The Impact of Approved Anti-obesity Medications on the Incidence of Cardiovascular Disease, Healthcare Resource Use and Costs Among Patients with Obesity: A Retrospective Cohort Study

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OBJECTIVES

This study analyzed the impact of two anti-obesity medications (AOMs) on cardiovascular disease (CVD) incidence, healthcare resource utilization (HCRU), and costs among US patients with obesity, a major driver of healthcare expenditures.

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] Direct medical costs associated with obesity are estimated at $147 billion annually.[3] Weight loss is crucial for preventing heart disease, and new anti-obesity medications (AOMs), including semaglutide and tirzepatide, are promising.[4,5] However, comparative research on their cardiovascular benefits is lacking.

METHODS

Setting

Retrospective cohort study assessing the Kythera data population; the identification period ranged from November 1 to December 31, 2023, with 12-month baseline and 6-month follow-up periods (**Figure 1**).

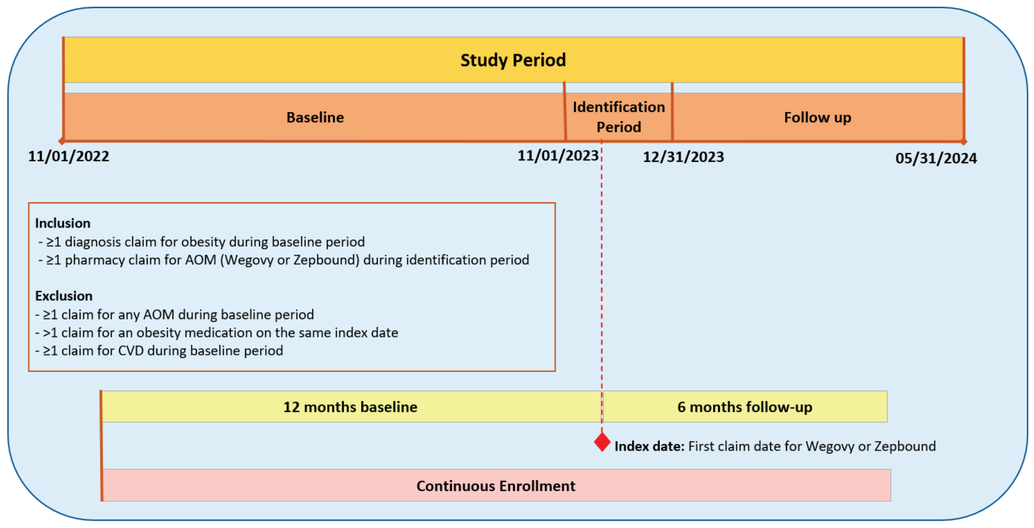
Sample

Patients with obesity in two cohorts:

- **AOM cohort:** Patients with evidence of tirzepatide (Zepbound) or semaglutide (Wegovy) use during the identification period; the first AOM claim was considered the index date.
- **Non-AOM cohort:** No evidence of AOM use, 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

Outcomes

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

Analysis

- Descriptive statistics (means and percentages) were used to describe the sociodemographic and clinical characteristics and outcomes of both cohorts. Chi-square tests were performed for categorical variables (e.g., hospital admissions, emergency visits), and two-sample t-tests were conducted for continuous variables (e.g., length of stay, healthcare expenditures).
- Standardized differences were calculated to assess balance between the cohorts, with values <0.1 considered negligible. P-values were reported for each outcome.
- Subgroup analysis comparing outcomes between semaglutide and tirzepatide users was also included.
- Outcomes were adjusted for demographics, comorbidities, and socioeconomic factors.

RESULTS

We identified 22,620 patients with obesity and AOM utilization (Wegovy: 19,801 patients, Zepbound: 2,819 patients) and 84,427 patients without AOM use.

The AOM cohort was younger, had a higher proportion of women, significantly higher comorbidity scores, and more CVD-related comorbidities than the non-AOM cohort. Additionally, more patients in the non-AOM cohort resided in low-SES areas vs those in the AOM cohort (**Table 1**).

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

Table 1. Baseline descriptive characteristics

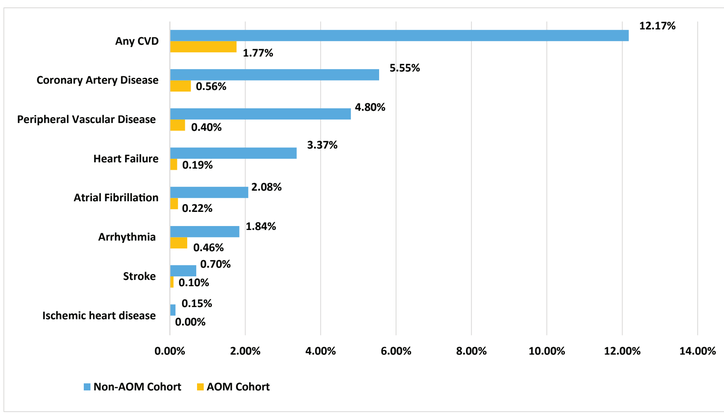
Characteristics	AOM Cohort (Wegovy or Zepbound) (N = 22,620)	Non-AOM Cohort (N = 84,427)	*P*-value	SMD
Age (years), mean (SD)	45.50 (12.15)	50.67 (18.15)	<0.0001	0.3035
Age group, n (%)				
18-40 years	7,615 (33.66)	19,346 (22.91)	<0.0001	0.2489
41-60 years	12,338 (54.54)	32,580 (38.59)	<0.0001	0.3262
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)

AOM users demonstrated significantly lower incidence of cardiovascular events than non-AOM users (1.77% vs 12.17%, p<0.0001 for all outcomes; **Figure 2**).

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



AOM: anti-obesity medication; CVD: cardiovascular disease

The AOM cohort had lower hospital admission rates (1.63% vs 6.62%, p<0.0001), shorter length of stay (0.12 vs 1.27 days, p<0.0001), and lower emergency department (ED) (6.23% vs 13.06%, p<0.0001) and outpatient visit rates (80% vs 82%, p<0.0001) than the non-AOM cohort (**Table 2**).

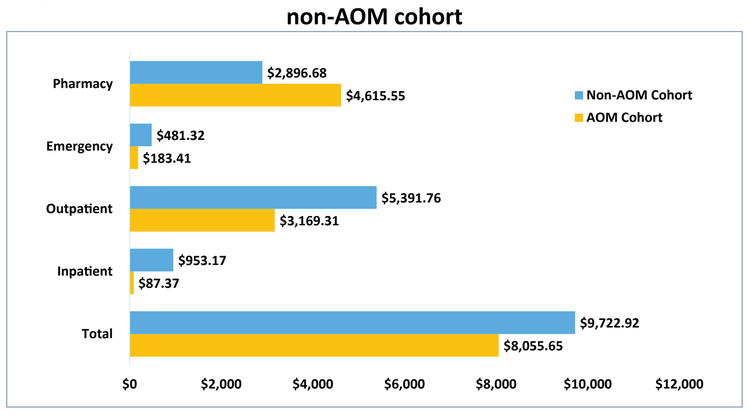
Table 2. Healthcare utilization among patients with obesity: AOM vs non-AOM cohort

	AOM Cohort (Wegovy or Zepbound) (N = 22,620)		Non-AOM Cohort (N = 84,427)		*P*-value	SMD
Outcome	**N/Mean**	**%/SD**	**N/Mean**	**%/SD**		
Healthcare Utilization						
Hospital admissions	368	1.63%	5,588	6.62%	<0.0001	0.2186
Length of stay (days)	0.12	1.83	1.27	10.29	<0.0001	0.1253
Emergency visits	1,410	6.23%	11,026	13.06%	<0.0001	0.2138
Outpatient visits	18,095	80.00%	69,009	81.74%	<0.0001	0.0448

AOM: anti-obesity medication; SD: standard deviation; SMD: standard mean difference

The AOM cohort incurred lower total health expenditures ($8,055.65 vs $9,722.92, p<0.0001; **Figure 3**).

Figure 3. Health expenditures among patients with obesity: AOM vs non-AOM cohort



AOM: anti-obesity medication

Zepbound users had a lower incidence of any cardiovascular event (1.14% vs 1.86%, p=0.0064), shorter length of stay (0.07 vs 0.12 days, p=0.0225), lower ED visit (3.33% vs 6.65%, p<0.0001), and outpatient visit rates (77.19% vs 80.39%, p<0.0001; **Table 3**), and lower total healthcare costs ($7,184.25 vs $8,179.71, p<0.0001) than Wegovy users.

Table 3. HCRU among obesity patients with semaglutide (Wegovy) vs tirzepatide (Zepbound) use

	Patients with Wegovy Use (N = 19,801)		Patients with Zepbound Use (N = 2,819)		*P*-value	SMD
Outcome	**N/Mean**	**%/SD**	**N/Mean**	**%/SD**		
Healthcare utilization						
Hospital admissions (%)	330	1.67%	38	1.35%	0.2109	0.0252
Length of stay (days)	0.12	1.93	0.07	0.93	0.0225	0.0276
Emergency visits (%)	1,316	6.65%	94	3.33%	<0.0001	0.1371
Outpatient visits (%)	15,919	80.39%	2,176	77.19%	<0.0001	0.0801

HCRU: healthcare resource utilization; SD: standard deviation; SMD: standard mean difference

CONCLUSION

AOM use was associated with a significantly lower incidence of cardiovascular events, lower HCRU, and lower total health expenditures, than non-AOM use, highlighting these medications as promising interventions in obesity management and decreasing the economic burden of CVD.

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