

SUPPLEMENTARY DATA

Supplementary Table 1. Quartiles (Q) of BMI change in the treatment groups of the Diabetes Control and Complications Trial (DCCT). Values represent the differences between baseline and closeout visits in the DCCT.

		Mean	Std Dev	Min	Max
Intensive	Q1	-0.09	1.12	-6.16	1.06
	Q2	1.87	0.40	1.07	2.60
	Q3	3.49	0.60	2.62	4.56
	Q4	6.83	2.22	4.56	17.08
Conventional	Q1	-0.097	1.38	-8.74	0.30
	Q2	0.80	0.31	0.31	1.31
	Q3	1.87	0.31	1.32	2.42
	Q4	3.83	1.28	2.43	9.65

Units are kg/m².

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Supplementary Table 2. Clinical characteristics of DCCT/EDIC treatment groups at the DCCT closeout visit by quartiles of weight gain.

Characteristics	Intensive			Conventional		
	Minimal Gainers	Excessive Gainers	<i>P</i> -value*	Minimal Gainers	Excessive Gainers	<i>P</i> -value*
N	453	151		457	152	
Age (yr)	35 ± 6	37 ± 6	0.0149	35 ± 6	35 ± 6	0.4978
Female sex (%)	44	64	<0.0001	43	49	0.1964
Weight (kg)	75 ± 13	90 ± 15	<0.0001	74 ± 12	80 ± 14	<0.0001
BMI (kg/m ²)						
At baseline	23 ± 3	24 ± 3	<0.0001	24 ± 3	24 ± 3	0.2917
At closeout	25 ± 3	31 ± 4	<0.0001	24 ± 3	27 ± 3	<0.0001
Iliac crest waist circumference (cm)	88 ± 9	103 ± 16	<0.0001	87 ± 8	93 ± 10	<0.0001
Secondary cohort (%)	52	54	0.6048	51	50	0.8700
Duration of diabetes (year)	12 ± 5	12 ± 5	0.7239	12 ± 5	12 ± 5	0.0992
Current cigarette smoker (%)	28	22	0.1361	30	22	0.0785
Blood pressure (mm Hg)						
Systolic	116 ± 11	118 ± 12	0.0415	116 ± 12	119 ± 13	0.0317
Diastolic	75 ± 9	76 ± 8	0.0117	74 ± 9	75 ± 10	0.3202
Lipids [mg/dl (mmol/l)]						
Total cholesterol	178 ± 29 (4.6 ± 0.7)	192 ± 30 (5.0 ± 0.8)	<0.0001	183 ± 33 (4.7 ± 0.9)	190 ± 36 (4.9 ± 0.9)	0.0285
Triglycerides	77 ± 43 (2.0 ± 1.1)	96 ± 64 (2.5 ± 1.7)	<0.0001	81 ± 41 (2.1 ± 1.1)	96 ± 53 (2.5 ± 1.4)	0.0030
LDL cholesterol	111 ± 26 (2.9 ± 0.7)	123 ± 27 (3.2 ± 0.7)	<0.0001	114 ± 30 (2.9 ± 0.8)	118 ± 30 (3.1 ± 0.8)	0.1201
HDL cholesterol	52 ± 14 (1.3 ± 0.4)	50 ± 12 (1.3 ± 0.3)	0.0462	52 ± 13 (1.3 ± 0.3)	53 ± 14 (1.4 ± 0.4)	0.7936
Non-HDL cholesterol	126 ± 30 (3.3 ± 0.8)	142 ± 30 (3.7 ± 0.8)	<0.0001	130 ± 34 (3.4 ± 0.9)	138 ± 35 (3.6 ± 0.9)	0.0201
Renal function (%)						
AER ≥40 mg/24 hr	5	5	0.9911	11	12	0.6832
AER ≥300 mg/24 hr	1	0	0.1561	2	3	0.5472
Insulin dose (u/kg/day)	0.64 ± 0.20	0.74 ± 0.23	<0.0001	0.61 ± 0.16	0.67 ± 0.19	0.0002
HbA1c [% (mmol/mol)]	7.3 ± 1.1 (56 ± 12)	7.4 ± 1.0 (58 ± 11)	0.0267	9.2 ± 1.5 (77 ± 16)	8.9 ± 1.5 (74 ± 17)	0.1970
DCCT updated mean HbA1 [% (mmol/mol)]	7.1 ± 0.8 (54 ± 9)	7.2 ± 0.7 (55 ± 8)	0.0868	9.0 ± 1.3 (75 ± 14)	8.9 ± 1.2 (74 ± 13)	0.3861

See text for definition of minimal and excessive weight gain groups. Data are means ± SD or %. AER=albumin excretion rate, BMI=body mass index, HDL=high-density lipoprotein, LDL=low-density lipoprotein. * *P*-value from the Wilcoxon rank-sum test or the chi-square test comparing minimal vs. excessive gainers.

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Supplementary Table 3. Clinical characteristics of DCCT/EDIC participants during EDIC years 5, 10, and 15 by quartiles of weight gain in the *conventionally* treated group

Characteristics	EDIC Year 5		EDIC Year 10		EDIC Year 15	
	Minimal Gainers	Excessive Gainers *	Minimal Gainers	Excessive Gainers *	Minimal Gainers	Excessive Gainers *
N, Subjects at risk for CVD	452	152	434	142	425	140
Any medication use up to visit (%)						
Anti-hypertensive medication†	17	22	37	46	46	55
Lipid-lowering medication	6	13 *	26	32	48	54
Aspirin	12	11	33	35	43	44
Hormone replacement therapy	5	4	5	6	4	4
DCCT/EDIC Time-weighted Means						
Weight (kg)	75 ± 12	78 ± 13	77 ± 13	80 ± 14	79 ± 13	81 ± 14
BMI (kg/m ²)	25 ± 3	26 ± 3 *	25 ± 3	27 ± 4 *	26 ± 3	28 ± 4 *
EDIC waist circumference (cm)	84 ± 9	88 ± 11 *	86 ± 10	89 ± 11 *	88 ± 10	90 ± 11
Systolic blood pressure (mm Hg)	116 ± 8	119 ± 9 *	118 ± 8	120 ± 9	118 ± 8	120 ± 8
Diastolic blood pressure (mm Hg)	74 ± 5	75 ± 5	75 ± 5	76 ± 5	74 ± 5	75 ± 5
HDL cholesterol (mg/dl)	54 ± 12	54 ± 12	54 ± 12	55 ± 13	55 ± 12	56 ± 13
	(1.4 ± 0.3)	(1.4 ± 0.3)	(1.4 ± 0.3)	(1.4 ± 0.3)	(1.4 ± 0.3)	(1.4 ± 0.3)
LDL cholesterol (mg/dl)	113 ± 25	118 ± 26	112 ± 23	115 ± 23	109 ± 21	110 ± 19
	(2.9 ± 0.6)	(3.1 ± 0.7)	(2.9 ± 0.6)	(3.0 ± 0.6)	(2.8 ± 0.5)	(2.8 ± 0.5)
Total cholesterol (mg/dl)	183 ± 28	190 ± 29	182 ± 25	188 ± 27	180 ± 24	182 ± 23
	(4.7 ± 0.7)	(4.7 ± 0.7)	(4.7 ± 0.6)	(4.9 ± 0.7)	(4.7 ± 0.6)	(4.7 ± 0.6)
Triglycerides (mg/dl)	81 ± 37	91 ± 40 *	80 ± 37	89 ± 38 *	80 ± 38	84 ± 35
	(2.1 ± 1.0)	(2.4 ± 1.0)	(2.1 ± 1.0)	(2.3 ± 1.0)	(2.1 ± 1.0)	(2.2 ± 0.9)
DCCT HbA1c (%)	9.0 ± 1.3	8.9 ± 1.2	9.0 ± 1.2	8.9 ± 1.2	9.0 ± 1.2	8.9 ± 1.2
	(75 ± 14)	(74 ± 13)	(75 ± 13)	(74 ± 13)	(75 ± 13)	(74 ± 13)
EDIC HbA1c (%)	8.3 ± 1.2	8.2 ± 1.2	8.1 ± 1.1	8.0 ± 1.0	7.9 ± 1.0	8.0 ± 1.0
	(67 ± 13)	(66 ± 13)	(75 ± 12)	(64 ± 11)	(63 ± 11)	(64 ± 11)
DCCT/EDIC HbA1c (%)	8.7 ± 1.1	8.6 ± 1.1	8.4 ± 1.0	8.4 ± 1.0	8.2 ± 0.9	8.2 ± 0.9
	(72 ± 12)	(70 ± 12)	(68 ± 11)	(68 ± 11)	(66 ± 10)	(66 ± 10)

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Data are means \pm SD or %. BMI=body mass index, HDL=high-density lipoprotein, LDL=low-density lipoprotein. * *P*-value < 0.01 from the Wilcoxon rank-sum test or the chi-square test comparing minimal vs. excessive gainers. † Includes angiotensin converting enzyme inhibitors, angiotensin receptor blockers, beta blockers, and calcium channel blockers.

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Supplementary Table 4. Association in the DCCT *conventionally* treated group between quartiles of weight gain during DCCT and subsequent cardiovascular events throughout EDIC follow-up.

	Overall		Minimal Gainers (n=457)		Excessive Gainers (n=152)		Unadjusted	Partially Adjusted	Fully Adjusted
	No. of Patients (%)*	No. of Events	No. of Patients (%)*	No. of Events	No. of Patients (%)*	No. of Events	Hazard Ratio (95% CI)		
1. Any cardiovascular disease event	86 (14)	171	63 (14)	107	23 (15)	64	1.06 (0.66-1.71)	1.08 (0.67-1.75)	1.07 (0.65-1.74)
2. Nonfatal acute myocardial infarction	24 (4)	28	15 (3)	17	9 (6)	11			
3. Nonfatal cerebrovascular event	12 (2)	13	9 (2)	10	3 (2)	3			
4. Death from cardiovascular disease	9 (1)	9	8 (2)	8	1 (1)	1			
5. Silent myocardial infarction	24 (4)	25	17 (4)	18	7 (5)	7			
6. Confirmed angina	14 (2)	23	9 (2)	12	5 (3)	11			
7. Revascularization	43 (7)	63	29 (6)	37	14 (9)	26			
Congestive Heart Failure	8 (1)	10	4 (1)	5	4 (3)	5			
Nonfatal myocardial infarction or stroke or death from cardiovascular disease (MACE)	40 (7)	50	28 (6)	35	12 (8)	15	1.25 (0.64-2.46)	1.24 (0.62-2.50)	1.49 (0.72-3.11)
1. Nonfatal acute myocardial infarction	24 (4)	28	15 (3)	17	9 (6)	11			
2. Nonfatal cerebrovascular event	12 (2)	13	9 (2)	10	3 (2)	3			
3. Death from cardiovascular disease	9 (1)	9	8 (2)	8	1 (1)	1			

* Number of patients with each type of event, regardless of whether or not it is the initial event for that subject. † Cox proportional hazard regression models unadjusted; partially adjusted for DCCT closeout age, sex, and the following time-dependent covariates: smoking, sustained AER ≥ 30 or ESRD, eGFR < 15 or ESRD, aspirin use, hormone replacement therapy use, and DCCT/EDIC time-weighted mean HbA1c; and fully adjusted to also include the following time-dependent covariates: systolic and diastolic blood pressure, anti-hypertensive medication use, total cholesterol, triglycerides, and lipid-lowering medication use.

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Supplementary Table 5. Association in the DCCT *intensively* treated group between quartiles of weight gain during DCCT and subsequent cardiovascular events throughout EDIC follow-up.

	Overall		Minimal Gainers (n=453)		Excessive Gainers (n=151)		Unadjusted	Partially Adjusted	Fully Adjusted
	No. of Patients (%)*	No. of Events	No. of Patients (%)*	No. of Events	No. of Patients (%)*	No. of Events			
Any cardiovascular disease event	73 (12)	133	50 (11)	93	23 (15)	40	1.35 (0.83-2.22)	1.14 (0.68-1.91)	1.02 (0.60-1.75)
1. Nonfatal acute myocardial infarction	22 (4)	24	16 (4)	17	6 (4)	7			
2. Nonfatal cerebrovascular event	8 (1)	9	6 (1)	7	2 (1)	2			
3. Death from cardiovascular disease	6 (1)	6	4 (1)	4	2 (1)	2			
4. Silent myocardial infarction	20 (3)	21	15 (3)	16	5 (3)	5			
5. Confirmed angina	15 (2)	15	11 (2)	11	4 (3)	4			
6. Revascularization	36 (6)	57	23 (5)	37	13 (9)	20			
7. Congestive Heart Failure	1 (<1)	1	1 (<1)	1	0 (0)	0			
Nonfatal myocardial infarction or stroke or death from cardiovascular disease (MACE)	34 (6)	39	25 (6)	28	9 (6)	11	1.04 (0.48-2.22)	0.87 (0.39-1.92)	1.01 (0.45-2.28)
1. Nonfatal acute myocardial infarction	22 (4)	24	16 (4)	17	6 (4)	7			
2. Nonfatal cerebrovascular event	8 (1)	9	6 (1)	7	2 (1)	2			
3. Death from cardiovascular disease	6 (1)	6	4 (1)	4	2 (1)	2			

See text for definition of minimal and excess weight gainers. * Number of patients with each type of event, regardless of whether or not it is the initial event for that subject. † Cox proportional hazard regression models unadjusted; partially adjusted for DCCT closeout age, sex, and the following time-dependent covariates: smoking, sustained AER ≥ 30 or ESRD, eGFR < 15 or ESRD, aspirin use, hormone replacement therapy use, and DCCT/EDIC time-weighted mean HbA1c; and fully adjusted to also include the following time-dependent covariates: systolic and diastolic blood pressure, anti-hypertensive medication use, total cholesterol, triglycerides, and lipid-lowering medication use.