Measuring the Cardiovascular Benefits of Anti-Obesity Medications

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BACKGROUND

Obesity affects nearly half of Americans and 604 million adults globally and is recognized as a significant risk factor for cardiovascular disease (CVD).[1,2] Weight loss is crucial for preventing heart disease, and new anti-obesity medications (AOMs), including semaglutide and tirzepatide, are promising.[3,4] However, comparative research on their cardiovascular benefits is lacking.

OBJECTIVES

This study aimed to evaluate the impact of AOM use on CVD risk among US patients with obesity.

METHODS

Setting

Retrospective cohort study using 2022-2024 Kythera data, with an identification period from November 1 to December 31, 2023, a 12-month baseline, and a 6-month follow-up (**Figure 1**).

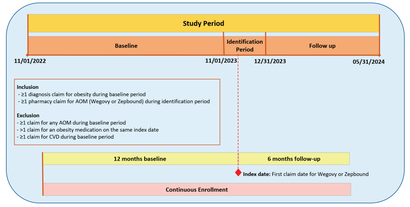
Sample

Patients with obesity in two cohorts:

- **AOM cohort**: Received tirzepatide (Zepbound) or semaglutide (Wegovy) during the identification period, with the first AOM claim considered the index date.
- **Non-AOM cohort**: Not prescribed AOMs, with random index dates matching the AOM cohort. A 1% random sample was analyzed.

Detailed inclusion and exclusion criteria are outlined in **Figure 1**.

Figure 1. Study design



AOM: anti-obesity medication; CVD: cardiovascular disease

METHODS (cont'd)

Outcomes

Risk of coronary artery disease (CAD), heart failure (HF), atrial fibrillation (AF), arrhythmia, ischemic heart disease, stroke, and peripheral vascular disease (PVD) were assessed during the follow-up.

Analysis

- Descriptive analysis of sociodemographic and clinical characteristics.
- Cox regression examined CVD risk and AOM use, adjusting for demographics, comorbidities, and socioeconomic factors, with additional analyses comparing outcomes between tirzepatide and semaglutide users.

RESULTS

We identified 22,620 patients in the AOM cohort (19,801 semaglutide and 2,819 tirzepatide users) and 84,427 patients in the non-AOM cohort who met the inclusion criteria. Patients in the AOM cohort were younger, more likely to be female, had significantly higher comorbidity scores, and had more CVD-related comorbidities than the non-AOM cohort. More patients in the non-AOM cohort lived in low-SES areas than in the AOM cohort (**Table 1**).

Among the AOM cohort, semaglutide users were slightly younger (45.39 vs 46.23 years, p=0.0004) and more likely to live in low-SES areas (28.21% vs 24.69%, p=0.0001) than tirzepatide users.

Table 1. Baseline characteristics of the study and comparison cohorts

Characteristics	AOM Cohort (Wegovy or Zepbound) (N=22,620)	Non-AOM Cohort (N=84,427)	*P*-value	SMD
Age (years), mean (SD)	45.50 (12.15	50.67 (18.15	<0.0001	0.3035
Age group, n (%)				
18-40 years	7,615 (33.66)	19,346 (22.91)	<0.0001	0.2489
41-60 years	12,338 (54.54)	32,580 (38.59)	<0.0001	0.3262
61-80 years	2,461 (10.88)	25,355 (30.03)	<0.0001	0.4438
80+ years	20 (0.09)	3,101 (3.67)	<0.0001	0.2139
Sex, n (%)				
Male	4,671 (20.65)	34,988 (41.44)	<0.0001	0.4373
Female	17,949 (79.35)	49,439 (58.56)	<0.0001	0.4373
Comorbidity scores, n (%)				
CCI ≥2	1,151 (5.09)	2,519 (2.98)	<0.0001	0.1158
CDS ≥2	11,898 (52.60)	6,525 (7.73)	<0.0001	1.3595
Elixhauser Score ≥2	14,017 (61.97)	11,395 (13.50)	<0.0001	1.2868
SES, n (%)				
Low	6,282 (27.77)	28,311 (33.53)	<0.0001	0.1233
Medium	7,389 (32.67)	27,160 (32.17)	0.1565	0.0106
High	8,523 (37.68)	27,080 (32.08)	<0.0001	0.1191
Baseline CVD-related comorbidities, n (%)				
Hypertension	7,812 (34.54)	8,872 (10.51)	<0.0001	0.6881
Hyperlipidemia	4,105 (18.15)	4,201 (4.98)	<0.0001	0.5026
Type 2 diabetes	1,084 (4.79)	4,687 (5.55)	<0.0001	0.0336
COPD	2,754 (12.18)	2,538 (3.01)	<0.0001	0.4294
Smoking history	1,076 (4.76)	845 (1.00)	<0.0001	0.2848
GERD	386 (1.71)	291 (0.34)	<0.0001	0.1722
Alcohol use disorder	96 (0.42)	168 (0.20)	<0.0001	0.0455
Chronic kidney disease	11,844 (52.36)	13,087 (15.50)	<0.0001	0.9332
Any CVD-related comorbidities	7,812 (34.54)	8,872 (10.51)	<0.0001	0.6881

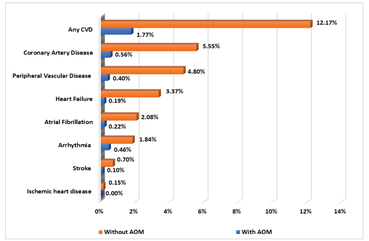
AOM: anti-obesity medication; CCI: Charlson comorbidity index; CDS: chronic disease score; COPD: chronic obstructive pulmonary disease; CVD: cardiovascular disease; GERD: gastroesophageal reflux disease; SES: socioeconomic status; SD: standard deviation; SMD: standardized mean difference

RESULTS (cont'd)

The unadjusted analysis showed that AOM users had a significantly lower incidence of cardiovascular events than non-AOM users (p<0.0001 for all outcomes; **Figure 2**).

After comparing semaglutide with tirzepatide, there were no significant differences for individual CVDs (all p>0.05); however, the likelihood of any CVD was higher for semaglutide users (1.86% vs 1.14%, p=0.0064).

Figure 2. Unadjusted outcome measures among patients in AOM and non-AOM cohorts



AOM: anti-obesity medication; CVD: cardiovascular disease

Adjusted analyses showed that AOM use was associated with a 63% reduction in CVD risk. Individuals residing in low-SES and medium-SES regions exhibited an increased risk of CVD compared with those in high-SES regions. A CCI score of >2 and smoking were associated with increased risk of CVD (**Table 2**).

Table 2. Cox regression results for time to CVD

Characteristics	HR	CI limit		*P*-value
		Lower	Upper	
Treatment				
Yes	0.37	0.34	0.42	0.0001
No	1.00	1.00	1.00	
Age (years)				
18-40	0.12	0.11	0.14	0.0001
41-60	0.57	0.53	0.60	0.0001
61-80	1.76	1.66	1.87	0.0001
80+	1.00	1.00	1.00	
Sex				
Male	0.82	0.80	0.85	0.0001
Female	1.00	1.00	1.00	
Comorbidity scores				
CCI score ≥2	2.11	1.90	2.34	0.0001
SES score				
Low	1.16	1.11	1.21	0.0001
Medium	1.11	1.07	1.16	0.0001
High	1.00	1.00	1.00	
Comorbidities				
Hypertension	0.72	0.67	0.77	0.0001
Hyperlipidemia	0.81	0.75	0.88	0.0001
Type 2 diabetes	0.78	0.71	0.85	0.0001
COPD	0.87	0.79	0.96	0.0050
Smoking history	1.18	1.03	1.35	0.0195
Alcohol use disorder	1.15	0.87	1.52	0.3176
Chronic kidney disease	1.15	0.87	1.54	0.3266

CCI: Charlson comorbidity index; CI: confidence interval; COPD: chronic obstructive pulmonary disease; CVD: cardiovascular disease; HR: hazard ratio

RESULTS (cont'd)

Semaglutide users had a 53% higher risk of CVD than tirzepatide users. Female sex, high CCI score, and smoking increased the CVD risk among the AOM cohort (**Table 3**).

Table 3. Cox regression results for time to CVD: Semaglutide (Wegovy) vs tirzepatide (Zepbound)

Characteristics	HR	CI limit		*P*-value
		Lower	Upper	
Treatment				
Wegovy	1.53	1.06	2.20	0.0215
Zepbound	1.00	1.00	1.00	
Age (years)				
18-40	0.52	0.16	1.66	0.2684
41-60	1.05	0.34	3.31	0.9284
61-80	2.81	0.89	8.87	0.0786
80+	1.00	1.00	1.00	
Gender				
Male	0.66	0.53	0.81	0.0001
Female	1.00	1.00	1.00	
Comorbidity scores				
CCI score ≥2	1.81	1.28	2.56	0.0008
SES score				
Low	1.16	0.91	1.48	0.2218
Medium	1.07	0.85	1.36	0.5697
High	1.00	1.00	1.00	
Comorbidities				
Hypertension	1.50	1.18	1.91	0.0010
Hyperlipidemia	1.41	1.14	1.76	0.0018
Type 2 diabetes	1.03	0.70	1.50	0.8949
COPD	1.15	0.87	1.52	0.3339
Smoking history	1.79	1.32	2.42	0.0002
Alcohol use disorder	0.97	0.50	1.90	0.9357
Chronic kidney disease	0.57	0.18	1.80	0.3407

CCI: Charlson comorbidity index; CI: confidence interval; COPD: chronic obstructive pulmonary disease; CVD: cardiovascular disease; HR: hazard ratio; SES: socioeconomic status

CONCLUSION

Weight reduction is crucial in reducing the incidence and CVD. The use of AOMs offers a promising solution to lessen the clinical burden of CVD in the United States. Our findings highlight a clear association between newly approved AOMs and a lower prevalence of CVD, reinforcing their effectiveness in managing cardiovascular conditions.

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Presented at Obesity Week 2024
November 3-6, 2024, San Antonio, TX