (84.4)	148.0 (112.2)	147.9 (105.7)
mmol/l	1.7 (0.9)	1.8 (0.9)	1.7 (1.3)	1.7 (1.2)
eGFR, ml/min/1.73 m²	81.0 (19.1)	81.9 (21.8)	83.7 (22.0)	81.0 (23.7)
Complications				
Microvascular disease, %	37.9	50.5	16.4	21.0
Macrovascular disease, %	4.2	4.4	7.4	36.0
Diabetes therapy				
Metformin, %	43.6	42.0	50.5	28.1
Sulphonylurea, %	24.3	24.2	6.7	3.4
Bolus insulin, %	11.1	17.3	4.6	3.0
Basal insulin, %	6.7	13.2	4.9	3.9

ESM Tab. 2. Variables independently associated with weight loss $\geq 10\%$. The table shows results of a logistic regression analysis, where the dependent variable was the weight loss $\geq 10\%$ and independent variables were those differing upon univariate analysis.

a) Cohort 1

Variable	OR (95% C.I.)	p
Female sex	1.34 (1.04; 1.72)	0.024
BMI	1.06 (1.03; 1.08)	<0.001
HbA_{1c}	1.11 (1.04; 1.18)	<0.001
Use of sulphonylurea	0.52 (0.37; 0.73)	<0.001
Use of metformin	1.12 (0.86; 1.47)	0.400
Use of bolus insulin	0.39 (0.23; 0.65)	<0.001
History of cancer	1.78 (1.09; 2.87)	0.021
Inflammatory disease	1.62 (1.14; 2.31)	0.007
RxRisk comorbidity index	1.04 (1.02; 1.07)	<0.001

b) Cohort 2

Variable	OR (95% C.I.)	p
Female sex	1.42 (1.26; 1.61)	<0.001
Diabetes duration	0.69 (0.65; 0.73)	<0.001
BMI	1.04 (1.03; 1.05)	<0.001
HbA_{1c}	1.05 (1.02; 1.09)	0.002
Total cholesterol	1.00 (0.99; 1.00)	0.581
Macroangiopathy	1.16 (0.87; 1.55)	0.318
RxRisk index	1.02 (1.01; 1.03)	0.001
DPP-4 inhibitors	0.88 (0.59; 1.33)	0.546
Statins	0.97 (0.84; 1.12)	0.655
Anti-platelet agents	0.88 (0.74; 1.04)	0.131

ESM Tab. 3. Outcomes. Differences between groups in the change over time of continuous outcome variables. Results are from adjusted MMRM. Negative values indicate a reduction in the weight loss versus the control group.

	Cohort 1 (5 years)		Cohort 1 (20 years)		Cohort 2	
	Difference (95% CI)	p-value	Difference (95% CI)	p-value	Difference (95% CI)	p-value
Primary outcome						
HbA1c, mmol/mol %	-3.4 (-4.5, 2.4) -0.31 (-0.41, -0.22)	<0.001	-2.1 (-3.9, -0.3) -0.19 (-0.36, 0.03)	<0.001	-2.8 (-3.9, -1.7) -0.26 (-0.36, -0.16)	<0.001
Secondary outcomes						
No. GLM classes	0.03 (-0.05, 0.11)	0.470	-0.2 (-0.36, -0.07)	0.004	-0.05 (-1.0, 0.004)	0.072
Systolic blood pressure, mm Hg	-2.7 (-3.7, -1.7)	<0.001	-1.9 (-3.8, -0.03)	0.047	-4.4 (-6.2, -2.6)	<0.001
HDL cholesterol, mg/dl mmol/l	1.4 (0.4, 2.3) 0.04 (0.01, 0.06)	0.005	1.4 (-0.1, 2.9) 0.04 (-0.00, 0.07)	0.071	2.1 (1.3, 2.9) 0.05 (0.03, 0.07)	<0.001
Triglycerides, mg/dl mmol/l	-11.2 (-17.2, -5.3) -0.1 (-0.2, -0.1)	<0.001	-0.9 (-9.6, 7.7) 0.0 (-0.1, 0.1)	0.833	-16.7 (-23.4, -10.1) -0.2 (-0.3, -0.1)	<0.001
LDL cholesterol, mg/dl mmol/l	0.5 (-2.5, 3.6) 0.01 (-0.06, 0.09)	0.725	6.8 (2.9, 10.6) 0.17 (0.07, 0.27)	0.001	1.5 (-1.2, 4.1) 0.04 (-0.01, 0.11)	0.273
eGFR, ml/min/1.73 m ²	1.5 (-0.02, 3.0)	0.052	2.4 (0.2, 4.7)	0.035	-0.6 (-2.6, 1.4)	0.549
UACR, mg/g mg/mmol	11.0 (-3.9, 25.9) 1.2 (-0.4, 2.9)	0.146	0.1 (-49.3, 49.6) 0.0 (-5.6, 5.6)	0.996	-11.8 (-41.2, 17.6) -1.3 (4.7, 2.0)	0.433

ESM Tab. 4. Characteristics of participants by diabetes remission status.

	Cohort 1				Cohort 2			
	All	Remission	No remission	p-value	All	Remission	No remission	p-value
Number	1934	145	1706		13277	649	10557	
Age, years	62.7 (11.7)	61.6 (11.3)	62.8 (11.7)	0.266	61.6 (12.7)	60.8 (12.0)	61.7 (12.6)	0.076
Male, %	57.3	60.0	56.7	0.447	58.9	60.6	58.4	0.283
Diabetes duration, years	0.8 (1.8)	0.4 (0.6)	0.8 (1.8)	0.008	1.0 (1.3)	0.5 (1.1)	1.0 (1.4)	<0.001
Body mass index, kg/m²	29.5 (5.2)	29.5 (4.7)	29.6 (5.2)	0.894	30.1 (5.7)	30.8 (6.1)	30.2 (5.7)	0.009
Lab & risk factors								
HbA_{1c}, mmol/mol	64 (17)	64 (16)	65 (17)	0.577	57 (13)	62 (14)	59 (13)	0.001
%	8.0 (2.1)	8.0 (2.0)	8.1 (2.1)		7.4 (1.7)	7.8 (1.7)	7.6 (1.7)	
Systolic blood pressure, mm Hg	140.5 (20.3)	139.0 (22.5)	141.0 (20.2)	0.270	137.8 (19.4)	139.5 (19.3)	137.9 (19.5)	0.041
Diastolic blood pressure, mm Hg	83.1 (10.7)	83.4 (11.7)	83.2 (10.7)	0.875	80.7 (10.6)	82.0 (10.6)	80.8 (10.6)	0.008
Total cholesterol, mg/dl	206.8 (48.3)	213.7 (48.5)	206.9 (48.7)	0.172	189.1 (43.3)	193.2 (43.1)	190.0 (43.4)	0.087
mmol/l	5.3 (1.7)	5.5 (1.7)	5.3 (1.7)		4.8 (1.5)	5.0 (1.5)	4.9 (1.5)	
HDL cholesterol, mg/dl	49.8 (14.9)	48.5 (15.5)	49.9 (14.9)	0.376	49.0 (13.7)	48.1 (13.2)	48.8 (13.7)	0.239
mmol/l	1.3 (0.5)	1.2 (0.5)	1.3 (0.5)		1.3 (0.5)	1.2 (0.5)	1.3 (0.5)	
LDL cholesterol, mg/dl	124.5 (39.6)	129.0 (40.0)	124.5 (39.9)	0.314	110.7 (36.9)	113.5 (36.2)	111.0 (37.0)	0.138
mmol/l	3.2 (1.4)	3.3 (1.4)	3.2 (1.4)		2.8 (1.3)	2.9 (1.2)	2.8 (1.3)	
Triglycerides, mg/dl	150.0 (77.0)	163.7 (82.4)	150.4 (76.9)	0.119	148.0 (112.2)	152.9 (100.7)	152.2 (118.6)	0.884
mmol/l	1.7 (0.9)	1.8 (0.9)	1.7 (0.9)		1.7 (1.3)	1.7 (1.1)	1.7 (1.3)	
eGFR, ml/min/1.73 m²	81.0 (19.1)	81.3 (20.9)	81.2 (18.8)	0.937	83.7 (22.0)	83.1 (20.5)	84.1 (22.1)	0.307
UACR, mg/g	43.0 (137.2)	41.6 (90.5)	44.3 (144.4)	0.912	51.6 (223.9)	41.7 (107.6)	53.5 (229.9)	0.630
Complications								
eGFR<60 ml/min/1.73 m²	14.1	13.8	13.8	0.995	10.3	10.9	9.9	0.404
UACR >30 mg/g	20.2	20.0	25.7	0.422	5.3	2.8	5.9	<0.001
Retinopathy, %	18.7	0.0	19.5	0.122	1.3	0.8	1.4	0.184
Cardiovascular disease, %	2.4	0.0	2.6	0.050	2.6	1.8	2.7	0.170
Macrovascular disease, %	4.2	0.0	4.5	0.009	16.4	14.0	16.6	0.081
Microvascular disease, %	37.9	37.5	38.3	0.911	7.4	3.9	7.8	<0.001
Comorbidities								
History of cancer, %	5.7	6.9	5.5	0.466	N/A	N/A	N/A	N/A
Inflammatory diseases, %	12.2	13.8	12.0	0.516	N/A	N/A	N/A	N/A
RxRisk comorbidity index	4.7 (5.1)	4.3 (5.2)	4.7 (5.1)	0.433	4.0 (5.4)	4.2 (5.9)	3.9 (5.4)	0.217
Diabetes therapy								
Metformin, %	43.6	23.4	46.9	<0.001	50.5	35.4	56.5	<0.001
Sulphonylurea, %	24.3	9.0	26.4	<0.001	6.7	2.2	7.9	<0.001
DPP-4 inhibitors, %	1.8	0.7	1.9	0.284	3.5	0.3	4.3	<0.001

GLP-1 receptor agonists, %	0.7	0.0	0.8	0.274	0.7	0.5	0.9	0.270
SGLT2 inhibitors, %	0.3	0.0	0.2	0.560	0.6	0.0	0.7	0.028
Thiazolidinediones, %	0.3	0.0	0.4	0.475	0.8	0.5	0.9	0.279
Bolus insulin, %	11.1	8.3	11.8	0.204	4.6	2.0	5.4	<0.001
Basal insulin, %	6.7	5.5	7.0	0.490	4.9	1.1	6.0	<0.001
Other therapies								
Statins, %	25.6	20.7	26.1	0.153	37.8	33.3	38.7	0.006
Anti-platelet agents, %	51.8	49.0	51.8	0.510	25.8	23.7	25.8	0.245
RAS blockers, %	41.0	43.4	40.9	0.552	45.0	46.8	45.2	0.405
Beta blockers, %	16.6	15.9	16.8	0.766	20.3	21.9	20.0	0.253
Calcium channel blockers, %	16.6	16.6	16.5	0.995	15.0	14.9	15.0	0.947
Diuretics, %	28.1	33.1	27.4	0.144	29.2	32.5	29.0	0.054

ESM Tab. 5. Characteristics of Cohort 1 divided in three groups based on weight loss. Group 0: <5% weight loss. Group 1: 5% to <10% weight loss, group 2: 10% or more weight loss. p1 indicates the p-values for the comparison of group 1 vs group 0, p2 indicates the p-values for the comparison between group 2 vs group 0, p3 indicates the p-values for the comparison of group 1 vs group 2.

	Group 2	Group 1	Group 0	p1	p2	p3
Number	308	545	1081			
Demographics						
Female, %	50.3	46.4	38.7	0.003	<0.001	0.274
Age, years	62.0 (12.5)	63.7 (12.0)	62.4 (11.2)	0.044	0.513	0.050
Diabetes duration, years	0.8 (1.8)	0.8 (1.6)	0.8 (1.8)	0.726	0.743	0.962
Risk factors and lab						
Body mass index, kg/m ²	31.1 (5.8)	30.0 (5.4)	28.7 (4.7)	<0.001	<0.001	0.007
Lab & risk factors						
HbA _{1c} , mmol/mol	66 (17)	64 (16)	63 (18)	0.326	0.035	0.201
%	8.2 (2.1)	8.0 (2.0)	7.9 (2.2)			
Systolic blood pressure, mm Hg	141.2 (21.7)	141.2 (19.6)	140.0 (20.2)	0.238	0.371	0.967
Diastolic blood pressure, mm Hg	83.9 (11.8)	83.0 (10.2)	82.9 (10.7)	0.854	0.183	0.276
Total cholesterol, mg/dl	208.8 (51.5)	207.6 (45.5)	205.8 (48.9)	0.548	0.434	0.766
mmol/l	5.4 (1.8)	5.3 (1.6)	5.3 (1.7)			
HDL cholesterol, mg/dl	49.3 (14.2)	48.7 (14.6)	50.5 (15.2)	0.063	0.303	0.655
mmol/l	1.3 (0.5)	1.2 (0.5)	1.3 (0.5)			
LDL cholesterol, mg/dl	123.6 (41.3)	126.4 (39.1)	123.9 (39.3)	0.349	0.942	0.459
mmol/l	3.2 (1.4)	3.2 (1.3)	3.2 (1.4)			
Triglycerides, mg/dl	158.6 (91.1)	158.2 (79.2)	143.4 (70.7)	0.003	0.018	0.962
mmol/l	1.8 (1.0)	1.8 (0.9)	1.6 (0.8)			
eGFR, ml/min/1.73 m ²	82.3 (21.3)	79.2 (18.8)	81.6 (18.5)	0.061	0.651	0.083
UACR, mg/g	25.6 (56.1)	48.1 (157.0)	45.7 (142.9)	0.877	0.228	0.233
mg/mmol	2.9 (6.3)	5.4 (17.8)	5.2 (16.2)			
Complications						
Cardiovascular disease, %	2.9	2.6	2.1	0.574	0.413	0.760
Coronary artery disease, %	2.6	2.2	2.0	0.825	0.550	0.714
Heart failure, %	0.0	8.8	2.5	0.040	0.335	0.065
Atrial fibrillation, %	0.6	0.4	1.3	0.074	0.349	0.563
Macrovascular disease, %	4.2	4.0	4.3	0.835	0.979	0.897
CKD, %	19.6	23.7	19.9	0.144	0.897	0.237
eGFR<60 ml/min/1.73 m ²	14.4	16.8	12.5	0.061	0.472	0.458
Microvascular disease, %	35.9	38.2	38.3	0.978	0.631	0.670
Retinopathy, %	13.8	15.0	21.3	0.304	0.360	0.882
Cerebrovascular disease, %	0.3	0.4	0.1	0.224	0.344	0.920
Carotid atherosclerosis, %	1.0	2.2	2.3	0.888	0.141	0.190
Peripheral arterial disease, %	50.0	22.2	66.7	0.046	0.679	0.476
Comorbidities						
History of cancer, %	8.1	5.3	5.2	0.904	0.052	0.108

Inflammatory diseases, %	17.2	12.1	10.7	0.405	0.002	0.039
RxRisk comorbidity index	5.8 (6.5)	4.4 (4.9)	4.5 (4.7)	0.904	<0.001	<0.001
Diabetes therapy						
Metformin, %	50.3	42.4	42.4	0.995	0.013	0.025
Sulphonylurea, %	16.2	23.3	27.1	0.098	<0.001	0.014
Glitazones, %	0.0	0.2	0.5	0.381	0.232	0.453
SGLT2 inhibitors, %	0.6	0.0	0.3	0.219	0.337	0.060
GLP-1RA, %	0.6	1.1	0.6	0.225	0.847	0.512
DPP-4 inhibitors, %	2.9	2.0	1.3	0.263	0.048	0.403
Bolus insulin, %	7.1	9.9	12.9	0.083	0.006	0.174
Basal insulin, %	6.8	6.2	6.9	0.595	0.942	0.741
Any insulin, %	10.7	11.6	15.4	0.038	0.040	0.708
Other therapies						
RAS blockers, %	43.2	41.8	40.0	0.468	0.311	0.703
Calcium channel blockers, %	16.9	17.2	16.3	0.621	0.802	0.892
Alpha blockers, %	4.2	4.6	4.1	0.626	0.907	0.804
Beta blockers, %	17.9	16.9	16.1	0.687	0.463	0.717
Anti-platelet, %	54.2	53.4	50.2	0.229	0.217	0.816
Diuretics, %	32.1	28.6	26.6	0.397	0.058	0.281
Statins, %	26.9	23.1	26.5	0.144	0.863	0.212

eGFR, estimated glomerular filtration rate. UACR, urinary albumin creatinine ratio. CKD, chronic kidney disease. RAS, renin angiotensin system.

ESM Tab. 6. Characteristics of cohort 2 divided in three groups based on weight loss. Group 0: <5% weight loss. Group 1: 5% to <10% weight loss, group 2: 10% or more weight loss. p1 indicates the p-values for the comparison of group 1 vs group 0, p2 indicates the p-values for the comparison between group 2 vs group 0, p3 indicates the p-values for the comparison of group 1 vs group 2.

	Group 2	Group 1	Group 0	p1	p2	p3
Number	1167	2304	9806			
Demographics						
Age, years	61.4 (13.2)	62.1 (12.8)	61.5 (12.6)	0.046	0.758	0.129
Sex male %	49.3	55.3	60.9	<0.001	<0.001	<0.001
Diabetes duration, years	0.5 (1.0)	0.7 (1.2)	1.1 (1.4)	<0.001	<0.001	<0.001
Risk factors and lab						
Weight, kg	88.4 (20.8)	85.7 (18.5)	82.8 (17.2)	<0.001	<0.001	<0.001
Body mas index, kg/m ²	32.0 (6.4)	30.8 (5.8)	29.7 (5.5)	<0.001	<0.001	<0.001
Waist cm	107.6 (13.7)	105.8 (13.2)	103.1 (12.7)	<0.001	<0.001	0.002
Systolic blood pressure, mm Hg	139.2 (20.5)	139.6 (19.2)	137.3 (19.4)	<0.001	0.002	0.566
Diastolic blood pressure, mm Hg	81.3 (11.0)	81.5 (10.5)	80.5 (10.5)	<0.001	0.026	0.489
Fasting glucose, mg/dl	150.0 (56.3)	150.8 (53.3)	145.7 (54.7)	<0.001	0.012	0.687
HbA _{1c} , mmol/mol	57 (14)	58 (12)	56 (13)	<0.001	<0.001	0.069
%	7.4 (1.8)	7.5 (1.6)	7.3 (1.7)			
Total cholesterol, mg/dl	189.1 (44.0)	192.3 (43.6)	187.8 (43.1)	<0.001	<0.001	0.417
mmol/l	4.8 (1.5)	4.9 (1.5)	4.8 (1.5)			
HDL cholesterol, mg/dl	49.0 (14.2)	48.4 (13.4)	49.2 (13.7)	0.018	0.059	0.884
mmol/l	1.3 (0.5)	1.2 (0.5)	1.3 (0.5)			
Triglycerides, mg/dl	148.1 (120.7)	156.9 (120.8)	144.7 (108.8)	<0.001	<0.001	0.695
mmol/l	1.7 (1.3)	1.8 (1.3)	1.6 (1.2)			
LDL cholesterol, mg/dl	110.7 (37.0)	112.9 (37.7)	109.8 (36.6)	0.001	0.002	0.518
mmol/l	2.8 (1.3)	2.9 (1.3)	2.8 (1.3)			
eGFR, ml/min/1.73 m ²	83.7 (21.6)	82.6 (23.8)	84.0 (21.5)	0.011	0.246	0.532
Albuminuria, mg/g	51.7 (263.0)	71.8 (289.0)	45.4 (200.3)	0.008	0.114	0.740
mg/mmol	5.8 (29.7)	8.1 (32.7)	5.1 (22.6)			
Complications						
CKD stage III+, %	11.0	11.3	9.9	0.052	0.261	0.780
Pathologic albuminuria, %	6.2	6.1	5.1	0.040	0.081	0.875
Retinopathy, %	0.8	1.2	1.4	0.498	0.129	0.338
Peripheral arterial disease, %	0.8	0.9	0.9	0.718	0.551	0.767
Stroke / TIA, %	0.0	0.0	0.2	0.060	0.181	N/D
Ischemic heart disease, %	2.5	1.8	2.1	0.365	0.419	0.193
Heart failure, %	0.2	0.1	0.2	0.392	0.948	0.488
Any site revascularization, %	1.4	0.9	1.4	0.075	0.987	0.213
Microangiopathy, %	17.5	17.7	16.0	0.045	0.145	0.967
Macroangiopathy, %	5.0	6.2	8.0	0.004	<0.001	0.171
Established cardiovascular disease, %	2.7	2.3	2.7	0.266	0.953	0.427
RxRisk	4.5 (6.0)	4.1 (5.3)	3.9 (5.3)	0.087	<0.001	0.040

Diabete therapy						
Metformin, %	50.3	51.3	50.3	0.404	0.975	0.610
Sulphonylurea, %	5.7	5.6	7.0	0.016	0.076	0.987
DPP-4 inhibitors, %	2.2	2.3	3.9	<0.001	0.004	0.893
GLP-1RA, %	0.9	0.9	0.7	0.181	0.256	0.928
SGLT2 inhibitors, %	0.5	0.6	0.6	0.973	0.713	0.731
Pioglitazone, %	0.6	0.4	0.8	0.041	0.567	0.330
Acarbose, %	0.2	0.1	0.1	0.923	0.658	0.763
Bolus insulin, %	4.9	4.0	4.7	0.196	0.636	0.203
Basal insulin, %	3.8	4.3	5.2	0.054	0.032	0.497
Other therapies						
Statin, %	33.8	35.9	38.7	0.011	0.001	0.253
Anti-platelet agents, %	22.1	25.9	26.2	0.793	0.004	0.019
RAS blockers, %	43.7	46.9	44.8	0.069	0.484	0.076
Beta blockers, %	21.2	21.0	20.1	0.353	0.392	0.890
Calcium channel blockers, %	14.0	15.6	14.9	0.431	0.426	0.234
Diuretics, %	29.1	31.8	28.6	0.002	0.700	0.107

eGFR, estimated glomerular filtration rate. UACR, urinary albumin creatinine ratio. CKD, chronic kidney disease. RAS, renin angiotensin system.

ESM Tab. 7. Three-group analysis of the change over time of risk factors in over the observation period.**A) Cohort 1**

Variable	Group 1 vs 0	Group 2 vs 0	Group 2 vs 1
Primary endpoint			
HbA _{1c} , mmol/mol	-1.3 (0.3)*	-2.4 (0.5)*	-1.2 (0.5)*
%	-0.12 (0.03)*	-0.22 (0.05)*	-0.11 (0.05)*
Secondary endpoints			
Body weight, kg	-3.4 (0.3)*	-7.0 (0.4)*	-3.6 (0.4)*
Systolic blood pressure, mm Hg	-1.4 (1.0)	-1.6 (1.1)	-3.0 (1.2)*
HDL cholesterol, mg/dl	-1.3 (0.8)	1.7 (1.0)	3.0 (1.0)*
mmol/l	-0.03 (0.03)	0.04 (0.03)	0.08 (0.03)
Triglycerides, mg/dl	-5.1 (4.4)	-3.3 (4.9)	1.8 (5.1)
mmol/l	0.1 (0.0)	0.0 (0.1)	0.0 (0.1)
LDL cholesterol, mg/dl	0.1 (1.9)	5.4 (2.2)*	5.3 (2.3)*
mmol/l	0.00 (0.07)	0.14 (0.06)*	0.14 (0.06)*
eGFR, ml/min/1.73 m ²	-0.9 (1.2)	1.8 (1.4)	2.7 (1.5)
UACR, mg/g	6.3 (23.4)	-3.1 (26.0)	-9.4 (28.6)
mg/mmol	0.7 (2.6)	-0.4 (2.9)	-1.1 (3.2)

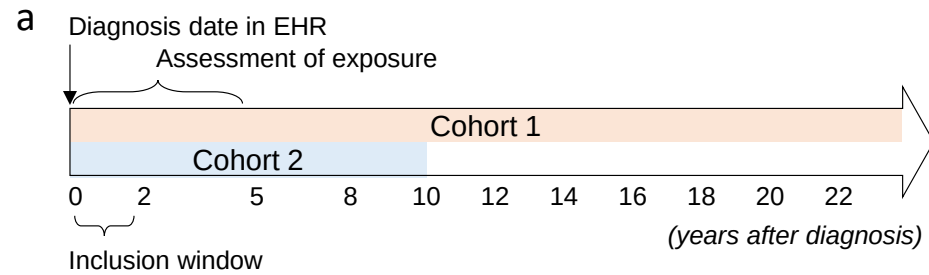
B) Cohort 2

Variable	Group 1 vs 0	Group 2 vs 0	Group 2 vs 1
Primary endpoint			
HbA _{1c} , mmol/mol	-1.4 (0.4)*	-3.1 (0.5)*	-1.6 (0.5)*
%	-0.13 (0.04)*	-0.28 (0.05)*	-0.15 (0.05)*
Secondary endpoints			
Body weight, kg	-4.4 (0.4)*	-8.6 (0.5)*	-4.2 (0.5)*
Systolic blood pressure, mm Hg	-1.6 (0.8)*	-4.8 (1.0)*	-3.1 (1.0)*
HDL cholesterol, mg/dl	0.8 (0.3)*	2.2 (0.4)*	1.3 (0.4)*
mmol/l	0.02 (0.01)*	0.06 (0.01)*	0.03 (0.01)*
Triglycerides, mg/dl	-7.5 (2.7)*	-17.8 (3.7)*	-10.4 (3.6)*
mmol/l	-0.1 (0.0)*	-0.2 (0.0)*	-0.1 (0.0)*
LDL cholesterol, mg/dl	-2.6 (1.1)*	-2.5 (1.4)	0.1 (1.4)
mmol/l	-0.07 (0.03)*	-0.06 (0.04)*	0.00 (0.01)
eGFR, ml/min/1.73 m ²	0.1 (0.5)	-0.1 (0.7)	-0.2 (0.6)
UACR, mg/g	32.4 (20.7)	1.9 (18.2)	-30.5 (20.7)
mg/mmol	3.7 (2.3)	0.2 (2.1)	-3.4 (2.3)

Group 0: weight loss less than 5%, Group 1: weight loss 5% to <10%, Group 2: weight loss 10% or more.

* $p < 0.05$ after correction for multiple comparisons.

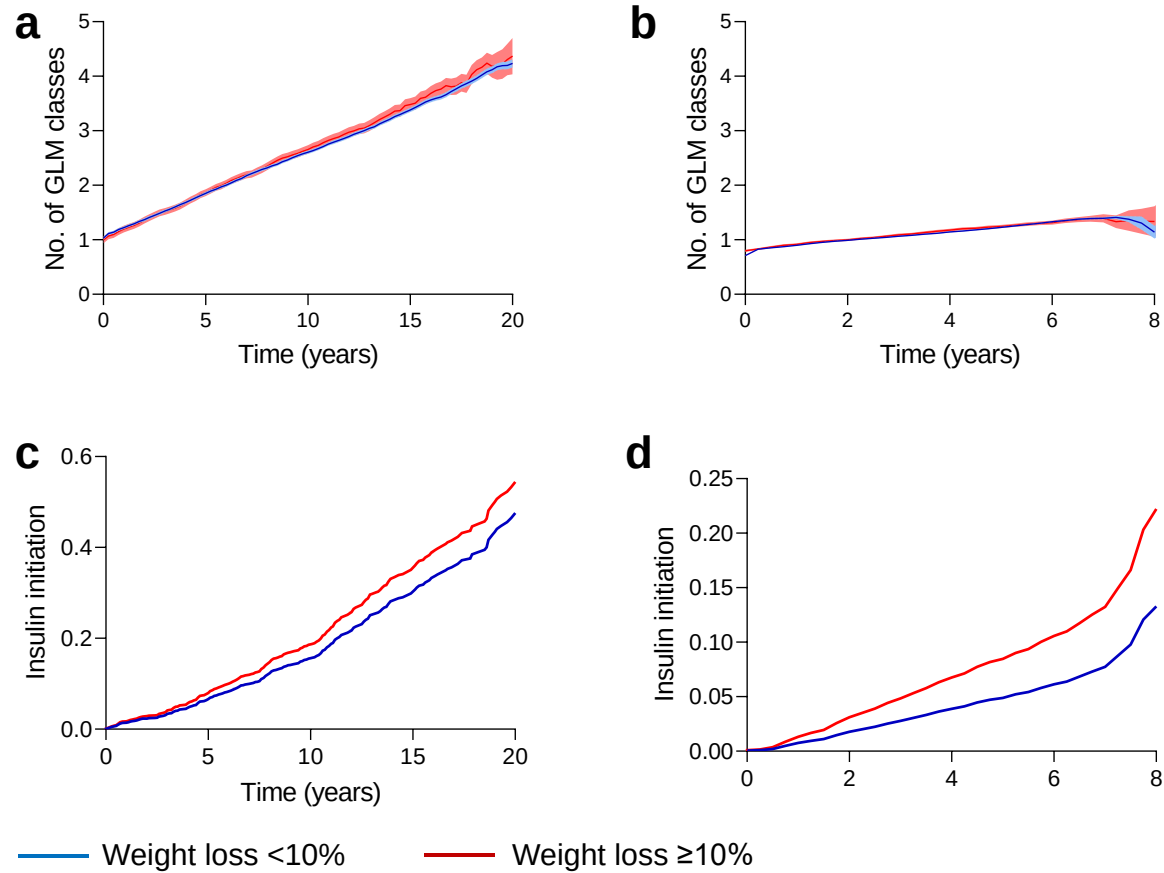
ESM Fig. 1. Study flowchart. a) Timeline of the two cohorts and windows of exposure (EHR, electronic health record). b) Number of patients and duration of observation in the two cohorts.



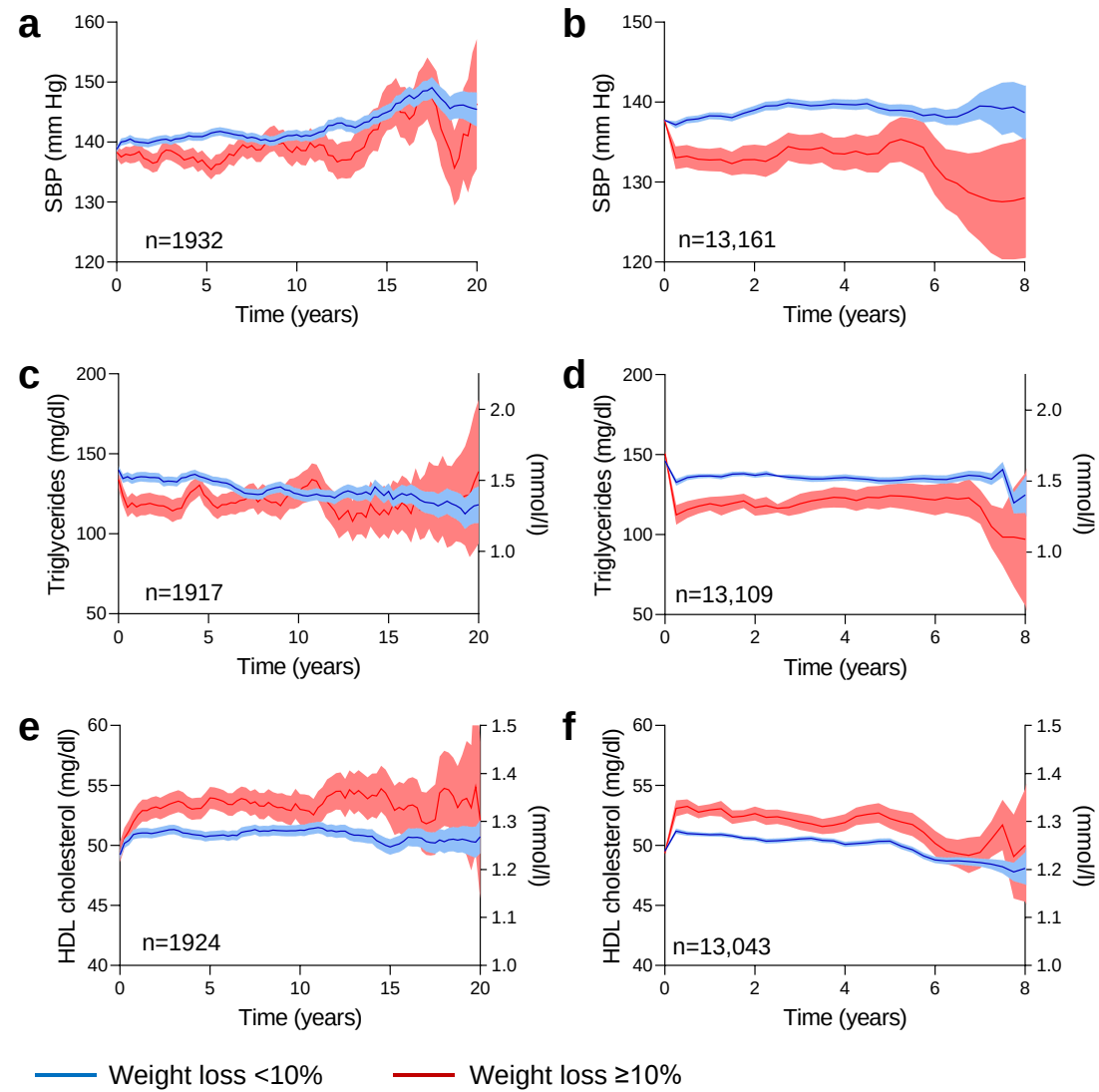
b

Step	Cohort 1	Cohort 2
Total, n	11,254	145,198
Included within 2 years after diagnosis, n	3970	50,080
Available data for assessment of exposure, n	3902	29,536
Available data for primary outcome, n	1934	13,277
Median observation, years	10.8	4.0
Max follow-up, years	24.0	8.5

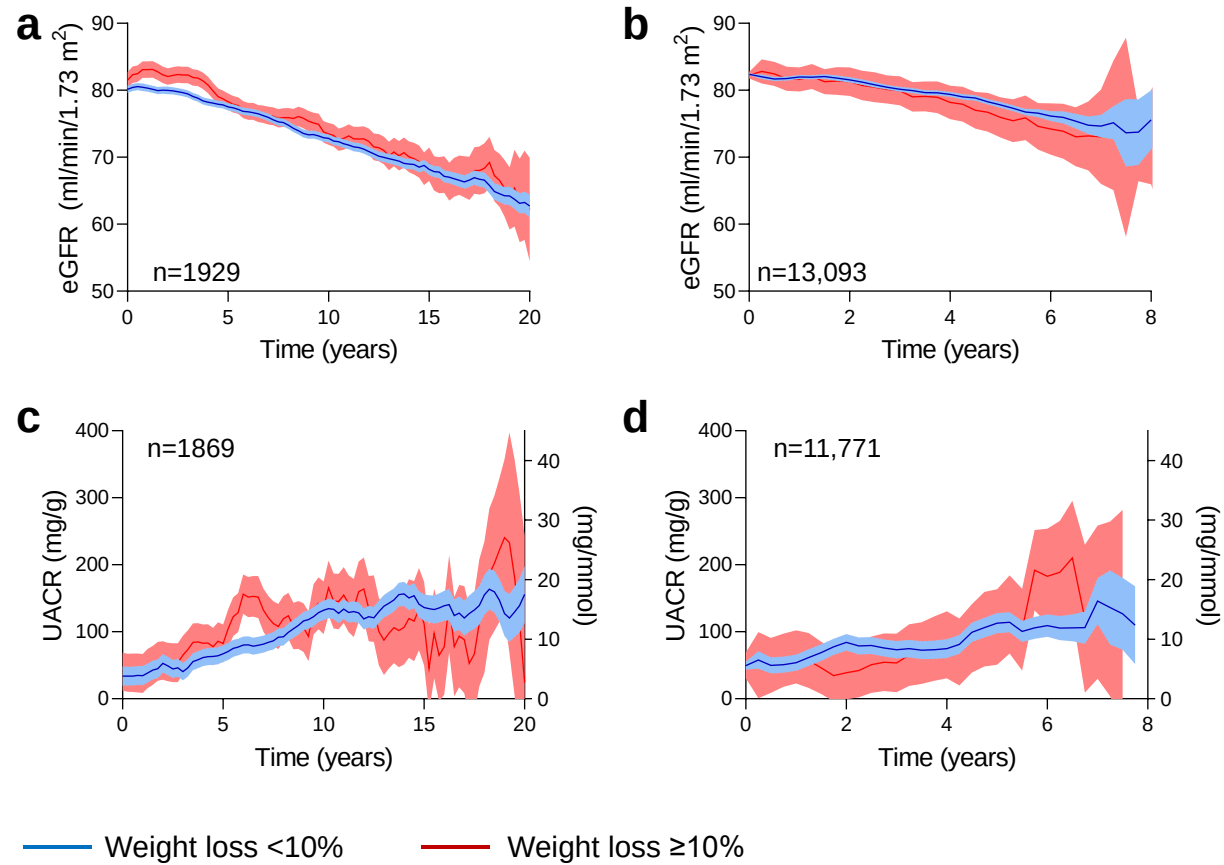
ESM Fig. 2. Weight loss and burden of therapy. a, b) The burden of therapy, defined as the number of glucose lowering medication (GLM) classes over time, is reported for the two groups of cohort 1 (a) and cohort 2 (b). The rates of insulin initiation analysed using the Cox regression model in cohort 1 (c) and cohort 2 (d). There were no missing data for these outcomes.



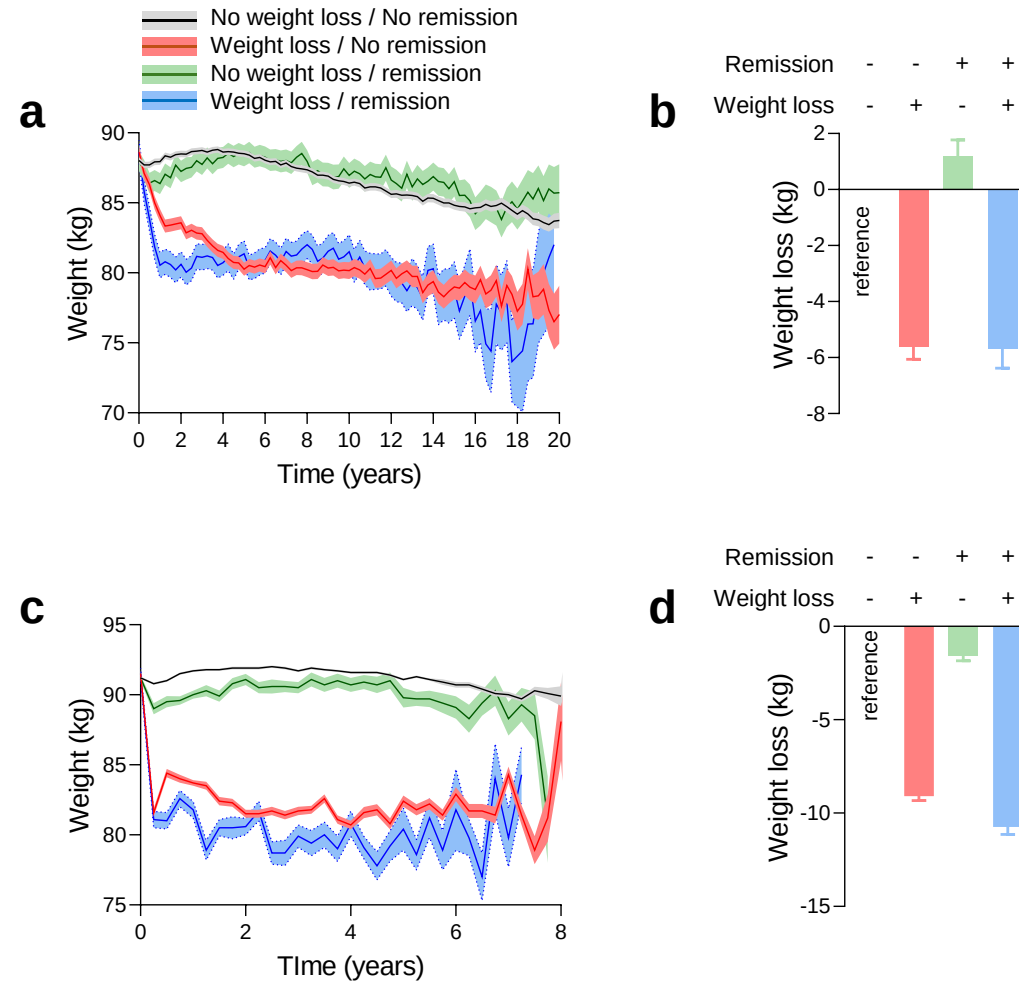
ESM Fig. 3. Weight loss and cardio-metabolic parameters. For cohort 1 (a, c, e) and cohort 2 (b, d, f), the change over time in systolic blood pressure (SBP), triglycerides, and HDL cholesterol are shown for the two groups. The number of patients with available data for each outcome is reported.



ESM Fig. 4. Weight loss and markers of kidney function and damage. For cohort 1 (a, c) and cohort 2 (b, d), the estimated glomerular filtration rate (eGFR) and the urinary albumin-to-creatinine ratio (UACR) are shown for both groups. The number of patients with available data for each outcome is reported.



ESM Fig. 5: Weight over time by weight loss group and remission status. Participants in Cohort 1 (a,b) and Cohort 2 (c,d) were divided into 4 groups based on whether or not they lost $\geq 10\%$ body weight and on whether or not they experienced remission within the first 5 years after diagnosis. For both cohorts, weight curves (a,c) are derived from an adjusted MMRM, while histograms (b,d) display the mean estimated difference in the entire period of observation (bars indicate standard error of the mean).



ESM Fig. 6. Main outcomes of participants in the two cohorts divided in 3 groups based on percentage of body weight. Data are presented separately for Cohort 1 (a-c) and Cohort 2 (d-f). a,d) Changes over time in body weight. b,e) Changes in HbA_{1c}. c,f) incidence of remission: adjusted hazard ratios (HR) are reported versus group 0 (reference) with their 95% confidence intervals.

