Effect of anti-obesity medications on cardiovascular events in the Veterans Affairs patient population

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BACKGROUND

Obesity is a significant public health challenge, and the US military veteran population is disproportionately affected, with an obesity rate of approximately 41% among veterans.[1] Anti-obesity medications (AOMs) are associated with clinically significant weight loss among veterans with overweight or obesity,[2] yet their beneficial effect on cardiovascular risk within this population has not been studied.

OBJECTIVES

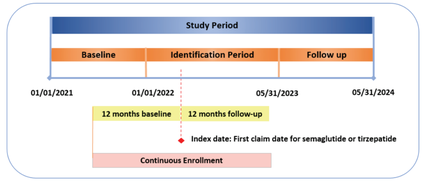
In the US Veterans Health Affairs (VHA) patient population, the effect of AOMs on the risk of cardiovascular events, specifically among patients with tirzepatide (Mounjaro) and semaglutide (Wegovy) use were examined.

METHODS

Setting

Retrospective cohort study of the VHA population (2021-2024) with an identification period from January 1, 2022, to May 31, 2023, and follow-up until May 31, 2024 (**Figure 1**).

Figure 1. Study Design



Sample

VHA patients with obesity (ICD-10: E66.9, E66.09, E66.1, E66.8, Z68.3) were categorized as follows:

- **AOM cohort**: Patients prescribed tirzepatide or semaglutide during the identification period (index date = first AOM claim)
- **Non-AOM Cohort**: Patients not prescribed AOMs, with randomly selected index dates

Detailed inclusion and exclusion criteria are listed in **Table 1**.

METHODS (cont'd)

Outcomes

Risk of the following conditions were assessed for the 1-year follow-up period: coronary artery disease (CAD; ICD-10: I25), heart failure (HF; ICD-10: I50), atrial fibrillation (AF; ICD-10: I48.91), arrhythmia (ICD-10: I49), ischemic heart disease (ICD-10: I25.9), stroke (ICD-10: I63.9), and peripheral vascular disease (PVD; ICD-10: I73.9).

Analysis

A descriptive analysis was conducted to assess sociodemographic and clinical characteristics and calculate cardiovascular disease outcomes.

Cox regression models were employed to examine the relationship between cardiovascular risk and AOM utilization, adjusting for baseline sociodemographic and clinical factors. Comparisons were made between AOM users and non-users, as well as between tirzepatide and semaglutide users.

RESULTS

In the AOM Cohort, 2,347 beneficiaries met the inclusion requirements (1,083 tirzepatide and 1,264 semaglutide users) and 11,055 patients were included in the non-AOM cohort (**Table 1**).

Table 1. Study attrition

	Inclusion criteria	AOM Cohort (tirzepatide or semaglutide) (n)	Non-AOM (n)
1)	≥1 pharmacy claim for an AOM (semaglutide or tirzepatide) during the identification period (1/1/22 - 5/31/23). The first prescription claim was considered the treatment initiation date.	16,076	N/A
2)	Not prescribed any obesity medications during the identification period (1/1/22 - 5/31/23). Index dates were randomly selected between the minimum and maximum index dates for the AOM cohort.	N/A	2,788,478
3)	≥1 claim with a diagnosis of obesity prior to index date	3,797	347,300
	Exclusion criteria		
1)	Prescribed any obesity medication during the study period	N/A	340,671
2)	≥1 claim with any obesity medications during the baseline	3,012	N/A
3)	>1 claim of obesity medication on the same index date	2,923	N/A
4)	≥1 claim with cardiovascular disease during the baseline	2,347	219,853
5)	Age ≥99 years on the index date	**2,347**	219,853
	Random 5% sample of patients with obesity and no AOM use		**11,055**

AOM: anti-obesity medication

Patients using AOMs were younger and more likely to be female than non-AOM users. The non-AOM cohort had a higher Charlson Comorbidity Index (CCI) score and more comorbidities but a lower Chronic Disease Score (CDS) than the AOM cohort (**Table 2**).

In the AOM cohort, semaglutide users were more likely to be younger (49.27 vs 53.79 years, p<0.001), female (75.79% vs 65.10%, p<0.001), have lower comorbidity scores (CCI score: 10.05% vs 30.01%, CDS: 56.65% vs 63.62%, Elixhauser: 72.39% vs 83.75%; all p<0.05), and were less likely to have any CVD-related comorbidity (57.67% vs 74.52%, p<0.0001) than tirzepatide users.

RESULTS (cont'd)

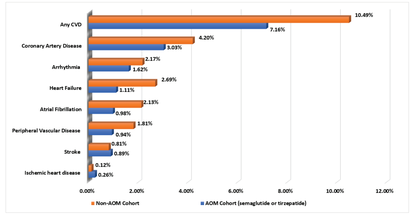
Table 2. Baseline Characteristics of Patients in the AOM and non-AOM cohorts

Characteristics	AOM Cohort (N = 2,347)	Non-AOM Cohort (N = 11,055)	P-value
Age (years), mean (SD)	51.36 (12.56)	58.95 (16.54)	<0.0001
Age_group, n (%)			
18-40 years	508 (21.64)	1,401 (12.67)	<0.0001
41-60 years	1,262 (53.77)	3,549 (32.10)	<0.0001
61-80 years	565 (24.07)	5,364 (48.52)	<0.0001
80+ years	12 (0.51)	621 (5.62)	<0.0001
Gender, n (%)			
Male	684 (29.14)	6,083 (55.02)	<0.0001
Female	1,663 (70.86)	4,971 (44.97)	<0.0001
Comorbidity scores, n (%)			
CCI ≥2	452 (19.26)	2,804 (25.36)	<0.0001
CDS ≥2	1,405 (59.86)	3,252 (29.42)	<0.0001
Elixhauser Score ≥2	1,822 (77.63)	8,427 (76.23)	0.1455
SES, n (%)			
Low	819 (34.90)	3,436 (31.08)	0.0003
Medium	741 (31.57)	3,514 (31.79)	0.8395
High	714 (30.42)	3,668 (33.18)	0.0097
Baseline CVD-related comorbidities, n (%)			
Hypertension	1,157 (49.30)	6,101 (55.19)	<0.0001
Hyperlipidemia	678 (28.89)	3,689 (33.37)	<0.0001
Type 2 diabetes	580 (24.71)	2,903 (26.26)	0.1206
COPD	71 (3.03)	837 (7.57)	<0.0001
Smoking history	185 (7.88)	1,165 (10.54)	0.0001
Alcohol use disorder	37 (1.58)	356 (3.22)	<0.0001
Chronic kidney disease	31 (1.32)	246 (2.23)	0.0052
Any CVD-related comorbidities	1,536 (65.45)	7,904 (71.50)	<0.0001

AOM: anti-obesity medication; CCI: Charlson comorbidity index; CDS: chronic disease score; COPD: chronic obstructive pulmonary disease; SES: socioeconomic status; SD: standard deviation

In the unadjusted analysis, there were no significant differences in ischemic heart disease, stroke, or arrhythmia between the AOM and non-AOM cohorts (all p>0.05). However, the non-AOM cohort had a higher likelihood of experiencing any CVD, CAD, HF, AF, or PVD than AOM users (**Figure 2**).

Figure 2. Cardiovascular-related outcomes among patients with vs without AOM use

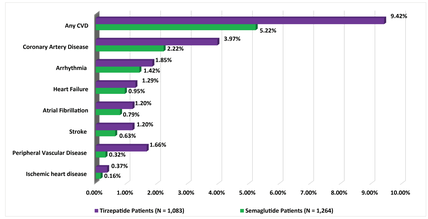


AOM: anti-obesity medication; CVD: cardiovascular disease

RESULTS (cont'd)

When comparing semaglutide to tirzepatide, no significant differences were found for arrhythmia, HF, AF, stroke, and ischemic heart disease (all p>0.05). However, tirzepatide users showed a significantly higher likelihood of experiencing any CVD, CAD, and PVD than semaglutide users (**Figure 3**).

Figure 3. Cardiovascular-related outcomes among patients with tirzepatide vs semaglutide use



AOM: anti-obesity medication; CCI: Charlson comorbidity index; CDS: chronic disease score; COPD: chronic obstructive pulmonary disease; CVD: cardiovascular disease; HR: hazard ratio; SES: socioeconomic status

After adjusting for sociodemographic and clinical factors, there were no statistically significant differences in cardiovascular risk for AOM vs non-AOM users, and semaglutide vs tirzepatide users.

CONCLUSION

While AOMs like tirzepatide and semaglutide promote weight loss, they do not significantly lower cardiovascular event risk compared with non-AOM users in the VHA population. Differences in patient characteristics emphasize the need for personalized treatment. Further research is needed to explore long-term cardiovascular outcomes of veteran patients with obesity and AOM use.

REFERENCES

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Presented at AMCP Nexus 2024
October 14-17, 2024, Las Vegas, NV