Anti-obesity Medications and Related Osteoarthritis Risk Among Patients with Obesity

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BACKGROUND

Obesity is a widespread health concern associated with increased risk of osteoarthritis (OA), a debilitating joint disease.[1,2] Excess weight places mechanical stress on joints and triggers metabolic inflammation, contributing to OA development.[3,4] Recently approved anti-obesity medications (AOMs), including tirzepatide (Zepbound) and semaglutide (Wegovy), offer promising avenues for weight management, but their impact on the risk of OA remains unclear.[5,6]

OBJECTIVES

The impact of newly approved AOM use on the risk of OA among US patients with obesity was evaluated.

METHODS

Setting

Utilizing the Kythera Labs data population, a retrospective cohort study was conducted for the period November 2022 - June 2024.

Sample

Patients with obesity in two cohorts:

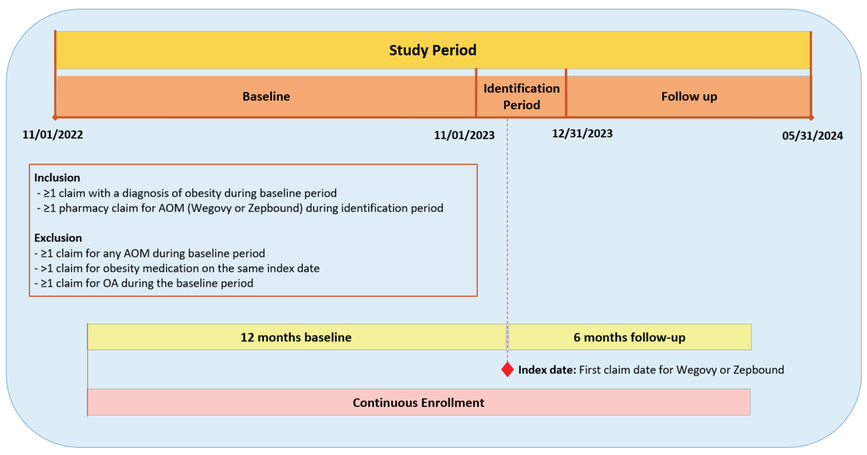
- **AOM cohort:** Evidence of tirzepatide or semaglutide use during the identification period; the first AOM claim date was designated as the index date
- **Non-AOM cohort:** No evidence of prescribed AOM use, with random index dates assigned for matching; a 1% random sample was assessed.

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

Outcomes

The risk of OA among patients with obesity was determined using Cox regression. Results among patients with tirzepatide and semaglutide use were also compared. Multivariable analysis was used to control for comorbidities and sociodemographic factors.

Figure 1. Study design and timeline



AOM: anti-obesity medication; OA: osteoarthritis

RESULTS

Of patients with obesity and AOM use (21,819), 19,087 had semaglutide use, and 2,732 had tirzepatide use; 85,018 patients were included in the non-AOM cohort (**Table 1**).

Table 1. Baseline characteristics of patients with vs without AOM use

	AOM Cohort (Wegovy or Zepbound) (N = 21,819)		Non-AOM Cohort (N = 85,798)		p-value	SMD
Characteristics	**N/Mean**	**%/SD**	**N/Mean**	**%/SD**		
Age	45.15	12.23	51.07	18.26	0.0000	0.3440
Age Group: 18-40	7,608	34.87%	19,125	22.29%	0.0000	0.2931
Age Group: 41-60	11,701	53.63%	32,937	38.39%	0.0000	0.3117
Age Group: 61-80	2,296	10.52%	26,249	30.59%	0.0000	0.4624
Age Group: 80+	29	0.13%	3,512	4.09%	0.0000	0.2229
Gender						
Male (%)	4,883	22.38%	36,256	42.26%	0.0000	0.4147
Female (%)	16,936	77.62%	49,540	57.74%	0.0000	0.4147
Comorbidity Scores						
Charlson Comorbidity Index Score (≥ 2)	1,529	7.01%	4,403	5.13%	0.0000	0.0822
Chronic Disease Score (≥ 2)	11,208	51.37%	6,920	8.07%	0.0000	1.3070
Elixhauser Score (≥ 2)	13,734	62.95%	13,564	15.81%	0.0000	1.2035
SES						
Low	6,050	27.73%	28,729	33.48%	0.0000	0.1232
Medium	7,082	32.46%	27,715	32.30%	0.6614	0.0033
High	8,262	37.87%	27,551	32.11%	0.0000	0.1223
Baseline Osteoarthritis-related Comorbidities						
Cerebrovascular Disease	186	0.85%	344	0.40%	0.0000	0.0645
Peripheral Vascular Disease	475	2.18%	1,255	1.46%	0.0000	0.0568
COPD	2,744	12.58%	3,089	3.60%	0.0000	0.4016
Depression	4,786	21.94%	3,266	3.81%	0.0000	0.7171
Metabolic Disorders	857	3.93%	300	0.35%	0.0000	0.3504
Visual Disturbances	351	1.61%	320	0.37%	0.0000	0.1573
Hearing Loss	170	0.78%	197	0.23%	0.0000	0.0943
Anxiety	6,233	28.57%	3,446	4.02%	0.0000	0.9142
Migraine	1,760	8.07%	809	0.94%	0.0000	0.4751
Gout	402	1.84%	274	0.32%	0.0000	0.1934
Fibromyalgia	395	1.81%	225	0.26%	0.0000	0.2052
Polymyalgia Rheumatica	7	0.03%	26	0.03%	0.8934	0.0010
Incidence						
Osteoarthritis	653	2.99%	12,382	14.43%	0.0000	0.3541

AOM: anti-obesity medication; COPD: chronic obstructive pulmonary disease; SD: standard deviation; SES: socioeconomic status; SMD: standardized mean difference

RESULTS (cont'd)

- Significant differences were observed in the proportions of patients with Elixhauser index score ≥2 (AOM cohort: 62.95% vs non-AOM cohort: 15.81%; standard mean difference [SMD]=1.2035; **Table 1**).
- AOM users demonstrated significantly lower incidence of OA (2.99%) than non-users (14.43%, p<0.0001; **Table 1**). Subgroup analysis of patients in the AOM cohort showed that the incidence of OA was higher in the semaglutide group at 3.08%, vs 2.42% in the tirzepatide group, but was not found to be significant (p=0.0584).

Adjusted Analysis

- After adjusting for sociodemographic and clinical characteristics, OA risk was 37% lower in AOM users vs non-users (hazard ratio [HR]=0.63, p<0.0001; **Table 2**). The adjusted risk of OA was 23% higher for patients with semaglutide vs tirzepatide use (HR=1.23, p=0.1126); the difference was not statistically significant.

Table 2. Cox regression results for time to osteoarthritis for patients with vs without AOM use

	HR	Conf. Interval		p-value
		Lower	Upper	
Treatment				
Yes	0.63	0.58	0.69	0.0000
No	1.00	1.00	1.00	
Characteristics				
Age Group: 18-40	0.15	0.13	0.17	0.0000
Age Group: 41-60	0.95	0.88	1.02	0.1550
Age Group: 61-80	2.21	2.07	2.37	0.0000
Age Group: 80+	1.00	1.00	1.00	
Gender				
Female	1.31	1.26	1.36	0.0000
Male	1.00	1.00	1.00	
Comorbidity Scores				
Charlson Comorbidity Score (≥ 2)	1.26	1.16	1.38	0.0000
Chronic Disease Score (≥ 2)	0.71	0.67	0.75	0.0000
Elixhauser Score (≥ 2)	0.45	0.42	0.47	0.0000
SES				
Low	1.10	1.05	1.15	0.0000
Medium	1.09	1.04	1.14	0.0001
High	1.00	1.00	1.00	
Comorbidities				
Cerebrovascular Disease	0.81	0.63	1.02	0.0781
Peripheral Vascular Disease	1.11	0.98	1.26	0.1158
COPD	0.99	0.91	1.09	0.9094
Depression	1.05	0.96	1.16	0.2656
Metabolic Disorders	0.78	0.60	1.01	0.0569
Visual Disturbances	0.97	0.76	1.23	0.7827
Hearing Loss	0.82	0.59	1.12	0.2131
Anxiety	0.77	0.70	0.84	0.0000
Migraine	0.87	0.73	1.02	0.0868
Gout	1.30	1.05	1.61	0.0169
Fibromyalgia	2.08	1.71	2.54	0.0000
Polymyalgia Rheumatica	1.57	0.79	3.15	0.2001

AOM: anti-obesity medication; COPD: chronic obstructive pulmonary disease; HR: hazard ratio; SES: socioeconomic status

CONCLUSION

AOM use was associated with a 37% lower adjusted risk of OA compared to non-use. Although no significant difference in OA risk reduction was observed between patients using semaglutide and tirzepatide, both medications demonstrated lower risk of OA. These results suggest that AOMs support weight management and may also help reduce the risk of developing OA in individuals with obesity.

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