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Use of Medications Associated with Weight Change Among Participants in the *All of Us* Research Program

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Abstract

Our objective was to describe the use of medications associated with weight change among U.S. adults with overweight/obesity, including anti-obesity medications (AOMs), weight-loss-promoting and weight-gain-promoting medications. We performed a cross-sectional analysis of data from the nationwide *All of Us* Research Program. We included adults with measured body mass index (BMI) ≥ 27 kg/m^2 enrolled between 2018–2022 across the United States. We used linked electronic health record data to determine medication use ± 12 months of BMI measure. Our 132,057 participants had mean age 54 years and mean BMI 34 kg/m^2. 60% of participants were women, 62% White, and 32% Black. Only 1% used any AOM, and 14% used at least one weight-loss-promoting medication. We found that 36% used at least one weight-gain-promoting medication, and approximately 20% used multiple weight-gain-promoting medications. While AOMs are underutilized by participants with overweight/obesity, weight-gain-promoting medication use is common. Our results raise concern about potential iatrogenic weight gain from medications. Future research is needed to estimate the long-term effect of weight-gain-promoting medications on weight status and determine whether weight-loss benefits occur with their discontinuation. Clinician education on AOMs and weight-loss-promoting medications may be needed to increase their use.

Keywords

Anti-obesity agents; Drug side effects; Body weight changes; Obesity

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Author Contributions

EA and KAG conceived the study. EA analysed data, and EA and KAG interpreted results. All authors were involved in writing the paper and had final approval of the submitted and published versions.

INTRODUCTION

Obesity affects more than 40% of U.S. adults and is a well-established risk factor for multi-morbidity and all-cause mortality (1–2). While multiple factors influence weight regulation, medications are an underappreciated iatrogenic factor contributing to weight change (3). A few medications, including anti-obesity medications (AOMs), may facilitate weight loss, while others promote weight gain through a variety of mechanisms (4–5). For example, commonly used medications used to treat weight-related comorbidities, such as sulfonylureas for type 2 diabetes mellitus and beta-blockers for hypertension, have been associated with weight gain.

AOMs are indicated for weight reduction in combination with a comprehensive lifestyle intervention for adults with a body mass index (BMI) ≥ 30 kg/m^2 or ≥ 27 kg/m^2 with weight-related comorbidities (6–7). Currently, multiple AOMs are approved by the U.S. Food and Drug Administration (FDA), and clinical practice guidelines recommend the use of AOMs (7). However, data suggests that these medications are underutilized (8–11). For example, estimates from 1999–2010 and 2012–2016 suggest that only 2% and <1% of patients with obesity, respectively, were prescribed AOMs (10–11). AOM underutilization has been attributed to several factors. Clinicians receive limited training in obesity care, lack familiarity with AOMs, and may have bias towards patients with obesity – all of which may negatively impact treatment (12–13). Evidence shows that certain populations, particularly women and patients with higher BMI, are more likely to use AOMs, which suggests that patient characteristics may influence the decision to prescribe pharmacotherapy (14–15). Finally, clinician and patient concerns regarding the efficacy, safety, and cost of AOMs have also been cited as chief reasons limiting use (13). Given the recent increase in the number of FDA-approved AOMs (16), a reassessment of AOM use in a real-world clinical sample is warranted.

In contrast to low AOM use, medications to manage weight-related comorbidities have widespread utilization, and these medications can impact weight. Drug classes with strong evidence of weight change include antidiabetic, antihypertensive, contraceptive, anticonvulsant, antidepressant, antipsychotic, and corticosteroid medications (3–5,17–18). These drugs are frequently used when treating weight-related comorbidities, such as type 2 diabetes mellitus, hypertension, and depression (4,19–20). This concern has led to clinical practice guidelines encouraging the selection of weight-neutral or weight-loss-promoting medications in patients with obesity at treatment initiation (3). To date, we know of only one study that reported the prevalence of weight-gain-promoting medications, which used data from the National Health and Nutrition Examination Survey (NHANES) (17). Little is known about the frequency of weight-gain-promoting and weight-loss-promoting medications in a real-world clinical population; therefore, the potential impact of medications on iatrogenic weight change remains unclear.

In this study, our aim was to describe the prevalence of use of medications associated with weight change, including anti-obesity, weight-loss-promoting, and weight-gain-promoting medications, among a large, clinical cohort of U.S. adults with overweight/obesity.

METHODS

Study Design and Data Source

We conducted a cross-sectional analysis of data from the *All of Us* Research Program, which is a precision-medicine initiative sponsored by the National Institutes of Health (NIH) (21). Since 2018, the Program has collected data from volunteer participants across the nation. Any person residing within the U.S. is eligible to participate, and the Program actively recruits participants from populations historically underrepresented in medical research. All data is volunteered by participants who are ≥ 18 years of age, able to provide informed consent, and live in a U.S. territory at the time of enrollment. The Program includes data from multiple sources including electronic health records (EHR), anthropometrics, and surveys. EHR data is standardized using the Observational Medical Outcomes Partnership (OMOP) Common Data Model, and includes information such as medications and diagnoses. For anthropometrics, height and weight is specifically measured for the Program by the participant or partnering health organizations, and BMI is calculated from this measurement. Upon enrollment, the baseline survey includes information on demographics as well as health and lifestyle. Additional details on the data curation process are publicly available at https://allofus.nih.gov/.

For this study, we used the "*All of Us* Controlled Tier Dataset v6", which contains EHR, anthropometric, and survey data collected between May 2018 — February 2022. We included adults with BMI ≥ 27 kg/m^2 (overweight or greater) calculated from their most recent weight measurement, as this group represents a population where weight reduction would likely be recommended, AOM use may be indicated, and avoiding weight-gain-promoting medications would be recommended (3,6–7). We excluded individuals who were deceased or lacked information on age, sex, or race/ethnicity. Given that an individual's weight may change over time, we limited extraction of most data elements within ± 12 months of their last weight measurement. The National Institutes of Health's *All of Us* Research Program Institutional Review Board approved the protocol and materials for the *All of Us* Research Program (8). The Johns Hopkins School of Medicine Institutional Review Board approved this study.

Outcomes

Our primary outcomes were use of anti-obesity, weight-loss-promoting, and weight-gain-promoting medications, which were all derived from EHR data.

We first created rosters of relevant medications for each of these groups (Table S1). For AOMs, we identified medications approved by the FDA for weight reduction during the study period based on prior studies and through the online FDA database (6,10–11,16). Some identified medications were FDA approved for short-term use (Benzphetamine, Diethylpropion, Phendimetrazine, Phentermine), while others were approved for long-term use (Liraglutide, Lorcaserin (approved only from 2012–2020), Naltrexone-Bupropion, Orlistat, Phentermine-Topiramate, Semaglutide). Liraglutide and Semaglutide were approved for both type 2 diabetes mellitus and obesity; however, we were unable to distinguish between prescriptions for these two indications in the dataset.

Therefore, we allocated all prescriptions for Liraglutide and Semaglutide as weight-loss-promoting medications rather than AOMs. Of note, we also identified two medications approved for other obesity indications – one medication was approved for treatment of certain types of rare genetic obesity (Setmelanotide) and another was approved for treatment of binge eating disorder (Lisdexamfetamine). We did not include these medications as AOMs, given that their specific treatment indications do not include common obesity. Therefore, we included 8 medications in our final list of AOMs. For weight-loss-promoting medications, we identified medications based on guidelines that included a variety of medications such as anticonvulsants, antidepressants, and medications to treat type 2 diabetes mellitus (3). We used the same approach for weight-gain-promoting medications, and identified medications within anticonvulsants, antidepressants, atypical antipsychotics, beta-blockers, contraceptives, corticosteroids, and medications to treat type 2 diabetes mellitus (3–5,17–18). Of note, we identified that some included medications were available as single agents or offered in combination with other medications (Table S2). We allocated components of combination medications to either weight-loss-promoting or weight-gain-promoting, as appropriate, in the estimates (Table S3).

We then identified participants with use of these medications documented in the EHR. Within the dataset, drug exposures are defined as an EHR entry for the start date of a prescription, the fill date of a prescription, or the administration date of a medication. We limited the sample to only oral formulations of medications (with the exception of insulins and glucagon-like peptide-1 (GLP-1) receptor agonists), as the weight change effect of other preparations (e.g., topical, ophthalmic, intravenous, etc) has not been well characterized. We defined use of each medication if exposure to that drug occurred within ± 12 months of their last weight measurement. We also individually calculated the number of participants with use of any anti-obesity, weight-loss-promoting, and weight-gain-promoting medications by identifying participants with a drug exposure to at least one medication in the relevant category. Finally, we individually determined counts of weight-loss-promoting and weight-gain-promoting medications by adding the number of drug exposures to unique medications in each category.

Other Measures

To characterize the sample included in this study, we examined other measures available in the dataset. We identified several weight-related comorbidities, including type 2 diabetes mellitus, within ± 12 months of their last weight measurement (2,6), which were derived from EHR data using the relevant 10th International Statistical Classification of Diseases and Related Health Problems (ICD-10) diagnostic codes. We also used data from two surveys in the dataset – *The Basics* and *Overall Health* questionnaires – collected within ± 36 months of their last weight measurement. Specifically, we examined educational attainment, annual household income, health insurance status and self-reported health status from these questionnaires.

Statistical Analysis

All analyses were conducted with Python 3 (Python Software Foundation, Wilmington, DE). We conducted descriptive analyses of all variables and report means and proportions, as

appropriate. We examined measures in the overall sample, as well as limited to participants with overweight (BMI ≥ 27 kg/m^2 and < 30 kg/m^2) and participants with obesity (BMI ≥ 30 kg/m^2). Additionally, we examined measures among a subset of participants with type 2 diabetes mellitus. Data visualization was completed with Microsoft Excel version 16.70 (Microsoft Corporation, Redmond,WA).

RESULTS

Physical measurement and EHR data were available for 306,179 and 258,415 participants, respectively. 132,057 participants had both physical measurement and EHR data, and met the inclusion criteria for our study. Table 1 displays the attributes of our sample. Mean age was 54 years (SD 16), 60.4% were women, and race was predominantly White (62.0%) and Black (31.7%). The population had high levels of education (68.1% with some college or greater) and nearly all participants were insured (90.2%). The most common weight-related comorbidity was hypertension (30.7%). In the sample, 30.1% were participants with overweight (27 kg/m^2 ≤ BMI < 30 kg/m^2) and 69.9% with obesity (BMI ≥ 30 kg/m^2). There were some differences between these groups – as compared to overweight, the group with obesity was comprised of more participants who were women (64.5% vs. 50.9%), identified as Black (34.4% vs. 25.3%), and reported fair/poor health status (29.5% vs. 16.9%). Of note, only 21.9% of included participants had a diagnosis of overweight/obesity in their medical record.

Anti-Obesity and Weight-Loss-Promoting Medications

Table 2 presents the prevalence of use of AOMs and weight-loss-promoting medications. We found that only 1.0% of participants used any AOM during the study period, and Phentermine was the most commonly used medication (0.8%). Participants with obesity had higher use of AOMs than participants with overweight (1.3% vs 0.4%, respectively). Overall, 14.3% of participants used at least one weight-loss-promoting medication, and the most commonly used medications were metformin (8.6%) and bupropion (4.1%). Very few participants used more than one weight-loss-promoting medication (Figure 1). Participants with obesity had higher use of weight-loss-promoting medications than participants with overweight (16.5% vs 9.0%, respectively).

Weight-Gain-Promoting Medications

Table 3 presents the prevalence of use of weight-gain-promoting medications. Overall, 35.8% of participants used weight-gain-promoting medications. The most commonly used weight-gain-promoting medications were insulin formulations (14.1%), gabapentin (11.7%), prednisone (10.4%), and metoprolol formulations (10.6%). Approximately, 20% of participants used multiple weight-gain-promoting-medications (Figure 2), and over 300 participants used 9 or more weight-gain-promoting medications (n=343, 0.3%). Participants with obesity had higher use of weight-gain-promoting medications than participants with overweight (38.1% vs 30.6%, respectively). Of note, 11.1% of participants used both weight-loss-promoting and weight-gain-promoting medications.

Subgroup of Participants with Type 2 Diabetes Mellitus and Overweight/Obesity

Overall, 19,180 participants in our cohort had a diagnosis of type 2 diabetes mellitus and overweight/obesity (14.5%). Table S4 presents the demographic characteristics of this subgroup. Mean age was 60 years (SD 12), 57.6% were women, and race was predominately White (60.5%) and Black (33.8%). Table S5 presents prevalence of use of AOMs and weight-loss-promoting medications in this subgroup. In brief, 1.2% of these participants used any AOM and 50.3% used at least one weight-loss-promoting medication. The most commonly used weight-loss-promoting medications were: metformin (42.0%), bupropion (6.6%), dulaglutide (5.9%), empagliflozin (5.8%), and liraglutide (5.0%). Among the type 2 diabetes mellitus subgroup, participants with obesity had higher use of weight-loss-promoting medications than participants with overweight (51.6% vs 45.2%, respectively). Table S6 presents prevalence of use of weight-gain-promoting medications in this subgroup. Overall, 71.6% used at least one weight-gain-promoting medication, and most commonly used were insulin formulations (75.9%), metoprolol formulations (26.9%), and gabapentin (25.8%). Participants with obesity had higher use of weight-gain-promoting medications than participants with overweight (72.3% vs 68.4%, respectively).

DISCUSSION

We found that the use of AOMs and weight-loss-promoting medications among a real-world sample of adults with overweight/obesity was low. In contrast, the use of weight-gain-promoting medications was relatively high – 35.8% used at least one weight-gain-promoting medication, whereas only 14.3% used any weight-loss-promoting medications and AOM use was even lower at 1.0%. Given our results, a substantial number of patients with overweight/obesity, including patients with concomitant type 2 diabetes mellitus, could be impacted by potential iatrogenic weight-change effects from medications.

An analysis of NHANES data from 1999–2018 showed that the overall use of weight-gain-promoting medications rose from 13.2% in 1999–2000 to 20.3% in 2017–2018 across all individuals (17). This study also found that the use of weight-gain-promoting medications correlated with weight status, where higher BMI groups were more likely to be prescribed a weight-gain-promoting medication – 11.5% of normal weight, 17.6% overweight, 23.9% class I/II obesity, and 25.6% class III obesity. In our real-world cohort, we found that 35.8% of participants with BMI ≥ 27 kg/m^2 used at least one weight-gain-promoting medication and approximately 20.0% used more than one. Another study found that individuals with low socioeconomic status (SES) may be more likely to use a weight-gain-promoting medication (22). A prior systematic review documented that the magnitude of weight gain varies by medication, although many randomized controlled trials included were short-term (4). Additional research is needed to examine how weight-gain-promoting medications impact weight status long-term as well as how the use of multiple weight-gain-promoting medications influences magnitude of weight gain.

Overall, the body of evidence shows that the use of weight-gain-promoting medications occurs commonly among individuals with known overweight/obesity – the same individuals who would most benefit from weight reduction. Prior trials have found that baseline use of weight-gain-promoting medications is linked to poor weight-loss outcomes (23–24). For

example, baseline insulin use was associated with less weight-loss among Look AHEAD trial participants taking part in an intensive lifestyle intervention (23). To date, clinical practice guidelines recommend avoiding initiation of weight-gain-promoting medications among patients with established obesity (3); however, none address how to manage patients with obesity already on weight-gain-promoting medications. Additional research is needed to determine whether weight-loss benefits might occur with discontinuation of weight-gain-promoting medications.

We found that the use of weight-loss-promoting medications was relatively low, and we believe that this is the first study to document prevalence of their use. Prior studies have focused only on FDA-approved AOMs. Many of the weight-loss-promoting medications that we examined are used in the treatment of weight-related conditions, and our results may highlight opportunities for modification of prescribing practices to help support weight reduction among patients with overweight/obesity. For example, we found relatively low use GLP-1 receptor agonists (2.8% among all formulations), which have demonstrated weight-loss benefits in clinical trials (25). Additionally, more participants were prescribed a weight-gain-promoting antidepressant (6.7% across all medications) as compared to Bupropion (4.1%), which is weight-loss-promoting. In theory, increased use of weight-loss-promoting medications for certain weight-related comorbidities, like diabetes mellitus or depression, could shift the population-level weight-status among patients with certain weight-related comorbidities, like diabetes mellitus and depression, to a lower mean BMI.

Similar to prior results, we found that the use of AOMs was very low at 1%. Previous studies examined the prevalence between 1999–2010 (2% use)(10), when there were fewer FDA-approved AOMs, and between 2012–2016 (<1% use)(11), when Naltrexone-Bupropion, Phentermine-Topiramate, and Lorcaserin had only recently been FDA approved (2012, 2014, and 2016 respectively)(13). A prior study using EHR data to examine AOM use found that the prevalence of use was 1.3% between 2009–2015 (27). In 2016, the American Association of Clinical Endocrinologists/American College of Endocrinology issued comprehensive practice guidelines for the medical care of patients with obesity, which encouraged use of AOMs (7). We theorized that AOM prescribing habits may have changed after publication of these guidelines. In contrast, we found that AOM use has remained the same between 2018–2022 within the EHR data examined.

Multiple factors likely contribute to the persistently low AOM use. Clinicians cite insufficient knowledge as a barrier to initiating weight-loss discussions, have limited experience with AOMs, and concerns about side effects and adverse events – all of which negatively impact their decision to prescribe AOMs (28). Obesity medicine training through board certification with the American Board of Obesity Medicine is associated with adherence to guideline-concordant obesity care and use of AOMs (29). Therefore, clinician education may be essential to increasing AOM use, perhaps through accessible, continuing medical education that reviews AOMs and weight-loss-promoting alternatives to commonly prescribed medications for weight-related comorbidities (30). In addition, insurance coverage for AOMs has typically been poor and has also been cited as a limitation to their use (11,31–32). Expansion of AOM coverage, such as that for federal employees

in 2023 (33), may help to increase use. Future studies will be needed to determine whether increased benefits coverage impacts AOM use.

We also conducted a subgroup analysis among participants with type 2 diabetes mellitus and overweight/obesity. In this subgroup, the use of AOMs was similar to the overall cohort at 1.2%. However, the use of weight-loss-promoting medications and weight-gain-promoting were both higher with 50.3% using any weight-loss-promoting medication and 71.6% using any weight-gain promoting medication. Clinicians should note that recent clinical practice guidelines for the treatment of patients with diabetes mellitus encourage the use of glucose-lowering agents that are weight-loss-promoting rather than weight-gain-promoting, when possible (34). We found that metformin was commonly used; however, we identified low use of GLP-1 receptor agonists and sodium-glucose co-transporter-2 (SGLT2) inhibitors among this subgroup. Given that our study dates precede these recent clinical practice guidelines, future research should reassess use of weight-loss-promoting hypoglycemic agents.

Our study has several limitations. This study uses data from an NIH initiative recruiting volunteer participants, which may introduce selection bias. Participants in our cohort had high levels of education and were mostly insured, which may reflect high SES. A recent NHANES analysis found that low SES is associated with greater use of weight-gain-promoting medications in adults with overweight/obesity, while AOM use was low irrespective of SES (23). Therefore, our study may underestimate the use of weight-gain-promoting medications as compared to what might be expected among people an entire U.S. sample. Despite this possible selection bias, it is important to note that the *All of Us* Research Program has prioritized recruiting historically underrepresented groups in medical research, and approximately 32% of our sample identified as Black. While participants from the *All of Us* Research Program are not necessarily representative of the entire U.S. population, this observational study adds valuable information on medications associated with weight change that is inclusive of racial and ethnic groups with limited representation in the medical literature (4). We determined eligibility into the sample by a single BMI measure and captured medication use within ±12 month window of the measurement. Therefore, we are unable to determine how the relevant medications may have affected weight status and duration of medication use is unknown. We were unable to explore factors associated with use of anti-obesity, weight-loss-promoting, and weight-gain-promoting medications, as the data use agreement for the Program prohibits examining such participant-level data. Future studies should examine patient and clinician-factors associated with differences in these prescribing patterns. Finally, we were unable to determine indication in the available medication data. Therefore, we were unable to distinguish whether liraglutide or semaglutide were prescribed for type 2 diabetes mellitus or obesity, and categorized all use together as weight-loss-promoting medications. Of note, as a proxy to identify anti-obesity as the indication for prescribing, we examined liraglutide and semaglutide use among participants with obesity and without type 2 diabetes mellitus (use of both was low); however, this approach may still underestimate use of these medications for weight reduction. We could not determine whether a weight-loss-promoting medication was being prescribed off-label for obesity (e.g., prescribing Bupropion and Naltrexone individually rather than the Naltrexone-Bupropion combination). As a result, the prevalence of AOM use may be underestimated.

In conclusion, AOMs and weight-loss-promoting medications are used infrequently among individuals with overweight/obesity as compared to weight-gain-promoting medications. Our results raise concern about the potential impact of iatrogenic weight gain from medications as a driver of the obesity epidemic. Future research is needed to estimate the long-term effect of weight-gain-promoting medications on weight status and to determine whether weight-loss benefits occur with their discontinuation. Clinician education and increased insurance coverage for AOMs may be needed to increase utilization of weight-loss-promoting medications.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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CONFLICTS OF INTEREST

KAG serves as the medical director for the American Board of Obesity Medicine, has a research grant from Novo Nordisk, and is a paid consultant to Eli Lilly. JLS is a co-investigator on a research grant from Novo Nordisk. All other authors declare that they have no competing interests.

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WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Anti-obesity medications have historically been underused among eligible patients with overweight/obesity.
- Medications to manage weight-related comorbidities have widespread use and some medications can impact weight – both weight gain and loss.

WHAT THIS STUDY ADDS

- Use of anti-obesity medications remains low despite clinical practice guidelines supporting their use.
- First study describing weight-loss-promoting medications, which are used by ~1 in 7 participants.
- More than 1 in 3 participants with overweight/obesity use weight-gain-promoting medications, and 1 in 5 used multiple of these medications.

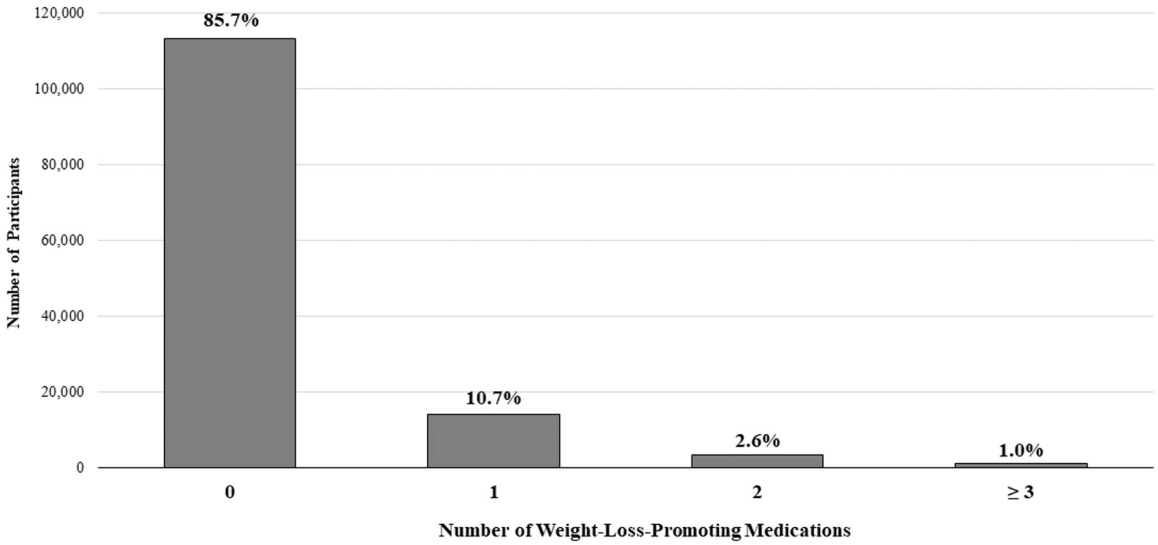

Figure 1. Weight-Loss-Promoting Medication Use among Included Participants in the *All of Us* Research Program.

Among adults with BMI ≥ 27 kg/m^2, we report the count of all weight-loss-promoting medications identified in the electronic health record within ± 12 months of weight measurement. Upper limit was defined as a count of ≥ 3 weight-loss-promoting medications (excluding anti-obesity medications).

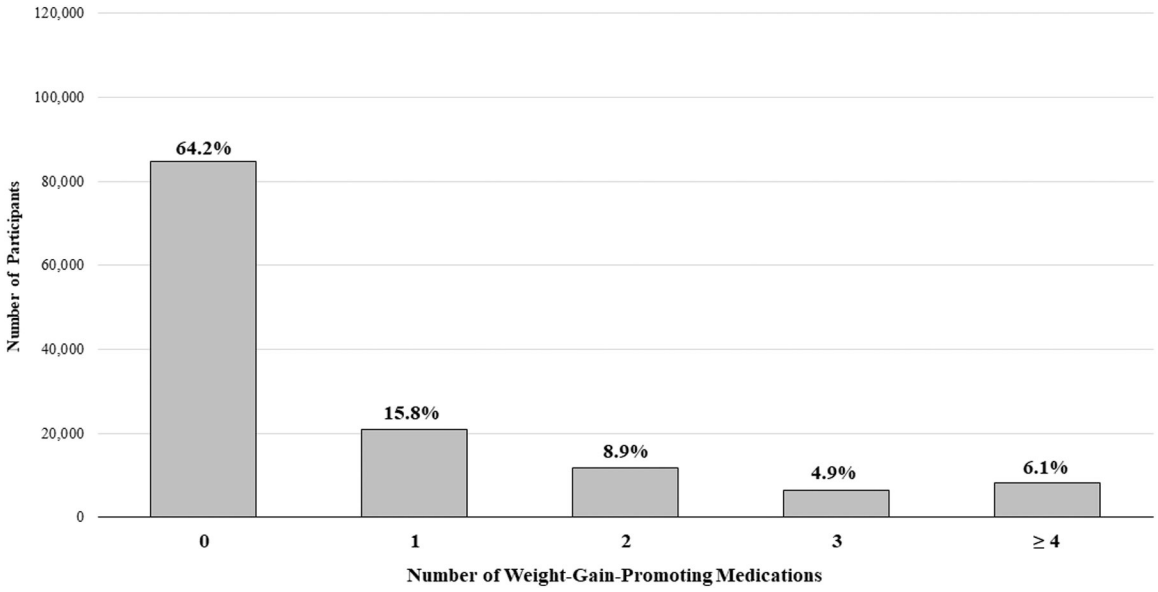

Figure 2. Weight-Gain-Promoting Medication Use among Included Participants in the *All of Us* Research Program.

Among adults with BMI ≥ 27 kg/m^2, we report the count of all weight-gain-promoting medications identified in the electronic health record within ± 12 months of weight measurement. Upper limit was defined as a count of ≥ 4 weight-gain-promoting medications.

Table 1.

Characteristics of Included Participants from the *All of Us* Research Program

	Overweight* (n=39,799)	Obesity* (n=92,258)	Overall (n=132,057)
Demographics			
Age (years), Mean ± SD	55 ± 17	53 ± 15	54 ± 16
Sex, n (%)			
Men	19,535 (49.1)	32,770 (35.5)	52,305 (39.6)
Women	20,264 (50.9)	59,488 (64.5)	79,752 (60.4)
Race, n (%)			
White	26,599 (66.8)	55,221 (59.8)	81,811 (62.0)
Black	10,078 (25.3)	31,737 (34.4)	41,815 (31.7)
Asian	1,392 (3.5)	1,401 (1.5)	2,793 (2.1)
Native Hawaiian or Pacific Islander	57 (0.1)	197 (0.2)	254 (0.2)
Middle Eastern or North African	347 (0.9)	525 (0.6)	872 (0.7)
Other	1,326 (3.3)	3,186 (3.5)	4,512 (3.4)
Hispanic, n (%)	1,079 (2.7)	2,731 (3.0)	3,810 (2.9)
Educational Attainment, n (%)**			
Never Attended	12 (0.0)	27 (0.0)	39 (0.0)
Grades 1–8	395 (1.0)	990 (1.1)	1,385 (1.0)
Grades 9–12	9,239 (23.2)	26,548 (28.8)	35,787 (27.1)
Some College/College	19,144 (48.1)	46,649 (50.6)	65,793 (49.8)
Advanced Degree	9,509 (23.9)	14,723 (16.0)	24,232 (18.3)
Annual Household Income, n (%)**			
Less than $34,999	11,930 (30.0)	35,546 (38.5)	47,476 (36.0)
$35,000-$149,999	15,538 (39.0)	33,404 (36.2)	48,942 (37.1)
$150,000 or more	4,996 (12.6)	6,569 (7.1)	11,565 (8.8)
Insurance Status, n (%)**			
Insured	36,087 (90.7)	83,082 (90.1)	119,169 (90.2)
Uninsured	2,124 (5.3)	5,542 (6.0)	7,666 (5.8)
Health Status			
Body Mass Index, Mean ± SD	28 ± 1	37 ± 7	34 ± 7
Diagnosed Comorbid Conditions, n (%)***			
Atherosclerosis	659 (1.7)	1,497 (1.6)	2,156 (1.6)
Essential Hypertension	10,145 (25.5)	30,411 (33.0)	40,556 (30.7)
Gastroesophageal Reflux Disease	5,909 (14.8)	16,764 (18.2)	22,673 (17.2)
Hyperlipidemia	7,953 (20.0)	19,697 (21.3)	27,650 (20.9)
Low Back Pain	589 (1.5)	1,752 (1.9)	2,341 (1.8)
Nonalcoholic Fatty Liver Disease	815 (2.0)	3,725 (4.0)	4,540 (3.4)
Obstructive Sleep Apnea	2,441 (6.1)	12,736 (13.8)	15,177 (11.5)
Osteoarthritis	8,187 (20.6)	23,430 (25.4)	31,617 (23.9)
Overweight/Obesity	2,437 (6.1)	26,468 (28.7)	28,905 (21.9)

	Overweight* (n=39,799)	Obesity* (n=92,258)	Overall (n=132,057)
Type 2 Diabetes Mellitus	3,678 (9.2)	15,502 (16.8)	19,180 (14.5)
Self-Reported Health Status, n (%)**			
Excellent	4,582 (11.5)	4,975 (5.4)	9,557 (7.2)
Very Good	14,102 (35.4)	21,419 (23.2)	35,521 (26.9)
Good	12,991 (32.6)	35,758 (38.8)	48,749 (36.9)
Fair	5,616 (14.1)	22,197 (24.1)	27,813 (21.1)
Poor	1,123 (2.8)	4,974 (5.4)	6,097 (4.6)

*Overweight includes participants with body mass index ≥ 27 kg/m^2 and < 30 kg/m^2. Obesity includes participants with body mass index ≥ 30 kg/m^2. Body mass index was calculated from measured height and weight.

**Data derived from survey data collected ± 36 months of weight measurement. Columns do not add up to 100% due to missing data.

***Comorbid conditions identified via diagnosis codes within the electronic health record.

Table 2.

Anti-Obesity and Weight-Loss-Promoting Medication Use among Included Participants in the *All of Us* Research Program*

	Overweight** (n=39,799)	Obesity** (n=92,258)	Overall (n=132,057)
Anti-Obesity Medications, by Type			
Short-term AOMs, n (%)			
Benzphetamine	0 (0.0)	1 (0.0)	1 (0.0)
Diethylpropion	1 (0.0)	5 (0.0)	6 (0.0)
Phendimetrazine	3 (0.0)	8 (0.0)	11 (0.0)
Phentermine	140 (0.4)	871 (0.9)	1,011 (0.8)
Long-term AOMs, n (%)			
Lorcaserin***	11 (0.0)	95 (0.1)	106 (0.1)
Naltrexone-Bupropion	14 (0.0)	151 (0.2)	165 (0.1)
Orlistat	8 (0.0)	75 (0.1)	83 (0.1)
Phentermine-Topiramate	0 (0.0)	77 (0.1)	77 (0.1)
Any AOM, n (%)	**167 (0.4)**	**1,165 (1.3)**	**1,332 (1.0)**
Weight-Loss-Promoting Medications, by Type			
Anticonvulsants, n (%)			
Felbamate	1 (0.0)	1 (0.0)	2 (0.0)
Topiramate	497 (1.2)	2,371 (2.6)	2,868 (2.2)
Zonisamide	46 (0.1)	159 (0.2)	205 (0.2)
Antidepressants, n (%)			
Bupropion	1,249 (3.1)	4,204 (4.6)	5,453 (4.1)
GLP-1 Receptor Agonists, n (%)			
Dulaglutide	178 (0.4)	1,209 (1.3)	1,387 (1.1)
Exenatide	31 (0.1)	218 (0.2)	249 (0.2)
Liraglutide****	165 (0.4)	1,158 (1.3)	1,323 (1.0)
Lixisenatide	4 (0.0)	16 (0.0)	20 (0.0)
Semaglutide****	82 (0.2)	657 (0.7)	739 (0.6)
Other Glucose-Lowering Agents, n (%)			
Metformin	1,928 (4.8)	9,380 (10.2)	11,308 (8.6)
Pramlintide	2 (0.0)	6 (0.0)	8 (0.0)
SGLT2 Inhibitors, n (%)			
Canagliflozin	51 (0.1)	208 (0.2)	259 (0.2)
Dapagliflozin	29 (0.1)	178 (0.2)	207 (0.2)
Empagliflozin	238 (0.6)	1,036 (1.1)	1,274 (1.0)
Ertugliflozin	9 (0.0)	49 (0.1)	58 (0.0)
Any Weight-Loss-Promoting Medication, n (%)	**3,566 (9.0)**	**15,261 (16.5)**	**18,827 (14.3)**

Abbreviations: AOM – anti-obesity medication; GLP-1 – glucagon-like peptide-1; SGLT2 – sodium-glucose co-transporter-2.

*We include medication use reported within ± 12 months of weight measurement.

** Overweight defined as a body mass index ≥ 27 kg/m^2 and < 30 kg/m^2. Obesity defined as body mass index ≥ 30 kg/m^2.

*** Lorcaserin was FDA-approved during study time frame; however, has since been removed from the market.

**** Liraglutide and semaglutide are approved by the Food and Drug Administration for both the treatment of diabetes mellitus and obesity. We are unable to distinguish between prescriptions for these two conditions; therefore, only list them under weight-loss-promoting medications. We conducted a sensitivity analysis reporting the prevalence of use of these medications among participants with obesity and without a diagnosis of type 2 diabetes mellitus (n=76,756) as a proxy for potential use as an AOM. This analysis found that 325 participants used liraglutide (0.4%) and 191 used semaglutide (0.2%).

Table 3.

Weight-Gain-Promoting Medication Use among Included Participants in the *All of Us* Research Program*

	Overweight* (n=39,799)	Obesity* (n=92,258)	Overall (n=132,057)
Weight-Gain-Promoting Medications, by Type			
Anticonvulsants, n (%)			
Carbamazepine	109 (0.3)	341 (0.4)	450 (0.3)
Divalproex sodium	188 (0.5)	603 (0.7)	791 (0.6)
Gabapentin	3,683 (9.3)	11,726 (12.7)	15,409 (11.7)
Pregabalin	473 (1.2)	2,000 (2.2)	2,473 (1.9)
Valproic acid	88 (0.2)	231 (0.3)	319 (0.2)
Vigabatrin	0 (0.0)	1 (0.0)	1 (0.0)
Antidepressants, n (%)			
Amitriptyline	492 (1.2)	1,712 (1.9)	2,204 (1.7)
Citalopram	672 (1.7)	2,123 (2.3)	2,795 (2.1)
Mirtazapine	489 (1.2)	1,126 (1.2)	1,615 (1.2)
Nortriptyline	276 (0.7)	856 (0.9)	1,132 (0.9)
Paroxetine	258 (0.6)	838 (0.9)	1,096 (0.8)
Atypical Antipsychotics, n (%)			
Clozapine	18 (0.0)	47 (0.1)	65 (0.0)
Olanzapine	260 (0.7)	706 (0.8)	966 (0.7)
Perphenazine	99 (0.2)	308 (0.3)	407 (0.3)
Quetiapine	545 (1.4)	1,541 (1.7)	2,086 (1.6)
Risperidone	196 (0.5)	664 (0.7)	860 (0.7)
Beta-Blockers, n (%)			
Atenolol	524 (1.3)	1,521 (1.6)	2,045 (1.5)
Metoprolol***	3,609 (9.1)	10,407 (11.3)	14,016 (10.6)
Propranolol	444 (1.1)	1,244 (1.3)	1,688 (1.3)
Contraceptives, n (%)			
Medroxyprogesterone	246 (0.6)	1,089 (1.2)	1,335 (1.0)
Corticosteroids (oral), n (%)			
Budesonide	205 (0.5)	600 (0.7)	805 (0.6)
Cortisone	47 (0.1)	140 (0.2)	187 (0.1)
Dexamethasone	1,585 (4.0)	4,263 (4.6)	5,848 (4.4)
Hydrocortisone	283 (0.7)	767 (0.8)	1,050 (0.8)
Methylprednisolone	2,251 (5.7)	6,783 (7.4)	9,034 (6.8)
Prednisolone	117 (0.3)	296 (0.3)	413 (0.3)
Prednisone	3,341 (8.4)	10,401 (11.3)	13,742 (10.4)
Insulins, n (%)			
Insulin	2 (0.0)	20 (0.0)	22 (0.0)
Insulin Aspart	836 (2.1)	3,218 (3.5)	4,054 (3.1)
Insulin Degludec	101 (0.3)	421 (0.5)	522 (0.4)

	Overweight* (n=39,799)	Obesity* (n=92,258)	Overall (n=132,057)
Insulin Detemir	161 (0.4)	606 (0.7)	767 (0.6)
Insulin Glargine	833 (2.1)	3,779 (4.1)	4,612 (3.5)
Insulin Glulisine	10 (0.0)	62 (0.1)	72 (0.1)
Insulin Isophane	84 (0.2)	428 (0.5)	512 (0.4)
Insulin Isophane Regular	90 (0.2)	496 (0.5)	586 (0.4)
Insulin Lente	0 (0.0)	3 (0.0)	3 (0.0)
Insulin Lispro	993 (2.5)	4,307 (4.7)	5,300 (4.0)
Insulin Regular	468 (1.2)	1,768 (1.9)	2,236 (1.7)
Meglitinides, n (%)			
Nateglinide	6 (0.0)	17 (0.0)	23 (0.0)
Repaglinide	30 (0.1)	101 (0.1)	131 (0.1)
Sulfonylureas, n (%)****			
Glimepiride	159 (0.4)	785 (0.9)	944 (0.7)
Glipizide	383 (1.0)	1,786 (1.9)	2,169 (1.6)
Glyburide	29 (0.1)	180 (0.2)	209 (0.2)
Tolbutamide	0 (0.0)	1 (0.0)	1 (0.0)
Thiazolidinediones, n (%)			
Pioglitazone	164 (0.4)	656 (0.7)	820 (0.6)
Rosiglitazone	0 (0.0)	2 (0.0)	2 (0.0)
Any Weight-Gain-Promoting Medication, n (%)	**12,192 (30.6)**	**35,111 (38.1)**	**47,303 (35.8)**

* We include medication use reported within ± 12 months of weight measurement.

** Overweight defined as a body mass index ≥ 27 kg/m^2 and < 30 kg/m^2. Obesity defined as body mass index ≥ 30 kg/m^2.

*** Includes prescriptions for metoprolol, metoprolol succinate and metoprolol tartrate.

**** We identified no prescriptions for the following sulfonylureas: Chlorpropamide, Glibenclamide, Glicazide, and Tolazamide.