# Cardiovascular benefits of weight loss medications: An analysis of tirzepatide (Mounjaro) and semaglutide (Wegovy) in the US Medicare population

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## BACKGROUND

Obesity and cardiovascular disease (CVD) pose significant health challenges for older adults in the United States, with approximately 41.5% of adults aged 60 and over experiencing obesity.[1] Recently, new anti-obesity medications (AOMs) such as tirzepatide and semaglutide have emerged, showing promising results in clinical trials with significant weight loss and cardiovascular benefits.[2,3] However, the real-world impact of these medications on cardiovascular outcomes in the Medicare population remains understudied.

## OBJECTIVES

To compare the risk of CVD between Medicare patients using AOMs and those not using AOMs, as well as between patients using tirzepatide and those using semaglutide.

## METHODS

**Setting**

Retrospective cohort study using 2021-2024 Kythera Medicare claims data with an identification period from January 1, 2022, to May 31, 2023, and a 1-year follow-up to assess cardiovascular event risk (**Figure 1**).

**Sample**

Medicare beneficiaries diagnosed with obesity (ICD-10: E66.9, E66.09, E66.1, E66.8, Z68.3) comprising two cohorts:

- **AOM cohort**: Patients who received tirzepatide or semaglutide during the identification period (first AOM claim = index date). **Figure 1** provides detailed inclusion and exclusion criteria.
- **Non-AOM cohort**: Patients who were not prescribed AOMs during the study period. Index dates were randomly selected between the minimum and maximum index dates for the AOM cohort. The non-AOM-related inclusion/exclusion criteria were the same as for the AOM cohort. A random sample of 5% of patients who met the criteria was included in the analysis.

**Outcomes**

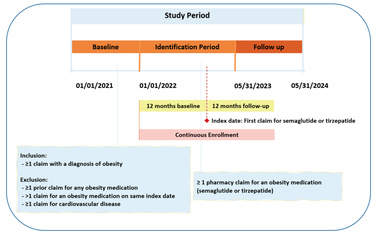
Risk of coronary artery disease (CAD) (ICD-10: I25), heart failure (HF) (ICD-10: I50), atrial fibrillation (AF) (ICD-10: I48.91), arrhythmia (ICD-10: I49), ischemic heart disease (ICD-10: I25.9), stroke (ICD-10: I63.9), and peripheral vascular disease (PVD) (ICD-10: I73.9) assessed during the 1-year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

## METHODS (cont'd)

**Analysis**

- A descriptive analysis was performed to ascertain the sociodemographic and clinical characteristics and calculate CVD outcomes.
- Cox regression models were used to analyze the association between cardiovascular risk and medication use, adjusting for demographics, comorbidity scores, socioeconomic status, and baseline cardiovascular-related comorbidities. The models compared users and non-users of AOMs and tirzepatide and semaglutide users.

**Figure 1. Study Design**




## RESULTS

The AOM cohort comprised 4,384 beneficiaries who met the inclusion criteria. Of these, 2,794 used tirzepatide and 1,590 used semaglutide. The non-AOM cohort comprised 33,536 Medicare enrollees.

Patients in the AOM cohort tended to be younger, female, have higher comorbidity scores, and reside in low-SES areas than the non-AOM cohort (**Table 1**). Among the AOM cohort, tirzepatide users were more likely to be older (66.64 vs 65.54, p<0.001), male (32.43% vs 20.0%, p<0.001), have higher Charlson Comorbidity Index (CCI) score (44.20% vs 17.30%, p<0.001), and have any cardiovascular-related comorbidities (85.5% vs 72.33%, p<0.001) than semaglutide users.

Unadjusted analysis showed no significant differences in CVD between AOM and non-AOM cohorts (p>0.05 for each outcome) (**Figure 2**).

Comparing semaglutide vs tirzepatide, there were no significant differences for HF, AF, arrhythmia, ischemic heart disease, and stroke outcomes (all p>0.05). However, for tirzepatide users, the likelihood of any CVD, CAD, and PVD was higher than for semaglutide users (6.16% vs 4.09%, p=0.0036 and (2.54% vs 1.38%, p=0.0106, respectively).

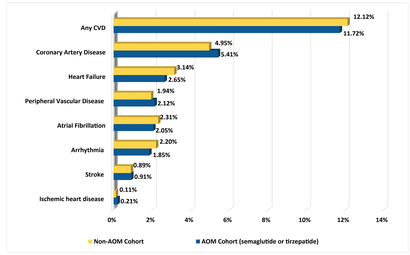
## RESULTS (cont'd)

**Table 1. Baseline characteristics for patients with vs without AOM use**

| Characteristics | AOM Cohort (semaglutide or tirzepatide) (N =4,384) | Non-AOM Cohort (N = 33,536) | P-value | Std. Diff. |
|---|---|---|---|---|
| Age (years), mean (SD) | 66.24 (10.11) | 70.34 (45.08) | <0.0001 | 0.0964 |
| **Age group, n (%)** | | | | |
| 65-70 years | 1,724 (39.32) | 10,227 (30.50) | <0.0001 | 0.1904 |
| 71-80 years | 1,417 (32.32) | 14,853 (44.29) | <0.0001 | 0.2425 |
| 80+ years | 164 (3.74) | 4,734 (14.12) | <0.0001 | 0.3109 |
| **Gender, n (%)** | | | | |
| Male | 1,224 (27.92) | 13,045 (38.90) | <0.0001 | 0.2272 |
| Female | 3,160 (72.08) | 20,491 (61.10) | <0.0001 | 0.2272 |
| **Comorbidity scores, n (%)** | | | | |
| CCI score ≥2 | 1,510 (34.44) | 9,521 (28.39) | <0.0001 | 0.1334 |
| CDS ≥2 | 3,419 (77.99) | 12,987 (38.73) | <0.0001 | 0.8192 |
| Elixhauser Index Score ≥2 | 3,756 (85.68) | 26,901 (80.22) | <0.0001 | 0.1389 |
| **SES, n (%)** | | | | |
| Low | 1,529 (34.88) | 10,797 (32.20) | 0.0004 | 0.0573 |
| Medium | 1,327 (30.27) | 10,991 (32.77) | 0.0009 | 0.0535 |
| High | 1,462 (33.35) | 11,227 (33.48) | 0.8649 | 0.0027 |
| **Baseline CVD-related comorbidities, n (%)** | | | | |
| Hypertension | 2,846 (64.92) | 22,076 (65.83) | 0.2326 | 0.0192 |
| Hyperlipidemia | 1,516 (34.58) | 11,656 (34.76) | 0.8176 | 0.0037 |
| Type 2 diabetes | 1,748 (39.87) | 9,071 (27.05) | <0.0001 | 0.2852 |
| COPD | 296 (6.75) | 2,354 (7.02) | 0.5136 | 0.0105 |
| Smoking history | 373 (8.51) | 2,826 (8.43) | 0.8552 | 0.0029 |
| Alcohol use disorder | 41 (0.94) | 405 (1.21) | 0.1156 | 0.0253 |
| Chronic kidney disease | 101 (2.30) | 837 (2.50) | 0.4415 | 0.0124 |
| Any CVD-related comorbidities | 3,539 (80.73) | 26,633 (79.42) | 0.0432 | 0.0325 |

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

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




AOM: anti-obesity medication; CVD: cardiovascular disease

## RESULTS (cont'd)

After adjusting for sociodemographic and clinical factors, AOM usage among patients with obesity was associated with a 10% reduction in the risk of CVD compared with patients not using AOMs (p=0.0149).

Moreover, the risk of CVD increased with age, being male, and having higher comorbidity scores and individual comorbidities (**Table 2**).

However, no significant difference in CVD risk was found between semaglutide vs tirzepatide users.

**Table 2. CVD risk among patients with obesity and AOM use**

| | Hazard Ratio | Conf. Interval | | p-value |
|---|---|---|---|---|
| | | Lower | Upper | |
| Treatment | 0.90 | 0.82 | 0.98 | 0.0149 |
| No Treatment | 1.00 | 1.00 | 1.00 | |
| **Age Group** | | | | |
| 65-70 | 0.76 | 0.71 | 0.82 | <0.0001 |
| 71-80 | 1.02 | 0.96 | 1.08 | 0.5005 |
| 80+ | 1.00 | 1.00 | 1.00 | |
| **Sex** | | | | |
| Female | 0.75 | 0.72 | 0.79 | <0.0001 |
| Male | 1.00 | 1.00 | 1.00 | |
| **Comorbidity Scores** | | | | |
| CCI Score (≥2) | 1.46 | 1.37 | 1.55 | <0.0001 |
| CDS (≥2) | 1.12 | 1.06 | 1.18 | <0.0001 |
| Elixhauser Index Score (≥2) | 1.24 | 1.14 | 1.34 | <0.0001 |
| **SES** | | | | |
| Low | 1.03 | 0.97 | 1.10 | 0.3152 |
| Medium | 1.01 | 0.95 | 1.08 | 0.6547 |
| High | 1.00 | 1.00 | 1.00 | |
| **Comorbidities** | | | | |
| Hypertension | 1.16 | 1.09 | 1.23 | <0.0001 |
| Hyperlipidemia | 1.03 | 0.98 | 1.09 | 0.2548 |
| Type 2 Diabetes | 1.01 | 0.95 | 1.07 | 0.8686 |
| COPD | 1.41 | 1.30 | 1.53 | <0.0001 |
| Smoking History | 1.22 | 1.13 | 1.32 | <0.0001 |
| Alcohol Use Disorder | 0.96 | 0.77 | 1.19 | 0.7109 |
| Chronic Kidney Disease | 1.29 | 1.14 | 1.46 | <0.0001 |

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

## CONCLUSION

**Both tirzepatide and semaglutide deliver significant cardiovascular benefits in addition to weight loss, offering a powerful tool to reduce healthcare costs tied to heart disease. Given these proven advantages, expanding Medicare coverage for these medications could lead to long-term savings by preventing costly cardiovascular events.**

## REFERENCES

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