Effectiveness of combining antiobesity medication with an employer-based weight management program for treatment of obesity: a randomized clinical trial[1]

Kevin M. Pantalone, DO; B. Gabriel Smolarz, MD; Abhilasha Ramasamy, MSc, MS; Merav Baz Hecht, MD; Brian J. Harty, MA; Bruce Rogen, MD; Marcio L. Griebeler, MD; Elena Borukh, MD; James B. Young, MD; Bartolome Burguera, MD, PhD

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What is a pragmatic trial?[2,3]

- **Pragmatic clinical trials (PCTs)** help measure the relative effectiveness of treatment strategies in real-world clinical practice. PCTs aim to provide evidence regarding real-world impact of a treatment strategy in routine clinical practice while retaining the core strength of randomized controlled trials
- **Randomized-controlled trials (RCTs)** confirm a physiological or clinical hypothesis under ideal conditions. They are the gold standard for evaluating the efficacy and safety of treatments

Differences and similarities between PCTs and RCTs[3-5]

	PCT	RCT
Objective	To study the effectiveness of a treatment/intervention in a real-world clinical practice	To determine, under controlled conditions, whether a treatment/intervention produces the expected results
Design	Study health intervention in a real-world setting, similar to the one where the intervention will be applied	Demonstrate safety and efficacy of an intervention under highly controlled conditions
Methodology	Randomized, multi-arm	Randomized, multi-arm
Study population	A diverse, representative population using broader inclusion and exclusion criteria	Carefully selected population using a set of well-defined inclusion and exclusion criteria

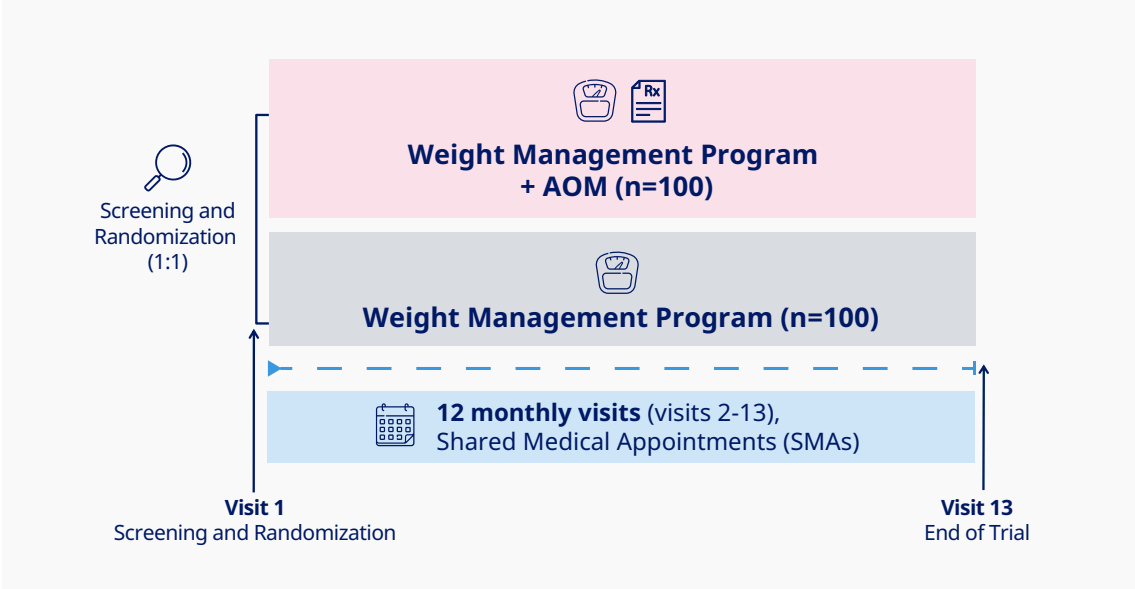
Effectiveness of combining an employer-based WMP with AOMs—real-world evidence from a pragmatic trial[1]

What was the purpose of the study?

- The primary objective was to compare the effectiveness of an employer-based WMP+AOMs[a] with WMP without AOMs on weight loss in people with obesity
- This study is the first pragmatic clinical trial evaluating the real-world effectiveness of AOMs

How was the study conducted?

- A 1-year, single-center, open-label, parallel-group, real-world, randomized, pragmatic trial
- Study involved 200 members of the Cleveland Clinic Employee health plan (aged ≥18 years; mean age 50 years) with obesity (BMI ≥30 kg/m^2)[b]
- Study conducted from January 7, 2019 to May 22, 2020



AOM=anti-obesity medication; BMI=body mass index; WMP=weight management program.

[a]No drug-drug comparisons were made as part of the analysis.
[b]Key exclusion criteria included contraindications to FDA-approved AOMs, prior (≤90 days) treatment with any medication with the intention of weight loss, previous 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 (A1C) ≥6.5% at screening or within 90 days prior to randomization.

Baseline weight-related characteristics (full analysis set)[1]

	By Treatment		
	Total (n=200)	WMP+AOM (n=100)	WMP (n=100)
Age, mean (SD), years	50.0 (10.3)	51.0 (10.4)	49.1 (10.1)
Sex (%)			
Male	23 (11.5)	12 (12.0)	11 (11.0)
Female	177 (88.5)	88 (88.0)	89 (89.0)
Race (%)[a]			
White	146 (73.0)	80 (80.0)	66 (66.0)
Black or African American	52 (26.0)	19 (19.0)	33 (33.0)
Other[b]	2 (1.0)	1 (1.0)	1 (1.0)
Body weight (kg), mean (SD)	105.0 (19.0)	104.4 (16.2)	105.7 (21.5)
BMI (kg/m^2), mean (SD)	38.9 (6.6)	39.1 (6.1)	38.8 (7.1)
BMI category, n (%)			
30 kg/m^2 to <35 kg/m^2	60 (30.0)	23 (23.0)	37 (37.0)
35 kg/m^2 to <40 kg/m^2	75 (37.5)	44 (44.0)	31 (31.0)
≥40 kg/m^2	65 (32.5)	33 (33.0)	32 (32.0)

SD=standard deviation.

[a]Post hoc analysis of the primary end point accounting for the imbalance in race indicated no influence on observed treatment effect.
[b]Other race subcategory included Asian and White (n=1) individuals and people from India (n=1).

Study design (cont)[1]

Cleveland Clinic's integrated WMP included

- Monthly SMAs with a physician and a nutritionist, with extensive dietary and nutritional counseling
  - Due to COVID-19, on March 23, 2020, all SMAs were switched to virtual SMAs after receiving Institutional Review Board approval
- Referral to an exercise physiologist
- Behavioral health counseling (as needed)

AOMs for chronic weight management

- At any time during the study period, participants in the WMP+AOM group could receive 1 of 5 AOMs approved by the US Food and Drug Administration for chronic weight management

Copays[a]

- All participants were responsible for applicable specialty visit copayments for each SMA attended (per Cleveland Clinic health plan)
- In the WMP+AOM group, a copay-like fee of $25 was paid by the participants for each monthly prescription to simulate a real-world access setting

The primary estimand[1]

- The primary estimand was the "effectiveness" or intention-to-treat (ITT) estimand in this study

This ITT estimand was used to quantify the average treatment effect for all end points in all randomized subjects, **regardless of adherence to randomized treatment**

Primary and secondary endpoints

Primary endpoint[b]

- Change from baseline (month 0) to month 12 (visit 13) in body weight (%)

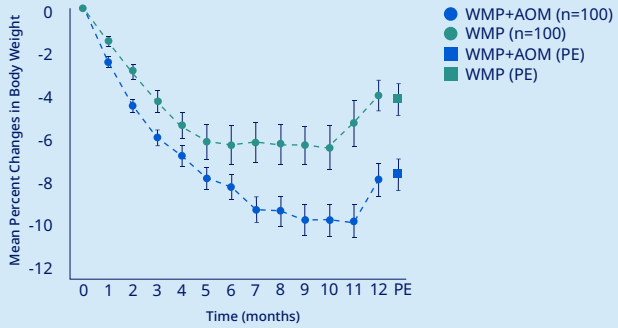
Secondary endpoints

- Percentage of participants who achieved (yes/no) ≥5% and ≥10% weight loss from baseline
- Number of SMAs attended and percentage of subjects attending ≥9 SMA visits
- Proportion of days covered by AOMs and percentage subjects covered by prescription claims for at least 80% of days[c]
- Work limitation change from baseline (Work Limitations Questionnaire Short-Form)
- Work productivity change from baseline (Work Productivity and Activity Impairment Questionnaire Specific Health Problem)

[a]Novo Nordisk covered the costs of all AOMs used in this study and patients were only responsible for a $25 copay to mimic real-world copay amounts.
[b]For subjects not attending the month 12 SMA, a stepwise approach to obtaining weight data within the visit window was applied that included calling subject in for a month 12/visit 13 weight measurement, extracting recent weight data from the electronic medical record, and using recent subject-reported weight.
[c]Only in subjects randomized to the weight management program in combination with medication for chronic weight management.

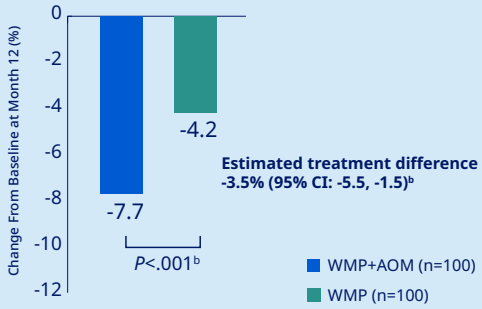
Significantly greater weight loss was achieved with WMP+AOM compared with WMP alone[1]

Observed Mean Weight Loss[2,a]
Mean baseline body weight: 231.5 lb (105.0 kg)



PE=Estimates from analysis of primary estimand of the primary endpoint at month 12.
[a]The body weights that were captured at the end of the study were based on ITT analysis. In other words, all subjects (including those not adherent to the program) were required to submit their weight at the end of the study period. Additionally, the COVID pandemic began at month 10 of the study, forcing some patients to switch from in-person to virtual SMA visits.

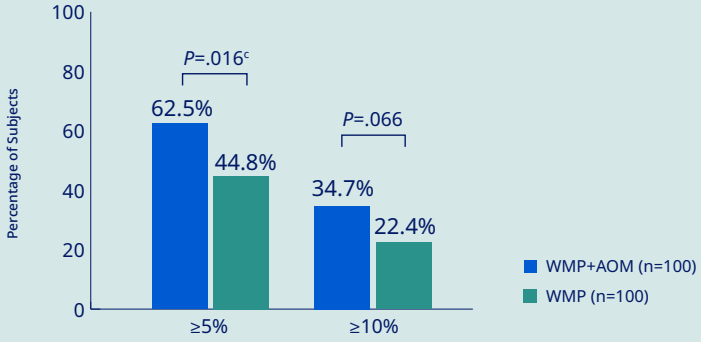
Primary Estimand[1]
Percent change from baseline at month 12
Mean baseline body weight: 231.5 lb (105.0 kg)



[b]Statistically significant difference.

Patients achieving ≥5% and ≥10% weight loss with WMP+AOM compared with WMP alone[1,2]

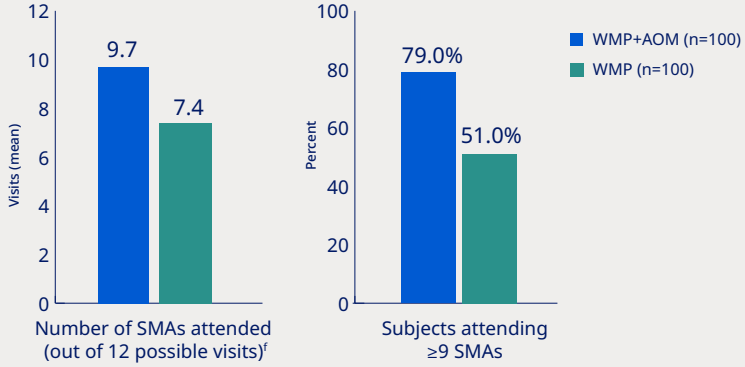
Categorical weight loss achieved at 12 months
Primary estimand



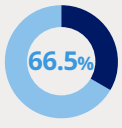
[c]Statistically significant difference: 62.5% vs 44.8%.

A higher adherence was observed among patients who received an AOM for chronic weight management compared with those that were not prescribed an AOM[1,d]

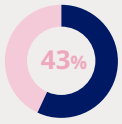
Adherence to SMAs[e]
SMA attendance



Adherence to AOMs[e]
Prescription claims coverage



Mean percentage of days during the trial that patients were covered for prescription claims



Proportion of patients covered ≥80% of days

[d]Not tested for statistical significance.
[e]Adherence was defined as attending ≥9 of 12 SMAs (both arms) and prescription coverage ≥80% of expected (WMP+AOM arm).
[f]Graph depicts mean number of SMAs attended. Detailed results (mean [SD]) were 9.7 (3.0) visits for the WMP + AOM group and 7.4 (3.9) visits for the WMP group.

Key study findings[1]

- Significantly greater weight loss was achieved when participants received an AOM for chronic weight management in addition to the WMP compared with the WMP alone
- Participants who received an AOM for chronic weight management were more adherent to the WMP compared with participants who did not receive an AOM
- This study demonstrated that significantly greater, clinically meaningful mean weight loss was achieved when AOMs were available in a real-world setting of an employer health plan compared with no access to AOMs

Study limitations[1]

- This study was small and, therefore, was not powered to examine subgroups (eg, BMI category), evaluate heterogeneity of effect, or investigate characteristics predicting individual response to AOMs
- The transition to virtual SMAs due to the COVID-19 pandemic resulted in more self-reported body weight assessments than expected and more missing patient-reported outcome data; however, supplementary analyses evaluating the potential impact of this transition indicated no impact on observed treatment effect on weight loss
- This was a single-employer study. While the prevalence of obesity is similar between sexes, the population was predominately female (88.5%); however, this is consistent with the predominance of female participants in WMPs and with new users (82.2%) of AOMs

References: 1. Pantalone KM, Smolarz BG, Ramasamy A, et al. Effectiveness of combining antiobesity medication with an employer-based weight management program for treatment of obesity: a randomized clinical trial. *JAMA Network Open*. 2021;4(7):e2116595. **2.** Data on file. Novo Nordisk Inc; Plainsboro, NJ. **3.** Gartlehner G, Hansen RA, Nissman D, Lohr KN, Carey TS. Criteria for Distinguishing Effectiveness From Efficacy Trials in Systematic Reviews. Rockville, MD: Agency for Healthcare Research and Quality (US); 2006. **4.** NIH Collaboratory Living Textbook on Pragmatic clinical trials. What is a pragmatic clinical trial. Section 4. Pragmatic elements: an introduction to PRECIS-2. https://rethinkingclinicaltrials.org/chapters/pragmatic-clinical-trial/post-6366/. Accessed March 2, 2021. **5.** NIH Collaboratory Living Textbook on Pragmatic clinical trials. What is a pragmatic clinical trial. Section 3. Differentiating between RCTs, PCTs, and quality improvement activities. https://rethinkingclinicaltrials.org/chapters/pragmatic-clinical-trial/what-is-a-pragmatic-clinical-trial-3/. Accessed March 2, 2021.

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