Effectiveness of Combining Antiobesity Medication With an Employer-Based Weight Management Program for Treatment of Obesity
A Randomized Clinical Trial

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Abstract

IMPORTANCE The clinical efficacy of antiobesity medications (AOMs) as adjuncts to lifestyle intervention is well characterized, but data regarding their use in conjunction with workplace wellness plans are lacking, and coverage of AOMs by US private employers is limited.

OBJECTIVE To determine the effect of combining AOMs with a comprehensive, interdisciplinary, employer-based weight management program (WMP) compared with the WMP alone on weight loss, treatment adherence, and work productivity and limitations.

DESIGN, SETTING, AND PARTICIPANTS This 1-year, single-center, open-label, parallel-group, real-world, randomized clinical trial was conducted at the Cleveland Clinic's Endocrinology and Metabolism Institute in Cleveland, Ohio, from January 7, 2019, to May 22, 2020. Participants were adults with obesity (body mass index [BMI; calculated as weight in kilograms divided by height in meters squared] ≥30) enrolled in the Cleveland Clinic Employee Health Plan.

INTERVENTIONS In total, 200 participants were randomized 1:1, 100 participants to WMP combined with an AOM (WMP+Rx), and 100 participants to WMP alone. The WMP was the Cleveland Clinic Endocrinology and Metabolism Institute's employer-based integrated medical WMP implemented through monthly multidisciplinary shared medical appointments. Participants in the WMP+Rx group initiated treatment with 1 of 5 US Food and Drug Administration–approved medications for chronic weight management (orlistat, lorcaserin, phentermine/topiramate, naltrexone/bupropion, and liraglutide, 3.0 mg) according to standard clinical practice.

MAIN OUTCOMES AND MEASURES The primary end point was the percentage change in body weight from baseline to month 12.

RESULTS The 200 participants were predominately (177 of 200 [88.5%]) women, had a mean (SD) age of 50.0 (10.3) years, and a mean (SD) baseline weight of 105.0 (19.0) kg. For the primary intention-to-treat estimand, the estimated mean (SE) weight loss was −7.7% (0.7%) for the WMP+Rx group vs −4.2% (0.7%) for the WMP group, with an estimated treatment difference of −3.5% (95% CI, −5.5% to −1.5%) (P < .001). The estimated percentage of participants achieving at least 5% weight loss was 62.5% for WMP+Rx vs 44.8% for WMP (P = .02). The rate of attendance at shared medical appointments was higher for the WMP+Rx group than for the WMP group. No meaningful differences in patient-reported work productivity or limitation measures were observed.

CONCLUSIONS AND RELEVANCE Clinically meaningful superior mean weight loss was achieved when access to AOMs was provided in the real-world setting of an employer-based WMP, compared

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with the WMP alone. Such results may inform employer decisions regarding AOM coverage and guide best practices for comprehensive, interdisciplinary employer-based WMPs.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03799198

Introduction

Obesity, a growing public health threat, poses significant health and economic burdens. The estimated prevalence of obesity among US adults of 42.4% in 2017 to 2018 is projected to increase to 48.9% by 2030. Associated with increased mortality and substantial morbidity from a multitude of diseases, obesity is the largest contributor to chronic disease burden in the US. In 2016, the estimated economic burden attributable to overweight and obesity in the US was $480.7 billion in direct health care costs and $1.24 trillion in indirect costs due to lost productivity. Much of this burden affects employers. As health care purchasers for most US employees (56%), employers face both the direct and indirect economic burdens of obesity.

Lifestyle interventions (eg, reduced caloric intake or increased physical activity) are the foundation of obesity prevention and treatment, but this conventional approach is often limited in its effectiveness, and most people with obesity struggle to achieve and maintain clinically meaningful weight loss. Medications approved by the US Food and Drug Administration (FDA) for chronic weight management, antiobesity medications (AOMs), can be useful adjuncts to lifestyle interventions. Although data showing the clinical efficacy of AOMs are robust, data regarding their use in conjunction with workplace wellness plans are lacking, and coverage of AOMs by US private employers is limited. Unlike other chronic diseases, employers must opt in to include AOMs in employee health care, even when AOMs are on formulary.

Pragmatic study designs can bridge the gap between clinical trials and clinical practice, providing valuable real-world effectiveness evidence, with the rigor of randomized clinical trials (RCTs), to inform treatment decisions of payers, clinicians, employers, and patients. To our knowledge, this is the first pragmatic RCT addressing an evidence gap of the real-world effectiveness of AOMs by examining the effect of access to AOMs on weight loss, weight management program (WMP) adherence, and work productivity and work limitations of AOM access within a comprehensive, interdisciplinary employer-based WMP.

Methods

Study Design

This was a 1-year, single-center, open-label, parallel-group, real-world, pragmatic RCT comparing an employer-based integrated medical WMP combined with AOM therapy (hereafter referred to as WMP+Rx) with the WMP alone among participants with obesity. The study was conducted at the Cleveland Clinic’s Endocrinology and Metabolism Institute in Cleveland, Ohio, from January 7, 2019, to May 22, 2020. The Consolidated Standards of Reporting Trials (CONSORT) reporting guideline for RCTs was followed. The Cleveland Clinic institutional review board approved the study protocol, which is available in Supplement 1. Participants provided written informed consent prior to participation. No one received compensation or was offered any incentive for participating in this study; however participants were eligible for copayment reimbursement according to the Cleveland Clinic’s health plan predefined compliance criteria for the WMP.
Study Population
Eligible participants included adults (aged ≥18 years) with obesity (body mass index [BMI; calculated as weight in kilograms divided by height in meters squared] ≥ 30) enrolled in the Cleveland Clinic Employee Health Plan. Key exclusion criteria included contraindications to all US FDA-approved AOMs (precluding prescription of AOM of any type), prior (≥ 90 days) treatment with any medication with the intention of weight loss, previous or current participation in this specific WMP, history of or plans during the study period for bariatric surgery or use of minimally invasive weight loss devices, history of type 1 or type 2 diabetes, or glycated hemoglobin (hemoglobin A1c) 6.5% or higher of total hemoglobin (to convert to proportion of total hemoglobin, multiply by 0.01). To comply with reporting requirements, participants self-identified with protocol-defined race and ethnicity categories.

Randomization and Interventions
Eligible participants were randomized 1:1 via centralized allocation to either WMP+Rx or WMP. The WMP was administered through monthly shared medical appointments (SMAs), a concept based on the chronic care model18 that combines group appointments for up to 10 patients in a multidisciplinary approach, consisting of encounters with a nutritionist, endocrinologist or obesity medicine specialist, and an ancillary team including nursing staff.19-22 The first study visit (baseline) included a comprehensive 1-on-1 evaluation with a physician, development of an individualized treatment plan, and diet selection (protein-sparing–modified fast, Mediterranean diet, or meal replacement), followed by a shared appointment with a nutritionist. Participants received dietary guidance but were responsible for their own meals, including payment of meal replacement products as applicable. All participants were offered a referral to an exercise physiologist; mental health or sleep clinic referrals occurred as applicable. After the baseline visit, participants attended 12 monthly SMA study visits that focused on accomplishing a healthier lifestyle and addressed the 5 components of the WMP: (1) nutrition; (2) physical activity; (3) appetite control; (4) sleep issues; and (5) anxiety, depression, and/or stress. Per the Cleveland Clinic Employee Health Plan, all participants were responsible for applicable specialty visit copayments and were eligible for copayment reimbursement according to predefined WMP compliance criteria.

Participants randomly assigned to WMP+Rx received a prescription for 1 of the following US FDA-approved AOMs at study initiation: orlistat, lorcaserin or lorcaserin extended release, phentermine-topiramate extended release, naltrexone-bupropion extended release, or liraglutide, 3.0 mg. Medication selection and subsequent management, including dose, dose escalation, medication switches, and temporary or permanent discontinuations throughout the study, were conducted per routine clinical practice. Participants received monthly AOM prescriptions at their SMAs and were responsible for a $25 fee simulating a typical copayment. Lorcaserin was withdrawn from the market on February 13, 2020.23 The 8 participants receiving lorcaserin at the time were notified immediately and either switched (n = 4) or discontinued (n = 4) AOM use owing to proximity to the end of the study. Other than the AOM prescribed for WMP+Rx, use of any medication for the primary intent of weight loss was not allowed in either treatment group.

Study End Points and Assessments
The primary end point was percentage change in body weight from baseline to month 12. Secondary end points included the percentage of participants who achieved at least 5% and at least 10% reduction in weight from baseline to month 12, the number of SMAs attended, the percentage of participants who attended 9 or more SMAs, the proportion of days covered (PDC) by AOM (WMP+Rx only), the percentage of participants with PDC 80% or higher (WMP+Rx only), and change from baseline to month 12 in the Work Productivity and Activity Impairment Questionnaire: Specific Health Problem v2.0 (WPAI:SHP v2.0) 4 domain scores, the Work Limitations Questionnaire 8-Item (WLQ-8) 4 domain scores, and the WLQ-8 overall index score. The WPAI:SHP v2.0 assesses percentage impairment (0%-100%) in 4 domain scores (absenteeism, presenteeism, work
productivity loss, and activity impairment) due to excess weight, with higher scores indicating greater impairment. The WLQ-8 assesses the amount of time (1 [none of the time (0%)] to 5 [all of the time (100%)]) excess weight made the task difficult in 4 domain scores (time management, physical tasks, mental or interpersonal tasks, and output tasks) along with an index of overall at-work productivity loss, with higher scores indicating greater impairment.

Weight was measured at baseline and during monthly SMAs on a designated calibrated scale. For participants who did not attend a month 12 SMA, weight was alternatively obtained during the visit window by the following hierarchy: (1) participant called into the office, (2) weight was extracted from the electronic medical record, or (3) participant self-reported. This hierarchy was also used following the transition to virtual SMAs on March 23, 2020, because of the COVID-19 pandemic. The PDC was the total number days' supply of AOM (trial pharmacy card) divided by the total planned study duration, multiplied by 100. Patient-reported outcome (PRO) work productivity and limitations were assessed at baseline and month 12 through self-administration of the WPAI:SHP v2.0 and the WLQ-8. After the transition to virtual SMAs, PROs were completed by mail. The safety data that were collected included serious adverse events and pregnancy.

Statistical Analysis
This study assessed the real-world effectiveness of AOMs as a class. Therefore, no analysis was conducted assessing the effect of an individual medication.

Two estimands were defined. The primary intention-to-treat (ITT) estimand quantified the mean treatment effect for all end points, in all randomized participants and regardless of adherence to randomized treatment. The secondary “if all participants had adhered” (efficacy) estimand quantified the mean treatment effect for body weight loss, categorical weight loss, and PROs in all randomized participants had they adhered to their randomized treatment for the entire study duration, with adherence defined by 9 or more SMAs attended (both groups) and PDC of at least 80% (WMP+Rx only). For participants nonadherent to the program or medication, the secondary (efficacy) estimand used data prior to nonadherence to estimate month 12 end points had they adhered. Both estimands were based on the full analysis set comprising all randomized participants analyzed according to their allocated treatment group. The primary end point analysis was supplemented with a completer analysis using the subset of participants with month 12 weight data who were adherent up to and including month 12. In addition, supplementary analyses evaluated the effect of the transition to virtual SMAs on treatment.

For the primary (ITT) estimand analyses, missing month 12 weight and PRO data were imputed based on a jump-to-reference multiple imputation (x = 100) approach for the primary end point and for the secondary categorical weight loss and PRO end points. A sensitivity analysis of the primary (ITT) estimand for the primary end point was conducted using the multiple imputation approach described by McEvoy,24 in which missing month 12 body weight was imputed from retrieved dropouts in the corresponding treatment group.

The study had 80% power to detect a 4% difference in percentage weight change from baseline to month 12 between the WMP+Rx and WMP groups at a 5% (2-sided) significance level. Treatment groups were compared using an analysis of covariance model (primary [ITT] estimand, and completer analysis) or mixed model for repeated measures (secondary [efficacy] estimand) for continuous end points and logistic regression for categorical end points with the baseline value as a covariate. No adjustments for multiplicity were made; inferences drawn from secondary end points may not be reproducible.

All statistical analyses were conducted using SAS, version 9.4 (SAS Institute Inc). The statistical analysis plan is available in Supplement 1.
Results

Study Population
Participants were predominately (177 of 200 [88.5%]) women (vs 23 of 200 [11.5%] men) and had a mean (SD) age of 50.0 (10.3) years, a mean (SD) baseline weight of 105.0 (19.01) kg, and a mean (SD) BMI of 38.9 (6.63). Of 200 participants, 178 (89.0%) had 1 or more obesity-related comorbid conditions, and 118 participants (59.0%) had 3 or more obesity-related comorbid conditions. The 100 participants randomly assigned to the WMP+Rx group, and the 100 participants randomly assigned to the WMP group comprised the full analysis set. Treatment groups were similar in baseline characteristics, except for an imbalance in race (Table). The first AOM prescribed after randomization (WMP+Rx only) is summarized in eTable 1 in Supplement 2. The rates of month 12 SMA attendance were 74.0% for the WMP+Rx group and 55.0% for the WMP group. Month 12 weight was obtained for 96 of 100 participants (96.0%) in the WMP+Rx group and 91 of 99 participants (92.0%) in the WMP group, with higher-than-planned (52 of 96 obtained measurements [54.2%] for the WMP+Rx group, and 47 of 91 obtained measurements [51.6%] for the WMP group) self-reported weight owing to the transition to virtual SMAs (Figure 1).

Primary End Point
For the primary end point, superior percentage body weight loss at month 12 was observed in the WMP+Rx group vs the WMP group for all analyses (Figure 2). For the primary (ITT) estimand, the estimated mean (SE) weight loss was −7.7% (0.7%) for WMP+Rx compared with −4.2% (0.7%) for WMP, for an estimated treatment difference (ETD) of −3.5% (95% CI, −5.5% to −1.5%) (P < .001). The mean (SE) weight loss per the secondary (efficacy) estimand was −9.2% (0.6%) for WMP+Rx vs −4.1% (0.6%) for WMP, for an ETD of −5.0% (95% CI, −6.7% to −3.4%) (P < .001). For the analysis of data from completers, the mean (SE) weight loss was −10.6% (0.9%) for WMP+Rx vs −5.4% (0.9%) for WMP, for an ETD of −5.2% (95% CI, −8.0% to −2.4%) (P < .001).

The results of the sensitivity analysis of the multiple imputation method were consistent with the primary (ITT) estimand. In addition, post hoc analysis of the primary end point, including race in the imputation model and as a factor in the analysis of covariance model, indicated no effect on the observed treatment (eAppendix and eTable 2 in Supplement 2). Supplemental analyses evaluating the effect of the transition to virtual SMAs indicated no effect on the analysis of the primary end point (eAppendix, eTable 3, and eTable 4 in Supplement 2).

Secondary End Points
Compared with the WMP group, a significantly higher percentage of participants in the WMP+Rx group achieved the secondary end points of at least 5% weight loss for the primary (ITT) estimand (62.5% vs 44.8%, P = .02) and secondary (efficacy) estimand (80.8% vs 39.6%, P < .001) and at least 10% weight loss for the secondary (efficacy) estimand (34.3% vs 16.7%, P = .005) (Figure 3). The rate of SMA attendance was higher for participants in the WMP+Rx group than for participants in the WMP group. Of 12 planned SMA visits, the mean (SD) number of SMAs attended was 9.7 (3.0) visits for the WMP+Rx group vs 7.4 (3.9) visits for the WMP group. The rate of attendance at 9 or more SMAs was 79.0% for the WMP+Rx group and 51.0% for the WMP group. The mean (SD) rate of PDC by AOM (WMP+Rx only) was 66.5% (27.1%), with 43 of 100 participants (43.0%) covered 80% or more of the time. Minimal change in the WPAI:SHP v2.0 and WLQ-8 scores at 12 months across all domains was observed, with no meaningful differences between groups (Figure 4). Month 12 WPAI:SHP v2.0 completion rates were 62.0% for participants in the WMP+Rx group and 56.6% for those in the WMP group. Month 12 WLQ-8 completion rates were 62.0% for participants in the WMP+Rx groups and 55.6% for those in the WMP group.
### Table. Baseline Characteristics of Participants by Treatment Group

| Characteristic                                                                 | WMP + Rx (n = 100) | WMP (n = 100) | Total (N = 200) |
|--------------------------------------------------------------------------------|-------------------|---------------|-----------------|
| **Demographic and baseline clinical characteristics**                          |                   |               |                 |
| Age, mean (SD), y                                                              | 51.0 (10.4)       | 49.1 (10.1)   | 50.0 (10.3)     |
| Sex                                                                            |                   |               |                 |
| Male                                                                           | 12 (12.0)         | 11 (11.0)     | 23 (11.5)       |
| Female                                                                         | 88 (88.0)         | 89 (89.0)     | 177 (88.5)      |
| Racea                                                                          |                   |               |                 |
| White                                                                          | 80 (80.0)         | 66 (66.0)     | 146 (73.0)      |
| Black or African American                                                     | 19 (19.0)         | 33 (33.0)     | 52 (26.0)       |
| Otherb                                                                         | 1 (1.0)           | 1 (1.0)       | 2 (1.0)         |
| Ethnicity                                                                      |                   |               |                 |
| Hispanic or Latino                                                            | 4 (4.0)           | 0 (0)         | 4 (2.0)         |
| Not Hispanic or Latino                                                        | 96 (96.0)         | 100 (100)     | 196 (98.0)      |
| Body weight, mean (SD), kg                                                    | 104.4 (16.2)      | 105.7 (21.5)  | 105.0 (19.0)    |
| Height, mean (SD), m                                                           | 1.64 (0.08)       | 1.65 (0.07)   | 1.64 (0.08)     |
| BMI, mean (SD)                                                                 | 39.1 (6.1)        | 38.8 (7.1)    | 38.9 (6.6)      |
| BMI category                                                                   |                   |               |                 |
| 30 to <35                                                                      | 23 (23.0)         | 37 (37.0)     | 60 (30.0)       |
| 35 to <40                                                                      | 44 (44.0)         | 31 (31.0)     | 75 (37.5)       |
| ≥40                                                                            | 33 (33.0)         | 32 (32.0)     | 65 (32.5)       |
| **Participants with comorbid conditions**                                     |                   |               |                 |
| ≥1 Comorbid condition                                                         | 87 (87.0)         | 91 (91.0)     | 178 (89.0)      |
| ≥2 Comorbid conditions                                                        | 68 (68.0)         | 79 (79.0)     | 147 (73.5)      |
| ≥3 Comorbid conditions                                                        | 56 (56.0)         | 62 (62.0)     | 118 (59.0)      |
| Comorbid conditionsc                                                           |                   |               |                 |
| Dyslipidemia                                                                   | 43 (43.0)         | 46 (46.0)     | 89 (44.5)       |
| Hypertension                                                                   | 37 (37.0)         | 35 (35.0)     | 72 (36.0)       |
| Depression                                                                     | 33 (33.0)         | 37 (37.0)     | 70 (35.0)       |
| Anxiety                                                                        | 32 (32.0)         | 37 (37.0)     | 69 (34.5)       |
| Osteoarthritis                                                                 | 31 (31.0)         | 37 (37.0)     | 68 (34.0)       |
| Prediabetes                                                                    | 37 (37.0)         | 31 (31.0)     | 68 (34.0)       |
| Gastroesophageal reflux disease                                               | 29 (29.0)         | 35 (35.0)     | 64 (32.0)       |
| Metabolic syndrome                                                             | 27 (27.0)         | 28 (28.0)     | 55 (27.5)       |
| Obstructive sleep apnea                                                       | 23 (23.0)         | 27 (27.0)     | 50 (25.0)       |
| Urinary incontinence                                                          | 11 (11.0)         | 11 (11.0)     | 22 (11.0)       |
| Polycystic ovary syndrome                                                      | 8 (8.0)           | 8 (8.0)       | 16 (8.0)        |
| **Baseline WPAI:SHP v2.0 domain scores**                                       |                   |               |                 |
| Absenteeism                                                                    |                   |               |                 |
| No.                                                                            | 95                | 95            | 190             |
| Mean (SD)                                                                      | 0.96 (9.12)       | 0.42 (2.87)   | 0.69 (6.75)     |
| Presenteeism                                                                   |                   |               |                 |
| No.                                                                            | 95                | 95            | 190             |
| Mean (SD)                                                                      | 8.32 (15.89)      | 10.32 (21.26) | 9.32 (18.74)    |
| Work productivity loss                                                         |                   |               |                 |
| No.                                                                            | 95                | 95            | 190             |
| Mean (SD)                                                                      | 8.90 (17.87)      | 10.45 (21.43) | 9.67 (19.69)    |
| Activity impairment                                                            |                   |               |                 |
| No.                                                                            | 100               | 100           | 200             |
| Mean (SD)                                                                      | 21.90 (25.17)     | 19.90 (26.99) | 20.90 (26.05)   |

(continued)
### Table. Baseline Characteristics of Participants by Treatment Group (continued)

| Characteristic                              | Participants, No. (%) | WMP + Rx (n = 100) | WMP (n = 100) | Total (N = 200) |
|---------------------------------------------|-----------------------|--------------------|---------------|-----------------|
| **Baseline WLQ-8 domain scores**            |                       |                    |               |                 |
| Time management                             |                       |                    |               |                 |
| No.                                         | 98                    | 95                 | 193           |                 |
| Mean (SD)                                   | 1.46 (0.62)           | 1.73 (0.95)        | 1.59 (0.81)   |                 |
| Physical tasks                              |                       |                    |               |                 |
| No.                                         | 99                    | 98                 | 197           |                 |
| Mean (SD)                                   | 1.46 (0.70)           | 1.51 (0.88)        | 1.48 (0.80)   |                 |
| Mental or interpersonal tasks               |                       |                    |               |                 |
| No.                                         | 98                    | 97                 | 195           |                 |
| Mean (SD)                                   | 1.45 (0.80)           | 1.48 (0.82)        | 1.47 (0.81)   |                 |
| Output tasks                                |                       |                    |               |                 |
| No.                                         | 97                    | 98                 | 195           |                 |
| Mean (SD)                                   | 1.27 (0.52)           | 1.32 (0.69)        | 1.29 (0.61)   |                 |
| At-work productivity loss                   |                       |                    |               |                 |
| No.                                         | 100                   | 98                 | 198           |                 |
| Mean (SD)                                   | 1.41 (0.46)           | 1.51 (0.62)        | 1.46 (0.55)   |                 |

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); WLQ-8, Work Limitations Questionnaire 8-Item; WMP, weight management program; WMP+Rx, WMP in combination with medication for chronic weight management; WPAI:SHP v2.0, Work Productivity and Activity Impairment Questionnaire Specific Health Problem v2.0.

* Post hoc analysis of the primary end point accounting for the imbalance in race indicated no influence on observed treatment effect (eAppendix and eTable 2 in Supplement 2).

** Other race subcategory included Asian and White (n = 1) individuals and people from India (n = 1).

* Conditions reported in less than 5% of participants were atherosclerotic cardiovascular disease (3%), male hypogonadism (2%), nonalcoholic fatty liver disease (1.5%), chronic kidney disease (1%), and heart failure (0.5%).

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**Figure 1. Participant Disposition**

BW indicates body weight; EMR, electronic medical record; ITT, intention to treat; SMA, shared medical appointment; WMP, weight management program alone; and WMP+Rx, WMP in combination with medication for chronic weight management.
Safety

In total, 23 serious adverse events (8 in the WMP+Rx group and 15 in the WMP group) were reported for 19 participants (8 in the WMP+Rx group and 11 in the WMP group). There was no clustering of serious adverse events, and causality was deemed unlikely following review of all cases. One death due to dilated cardiomyopathy occurred in the WMP group. Two pregnancies (1 in each group) occurred, each resulting in a healthy term infant.

Discussion

This study addressed a research gap identified by the American College of Occupational and Environmental Medicine by assessing the use of AOMs in the workplace and showed that clinically meaningful superior mean weight loss may be achieved when access to AOMs is provided in the real-world setting of an employer-based WMP compared with no access to AOMs. The estimated

**Figure 2. Change in Percentage Body Weight From Baseline to 12 Months, Primary End Point**

![Graph showing change in percentage body weight from baseline to 12 months, with estimands for ITT, secondary efficacy, and completers analysis.]

**Figure 3. Secondary End Points of Categorical Weight Loss at 12 Months Compared With Baseline**

![Graph showing secondary end points of categorical weight loss at 12 months compared with baseline, with estimands for ITT and secondary efficacy.]

ITT indicates intention to treat; WMP, weight management program; and WMP+Rx, WMP plus antiobesity medication. Mean baseline indicates mean body weight at baseline, and error bars indicate 95% CI. All comparisons are significantly different at \( P < .001 \).
The treatment effect on the 12-month percentage weight loss of −3.5% (primary [ITT] estimand) and −5.0% (secondary [efficacy] estimand) is consistent with RCT data, in which the ETD of 12-month percentage weight loss due to individual medications compared with placebo ranges from −1.3% to −9.4%, with the majority between −3.0% and −5.4%. In addition, participants with access to AOMs were more likely than participants without access to AOMs to achieve at least 5% weight loss, a benchmark associated with clinically meaningful improvement in certain obesity-related comorbid conditions. These clinical benefits were observed without unexpected safety concerns.

The rate of SMA attendance was higher among participants who were provided access to AOMs compared with participants without access. Potential hypotheses for this result include the positive motivation participants had with increased weight loss and the continued monthly prescribing of AOMs associated with SMA attendance. This observation has clinical implications because SMA adherence is associated with greater weight loss, and a correlation has been observed between the number of SMAs attended and the magnitude of weight lost. Access to AOMs may increase the potential benefits of other interventions, long-term lifestyle changes, and maintenance of weight loss. However, maintenance of weight loss may diminish without long-term AOM use.

Less than half (43.0%) of the participants in the WMP+Rx group were considered adherent to AOMs (PDC ≥80%). However, adherence was based on pharmacy fills rather than on actual use, and this approach may underestimate adherence to AOMs, especially for medications requiring titration, with participants potentially taking lower doses than prescribed. Although there is not a measure consistently used in RCTs that is comparable to standard real-world measures of adherence,
completion rates in most weight loss RCTs range from 50% to 70%. The observed mean PDC (66.5%) is within the range of retrospective claims analysis of medications for 6 other chronic diseases: 35% (overactive bladder medications) to 72% (oral antidiabetic medications). Although higher SMA attendance among participants in the WMP+Rx group may account for some of the observed treatment effect, for the secondary estimand assessing “if all patients had adhered,” the magnitude of weight loss in the WMP+Rx group was higher than in the primary (ITT) estimand but was similar in the WMP group. This observation persisted in a sensitivity analysis of the primary estimand that used an alternative imputation approach. In addition, the magnitude of weight loss in the completers analysis was the highest for WMP+Rx (−10.6%) but only slightly higher for WMP (−5.4%). Although this study was not designed to assess the contribution of SMAs vs AOMs, these analyses may suggest that AOM adherence may affect weight loss more than WMP attendance. This observation is particularly relevant to inform coverage decisions regarding AOMs.

Obesity is associated with decreased workplace productivity, including absenteeism and presenteeism, but research assessing changes in work productivity following weight loss is limited, particularly with respect to the effect of AOMs. In the present study, changes in work productivity and limitation assessments were minimal, and differences between treatment groups were not meaningful. Although the study was not powered to assess these end points, a ceiling effect likely impacted the results. Low levels of baseline impairment were reported, perhaps related to the typically sedentary workplace of the present study setting. Obesity burden varies by employer industry; therefore, the effect of weight loss on productivity measures is influenced by industry setting. In addition, whereas the magnitude of weight loss was clinically significant, it may not have been large enough or the duration of follow-up long enough to affect these measures. Finally, the switch to virtual SMAs resulted in missing PRO data.

Antiobesity medications have limited access and coverage, deterring appropriate use. Better understanding of the cost-benefit balance of AOMs in employer-based settings, including their effect on indirect and direct costs attributable to obesity alongside drug-acquisition costs, is necessary to inform coverage decisions. The effect of AOMs on indirect costs through improved productivity remains an important area of research, targeting diverse workplace settings or populations with higher baseline impairment. Weight loss in patients with obesity is associated with significant reductions in direct health care costs. Owing to the 1-year duration, the present study did not assess health care resource use and costs. Potential cost savings may be estimated from the literature, but elucidation of the cost-benefit balance of AOMs requires further research.

Limitations

Although this study provides robust real-world effectiveness data for the effect of AOMs on weight and adherence end points, some study limitations are noted. This study was small and therefore was not powered to examine subgroups (eg, BMI category), assess response to individual medications, evaluate heterogeneity of effect, or investigate characteristics predicting individual response to AOMs. The PRO end points were underpowered and limited by the short duration of follow-up. Medication adherence was assessed by pharmacy fills rather than by actual use. Economic end points were not assessed. Finally, the transition to virtual SMAs due to the COVID-19 pandemic resulted in more self-reported body weight assessments than expected and more missing PRO data. However, supplementary analyses evaluating the potential effect of this transition indicated no influence on observed treatment effect for weight loss.

This was a single-employer study. The population was predominately (88.5%) female, whereas the prevalence of obesity is similar between sexes. This, however, is consistent with the predominance of female participants in WMPs and as new users of AOMs (82.2%), and highlights the need for interventions conducive to male participation.
Conclusions

This study addresses a critical gap in evidence in the real-world effectiveness of AOMs in employer-based settings. The results of this pragmatic RCT, which reflected real-world medical practice in the workforce, indicate that the use of AOMs in conjunction with an interdisciplinary wellness program for obesity management yields clinical benefits similar to those seen in RCTs. Such results should inform employer decisions regarding employee access to these medications and guide the development of best practices for comprehensive employer-based interdisciplinary weight management programs. Further research is needed regarding the economic effect of access to AOMs in real-world, employer-based settings, considering employee performance and function, medication costs, and reduction in other obesity-related medical costs. A long-term pragmatic RCT conducted in multiple, diverse industry settings may address these considerations and further elucidate the cost-benefit balance of AOMs.

ARTICLE INFORMATION

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SUPPLEMENT 2.

**eAppendix.** Supplementary Data and Additional Information Regarding Sensitivity, Post Hoc, and Supplementary Analyses of the Primary End Point

**eTable 1.** First Anti-Obesity Medication Prescribed After Randomization (WMP+Rx)

**eTable 2.** Change in Body Weight (%) at 12-Months Compared to Baseline – Primary End Point – Primary (ITT) Estimand Sensitivity and Post Hoc Analyses

**eTable 3.** Change in Body Weight (%) at 12-Months Compared to Baseline – Primary End Point – Supplementary Analyses of COVID-19 Impact – Primary (ITT) Estimand

**eTable 4.** Change in Body Weight (%) at 12-Months Compared to Baseline – Primary End Point – Supplementary Analyses of COVID-19 Impact – Secondary (Efficacy) Estimand

**eReference**

SUPPLEMENT 3.

Data Sharing Statement