

Weight Change in Diabetes and Glycemic and Blood Pressure Control

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OBJECTIVE— Weight loss in type 2 diabetes is undisputedly important, and data from community settings are limited. We evaluated weight change and resulting glycemic and blood pressure control in type 2 diabetic patients at an HMO.

RESEARCH DESIGN AND METHODS— Using electronic medical records, this retrospective cohort study identified 2,574 patients aged 21–75 years who received a new diagnosis of type 2 diabetes between 1997 and 2002. We estimated 3-year weight trajectories using growth curve analyses, grouped similar trajectories into four categories using cluster analysis, compared category characteristics, and predicted year-4 above-goal A1C and blood pressure by group.

RESULTS— The weight-trajectory groups were defined as higher stable weight ($n = 418$; 16.2%), lower stable weight ($n = 1,542$; 59.9%), weight gain ($n = 300$; 11.7%), and weight loss ($n = 314$; 12.2%). The latter had a mean weight loss of 10.7 kg (-9.8% ; $P < 0.001$) by 18 months, with near-complete regain by 36 months. After adjusting for age, sex, baseline control, and related medication use, those with higher stable weight, lower stable weight, or weight-gain patterns were more likely than those who lost weight to have above-goal A1C (odds ratio [OR] 1.66 [95% CI 1.12–2.47], 1.52 [1.08–2.14], and 1.77 [1.15–2.72], respectively). Those with higher stable weight or weight-gain patterns were more likely than those who lost weight to have above-goal blood pressure (1.83 [1.31–2.57] and 1.47 [1.03–2.10], respectively).

CONCLUSIONS— A weight-loss pattern after new diagnosis of type 2 diabetes predicted improved glycemic and blood pressure control despite weight regain. The initial period postdiagnosis may be a critical time to apply weight-loss treatments to improve risk factor control.

Diabetes Care 31:1960–1965, 2008

Almost all adults with diabetes are overweight; more than half are obese (1). Obesity is associated with worse blood glucose and other cardiovascular risk factor control (2). Results from the Look AHEAD trial show that weight loss in diabetes improves glycemic control, reduces blood pressure, and improves blood lipids (3). Observational studies also support a likely link between weight loss and reduced mortality in people with diabetes (2).

Limited data describe the extent to which weight loss, as well as resulting levels of glycemic and blood pressure control, is achieved in community-living

people with type 2 diabetes (4,5). Most weight information on these subjects comes from research volunteers (4,5). Prior studies of health effects of weight change have been plagued by confounding of low weight by disease burden and by difficulty separating intentional from unintentional weight loss (6,7).

This study used electronic medical records data to evaluate weight trajectories in the initial years following a new type 2 diabetes diagnosis, associated demographic and comorbidity factors, and resulting glycemic and blood pressure control. The initial period after a diabetes diagnosis is of particular interest because

this may be a time of heightened patient and clinician interest in patient behavior change (8).

RESEARCH DESIGN AND METHODS

The study design and procedures were approved by the study site's institutional review board.

Study site and data sources

The study was conducted at Kaiser Permanente Northwest (KPNW), a not-for-profit HMO in the Pacific Northwest with ~480,000 members. Electronic medical records include patient weight, blood pressure, height, smoking status, diagnoses, treatment procedures, medications, and laboratory results. The KPNW diabetes registry has been shown to be 99.5% specific and 99% sensitive for diabetes diagnosis compared with chart review (9). KPNW members with diabetes are demographically and clinically similar to the national population of patients with diabetes (9).

The study site's clinical guidelines for diabetes care are consistent with prevailing guidelines (10). Guidelines recommend lifestyle management for all people with diabetes and a stepped-care approach to medication use for control of risk factors. Most newly diagnosed members attend diabetes classes, and HMO weight-related health-education classes are available for a fee.

Study design and identification of participants

This retrospective cohort study evaluated 3-year weight trajectory patterns in subjects aged 21–75 years and newly diagnosed with type 2 diabetes, as well as the patterns' effects on A1C and blood pressure in year 4. We identified all men and women aged 21–75 years with any evidence of type 2 diabetes ($n = 38,430$). We then limited the population to those with newly diagnosed type 2 diabetes from 1 January 1997 to 31 December 2002 ($n = 17,403$) and then further limited it to those with 12 months' pre- and 36 months' postdiagnosis continuous HMO membership ($n = 8,540$). A diabetes diagnosis was assigned to those who met diabetes registry criteria: documentation of an inpa-

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Received 28 February 2008 and accepted 14 June 2008.

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tient or outpatient type 2 diabetes diagnosis, fasting plasma glucose >125 mg/dl, or diabetes medication dispensed. The first diagnosis date served as the index date. A diagnosis was considered new if the patient had not met the qualifying criteria in the 12 months before diabetes registry entry. We excluded 3,833 patients with a severe illness or condition associated with unintentional weight change in the 12 months preperiod or during trajectory: 69.0% ($n = 2,645$) with cancer, 12.0% ($n = 460$) on home oxygen, 5.0% ($n = 191$) with a pregnancy, 5.0% ($n = 193$) with amputation(s), and 9.0% ($n = 344$) with any of the following conditions: HIV, nutritional deficiency, bariatric surgery, dialysis, hospice, or care facility stay >30 days and BMI <20 kg/m² ($n = 4,707$ remained). Finally, we included only those with a weight measurement at baseline and at least five weight measurements in the 3 years postdiagnosis (to explore differently shaped weight-change curves); the final weight measurement had to occur 30 to 36 months postindex (final $n = 2,574$ patients). Those excluded as a result of weight requirements were younger (54.5 vs. 56.3 years; $P < 0.001$) and more likely to be male (52.3 vs. 47.3%; $P < 0.001$) and have a higher A1C (8.2 vs. 8.0%; $P = 0.023$), but they did not have significantly different blood pressure.

Study variables

The primary outcomes were above-goal A1C ($\geq 7\%$) and above-goal blood pressure ($\geq 130/80$ mmHg) (10) during the 4th year after the index date, using mean values. To adjust for baseline A1C, we defined baseline as A1C measures that were taken during year 1 because few participants had pre-diabetes diagnosis A1C measures. Additional analyses considered only patients with A1C measured in a 3-month window around the index date. Baseline blood pressure (above goal) was based on mean blood pressure in the 12 months before index.

We used all weight measurements to create a 3-year trajectory for each individual. Baseline was defined as the preperiod measurement of weight closest to the index date. The 3-year weight was the measure collected closest to the end of the 30- to 36-month interval.

We included a group of covariates traditionally associated with weight or weight change (11–13): age at index date

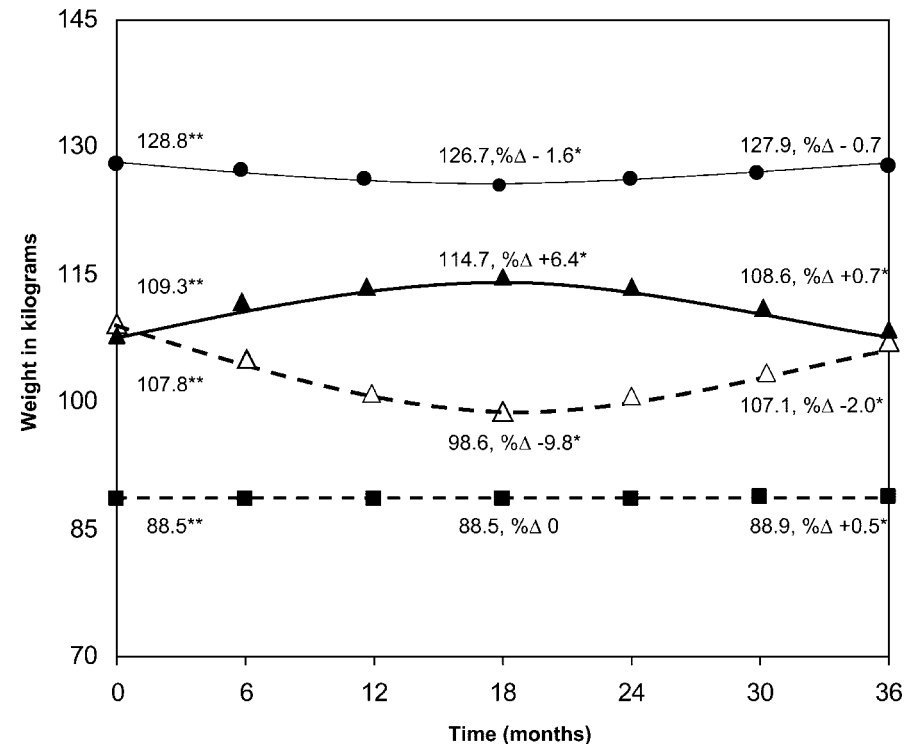


Figure 1—The four dominant weight-change trajectory patterns in the three years after diagnosis of type 2 diabetes. ●, group with higher stable weight ($n = 418$; 16.2%); △, weight-loss group ($n = 314$; 12.2%); ▲, weight-gain group ($n = 300$; 11.7%); ■, group with lower stable weight ($n = 1,542$; 59.9%); and %Δ, percentage weight change from baseline. **Estimated baseline weights differ from mean baseline weights in Table 1. *Percentage weight changes (month 0–month 18 and month 0–month 36) are significantly different from zero ($P < 0.001$ based on Wilcoxon’s signed-rank test).

(11), sex (12), whether the individual was in a group at “race-risk” for obesity (Black, Hispanic, Native American, and Pacific Islander, combined) (12), Medicaid enrollment, and family income <\$40,000 per year (11). Race data were available for 77% of patients. To approximate missing race data and to assign family income, we used participants’ mailing addresses to obtain census tract block data.

We used baseline weight and any available height to determine baseline BMI and obesity (BMI ≥ 30 kg/m²) status (1). Current smoking was noted using the preperiod record closest to the index date. We used the mean number of unique medications dispensed in the prediagnosis period as a measure of disease burden (14). We noted baseline diagnoses that could affect or be affected by weight or weight change: hypertension, dyslipidemia, cardiovascular disease (excluding congestive heart failure), microvascular disease (retinopathy, neuropathy, and nephropathy, combined), depression, and conditions that could interfere with activity (asthma, chronic obstructive pulmonary disease, and arthritis, combined) (13).

We used the following diabetes medication categories for any single medication dispensed for >30 days during year 4: “sulfonylureas” for patients dispensed sulfonylureas (but not metformin), “metformin” for those dispensed metformin (but not sulfonylureas), “sulfonylureas and metformin” for those dispensed both, thiazolidinedione, acarbose, and repaglinide. Insulin use was indicated for those to whom any insulin was dispensed during year 4. We used the blood pressure medication categories beta blocker, diuretic, ACE inhibitor, angiotensin receptor blocker, or “other antihypertensive” medication for those dispensed for >30 days during year 4.

Statistical analysis

Individual weight trajectories were estimated using growth curve analyses (multilevel modeling) with HLM 6.0. Time formed the first level of the model, with weight as the dependent variable. We used both linear and quadratic models to determine best fit for the data. The intercept and slope parameters describing individual weight trajectories were entered into a hierarchical cluster analysis, using

Table 1—Baseline characteristics of patients with new-onset type 2 diabetes by weight change–trajectory pattern

	Higher stable weight	Lower stable weight	Weight loss	Weight gain	P*
n (%)	418 (16.2)	1,542 (59.9)	314 (12.2)	300 (11.7)	
Age (years)	52.9 ± 8.9	57.7 ± 10.3	55.9 ± 9.7	54.4 ± 9.9	<0.001†
Female sex	174 (41.6)	876 (56.8)	165 (52.6)	141 (47.0)	<0.001
Weight (kg)	129.4 ± 17.7	89.0 ± 15.0	111.0 ± 20.5	108.0 ± 20.0	<0.001
BMI (kg/m ²)	43.1 ± 7.0	32.3 ± 5.2	38.9 ± 7.2	37.0 ± 7.0	<0.001†
BMI category (kg/m ²)					<0.001†
<25	0 (0.0)	97 (6.3)	1 (0.3)	7 (2.3)	
25 to <30	2 (0.5)	452 (29.3)	19 (6.1)	43 (14.3)	
30 to <40	147 (35.1)	869 (56.4)	170 (54.1)	157 (52.3)	
≥40	269 (64.4)	124 (8.0)	124 (39.5)	93 (31.0)	
Race risk‡	16 (3.8)	112 (7.3)	12 (3.8)	15 (5.0)	0.012
Family income <\$40,000/year	83 (19.9)	293 (19.0)	47 (15.0)	64 (21.3)	0.205†
Medicaid	17 (4.1)	68 (4.4)	10 (3.2)	15 (5.0)	0.703
Current smoker	61 (14.6)	254 (16.5)	53 (16.9)	65 (21.7)	0.084
No. of medications	7.5 ± 5.8	7.7 ± 5.7	7.9 ± 6.0	8.3 ± 6.0	0.241
Median (IQR)	6.5 (3–10)	7 (3–11)	7 (4–11)	7 (4–11.5)	
Depression	61 (14.6)	183 (11.9)	45 (14.3)	53 (17.7)	0.035
Hypertension	237 (56.7)	704 (45.7)	163 (51.9)	137 (45.7)	<0.001
Dyslipidemia	89 (21.3)	405 (26.3)	73 (23.3)	67 (22.3)	0.116
CVD (excluding CHF)	43 (10.3)	183 (11.9)	30 (9.6)	39 (13.0)	0.450
Microvascular disease§	40 (9.6)	114 (7.4)	25 (8.0)	22 (7.3)	0.517
Asthma/COPD/arthritis¶	126 (30.1)	393 (25.5)	80 (25.5)	89 (29.7)	0.153
A1C (year 1)¶	7.2 ± 1.1	7.1 ± 1.2	6.7 ± 1.0	7.3 ± 1.3	<0.001†
Median (IQR)	6.9 (6.3–7.8)	6.8 (6.3–7.6)	6.5 (6.0–7.3)	6.9 (6.4–8.0)	
A1C above goal	178 (47.7)	591 (43.6)	97 (33.9)	123 (46.6)	<0.001†
Systolic blood pressure#	140.1 ± 13.6	137.6 ± 15.1	138.3 ± 13.8	137.2 ± 15.7	<0.002
Median (IQR)	139 (132–147)	136 (127–147)	138 (128–147)	136 (127–147)	
Diastolic blood pressure#	85.9 ± 8.1	82.3 ± 8.0	83.9 ± 7.9	84.1 ± 9.2	<0.001
Median (IQR)	86 (80–91)	82 (77–87)	84 (79–89)	84 (79–89)	
Blood pressure above goal	369 (88.3)	1211 (78.5)	257 (81.9)	237 (79.3)	<0.001

Data are means ± SD or n (%) unless otherwise indicated. *Comparison across all four groups. †Comparison of weight-gain and weight-loss groups significant at $P < 0.05$. ‡Defined as any of the following: African American/Hispanic/American Indian/Pacific Islander. ¶Combined noncardiovascular diagnoses that may interfere with activity. §Retinopathy, neuropathy, and nephropathy grouped together. ¶A1C means based on 373 subjects (89.2%) in higher-stable, 1,355 (87.9%) in lower-stable, 286 (91.1%) in weight-loss, and 264 (88.0%) in weight-gain groups that had one or more measures during year 1. #Blood pressure means based on 418 subjects (100%) in higher-stable, 1,542 (100%) in lower-stable, 314 (100%) in weight-loss, and 299 (99.7%) in weight-gain groups that had one or more measures during the baseline year. CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; IQR, interquartile range.

Ward's Method in SPSS 15.0, to identify groups of patients with similar weight trajectories. We used ANOVA and χ^2 tests to compare characteristics of groups. Multiple logistic regression models estimated the unadjusted effect of membership in a weight-trajectory cluster on above-goal A1C and blood pressure in year 4, as well as the effect while controlling for factors that were statistically significant in univariate analyses and are known to affect glycemic and blood pressure control (3). Adjusted model one controlled for age, sex, and baseline A1C or blood pressure control, and model two added diabetes or blood pressure medication use at year 4. The weight loss–trajectory cluster was the reference group. We considered $P < 0.05$ to be statistically significant.

RESULTS—When estimating weight trajectories, we found that the quadratic model fit significantly better than the linear model ($P < 0.0001$). Therefore, three variables representing an individual's weight trajectory were included in the cluster analysis: intercept (estimated baseline weight), linear slope, and quadratic slope.

We found four weight-trajectory clusters (Figure 1). The group with a higher stable weight ($n = 418$; 16.2%) and the group with a lower stable weight ($n = 1,542$; 59.9%) largely maintained their weights. The weight-gain group ($n = 300$; 11.7%) began at a mean weight of 107.8 kg and gained weight until about 18 months, reaching a mean of 114.7 kg (6.4% gain; $P < 0.001$), followed by a

weight loss; ending mean weight was near baseline. The weight-loss group ($n = 314$; 12.2%) began at a mean weight of 109.3 kg and lost weight until about 18 months, reaching a mean of 98.6 kg (9.8% loss), followed by a regain to approximately baseline weight. Notably, the weight-gain and weight-loss groups began and ended at similar mean weights.

Table 1 compares baseline characteristics of the study subjects. The four groups were significantly different with respect to age, sex, baseline weight and BMI, race, diagnosed depression, and hypertension and blood pressure. Of note is that the mean baseline (year 1) A1C and the percent above goal were significantly different across groups and lower in the weight-loss compared with the weight-gain group.

Table 2—Glycemic and blood pressure in year 4 by 3-year weight change–trajectory pattern

	Higher stable weight	Lower stable weight	Weight loss	Weight gain	P*
A1C measurements					
n (%)	322 (16.9)	1,135 (59.4)	227 (11.9)	227 (11.9)	
Above-goal mean A1C (%)†	153 (47.5)	472 (41.6)	63 (27.8)	118 (52.0)	<0.0001
A1C (%)	7.2 ± 1.3 ^c	7.0 ± 1.2 ^{ad}	6.6 ± 1.1 ^{bcd}	7.3 ± 1.4 ^{ab}	<0.0001
Median (IQR)	6.9 (6.3–7.8)	6.8 (6.2–7.5)	6.4 (5.8–7.1)	7.0 (6.2–78.0)	
Mean A1C stratum (%)					<0.0001
<7	169 (52.5)	663 (58.4)	164 (72.2)	109 (48.0)	
7–8	87 (27.0)	277 (24.4)	41 (18.1)	59 (26.0)	
8–9	37 (11.5)	120 (10.6)	14 (6.2)	31 (13.7)	
≥9	29 (9.0)	75 (6.6)	8 (3.5)	28 (12.3)	
Blood pressure measurements					
n (%)	396 (16.4)	1447 (60.1)	285 (11.8)	281 (11.7)	
Above-goal mean blood pressure (mmHg)†	291 (73.5)	893 (61.7)	172 (60.4)	189 (67.3)	<0.0001
Systolic blood pressure (mmHg)	135.9 ± 12.9 ^{ab}	132.9 ± 14.0 ^a	131.6 ± 13.2 ^b	133.4 ± 13.3	<0.0001
Median (IQR)	135 (127–144)	132 (123–141)	131 (122–139)	132 (125–140)	
Diastolic blood pressure (mmHg)	80.1 ± 7.8 ^{ab}	77.1 ± 8.2 ^{bd}	77.4 ± 8.4 ^{ac}	79.3 ± 8.3 ^{cd}	<0.0001
Median (IQR)	80 (75–85)	77 (71–82)	79 (72–82)	80 (74–84)	
Mean systolic blood pressure stratum (mmHg)					0.0364
≤130	143 (36.1)	650 (44.9)	135 (47.4)	133 (47.3)	
130–139	110 (27.8)	389 (26.9)	81 (28.4)	69 (24.6)	
140–159	125 (31.6)	355 (24.5)	61 (21.4)	69 (24.6)	
≥160	18 (4.5)	53 (3.7)	8 (2.8)	10 (3.5)	
Mean diastolic blood pressure stratum (mmHg)					<0.0001
≤80	198 (50.0)	970 (67.0)	182 (63.9)	151 (53.7)	
80–89	155 (39.1)	385 (26.6)	82 (28.8)	104 (37.0)	
90–99	40 (10.1)	84 (5.8)	19 (6.6)	24 (8.6)	
≥100	3 (0.8)	8 (0.6)	2 (0.7)	2 (0.7)	

Data are n (%) and means ± SD unless otherwise indicated. *Comparison across all 4 groups. †Includes those with one or more measures during year 4. ^{abcd}Means with the same superscripts are significantly different from one another at $P < 0.05$. IQR, interquartile range.

Table 2 summarizes the unadjusted A1C and blood pressure results in year 4 by group. The weight-loss group had the lowest percentage of individuals with above-goal A1C (by year 4, the difference between it and other groups had become more prominent) and blood pressure and more favorable means and distributions of both measures. Metformin use in the weight-loss group remained stable (19.4% in year 1 vs. 23.6% in year 4), whereas use in the weight-gain group increased from 18.3% in year 1 to 41.3% in year 4 (data not shown).

Table 3 presents the logistic regression models comparing above-goal A1C in year 4 in the three other weight-change trajectories with that in the weight-loss group (limited to the 1,911 [74.2%] patients who had one or more A1C measures in both years 1 and 4). In the three models, the likelihood of above-goal A1C remained significantly higher among the groups with higher stable weight, lower stable weight, and weight gain than in the weight-loss

group. The magnitude of the effect is diminished by adding the covariates.

In the fully adjusted model 2, those with higher stable weight were 1.7 times more likely (95% CI 1.1–2.5) to have above-goal A1C than those in the weight-loss group, those with lower stable weight were 1.5 times more likely (1.1–2.1), and those with weight gain were 1.8 times more likely (1.2–2.7). Each year of age reduced the odds of above-goal A1C by 3% (odds ratio [OR] 0.97 [95% CI 0.96–0.98]). Those with above-goal A1C at year 1 were 2.4 times more likely to be above goal at year 4 (95% CI 2.7–4.0).

When analyses were restricted to 1,599 patients with a true baseline A1C measure, the odds of above-goal A1C in year 4 were 2.3 (95% CI 1.4–3.7) times higher in the weight-gain group than in the weight-loss group. Also, baseline BMI alone (vs. trajectory membership) did not significantly predict above-goal A1C in year 4 (data not shown).

Table 3 also presents logistic regression models comparing above-goal blood pres-

sure in year 4 in the other weight-change trajectories to blood pressure in the weight-loss group (limited to the 2,410 [93.6%] patients who had one or more blood pressure measures in year 4). In the fully adjusted model 2, those with higher stable weight were 1.8 times more likely (95% CI 1.3–2.6) than those in the weight-loss group to have above-goal blood pressure, and those with weight gain were 1.5 times more likely (1.1–2.1). Each year of age increased the odds of being above goal by 2% (OR 1.02 [95% CI 1.01–1.03]). Those with above-goal blood pressure at year 1 were 2.9 times more likely to be above goal at year 4 (95% CI 2.4–3.6).

CONCLUSIONS—We found that 12.2% of people with type 2 diabetes in our population had a mean 3-year weight-change trajectory that included a clinically significant (9.8% at 18 months) (2) mean weight loss. Despite weight regain during the 3-year period, those who initially lost weight had improved glycemic and blood pressure control in year 4 com-

Table 3—Impact of 3-year weight change–trajectory pattern and covariates on above-goal A1C* and blood pressure† at year 4

	Unadjusted model			Adjusted model 1			Adjusted model 2		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
A1C outcome									
Weight trajectory clusters									
Higher stable weight	2.36	1.64–3.39	<0.0001	1.96	1.34–2.87	0.0006	1.66	1.12–2.47	0.0118
Lower stable weight	1.85	1.35–2.53	<0.0001	1.83	1.32–2.55	0.0003	1.52	1.08–2.14	0.0158
Weight gain	2.82	1.91–4.16	<0.0001	2.59	1.72–3.91	<0.0001	1.77	1.15–2.72	0.0094
Weight loss	1.00	—	—	1.00	—	—	1.00	—	—
Age (years)				0.97	0.96–0.98	<0.0001	0.97	0.96–0.98	<0.0001
Male sex				1.02	0.84–1.24	0.861	1.07	0.87–1.31	0.541
A1C above goal (year 1)				3.35	2.76–4.07	<0.0001	2.42	1.97–2.98	<0.0001
Oral hyperglycemic medication class year 4‡									
Metformin							1.54	1.14–2.08	0.0047
Sulfonylureas							2.16	1.67–2.81	<0.0001
Metformin and sulfonylureas							4.40	3.30–5.86	<0.0001
Neither sulfonylureas nor metformin							1.00	—	—
Insulin							2.25	1.41–3.59	0.0006
Blood pressure outcome									
Weight-trajectory clusters									
Higher stable weight	1.82	1.31–2.52	0.0003	1.84	1.32–2.58	0.0004	1.83	1.31–2.57	0.0004
Lower stable weight	1.06	0.82–1.37	0.666	1.05	0.80–1.37	0.736	1.05	0.80–1.38	0.710
Weight gain	1.35	0.96–1.90	0.088	1.47	1.03–2.09	0.0348	1.47	1.03–2.10	0.0347
Weight loss	1.00	—	—	1.00	—	—	1.00	—	—
Age (years)				1.02	1.01–1.03	0.0001	1.02	1.01–1.03	0.0008
Male sex				0.81	0.68–0.96	0.0169	0.81	0.68–0.97	0.0203
Blood pressure above goal (baseline)§				3.02	2.45–3.73	<0.0001	2.94	2.37–3.64	<0.0001
Blood pressure medication class year 4									
β-blockers							0.88	0.73–1.07	0.193
Diuretics							1.05	0.86–1.29	0.609
ACE inhibitor/ARB							1.04	0.86–1.25	0.691
Other antihypertensives							1.33	1.05–1.69	0.0194

*A1C models include the 1,911 (74.2%) patients who had one or more A1C measure in both years 1 and 4; above-goal is A1C \geq 7%. †Blood pressure models include the 2,409 (93.6%) patients that had one or more blood pressure measurement at both baseline and year 4; above-goal is \geq 130/80 mmHg. ‡These subgroups also contain 23 (1.2%) patients taking a thiazolidinedione or acarbose during year 4. No patients were taking repaglinide during year 4. §Baseline blood pressure control based upon mean in 12-month pre-index of <130/80 mmHg. ||Includes all remaining classes of medication used for hypertension. ARB, angiotensin receptor blocker.

pared with that in groups with stable or weight-gain trajectories. These findings suggest that, even in the face of weight regain (15), losing weight can have long-lasting benefits in type 2 diabetes. The therapeutic advantage achieved through weight loss is exceedingly important given the close connection between glycemic and blood pressure control (especially in the first years postdiagnosis) and cardiovascular outcomes (16,17).

Although helping patients achieve weight loss can be overwhelming (18), physicians can feel encouraged by the weight trajectories we observed in free-living people with type 2 diabetes during the 3 years after initial diagnosis. Some people achieved weight loss despite the fact that the study site, similar to many communities (18), directs fewer resources to weight loss than to monitoring

and medications. Practitioners frustrated by the frequency of weight regain (15) may be reinvigorated by our finding that weight regain in diabetes may not imply lack of therapeutic benefits of weight loss.

The weight-loss group, on average, began regaining at about 18 months. This suggests that the first months postdiagnosis may provide a window to capitalize on patient and clinician motivation by actively applying weight-loss interventions. However, additional support for maintaining weight loss will be important.

Recent findings from the Look AHEAD weight loss in diabetes study revealed that the intensive lifestyle intervention group lost, on average, 8.6% of their initial weight at 1 year, compared with 0.7% in the education control group (3). The magnitude of weight change noted in our community weight-losing cohort was

similar. At year 4, the absolute A1C and blood pressure differences between those who lost or gained weight were small but similar to differences observed between intervention and control subjects in Look AHEAD (3). The A1C effects seen here are clinically significant: prior studies have concluded that every percentage point reduction in mean A1C correlates with a 37% reduction in risk of microvascular complications and a 21% reduction in risk of any diabetes-related end point and diabetes-related deaths. No threshold has been observed for these risks (19). Risk of death from ischemic heart disease and stroke also increases progressively and linearly starting from blood pressure levels as low as 115/75 mmHg (20).

Last, our models controlling for medication use in year 4 may have provided conservative estimates of effects of weight

trajectories on A1C control, in that diabetes medication use likely also affects weight trajectories (21). The weight-loss group had little change in metformin use (often associated with weight loss) (21). Thus, medication use patterns cannot explain the improved trajectory and A1C patterns in the weight-loss group.

Our study has several limitations. The study was conducted at one HMO in two states, so findings may not be generalizable to other settings. We studied only survivors, so we do not know weight-change patterns for everyone or how they related to outcomes. However, our study was strengthened by access to many measures taken in a large group of community-based diabetes patients, including diagnostic data that might suggest unintentional weight change. Our data were collected during clinical care; thus, weight and other measurements may not have been as precise or complete as they would be during a clinical trial. For example, we did not have a true baseline A1C on all patients and, instead, used year 1 findings. However, this was a conservative approach, and findings were largely unchanged when analyses were restricted to those with a baseline measure.

We did not evaluate possible mechanisms that might explain the improved A1C and blood pressure control observed in the weight-loss group. The lasting benefit, in spite of weight regain, may derive from increased insulin sensitivity remaining from weight loss (22); mechanisms related to "metabolic memory" (23); lifestyle changes accompanying weight loss, such as improved diet or increased activity; or other unmeasured factors that differed among the weight-trajectory groups. We did not evaluate which behaviors led to weight change. These areas should be the focus of future research. Interestingly, the strength of the trajectory method is highlighted by the finding that baseline BMI alone did not significantly predict above-goal A1C in year 4.

We conclude that, in this analysis, a weight-loss trajectory predicted improved glycemic and blood pressure control when compared with stable-weight or weight-gain trajectories. In light of previously reported positive effects of weight loss on therapeutic outcomes in people with diabetes (3,17,19) and our added findings of the natural history of weight loss and outcomes in diabetes in the community, more focus should be placed on helping clinicians implement programs to

manage weight trajectories in new diabetic patients.

Acknowledgments—This study was supported by grant R21 DK073546-02 (Weight in Secondary Prevention) from the National Institute of Diabetes and Digestive and Kidney Diseases.

We thank Martha Swain for editorial assistance and Chalinya Bruce for administrative support.

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