A Retrospective Analysis of the Impact of Approved Anti-Obesity Medications on the Risk of Cardiovascular Disease in Patients with Obesity

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BACKGROUND

Obesity is a prevalent and growing health concern in the United States, affecting over 42% of adults and contributing significantly to the burden of cardiovascular disease (CVD).[1,2] Recently, approved anti-obesity medications (AOMs) such as Zepbound and Wegovy have emerged as potential interventions to reduce weight and potentially lower CVD risk among individuals with obesity.[3,4]

OBJECTIVES

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

METHODS

Setting

Retrospective cohort study using 2022-2024 Kythera data, with an identification period from 01NOV2023 to 31DEC2023, a 12-month baseline, and a 6-month follow-up period (**Figure 1**).

Sample

Patients with obesity in two cohorts:

- **AOM cohort:** Received tirzepatide (Zepbound) or semaglutide (Wegovy) during the identification period; the first AOM claim was designated as 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**.

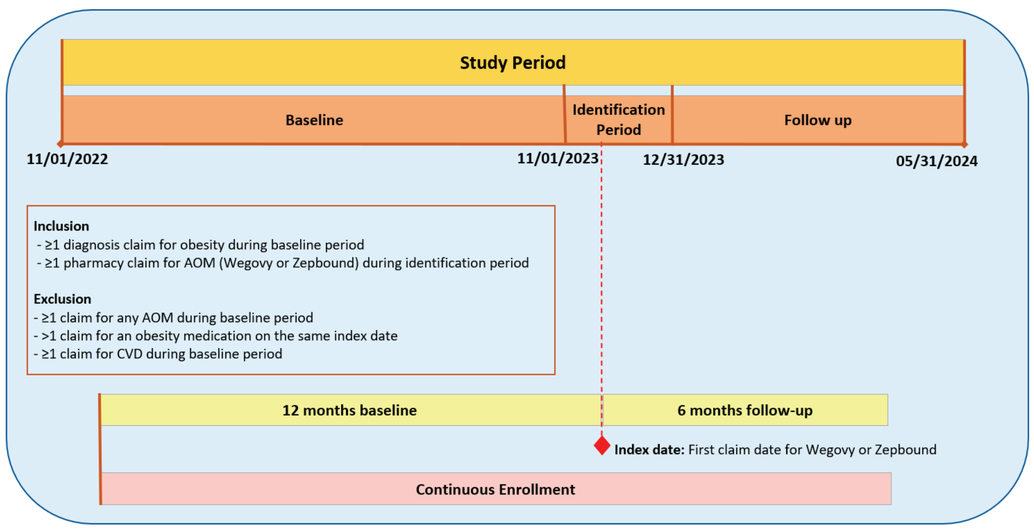
Outcomes

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

Analysis

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

Figure 1. Study design and timeline



AOM: anti-obesity medication; CVD: cardiovascular disease

RESULTS

We identified 22,620 patients with obesity and AOM use (19,801 semaglutide and 2,819 tirzepatide users), and 84,427 patients with obesity without AOM use.

Significant differences were observed in the proportion of patients with Elixhauser Index Score ≥2, comprising 61.97% in the AOM cohort vs 13.50% in the non-AOM cohort (std. diff.=1.2868; **Table 1**).

Table 1. Baseline characteristics of patients in the AOM and non-AOM cohorts

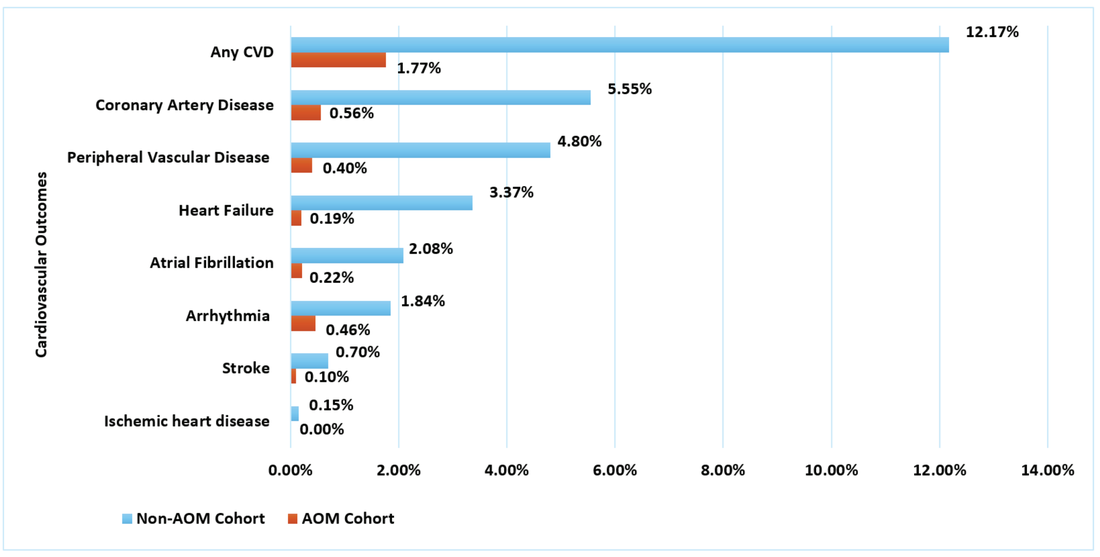
Characteristics	AOM Cohort (Wegovy or Zepbound) (N=22,620)	Non-AOM Cohort (N=84,427)	P-value	SMD
Age (years), mean (SD)	45.50 (12.15)	50.67 (18.15)	<0.0001	0.3035
Age group, n (%)				
18-40 years	7,615 (33.66)	19,346 (22.91)	<0.0001	0.2489
41-60 years	12,338 (54.54)	32,580 (38.59)	<0.0001	0.3262
61-80 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; GERD: gastroesophageal reflux disease; SES: socioeconomic status; SD: standard deviation; SMD: standardized mean difference

RESULTS (cont'd)

Patients with AOM use demonstrated significantly lower incidence of cardiovascular events (1.77%) than those without AOM use (12.17%, p<0.0001; **Figure 2**).

Figure 2. Unadjusted CVD-related outcomes among patients in the AOM and non-AOM cohorts



AOM: anti-obesity medication; CVD: cardiovascular disease

Adjusted Analysis

- Adjusted analyses confirmed that AOM use was associated with a substantially reduced risk of CVD (hazard ratio [HR]=0.37, p<0.0001; **Table 2**).
- Differences in specific cardiovascular outcomes between Zepbound and Wegovy users were observed, with Wegovy users showing a higher hazard of CVD than Zepbound users (HR=1.53, p=0.0215; **Table 3**).

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; SES: socioeconomic status

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	2.2	0.0215
Zepbound	1	1	1	
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	1	1	
Gender				
Male	0.66	0.53	0.81	0.0001
Female	1	1	1	
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	1	1	
Comorbidities				
Hypertension	1.5	1.18	1.91	0.001
Hyperlipidemia	1.41	1.14	1.76	0.0018
Type 2 diabetes	1.03	0.7	1.5	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	0.5	1.9	0.9357
Chronic kidney disease	0.57	0.18	1.8	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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