## Effect of Obesogenic Medications on Weight-Loss Outcomes in a Behavioral Weight-Management Program

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**Objective:** This study aimed to evaluate a possible association between the use of obesogenic medications and inadequate weight loss in a behavioral weight-management program.

**Methods:** This is a case-control, single-center study of 666 adult patients within a Veterans Health Administration health system who participated in the MOVE! behavioral weight-loss program. The cohort was divided into responders (n = 150), patients who achieved  $\ge 5\%$  total weight loss by the end of the MOVE! program, and nonresponders (n = 516), those who achieved < 5% total weight loss. We reviewed each patient's medical records for exposure to obesogenic medication during the time of treatment.

**Results:** Approximately 62% (n = 411) of patients entering MOVE! had a prescription for obesogenic medications. Obesogenic medication use was associated with worse weight-loss outcomes, and participants were 37% less likely to achieve a clinically meaningful ( $\ge 5\%$  total weight loss) outcome at the end of the MOVE! program (odds ratio, 0.633; 95% CI: 0.427-0.937; adjusted P = 0.022). Patients who received three or more medications (n = 72) had the greatest difficulty achieving 5% weight loss compared with the control group (odds ratio, 0.265; 95% CI: 0.108-0.646; adjusted P = 0.003).

**Conclusions:** The use of provider-prescribed obesogenic medications was associated with worse weightloss outcomes in a behavioral weight-loss program. Closer scrutiny of patient medications is necessary to help improve outcomes of weight-loss treatments.

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## Introduction

The prevalence of obesity continues to increase, with most recent estimates suggesting that 51% of the US population will have obesity by 2030 (1). Veterans are particularly affected; up to 78% of veterans have either overweight or obesity (2). The estimated annual medical cost for individuals with obesity is \$1,429 higher than for those with normal weight (3). To address this health problem, Veterans Health Administration (VHA) established the MOVE! program in 2005. The MOVE! program is an 8-week-long, patient-centered, comprehensive, evidence-based, multidisciplinary weight-management program. Behavioral weight-loss programs are a cornerstone of obesity care and are often offered as one of the first steps of obesity management.

However, the weight-loss outcomes from behavioral weight-loss programs are quite variable (4,5). Success rates of patients losing a clinically meaningful amount of weight by the end of the MOVE! program have been found to be 18% to 20% (6). Multiple factors have been implicated in the variability of these types of programs, including poor adherence and unrealistic patient expectations (7). Improving patient outcomes is a high priority, not only for decreasing a modifiable risk factor for some of the leading causes of preventable death but also for decreasing the financial burden associated with obesity on a national level.

The etiology of obesity is multifactorial, including genetics; easy access to energy-dense, nutrient-poor, highly palatable food; physical inactivity; and changes in sleep-wake cycles, among other factors (8).

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For example, a growing body of evidence shows that several frequently prescribed medications can cause weight gain and contribute to the obesity epidemic (9-12). The Endocrine Society clinical practice guidelines advise that obesogenic medications should be avoided in patients with obesity (13). Notably, obesogenic drugs fall into various categories of medications, including some of the most frequently prescribed medications in the United States, such as beta-blockers, antidepressants, antipsychotics, anticonvulsants, antidiabetic medications, antihistamines, and hormones (Table 1) (10-21). Given the frequent use of obesogenic medications could be a potential risk factor for poor weightloss outcomes in patients being treated for obesity.

Here, we present a retrospective case-control study that measures the impact of provider-prescribed obesogenic medications on weight-loss outcomes of the VHA San Diego MOVE! program. In particular, we hope to answer the following question: Do obesogenic medications affect the weight-loss response of patients to a behavioral weight-loss program? To do this, patients who participated in the MOVE! program between 2011 and 2015 were split into those who responded to therapy (5% weight loss after the intervention) and those who did not. We then

assessed whether exposure to any number of obesogenic medications affected whether a patient was a responder or not. Despite the retrospective study design, the short duration of the weight-loss program made it possible to collect homogenous data and correlate the use of obesogenic medications and weight-loss outcomes.

## Methods

### Study design and data source

This is a retrospective, single-center, case-control study of patients older than 18 years old who completed the MOVE! program at the VHA San Diego in California. This study had the approval of the Institutional Review Board of the VHA San Diego. We identified patients who participated from January 1, 2011, to December 31, 2015. The MOVE! program is available to veterans with BMI  $\ge$  30 who are referred by their primary care provider or other health care provider for weight loss. Participants who did not complete the MOVE! program were excluded. Completion of the program was defined as having more than 75% participation in the program activities.

Medication class (n)	Obesogenic medications (n)	Mechanism of weight gain (reference)		
Anticonvulsants ( <i>89</i> )	Carbamazepine ( <i>3</i> ) Gabapentin ( <i>72</i> )	Hypothalamic mediated increase in appetite and decrease in ener expenditure (15)		
	Pregabalin (12)			
	Valproic acid (2)			
Antidepressants/antianxiety ( <i>85</i> )	Amitriptyline (19)	Appetite increase stimulated via serotonergic pathways (12)		
	Fluoxetine (33)			
	Mirtazapine (18)			
	Nortriptyline (5)			
	Paroxetine (10)			
Antihistamines ( <i>125</i> )	Cetirizine (29)	Increased appetite and altered body weight regulation (16,17)		
	Diphenhydramine (18)			
	Fexofenadine (2)			
	Hydroxyzine (29)			
	Loratadine (47)			
Antipsychotics ( <i>36</i> )	Olanzapine (5)	Increased orexigenic and decreased anorexigenic neuropeptide		
	Quetiapine (17)	expression in the hypothalamus (15,18)		
	Risperidone (11)			
	Ziprasidone (3)			
Beta-blockers ( <i>205</i> )	Atenolol (80)	Inhibited sympathetic tone, decreased lipolysis, reduced exercise		
	Carvedilol (24)	tolerance, increased fatigue, and reduced resting energy		
	Metoprolol ( <i>79</i> )	expenditure (11)		
	Propanolol (22)			
Corticosteroids and hormones (15)	Medroxyprogesterone (2)	Altered energy intake and expenditure of the human body (10)		
	Oral contraceptives (2)	Altered energy intake and expenditure of the human body (10)		
	Prednisone (11)			
Diabetes medications (156)	Insulin ( <i>70</i> )	Anabolic and adipogenic hormone causing decreased daily energy		
		expenditure (19)		
	Sulfonylureas (58)	Increased secretion of insulin and water retention (20)		
	Thiazolidinediones (28)	Insulin sensitizer causing water retention (21)		

Common physician-prescribed obesogenic medications identified in Endocrine Society guidelines (13,14). The number of patients in our study who were taking these medications is also provided. Some medications identified in Endocrine Society guidelines were not taken by any individuals in our cohort, mainly because of them not being on the VHA formulary.

We divided our study population based on  $\ge 5\%$  total body weight loss (%TBWL) at the end of the MOVE! program. This level of weight loss is associated with clinically meaningful outcomes, such as improvements in blood pressure, glycemia, and triglycerides (22-24). Responders ("cases") were defined as patients who were able to lose 5% or more from their intake total weight by the end of the MOVE! program. Nonresponders ("controls") lost less than 5% of their total weight by the end of the 8-week program. Secondary outcomes included the number of obesogenic medications prescribed and the effects of specific medication classes (e.g., antidiabetic, beta-blockers, antidepressants) on weight loss outcomes. Pharmacy data were recorded from the VHA electronic medical records through manual chart review. These data included prescription regimens for 28 obesogenic medications (Table 1) ("exposure"), 4 leptogenic medications (Supporting Information Table S1), and 2 obesity pharmacotherapy drugs (Supporting Information Table S1). We defined obesogenic medications as drugs with a known side effect of weight gain of 2 kg or  $\geq 5\%$  from baseline, leptogenic medications as drugs for which weight loss is a known side effect, and obesity pharmacotherapy as drugs approved for the treatment of obesity. Obesogenic medications were selected from current practice guidelines (13,14). Outpatient prescriptions with a duration of 1 month or longer that were both filled and received by the patient were considered as medication use. For example, if during the intake visit at the MOVE! program the patient had an active prescription with a duration of 1 month or longer, and it was filled by the VHA pharmacy, this is considered as medication use. On the other hand, if a prescribed medication was not filled, it was not considered as used. Most prescriptions for nearly all the patients were filled by VHA pharmacies. To address potential non-VHA medication usage, primary care notes were screened for medications that were not included in the pharmacy records. By including all obesogenic medications without regard to duration, we are reducing potential confounding and overinterpretation of our data. Comorbidities and demographic data were also abstracted through manual electronic health record review.

## MOVE! program

The MOVE! program consists of eight weekly, 90-minute group classes led by licensed providers. During each session, instructors use tools including audiovisual materials, didactic instruction, and class exercises. Education is provided and covers topics such as health benefits of weight loss, goal setting, self-monitoring, identification of environmental cues that may affect eating and physical activity, mindful eating, food composition and dietary guidelines, portion control strategies, benefits of exercise, and barriers to physical activity. Patients have their weight checked during each class using a standardized digital scale, and this is recorded in their electronic medical records. Participants are given a pedometer with instructions. Patients have the option to keep food logs weekly that are reviewed by the weight-loss providers, and patients receive written feedback.

## Statistical analysis

We compared continuous and categorical outcomes across responders and nonresponders using two-sample t tests and Fisher exact tests, respectively. We report adjusted (adj) odds ratios (OR) derived from multivariable logistic regressions with control for potential confounders, including age of patient at the time of weight-loss clinic intake visit, gender, the use of obesogenic medications (defined as prescription for 1 month or longer of an obesogenic medication during the 8-week weight-loss intervention), leptogenic medications (defined as prescription for 1 month or longer of a leptogenic medication during the 8-week weight-loss intervention), and obesity pharmacotherapy (defined as prescription for 1 month or longer of a medication used for obesity treatment during the 8-week weight-loss intervention), and BMI.

## Results

## Patient characteristics

The study population included 724 adult individuals (see Supporting Information Figure S1 for breakdown of patients in this case-control study). We excluded 58 patients who did not meet the attendance criteria (at least 75% participation in MOVE! classes). Of the remaining 666 patients in our cohort, 150 patients (22.5%) were responders, reaching 5%TBWL or more at the end of the MOVE! program. The remaining 516 (77.5%), considered nonresponders, lost less than 5% of their total weight (Table 2). Responders were older (63.0 [SEM 0.8] vs. 59.4 [SEM [0.5] years; P < 0.001) and had a lower percentage of women compared with the nonresponders group (10.7% vs. 18.4%; P = 0.025). Age did not appear to correlate with weight loss (Supporting Information Figure S2). Responders had a higher percent excess weight loss after MOVE! compared with nonresponders (27.1% [SEM 2.0%] vs. 3.0% [SEM 0.5%], respectively; P < 0.001) and a higher %TBWL at the end of MOVE! compared with nonresponders (7.9% [SEM 0.5%] vs. 0.8% [SEM 0.1%], respectively). Absolute weight loss at the end of the MOVE! program was also higher for responders compared with the nonresponders (21.0 [SEM 1.4] lb vs. 1.9 [SEM 0.4] lb, respectively) (Table 2).

## Effects of obesogenic medications on excess weight loss

To investigate the effect of obesogenic medications on weight-loss outcomes at the end of the MOVE! program, we measured the usage of these drugs in responders and nonresponders. We found that more than 60% of the patients participating in the MOVE! program had at least one obesogenic medication prescribed (n = 411, 61.7%) (Table 2). Obesogenic medications were less frequently prescribed in responders than nonresponders (54% vs. 64%; adj P = 0.029), suggesting that obesogenic medication use is associated with a poor weight-loss outcome. Patients with any provider-prescribed obesogenic medications were 37% less likely to achieve 5%TBWL (adj OR, 0.633, 95% CI: 0.427-0.937; P = 0.022) (Figure 1).

# Effect of increased number of obesogenic medications

To further examine the influence of obesogenic drugs in weight-loss success, we calculated the OR of achieving 5%TBWL for different numbers of obesogenic medications prescribed. Patients prescribed three or more obesogenic medications were least likely to achieve 5%TBWL compared with the participants not using those drugs (adj OR, 0.265, 95% CI: 0.108-0.646; P = 0.003) (Figure 1). This suggests that with a greater number of obesogenic medications prescribed, it is more likely for a patient to have a poor weight-loss outcome. Moreover, patients with three or more obesogenic medications prescribed had the lowest absolute TBWL by the end of the program (Table 3).

*Demographics, n (%)* Age, mean (SEM) Gender (female)

**Black or African American** 

American Indian/Alaska Native

Native Hawaiian/Pacific Islander

Hispanic/Latino

Asian American

White

#### TABLE 2 Characteristics of study participants

All ( <i>N</i> = 666)	Responders ( $n = 150$ )	Nonresponders ( $n = 516$ )	P value
60.2 (0.4)	62.0 (0.9)	50.4.(0.5)	< 0.001
60.2 (0.4)	63.0 (0.8)	59.4 (0.5)	
111 (16.7)	16 (10.7)	95 (18.4)	0.025
241 (36.2)	45 (30.0)	196 (38.0)	0.152
129 (19.4)	21 (14)	108 (20.9)	
32 (4.8)	8 (5.3)	24 (4.7)	
12 (1.8)	5 (3.3)	7 (1.4)	
39 (5.9)	7 (4.7)	32 (6.2)	
7 (1.0)	0 (0.0)	7 (1.4)	
22 (3.3)	4 (2.7)	18 (3.5)	
256.1 (2.0)	263.3 (4.1)	254.1 (2.3)	0.057
38 (0.3)	38.9 (0.6)	37.8 (0.3)	0.076
()		()	

Other ethnicity	22 (3.3)	4 (2.7)	18 (3.5)	
Anthropomorphics, mean (SEM)				
Intake weight (lb)	256.1 (2.0)	263.3 (4.1)	254.1 (2.3)	0.057
Intake BMI (kg/m²)	38 (0.3)	38.9 (0.6)	37.8 (0.3)	0.076
Intake excess weight (lb)	87.6 (1.8)	93.5 (3.9)	85.9 (2.0)	0.079
Total weight loss at end of MOVE! (lb)	6.2 (0.5)	21.0 (1.4)	1.9 (0.4)	0.014
Total weight loss at end of MOVE! (%)	2.4 (0.2)	7.9 (0.5)	0.8 (0.1)	< 0.001
Excess weight loss at end of MOVE! (%)	8.5 (0.7)	27.1 (2.0)	3.0 (0.5)	< 0.001
Comorbidities, n (%)				
Hypertension	63.8 (425)	98 (65.3)	327 (63.4)	0.700
Type 2 diabetes	214 (32.1)	42 (28.0)	172 (33.3)	0.234
Dyslipidemia	392 (58.9)	95 (63.3)	297 (57.6)	0.221
Major depression	302 (45.3)	58 (38.7)	244 (47.3)	0.063
Coronary artery disease	83 (12.5)	18 (12.0)	65 (12.6)	1.000
Anxiety disorder	100 (15.0)	19 (12.7)	81 (15.7)	0.436
Seizure disorder	7 (1.0)	2 (1.3)	5 (1.0)	0.658
Psychoses	26 (3.9)	4 (2.7)	22 (4.3)	0.478
Weight-affecting medication, n (%)				
Obesogenic medications	411 (61.7)	81 (54.0)	330 (64.0)	0.029
Leptogenic medications	217 (32.6)	39 (26.0)	178 (34.5)	0.060
Antiobesity pharmacotherapy	14 (2.1)	2 (1.3)	12 (2.3)	0.746

Fisher exact test used for all comparisons except for all continuous variable comparisons (i.e., age, weight, and BMI), for which unpaired t test used.

## **Obesogenic medication class effects**

The study assessed the effect of different classes of obesogenic drugs on weight-loss outcomes. We found that compared with individuals who were not prescribed obesogenic drugs, participants who were on antidiabetic medications had lower odds of achieving an adequate weight loss of 5%TBWL at the end of MOVE! (adj OR, 0.387, 95% CI: 0.207-0.723; P = 0.003) (Figure 1).

## Effect of comorbidities on weight-loss outcome

We explored the possibility that comorbidities influence this difference in weight-loss outcome in patients using obesogenic medications (i.e., reverse causality). For instance, inadequate weight loss caused poor control of hypertension and that prompted the use of obesogenic medications. This is not supported from our data (Figure 2), as comorbidities were not different between responders and nonresponders (Table 2). Furthermore, the weight-loss outcome was inferior for patients with a specific comorbidity using obesogenic medications when compared with patients with the same comorbidity not taking these medications (Table 4). Moreover, a higher number of comorbidities was not associated with poor weight-loss outcomes (Table 5).

## Discussion

In this retrospective case-control study, 22.5% of 666 patients achieved 5%TBWL after the MOVE! behavioral weight-loss program. Our study showed that the patients prescribed any obesogenic medications were 37% less likely to have clinically meaningful weight loss by the end of the 8-week program. A stronger association was seen for those who were prescribed three or more obesogenic medications, as they had a 73% lower chance of achieving 5%TBWL. There is a need for larger studies that can determine whether there is a threshold of the number of medications for which the negative effects of obesogenic medications are realized, or whether specific medications have a particularly strong effect on outcomes. In 2014 alone, patients spent approximately \$2.5 billion on commercial or proprietary weight-loss services. Our study suggests that success rate of such programs may be impacted by a factor that was not previously considered, which is the use of provider-prescribed obesogenic medications (7).

There is significant variability in weight-loss outcomes with each obesity treatment modality including behavioral programs such as the MOVE! program and surgical interventions. In behavior-based

	Exposure	OR ( <i>CI</i> )	Р
Primary Outcome			
Obesogenic Medications -	⊢ <b>●</b> −−i	0.63 (0.43, 0.94)	0.022
# of Obe			
1 Obesogenic Medication -	<b>⊢●</b> −•	0.65 (0.42, 1.02)	0.061
2 Obesogenic Medications-	F-	0.68 (0.41, 1.12)	0.132
3+ Obesogenic Medications-	H <b></b> 1	0.26 (0.11, 0.65)	0.003
Type of O	besogenic Medication		
Antidiabetics -	⊨●1	0.39 (0.21, 0.72)	0.003
Leptogenic Medications-	·	1.59 (1.03, 2.47)	0.037
Antihistamines -	<b>⊢_</b> •	0.93 (0.53, 1.63)	0.798
Antipsychotics -		0.48 (0.14, 1.64)	0.242
Beta-Blockers-	<b>⊢_</b> •	0.96 (0.58, 1.59)	0.883
Anticonvulsants-	<b>⊢</b> •	0.97 (0.52, 1.81)	0.933
Antidepression/anti-anxiety-		0.80 (0.43, 1.50)	0.490
HRT/Oral Contraceptives-	۱ <u>ــــ</u> ۱	0.92 (0.24, 3.49)	0.906
	Comorbidity		
Type 2 Diabetes-		0.76 (0.46, 1.26)	0.287
Hyperlipidemia -		1.21 (0.81, 1.81)	0.349
Hypertension-		0.88 (0.57, 1.35)	0.550
Depression -	<b>⊢</b> ●	0.83 (0.56, 1.22)	0.349
Anxiety-	<b>⊢●</b> I	0.88 (0.51, 1.35)	0.648
Coronary Artery Disease-		0.73 (0.41, 1.32)	0.302
Pyschotic Disease-	<b>⊢</b> I	0.78 (0.26, 2.37)	0.659
	More More Obesogenic Leptogenic		
(	) 1 2 3 4 OR for ≥ 5% TBWL (95% CI)	 	

**Figure 1** Factors associated with worse weight outcomes at the end of the MOVE! program. OR and 95% CI for  $\ge$  5%TBWL at the end of the MOVE! program. *P* values from logistic regression adjusted for obesity pharmacotherapy and differences in baseline characteristics between responders and nonresponders, including age, gender, BMI, and obesogenic and leptogenic medications. Bold indicates *P* < 0.05. [Colour figure can be viewed at wileyonlinelibrary.com]

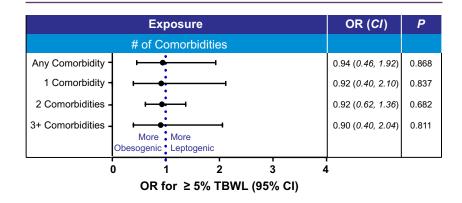
#### TABLE 3 Absolute weight loss for different numbers of obesogenic medications prescribed

Number of obesogenic medications	n (%)	TBWL ± SEM
0	255 (38.3)	$7.30 \pm 0.66$
1	204 (30.6)	$5.55 \pm 0.91$
2	135 (20.3)	6.84 ± 1.71
3+	72 (10.8)	2.90 ± 1.32

TBWL, total body weight loss (in pounds).

weight-control therapies, several factors, such as initial body weight, early weight loss, and other treatment factors and behavioral changes

have been found to account for 20% to 30% of observed variance in weight-loss success or failure (25). Our main conclusion is bolstered by a recent publication that showed that exposure to obesogenic medications had a significant effect on post-laparoscopic sleeve gastrectomy weight-loss outcomes. More specifically, patients on obesogenic medications lost significantly less weight 1 year after bariatric surgery compared with patients not using those drugs (53.8% of excess weight lost vs. 65.0%, respectively; P = 0.002) (26). Together, these studies show that regardless of patient population (i.e., predominantly male veterans, predominantly affluent women) and treatment modality (i.e., behavioral/dietary intervention, bariatric surgery), any exposure to obesogenic medications during treatment negatively affected weight-loss outcomes. For both studies, weight-loss outcomes were not associated with comorbidities. Hence, for all weight-loss treatment options, addressing the prescription of obesogenic medications could help to improve this observed variation in weight-loss success.



**Figure 2** Comorbidities were not associated with worse weight outcomes, and obesogenic effects could not be attributed to increased comorbidities. OR and 95% Cl for  $\geq$  5%TBWL at the end of the MOVE! program. *P* values from logistic regression adjusted for obesity pharmacotherapy and differences in baseline characteristics between responders and nonresponders, including age, gender, BMI, and obesogenic and leptogenic medications. [Colour figure can be viewed at wileyonlinelibrary.com]

#### TABLE 4 Weight-loss outcomes by comorbidity status

		Obesogenic medication group		onobesogenic dication group
Comorbidity	n	TBWL ± SEM	n	TBWL ± SEM
Hypertension	297	$6.32 \pm 0.89$	128	7.25 ± 0.99
Hyperlipidemia	270	$6.66 \pm 0.99$	122	$8.35 \pm 0.88$
Depression	200	5.48 ± 1.24	102	6.47 ± 1.12
Coronary artery disease	66	5.90 ± 1.50	17	7.62 ± 2.57
Type 2 diabetes	173	6.73 ± 1.41	41	9.43 ± 1.91
Anxiety	64	$5.05 \pm 1.42$	36	$6.32 \pm 1.74$
NAFLD	27	$6.54 \pm 1.57$	13	$6.68 \pm 2.46$
Psychoses	20	3.10 ± 1.74	6	$3.38 \pm 3.34$

TBWL, total body weight loss (in pounds); NAFLD, non-alcoholic liver disease.

TABLE 5 Weight-loss outcome analysis for different numbers of comorbidities

comorbidities	n (%)	TBWL ± SEM
0	54 (8.1)	6.08 ± 1.49
1	110 (16.5)	5.11 ± 1.32
2	188 (28.2)	$7.34 \pm 0.82$
3+	314 (47.1)	$5.92 \pm 0.87$

Our data support the 2015 clinical practice guidelines of the Endocrine Society, the European Society of Endocrinology, and the Obesity Society, which recommend leptogenic and weight-neutral medications as first- and second-line treatment in the management of patients with overweight and obesity with type 2 diabetes mellitus (13). Furthermore, identification of obesogenic medications in each clinical encounter is encouraged. Among the different classes of provider-prescribed obesogenic medications, patients on antihistamines, antidiabetic medications, and antipsychotics had significantly lower odds of achieving 5% weight loss in our study.

Understanding the obesogenic mechanism and impact of this drug class in the obesity epidemic and finding alternative agents could be important to improve weight-loss efforts. In 2012, 11.8% of the total prescriptions in the United States were for diabetes (27). The 2016 guidelines by the American Association of Clinical Endocrinologists and the American College of Endocrinology recommend early use of leptogenic or weight-neutral drug options, such as metformin, pramlintide, sodium/glucose cotransporter 2 inhibitors, dipeptidyl peptidase-4 inhibitors, or glucagon-like peptide-1 agonists, before using obesogenic medications such as insulin, sulfonylureas, and thiazolidinediones (19-21,28,29). In a prospective study of 3,234 patients, those metformin had greater weight loss compared with those in the placebo group (2.1 kg vs. 0.1 kg; P < 0.001) (30).

As obesogenic medications are frequently prescribed for common diseases, the use of alternatives is a challenging task requiring a multidisciplinary approach (31). Selecting a suitable alternative for disease management needs careful evaluation. Obstacles in the implementation of changes in prescription practices include exacerbation of a controlled disease and adverse effects from the new agent. Cost is also a considerable factor. For example, patients may require additional education and possibly extra care visits related to medication changes. Additionally, newer alternative agents could have increased cost compared with older agents; for example, on average, pramlintide costs \$250 for a month's supply versus the \$20 to \$30 cost for a glipizide prescription. Nevertheless, the benefits of weight loss, considering the tremendous negative effect of obesity in public health as well as each individual's morbidity and mortality, may outweigh possible risks and initial expenses. Previous experience from antibiotic safe prescription practices underlines that this multidisciplinary approach can be effective at different levels of the health care system, from societies and hospital policies to single providers. Change can be implemented in obesogenic drug use with a variety of strategies that focus on education and guidelines of safe practices, restricting agents based on indications, feedback from individual providers, computer assistance with information technology, and patient-specific recommendations (32,33). It should be noted that although published effects on weight for a given obesogenic agent may be modest, these effects should be considered as one of many factors that impact weight regulation and energy balance in a complex neurohormonal system, and efforts should be made to remove as many obstacles as possible for the difficult task of weight reduction.

Limitations of our study include a retrospective study design, unknown confounders that we could not identify and control, and data extraction from electronic records that were collected only for medical management purposes. We do not have data for adherence to the prescribed regimen. In addition, dosing and duration of treatment were not recorded for this study. Patients in our cohort had a VHA primary care physician and access to VHA pharmacies. Even though we cannot confirm that VHA pharmacies were the only source of medication dispensing, they have a lower cost, and, for most veterans, VHA is the single health care provider and use of outside pharmacies is limited (34). Nevertheless, primary care notes were screened for recorded medications prescribed outside of VHA. Moreover, we could not assess the use of over-the-counter drugs by our participants. However, over-the-counter drugs are more expensive than using VHA pharmacies, and frequency of their use was likely small. Finally, we excluded patients who did not complete the MOVE! program, some of whom may have quit the program because of lack of success. Whether these patients did not achieve 5%TBWL because of obesogenic medication or lack of participation would not be clear, and therefore their removal is justified. Of note, all of these factors would bias the results toward the null hypothesis. Our cohort of veterans consisted mostly of older Caucasian men, and generalization of these findings to the general population should be done cautiously. The short nature of the MOVE! program provides a unique cohort that is closely followed for 8 weeks. Inclusion in this study was dependent on both adequate participation, recorded intake weight, and recorded final weight upon completion of the program. Moreover, the short duration of the treatment program would bias the result toward the null hypothesis. Still, the effects of obesogenic medication on weight loss are robust enough to be detected in this scenario.

More research is necessary to evaluate the true impact of obesogenic drugs on weight-loss success after a behavioral weight-loss program. A prospective study would more accurately describe the effect of obesogenic drugs on weight-loss outcomes, such as randomization of patients to either continuation or discontinuation of obesogenic drugs prior to starting a weight-loss program.

## Conclusion

Despite growing evidence for medication-induced weight gain for numerous commonly prescribed medications, use of obesogenic medications in patients undergoing weight-loss efforts is frequent, and the impact on weight-loss outcomes has yet to be determined. This study was a retrospective case-control study that examined the effect of obesogenic medications on weight loss after an evidence-based behavioral weight-loss program. Obesogenic medication use was associated with a lower chance of achieving clinically meaningful weight loss. Our finding that higher numbers of obesogenic medications prescribed translates to worse weight-loss outcomes further supports this association. Antidiabetics showed a stronger association between exposure and weight-loss outcome. Improvement of prescription practices regarding commonly prescribed medications that cause weight gain could facilitate weight-loss efforts of patients undergoing behavioral weight-loss programs.**O** 

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