LDL Reductions Following Weight Loss Are Blunted in Patients Who Regain the Weight

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Key Findings:

- Patients who sustained a ≥10% weight loss over 18 months had an average LDL reduction of 6.2 mg/dL, compared to 2.7 mg/dL among patients who had little to no weight change and 1.9 mg/dL among those who lost and then regained weight.
- LDL decrease of 10 mg/dL or more was achieved by 41% of the sustained-loss group, compared to 33% in the steady group and 34% in the regain group.
- LDL increases from baseline of ≥10 mg/dL were more common in the regain group (32%) than in the steady (29%) or loss (27%) groups, indicating that weight regain blunts and may reverse cholesterol benefits.

Obesity is a major modifiable risk factor for cardiovascular disease, and weight loss is associated with improvements in cardiovascular health, including cholesterol levels.[1] However, many patients experience weight cycling (substantial weight loss followed by regain), which might impact cardiovascular health.[2] While previous research highlights the benefits of sustained weight loss, less is known about the lipid profiles of individuals who regain lost weight.

To understand the effects of weight cycling, we studied 156,096 adult patients with an obese BMI who had at least three BMI measurements over an 18-month period that demonstrated specific patterns in weight change. Patients were categorized into three weight patterns: sustained loss (≥10% reduction that was not regained), steady (weight remained within ±2% of baseline throughout), and regain (initial ≥10% reduction followed by return near baseline). LDL values were compared from baseline result around the time of their first qualifying BMI to an LDL result around the third BMI measurement. Patients were matched based on age, sex, BMI classification, social vulnerability, comorbidities, and use of lipid-lowering medications.

We found that the average change in LDL differed by weight pattern. Patients in the sustained loss group had the largest average reduction, with LDL levels decreasing by 6.2 mg/dL. This contrasts with only a 1.9 mg/dL reduction in the regain group, despite similar initial weight loss, suggesting that cholesterol benefits attenuate quickly when weight is regained. Patients who maintained steady weight experienced a modest average decline of 2.7 mg/dL. The average LDL for all groups decreased, including those with stable weight, which might reflect underlying characteristics of the study population, such as increased likelihood of lipid management among those with repeat LDL testing. However, even within this potentially health-engaged subgroup, the gradient of LDL improvement across weight patterns suggests that the observed differences remain clinically meaningful.

Average LDL Difference by Weight Change Group

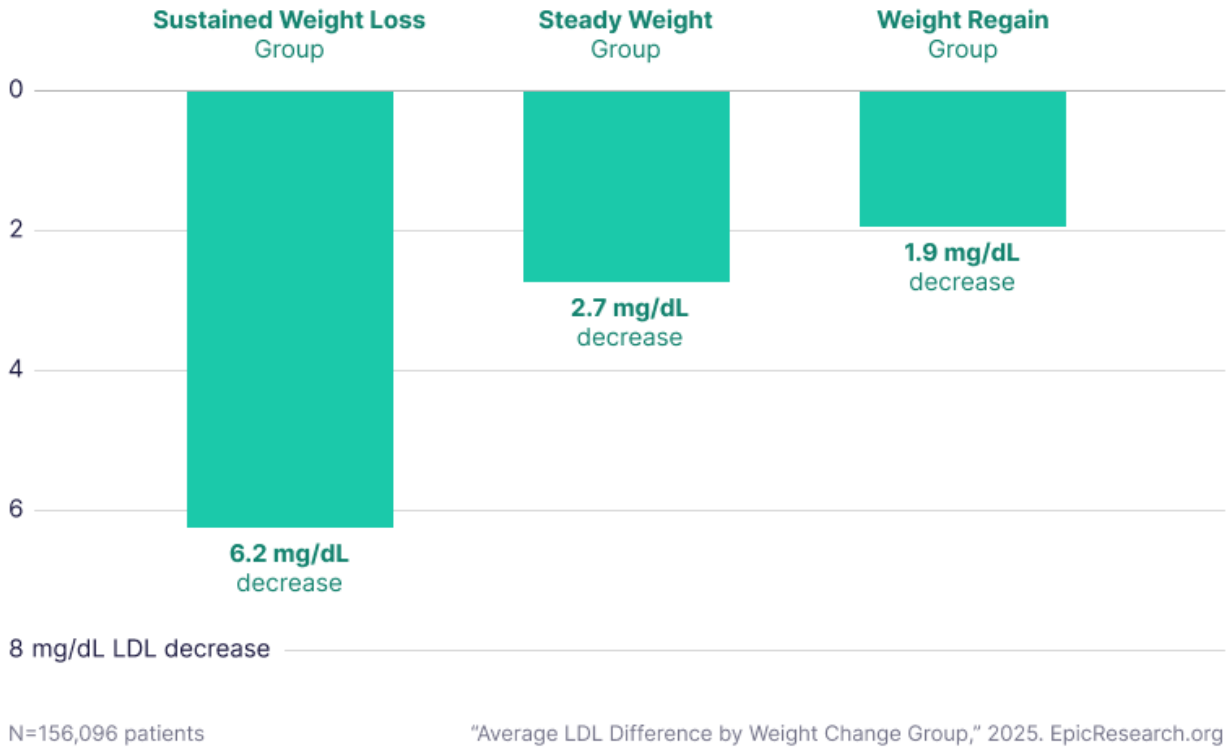

Figure 1. The average LDL difference by weight change group.

The distribution of LDL changes further contextualizes these average effects. Patients in the sustained loss group were more likely to experience large reductions in LDL, with a greater proportion achieving improvements of 10 mg/dL or more compared to the other groups: 41% of the loss group had LDL reductions of at least 10 mg/dL, compared to 33% in the steady group and 34% in the regain group. Patients in the regain group had a greater proportion experiencing LDL increases. Approximately 32% of regain patients had LDL increases of 10 mg/dL or more, compared to 29% of the steady group and 27% of the loss group. Previous research has shown that weight loss can lead to transient increases in LDL levels, which might be a factor contributing to the LDL increase among the sustained weight loss group.[3,4]

LDL Difference Distribution by Weight Change Group

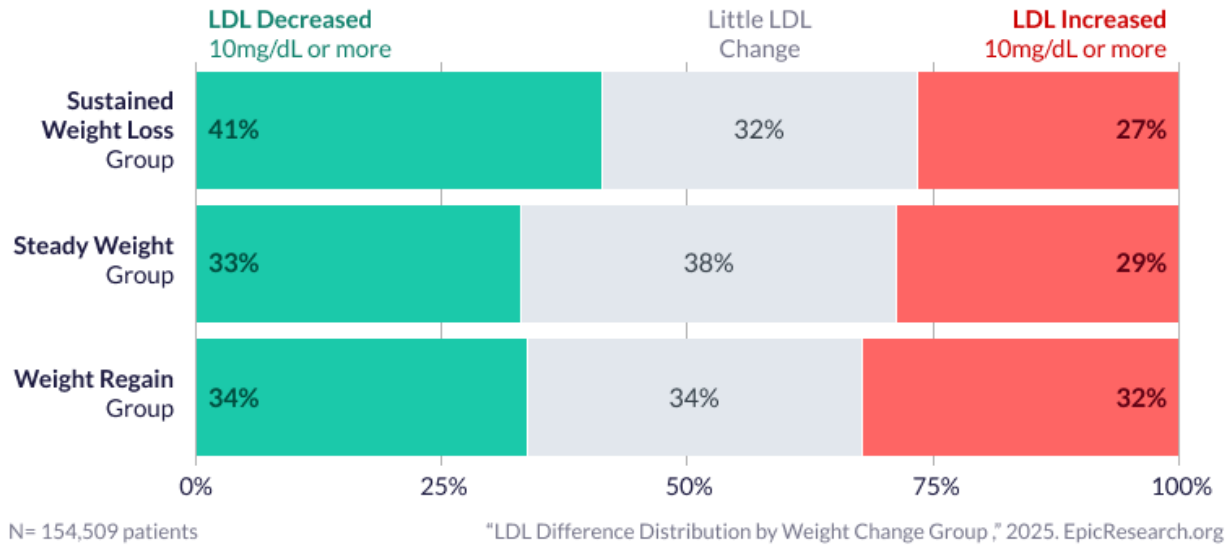

Figure 2. The distribution of LDL difference by weight change group.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 300 million patient records from 1,700 hospitals and more than 40,000 clinics from all 50 U.S. states, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

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2. Kakinami L, Knäuper B, Brunet J. Weight cycling is associated with adverse cardiometabolic markers in a cross-sectional representative US sample. J Epidemiol Community Health. 2020;74(8):662-667. doi:10.1136/jech-2019-213419
3. Surampudi, V., Biggs, K., & Li, Z. (2019). Weight loss and transient LDL increase (P12-057-19). Current Developments in Nutrition, 3(Suppl 1), nzz035.P12-057-19. https://doi.org/10.1093/cdn/nzz035.P12-057-19
4. Phinney, S. D., Tang, A. B., Waggoner, C. R., Tezanos-Pinto, R. G., & Davis, P. A. (1991). The transient hypercholesterolemia of major weight loss. The American Journal of Clinical Nutrition, 53(6), 1404–1410. https://doi.org/10.1093/ajcn/53.6.1404

Data Definitions

Term	Definition
Study period	1/1/2015 to 4/1/2025
Study population	Adult patients with: • A BMI of 30 or greater, another BMI reading 5-7 months later, and another 11-13 months later than the second reading

	• An LDL reading between one year before through two months after first qualifying BMI, using the latest if multiple • An LDL reading between two months before through one year after the third qualifying BMI, using the earliest if multiple Exclude patients with any of: 12 months before first BMI through 12 months after third BMI: Pregnancy: ICD-10-CM code O*, a pregnancy episode, or a birth record Between first BMI reading through final BMI **Amputations** Patients with any use of **medications with weight-related side-effects** during the observation period Patients with **weight-related conditions** Prior to end of observation: Cancer: C* (two incidences of the same parent level code (CXX) within a two-year period) Bariatric surgery: procedure with CPT code 43644, 43645, 43659, 43770, 43771, 43772, 43773, 43774, 43775, 43845, 43846, 43847, 43848, 43886, 43887, 43888, 43842, or 43843 Patients with any evidence of **noninfective enteritis or colitis** Any time: HIV: B20* Dementia/Alzheimer's disease: G30*, F01*, F02*, or F03*
Exposures	We select one sequence per patient that fit a pattern: • Steady: All three BMI readings were within +/- 2% of the baseline • Sustained loss: The mid and final BMI showed 10% loss from baseline • Regain: The mid BMI showed 10% loss from baseline and the final BMI showed reversion to -2% to +10% of the baseline Patients who did not meet one of the above buckets were excluded. When patients fit the pattern of multiple buckets at different times, we analyzed just their regain pattern if they had one. Otherwise, we analyzed their loss patterns.
Outcomes	Difference in **LDL** results between baseline and outcome value • Baseline value was the one closest to the initial BMI reading • Outcome value was taken between the third qualifying BMI through six months after, taking the closest to the BMI reading
Matching factors	Age • 18-34 • 35-49 • 50-64 • 65+ Legal sex Baseline BMI category • Class 1 Obese: 30-<35 • Class 2 Obese: 35-<40 • Class 3a Obese: 40-<45 • Class 3b Obese: 45+

	Social Vulnerability Index quintile Depression: ICD-10-CM code F32*, F33*, F06.31*, F06.32*, or F34.1* Diabetes: ICD-10-CM code E08*-E13* **Lipid-lowering medication** use during observation period
LDL	A lab result with LOINC code 13457-7, 18262-6, or 2089-1, excluding results outside of 30 to 400 mg/dL
Amputation	A diagnosis with ICD-10-CM code Z89.2*, Z89.6*, S78.011A, S98.011A, S78.012A, S98.012A, S78.019A, S98.019A, S78.021A, S98.021A, S78.022A, S98.022A, S78.029A, S98.029A, S78.111A, S98.111A, S78.112A, S98.112A, S78.119A, S98.119A, S78.121A, S98.121A, S78.122A, S98.122A, S78.129A, S98.129A, S78.911A, S98.131A, S78.912A, S98.132A, S78.919A, S98.139A, S78.921A, S98.141A, S78.922A, S98.142A, S78.929A, S98.149A, S88.011A, S98.211A, S88.012A, S98.212A, S88.019A, S98.219A, S88.021A, S98.221A, S88.022A, S98.222A, S88.029A, S98.229A, S88.111A, S98.311A, S88.112A, S98.312A, S88.119A, S98.319A, S88.121A, S98.321A, S88.122A, S98.322A, S88.129A, S98.329A, S88.911A, S98.911A, S88.912A, S98.912A, S88.919A, S98.919A, S88.921A, S98.921A, S88.922A, S98.922A, S88.929A, S98.929A Procedures with ICD-10-PCS code 0Y6[23478CDFGHJ]* or 0X6[012389BCDF]*
Noninfective enteritis or colitis	Chron's disease: ICD-10-CM K50* Ulcerative colitis: ICD-10-CM K51* Other: ICD-10-CM K52*
Medications with weight-related side effects	Glucocorticoids: Pharmaceutical class of "GLUCOCORTICOIDS" or a pharmaceutical subclass of "Glucocorticoids" and a route of "injection," "intra-articular," "intramuscular," "intravenous," or "oral" Diuretics: Pharmaceutical class with '*Diuretic*'
Weight-related conditions	Hypothyroidism: E03.9 Heart failure: ICD-10-CM code I50* or SNOMED codes 421518007, 56675007 Renal failure: N17*, N18*, or N19* Eating disorders: F50*
Lipid-lowering medication	Statin medications: a pharmaceutical subclass of "Antihyperlipidemic - HMG CoA Reductase Inhibitors (statins)" or "Antihyperlipidemic - HMG CoA Reductase Inhibitor and Niacin Comb" or a generic name of rosuvastatin calcium, simvastatin, atorvastatin calcium, pravastatin sodium, niacin/lovastatin, lovastatin, or fluvastatin sodium. Other lipid lowering medications: a pharmaceutical subclass of "Antihyperlipidemic - Bile Acid Sequestrants," "Antihyperlipidemic - Fibric Acid Derivatives," "Antihyperlipidemic - Selective Cholesterol Absorption Inhibitor," "Antihyperlipidemic - PCSK9 Inhibitors," "Antihyperlipidemic - ATP-Citrate Lyase (ACLY) Inhibitor," or "Antihyperlipidemic - Omega-3 Fatty Acid Type" or a generic name of alirocumab, evolocumab, inclisiran sodium, bempedoic acid, icosapent ethyl, omega-3 acid ethyl esters, niacin, cholestyramine, cholestyramine (with sugar), cholestyramine/aspartame, or cholestyramine/saccharin sod
Social Vulnerability Index	The social vulnerability quintile for the ZIP Code of the patient's most recent address

Table 1: Study Population Distributions

Characteristic	Overall	Loss	Regain	Steady
Patients	156,096	69,376	17,344	69,376
BMI 30-35	45%	45%	45%	45%
BMI 35-40	29%	29%	29%	29%
BMI 40-45	15%	15%	15%	15%
BMI 45 Plus	12%	12%	12%	12%
Avg Baseline BMI	37.9	38.9	37.3	37.1
Age 18-34	10%	10%	10%	10%
Age 35-49	26%	26%	26%	26%
Age 50-64	39%	39%	39%	39%
Age 65 Plus	25%	25%	25%	25%
Female	53%	53%	53%	53%
Male	47%	47%	47%	47%
SVI Q1	13%	13%	13%	13%
SVI Q2	19%	19%	19%	19%
SVI Q3	18%	18%	18%	18%
SVI Q4	21%	21%	21%	21%
SVI Q5	28%	28%	28%	28%
SVI None	1%	1%	1%	1%
Depression	32%	32%	32%	32%
Diabetes	39%	39%	39%	39%
Lipid Lowering Meds	53%	53%	53%	53%
GLP-1	14%	19%	11%	9%
Anorexiant	4%	6%	6%	2%
Anorexiant Or GLP-1	22%	27%	21%	17%
Baseline LDL Over100	51%	51%	50%	51%
Endpoint LDL Over100	46%	43%	48%	48%
IQR1 Baseline LDL	78.0	77.0	78.0	78.4
Median Baseline LDL	100.0	100.0	100.0	101.0
IQR3 Baseline LDL	125.0	125.0	124.0	125.0
IQR1 Endpoint LDL	73.0	71.0	75.0	75.0
Median Endpoint LDL	96.0	93.0	97.5	97.2
IQR3 Endpoint LDL	121.0	118.0	123.0	122.0
Baseline LDL Avg	103.1	103.2	102.5	103.2
Endpoint LDL Avg	98.9	96.9	100.6	100.5
LDL Delta Avg	(4.2)	(6.2)	(1.9)	(2.7)
Baseline LDL Std Dev	34.7	35.4	34.7	34.0
Endpoint LDL Std Dev	34.7	34.9	35.1	34.4
LDL Delta Std Dev	30.3	32.3	30.8	27.8