# Supplemental Online Content

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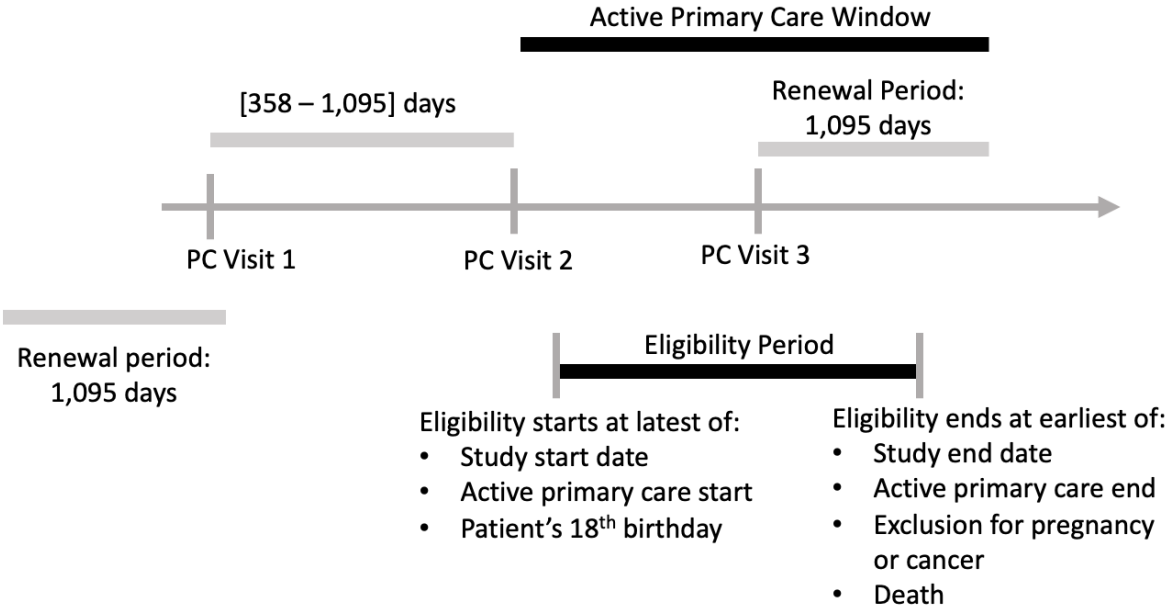
This supplemental material has been provided by the authors to give readers additional information about their work.

**eTable 1.** Procedure Codes Used for Pregnancy Exclusion

| Exclusion | Code Set | Codes |
|---|---|---|
| *Pregnancy* | | |
| Antepartum visits | CPT4 | 0500F, 0501F, 0502F, 0503F |
| Postpartum Visits | CPT4 | 0503F, 59430 |
| Delivery | CPT4 | 594xx, 595xx, 596xx, 598xx |




**eFigure 1.** Schematic Illustrating Time Periods Related to Cohort Selection

**eMethods.** Primary Care Cohort Selection

Active Primary Care

In this section we provide additional detail on how we identified periods of active primary care using data on primary care visits from the EHR. First, we identified all primary care visits between October 1, 2012, and March 23, 2020. We defined primary care visits as completed visits with a primary care provider, based on the provider's designated provider type.

Next, we identified all instances in which a patient had two primary care visits separated by [358 – 1,095] days. For each such instance, we defined the day of the second primary care visit as an index date. Then, using a renewal period of 1,095 days (~3 years), we identified periods of active primary care ending 1,095 days after the final primary care visit within the renewal period. Therefore, patients with active primary care all had at least two initial primary care visits separated by ≥ 358 days and had at least one primary care visit in the prior 3 years (1,095 days). See eFigure 1.

Cohort Eligibility

Patients were eligible for study inclusion during a period of active primary care. The start of each patient's eligibility period was the latest date among the beginning of the study period (October 1, 2015), the start of their active primary care window, or their 18$^{th}$ birthday. Likewise, the end of each patient's eligibility period was the earliest of the end of their active primary care window, the study period end date (March 23, 2020), or death. We initially included patients with ≥ 90 days of active primary care after these truncations and used the longest such window from patients with more than qualifying instance.

Exclusion Criteria

After identifying windows of active primary care as just described we excluded patients without 2 valid body mass index measurements (BMI) ≥ 90 days apart, with the valid range considered 12-100 kg/m$^2$. Next, we additional excluded patients with evidence of pregnancy or metastatic cancer by truncating their period of eligibility (active primary care window) using the following rules. We excluded potentially pregnant patients and patients with metastatic cancer because we considered the potential weight changes associated with these conditions outside the scope of this study. For pregnancy, we truncated eligibility at the earlier of 10 weeks before an

antepartum visit, 40 weeks before a delivery, or 44 weeks before a postpartum visit. For cancer, we truncated eligibility 6 months prior to the first evidence. After truncation, we excluded patients without at least 2 valid BMI measurements ≥ 90 days apart. We identified pregnancy related visits using Current Procedural Terminology (CPT4) codes; see eTable 1. We identified metastatic cancer using a pre-built flag based on the Elixhauser comorbidity index in our research data warehouse.

*Weight Management Treatment Definitions*

In this section we elaborate on the weight management treatment definitions.

Nutrition Counseling by a Registered Dietitian

We defined exposure to nutrition counseling by a Registered Dietitian (RD) using department and clinic names from visit data. In cross-sectional analyses we counted the number of unique days with visits during the follow-up periods. In the trajectory analysis, the time-varying nutrition counseling exposure is a flag representing whether a patient had one or more nutrition counseling visits in the prior 90 days.

Anti-Obesity Medications

We used provider orders to identify patients with exposure to AOMs, including orlistat, liraglutide, fixed-combination naltrexone/bupropion, and fixed-combination phentermine/topiramate. To account for off-label prescribing of brand name medications, we also included any overlapping exposures to either phentermine and topiramate or bupropion and naltrexone. We identified prescriptions from orders data using both generic and name brand drug names. The prescribed quantity of AOMs, including any refills, and the defined daily dose were used to construct an estimate of the number of days ordered. We assumed patients began taking the medication the day it was ordered and defined a patient as exposed to a medication for the

estimated number of active prescription days. Patients were assumed to have continuous exposure to a medication if there were fewer than 14 days between the expiration of one order and the start of the next.

Very low-calorie meal replacement

We identified patients participating in a very low-calorie meal replacement (MR) program using visits at the program location with program providers. This is a 24-month program, consisting of an initial and interval visits with a program physician, regular meetings with a program RD, physical activity recommendations, an initial intensive energy restriction phase of 800-900 kcal/d in the form of MR products (shakes +/- soups) for 3 months, and a gradual transition to a low calorie conventional food based diet.(cite) We considered patients active participants starting from their first visit with an RD at the program site, provided they had a visit with a program physician in the prior 90 days. We continued to consider patients active for any period over the subsequent two years in which they had a visit with any program provider (either an RD or physician) in the prior 90 days. Exposure to the MR program was divided into an "early" phase consisting of the first 6 months of engagement and a "late" phase encompassing months 6-24.

Bariatric Surgery

We identified bariatric surgery using procedure codes as detailed in eTable 4. When treated as an outcome in the cross-sectional analysis, we excluded patients with prior bariatric surgery. In the trajectory analysis, the time-varying bariatric surgery exposure was divided into indicators representing distinct periods after surgery: [0-90) days, [90-180) days, [180-365) days and $\geq$ 365 days.

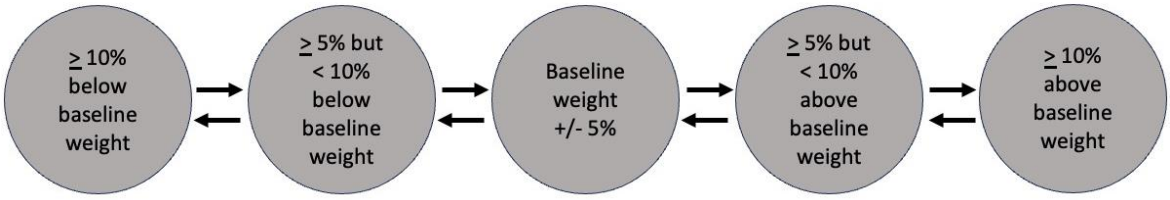
**eTable 2.** *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* and *International Classification of Diseases, Ninth Revision* Diagnosis Codes for Weight-Related Conditions

| Condition | ICD-10 | ICD-9 |
|---|---|---|
| Non-alcoholic fatty liver disease | K7581, K760, K740, K769 | 571.5, 571.8, 571.9 |
| Obstructive sleep apnea | G4730, G4733, G4739 | 780.53, 780.57 |
| Hyperlipidemia | E78.0, E78.00, E78.01, E78.1, E78.2, E78.2, E78.4, E78.41, E78.49, E78.5 | 272.0, 272.1, 272.2, 272.3, 272.4 |
| Hypertension | H35031, H35.032, H35.033, H35.039, I10, I11.0, I11.9, I12.0, I12.9, 113.0, I13.10, I13.11, I13.2, I14.0, I15.1, I15.2, I15.8, I15.9, I67.4, N26.2 | 362.11, 401.0, 401.1, 401.9, 402.01, 402.11, 402.90, 402.91, 403.00, 403.01, 403.10, 403.11, 403.90, 403.91, 404.00, 404.01, 404.02, 404.03, 404.10, 404.11, 404.12, 404.13, 404.90, 404.91, 404.92, 404.93, 405.01, 405.09, 405.11, 405.19, 405.91, 405.99, 437.2 |
| Type 2 Diabetes Mellitus | E11 (all codes) | 250.00, 250.02, 250.10, 250.12, 250.20, 250.22, 250.30, 250.32, 250.40, 250.42, 250.50, 250.52, 250.60, 250.62, 250.70, 250.72, 250.80, 250.82, 250.90, 250.92 |

**eTable 3.** Procedure Codes Used to Identify Weight Loss Surgery

| Procedure | Code Set | Codes |
|---|---|---|
| Weight loss surgery | CPT4 | 43644, 43645, 43770, 43775, 43842, 43843, 43846, 43847, 43845, 43848 |

*Multistate Markov Models*




**eFigure 2.** Illustration of Weight-Loss Status States Used in the Multistate Markov Model (MSM)
Circles represent weight-loss statuses observed within the electronic health record computed as percentages of each patient's baseline weight. Arrows represent transitions or changes in status which (here) are only allowed between adjacent states. The Markov model estimates the rates of transitions which depend on covariates which include time-varying exposures to weight loss treatment and baseline demographics. Conditional on being in one of these 5 states at a given point in time, the probabilities of being in any of the 5 states at a specific time in the future is computed by integrating over all possible transition combinations during the intervening time. In practice this is expressed through a mathematical concept known as matrix exponentiation and through algorithms for approximating these.

The longitudinal analysis of patients' weight status trajectories in this paper uses a Multistate Markov Model (MSM). Here "multistate" refers to one of 5 "states" representing a patient's weight status relative to baseline. These 5 states are illustrated in eFigure2. Each time a patient's weight is measured by the health system during their follow-up period we observe their weight status – or state – at that point in time, by comparing the weight measurement to their baseline weight.

In a traditional time-to-event or survival analysis the dependent variable is the timing of *transitions* from one state to another, e.g. the timing of a patient achieving 5% weight loss and transitioning from the "baseline +/- 5%" state to "≥ 5% but < 10% below baseline state". However, such models generally assume we observe the timing of the transition directly rather than observing their weight status or state at arbitrary times as we do here. Data like ours are known as *current-status* data and can be modeled using MSMs.

The “Markov” in Multistate Markov model refers to the Markov property – an assumption that the probability of each future state depends only on the current state and exposures and not on prior states. The instantaneous probabilities of transitions between adjacent states – or hazards – are modeled on the log-scale. The log hazards – or intensities – depend linearly on baseline covariates and time-varying exposures. The coefficients expressing this dependence are estimated using maximum likelihood. The likelihood is calculated from the probability of a patient being in observed states at observed times. Because of the Markov property, this likelihood is a product of successive pairs of observed states for each patient. The probability that a patient in state $x$ at time $t$ is in state $y$ at time $s$, is computed by integrating over all combinations of transitions leading from state $x$ to state $y$ in time $s - t$. Although there are infinitely many combinations of transitions, the integral can be expressed as a matrix exponential for which there exist approximation algorithms.

**eTable 4.** Demographics for Serial Cross-Sections Analysis

| Variable | Both, N (%) | 2017 only, N (%) | 2019 only, N (%) | Change (95% CI); p-value (2019 only less 2017 only) |
|---|---|---|---|---|
| Total, N | 76,277 | 33,267 | 29,138 | - |
| Age, mean (IQR) | 53.1[1] (42.4-64.9) | 48.8 (32.2-63.2) | 48.5 (32.7-62.9) | -0.26 (-0.55 to 0.04); p = 0.09 |
| Gender | | | | p < 0.001 |
| Female[2] | 43,239 (56.7) | 19,382 (58.3) | 16,188 (55.6) | -2.7 (-3.5 to -1.9) |
| Male | 33,038 (43.3) | 13,885 (41.7) | 12,950 (44.4) | 2.7 (1.9-3.5) |
| Race | | | | p < 0.001 |
| American Indian or Alaska Native | 308 (0.4) | 108 (0.3) | 137 (0.5) | 0.1 (0.0-0.2) |
| Asian | 4,585 (6.0) | 2,016 (6.1) | 1,818 (6.2) | 0.2 (-0.2 to 0.6) |
| Black or African American | 7,584 (10.3) | 2,943 (8.8) | 2,943 (10.1) | 1.3 (0.8-1.7) |
| Native Hawaiian or Other Pacific Islander | 57 (0.1) | 34 (0.1) | 14 (0.0) | -0.1 (-0.1 to -0.0) |
| White or Caucasian | 60,432 (79.2) | 26,807 (80.6) | 22,901 (78.6) | -2.0 (-2.6 to -1.4) |
| Other[3] | 3,041 (4.0) | 1,359 (4.1) | 1,325 (4.5) | 0.5 (0.1-0.8) |
| Ethnicity | | | | p < 0.001 |
| Hispanic | 2,156 (2.8) | 981 (2.9) | 1,088 (3.7) | 0.8 (0.5-1.1) |
| Non-Hispanic | 70,664 (92.6) | 30,818 (92.6) | 27,202 (93.4) | 0.7 (0.3-1.1) |
| Unknown | 3,457 (4.5) | 1,468 (4.4) | 848 (2.9) | -1.5 (-1.8 to -1.2) |
| Type-2 Diabetes | 1,608 (2.1) | 485 (1.5) | 1,824 (6.3) | 4.8 (4.5-5.1); p < 0.001 |
| Hyperlipidemia | 7,080 (9.3) | 1,624 (4.9) | 441 (1.5) | -3.4 (-3.6 to -3.1); p < 0.001 |
| Hypertension | 11,265 (14.8) | 2,896 (8.7) | 645 (2.2) | -6.5 (-6.8 to -6.1) |
| Non-alcoholic fatty liver disease | 937 (1.2) | 354 (1.1) | 40 (0.1) | -0.9 (-1.0 to -0.8); p < 0.001 |
| Obstructive sleep apnea | 294 (0.4) | 85 (0.3) | ≤ 11 (< 0.1) | -0.2 (-0.3 to -0.2); p < 0.001 |

1. Age are at time of BMI measurement, with age at the 2017 measurement used for 'Both'.
2. ≤11 individuals with undefined gender grouped with Female.
3. Includes Other, Patient Refused, and Unknown.

**eTable 5.** Unique Patients and Time at Risk by Exposure and State

| | **Weight Category State, n (person years at risk)** | | | | | |
|---|---|---|---|---|---|---|
| Exposure | **≥ 10% loss** | **5-10% loss** | **Baseline** | **5-10% gain** | **≥ 10% gain** | **Total** |
| Total | 2,800 (2,855) | 4,590 (3,331) | 10,180 (22,646) | 3,776 (3,138) | 1,663 (1,580) | 10,180 (33,549) |
| Weight Status Measures, n | 29,182 | 30,613 | 174,367 | 28,311 | 15,952 | 278,425 |
| *Controls* | | | | | | |
| Male | 916 (851) | 1,585 (1,164) | 3,536 (8,263) | 1,160 (960) | 453 (430) | 3,536 (11,700) |
| 1 PCP visit in past 365 days | 1,427 (603) | 2,190 (811) | 7,684 (6,018) | 2,115 (817) | 918 (387) | 8,486 (8,660) |
| 2 PCP visits in past 365 days | 2,401 (2,051) | 3,871 (2,252) | 9,437 (14,640) | 3,118 (2,013) | 1,345 (1,038) | 9,697 (22,054) |
| *Weight Management Treatments* | | | | | | |
| ≥1 Nutrition Counseling Appointment in prior 90 days | 252 (81) | 572 (139) | 2,702 (895) | 555 (127) | 242 (63) | 3,397 (1,316) |
| Low calorie meal replacement - Early Active | 82 (27) | 104 (19) | 164 (34) | 40 (4) | 24 (3) | 189 (88) |
| Low calorie meal replacement - Late Active | 65 (37) | 47 (12) | 45 (14) | ≤ 11 (< 1) | ≤ 11 (< 1) | 111 (66) |
| Weight management medications | 240 (116) | 359 (116) | 1,048 (450) | 300 (81) | 166 (55) | 1,428 (821) |
| *Days Since Bariatric Surgery* | | | | | | |
| 1-90 | 341 (45) | 330 (34) | 354 (33) | 57 (3) | 29 (3) | 520 (119) |
| 91-180 | 372 (82) | 101 (17) | 50 (8) | - | - | 446 (107) |
| 181-365 | 403 (171) | 67 (12) | 25 (5) | - | - | 428 (189) |
| > 365 (weight loss states) | 321 (410) | 53 (23) | - | - | - | 330 (432) |
| > 90 (baseline) | - | - | 62 (22) | - | - | 62 (22) |

**eTable 6.** Odds Ratios From Propensity Score Model for Probability of Prospective Weight Management Treatment Exposure

| Characteristic | Odds Ratio (95% CI) |
|---|---|
| Intercept, probability | 0.01(0.01-0.02) |
| Age (decades)[1] | 0.86 (0.84-0.88) |
| Baseline BMI (kg/m$^2$) | 1.06 (1.05-1.06) |
| Male | 0.67 (0.63-0.72) |
| *Race*[2] | |
| Asian | 1.25 (1.01-1.56) |
| Black or African American | 1.09 (1.01-1.19) |
| Other[3] | 1.09 (0.91-1.31) |
| Unknown or Patient Refused | 0.92 (0.67-1.01) |
| *Weight-related conditions* | |
| Hyperlipidemia | 1.46 (1.32-1.61) |
| Hypertension | 1.29 (1.19-1.41) |
| Non-alcoholic fatty liver disease | 1.07 (0.85-1.35) |
| Obstructive Sleep Apnea | 0.70 (0.46-1.05) |
| Type 2 Diabetes Mellitus | 2.11 (1.82-2.44) |
| Follow Up[3] (years) | 1.70 (1.65-1.75) |

BMI = Body Mass Index, CI = Confidence Interval

[1] Age is centered at the mean of 51.9 years and scale by 10 to represent decades.

[2] Reference category is White or Caucasian.

[3] Follow up is centered at a mean of 2.68 years.

[4] American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, Other, Multiple

**eTable 7.** Balance Assessment for Propensity Matching

In this table we assess covariate balance after propensity matching patients with weight management treatment exposures to those without. Matching was 1:1 and done within 16 strata defined by 4 binary variables: gender, race (White vs non-white), ethnicity (Hispanic vs non-Hispanic/unknown), and presence of any obesity related condition (hyperlipemia, hypertension, non-alcoholic fatty liver disease, obstructive sleep apnea or type 2 diabetes). By design, the cohorts were perfectly balanced by gender, White race, and Hispanic ethnicity. A Kolmogorov-Smirnov test failed to identify differences in the distributions of the linear predictors for the propensity (D = 0.002, p = 1.00).

| **Characteristic** | **WMT Exposed, N (%)** | **No WMT Exposure, N (%)** | **Standardized Mean Difference** |
|---|---|---|---|
| Baseline Age, mean (sd) | 49.9 (13.9) | 48.6 (15.0) | 0.092 |
| Baseline BMI, mean (sd) | 38.7 (7.1) | 38.9 (7.6) | -0.029 |
| Days at risk, mean (sd) | 1213.7 (399.2) | 1187.1 (399.5) | 0.066 |
| *Ethnicity* | | | |
| Non-Hispanic | 4,705 (92.4) | 4,754 (93.4) | -0.038 |
| Unknown | 185 (3.6) | 136 (2.7) | 0.055 |
| *Self-reported Race* | | | |
| Black or African American | 878 (17.2) | 863 (17.0) | 0.008 |
| Asian | 98 (1.9) | 91 (1.8) | 0.010 |
| Other | 209 (4.1) | 226 (4.4) | -0.017 |
| Unknown | 46 (0.9) | 51 (1.0) | -0.010 |
| *Obesity-Related Conditions* | | | |
| Hyperlipidemia | 674 (13.2) | 656 (12.9) | 0.010 |
| Hypertension | 1,160 (22.8) | 1,172 (23.0) | -0.006 |
| Non-alcoholic fatty liver disease | 88 (1.7) | 112 (2.2) | -0.034 |
| Obstructive Sleep Apnea | 28 (0.6) | 23 (0.5) | 0.014 |
| Type 2 Diabetes | 260 (5.1) | 306 (6.0) | -0.039 |

WMT = Weight Management Treatment

**eTable 8.** Hazard Ratios for Control Covariates
This table contains hazard ratios and 95% confidence intervals for control covariates from the multistate trajectory model described in the main paper. Hazard ratios for primary weight management treatment exposures are given in Table 2 of the main manuscript.

| Transition | Male | Age (1 SD) | Baseline BMI (per 5 kg/m$^2$) | 365-day PCP visits (0-2) |
|---|---|---|---|---|
| *Weight Loss Transitions* | | | | |
| 5-10% loss to > 10% loss | 1.07 (1.00-1.15) | 0.92 (0.89, 0.95) | 1.07 (1.04, 1.09) | 1.27 (1.18-1.35) |
| baseline to 5-10% loss | 1.07 (1.02-1.12) | 0.98 (0.96, 1.01) | 1.08 (1.07, 1.10) | 1.25 (1.20-1.31) |
| 5-10% gain to baseline | 1.09 (1.03-1.16) | 1.05 (1.01, 1.08) | 1.02 (1.00, 1.04) | 1.24 (1.18-1.31) |
| > 10% gain to 5-10% gain | 1.03 (0.93-1.14) | 1.29 (1.22, 1.35) | 1.06 (1.02, 1.09) | 1.24 (1.14-1.36) |
| *Weight Gain Transitions* | | | | |
| > 10% loss to 5-10% loss | 1.27 (1.17-1.38) | 1.01 (0.96-1.05) | 0.96 (0.93-0.98) | 1.19 (1.09-1.28) |
| 5-10% loss to baseline | 1.13 (1.07-1.20) | 0.88 (0.86-0.91) | 0.99 (0.97-1.01) | 1.28 (1.21-1.35) |
| baseline to 5-10% gain | 0.85 (0.81-0.90) | 0.73 (0.71-0.75) | 0.97 (0.96-0.99) | 1.18 (1.13-1.24) |
| 5-10% gain to > 10% gain | 0.91 (0.83-0.99) | 0.81 (0.78-0.85) | 0.97 (0.94-0.99) | 1.36 (1.26-1.46) |

**eTable 9.** Marginal Effects and Observed Population Attributable Fractions for Individual Weight Management Treatments (WMT)

We estimated the marginal effect of each class of WMT as utilized during the study period by comparing to a counterfactual assuming no patients receive that class of WMT, while holding other WMTs and control covariates fixed. Estimate are averaged over 47,280 patients with obesity and a full year of follow up from baseline. The observed population attributable fraction is the marginal effect over the reference probability from WMT use as observed.

| **WMT Counterfactual** | **Average Probability of ≥ 5% weight loss, % (95% CI)** | **Marginal effect, % (95% CI)** | **Population Attributable Fraction, % (95% CI)** |
|---|---|---|---|
| WMT as observed | 17.57 (17.13-18.04) | - | - |
| No WMT use | 17.08 (16.64-17.56) | 0.50 (0.48-0.52) | 2.81 (2.64-2.96) |
| No nutrition counselling | 17.49 (17.05-17.96) | 0.08 (0.06-0.10) | 0.47 (0.36-0.58) |
| No meal replacement | 17.51 (17.06-17.98) | 0.07 (0.06-0.08) | 0.39 (0.34-0.43) |
| No anti-obesity medications | 17.54 (17.09-18.01) | 0.04 (0.03-0.05) | 0.22 (0.17-0.26) |
| No bariatric surgery | 17.27 (16.83-17.74) | 0.30 (0.30-0.31) | 1.73 (1.66-1.79) |

WMT = Weight Management Treatment