

## BACKGROUND

Roughly 19% of active component service members have obesity, and approximately 68% experience obesity or overweight.<sup>1</sup> The use of weight loss prescriptions for US service members has risen significantly since 2018, when the Department of Defense (DoD) began approving coverage of medications for active-duty personnel struggling with body weight.<sup>1</sup> Anti-obesity medications (AOMs) like tirzepatide and semaglutide have displayed promising results in clinical trials, demonstrating substantial weight loss and cardiovascular benefits.<sup>2,3</sup> However, the impact of these medications on cardiovascular risk in this specific population has not yet been evaluated.

## **OBJECTIVES**

This study aimed to analyze the impact of tirzepatide (Mounjaro) and semaglutide (Wegovy) utilization on the likelihood of experiencing a cardiovascular event and to compare the risks associated with each medication among active US military personnel.

## METHODS

## Setting

Retrospective study using DoD data from January 1, 2021, to May 31, 2024, with 12-month baseline and follow-up (Figure 1).

## Population

- AOM cohort: Patients who received tirzepatide or semaglutide between January 1, 2022, and May 31, 2023 (identification period), with the first AOM claim serving as the index date. Patients with prior AOM use and those with >1 AOM claim on the same index date were excluded.
- Non-AOM cohort: Patients who had not received any AOM during the study period. A random index date was selected within the range of AOM cohort index dates, and a random sample of 5% of patients who met the criteria was included in the analysis.

Both groups were required to have an obesity diagnosis and no history of cardiovascular disease during the baseline, as well as continuous medical and pharmacy benefits for 12 months pre- and post-index date.

#### Outcomes

Risk of coronary artery disease, heart failure, atrial fibrillation, arrhythmia, ischemic heart disease, stroke, and peripheral vascular disease assessed during the 1-year follow-up.

# Effect of weight loss medications on cardiovascular risk among active US military personnel

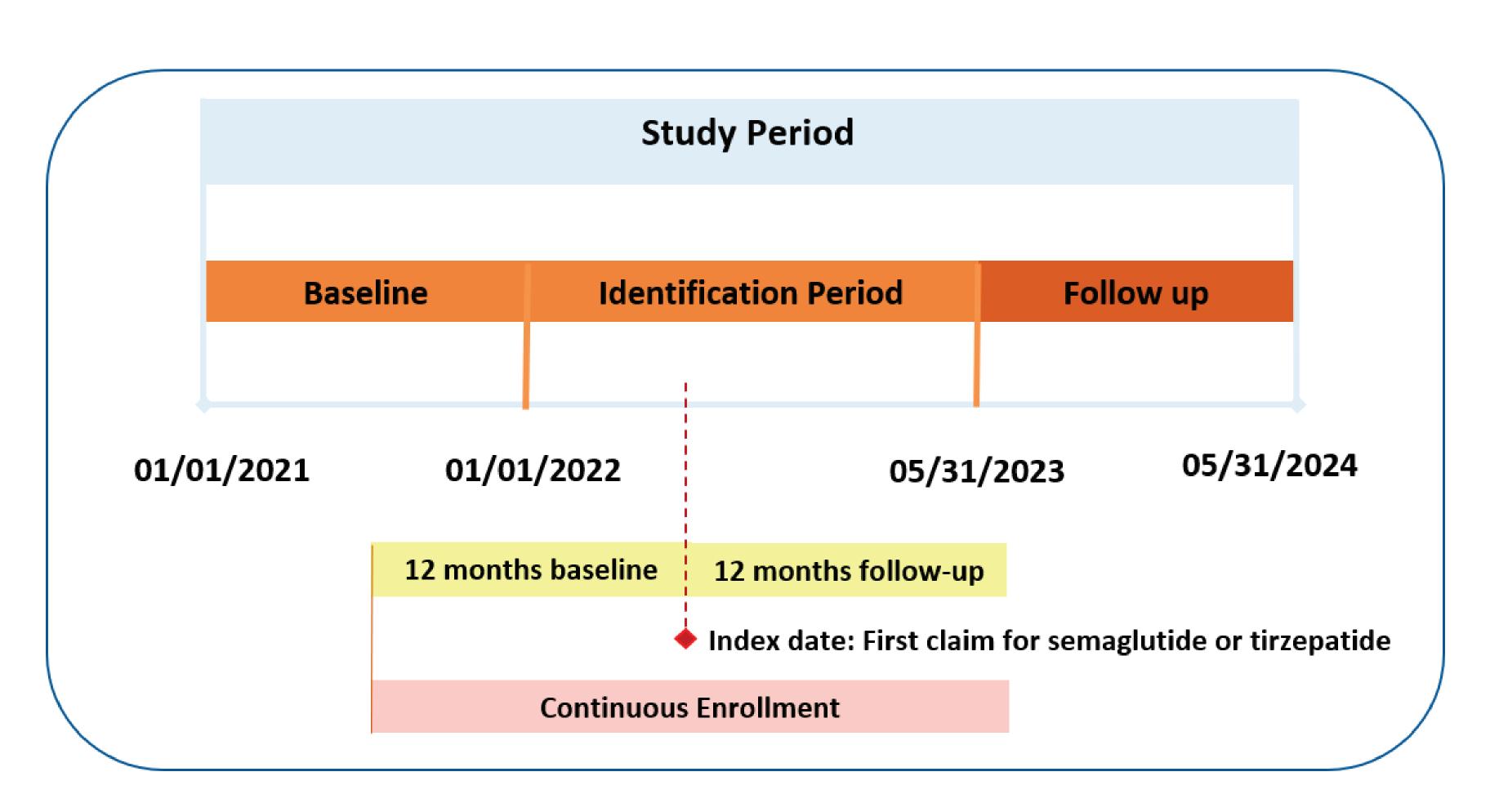
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# **METHODS (cont'd)**

## Analysis

- Descriptive analysis was conducted to determine patient sociodemographic and clinical features and to assess cardiovascular disease (CVD) outcomes.
- Cox regression models were used to examine the relationship between medication use and cardiovascular risk, while accounting for demographics, comorbidity scores, socioeconomic status, and baseline cardiovascular-related comorbidities.

This analysis compared individuals using AOMs with those not using them and further compared tirzepatide and semaglutide users.



#### Figure 1. Study Design

## RESULTS

We identified 3,687 beneficiaries who met the inclusion requirements in the AOM cohort (1,604 tirzepatide users and 2,083 semaglutide users) and 10,732 patients in the non-AOM cohort.

Patients in the AOM group were more likely to be younger, female, have higher chronic disease score (CDS), and have fewer cardiovascular-related comorbidities than the non-AOM cohort (Table 1). Within the AOM cohort, the semaglutide users were younger (46.01 vs 50.49 years, p<0.0001) and more likely to be female (84.78% vs 79.30, p<0.0001). They also had lower comorbidity scores (Charlson comorbidity index [CCI] score: 5.57% vs 22.38%, Elixhauser index score: 61.69% vs 70.64%, both p<0.0001), and were less likely to have any CVD-related comorbidities (43.30% vs 61.78%, p<0.0001) than tirzepatide users.



# **RESULTS (cont'd)**

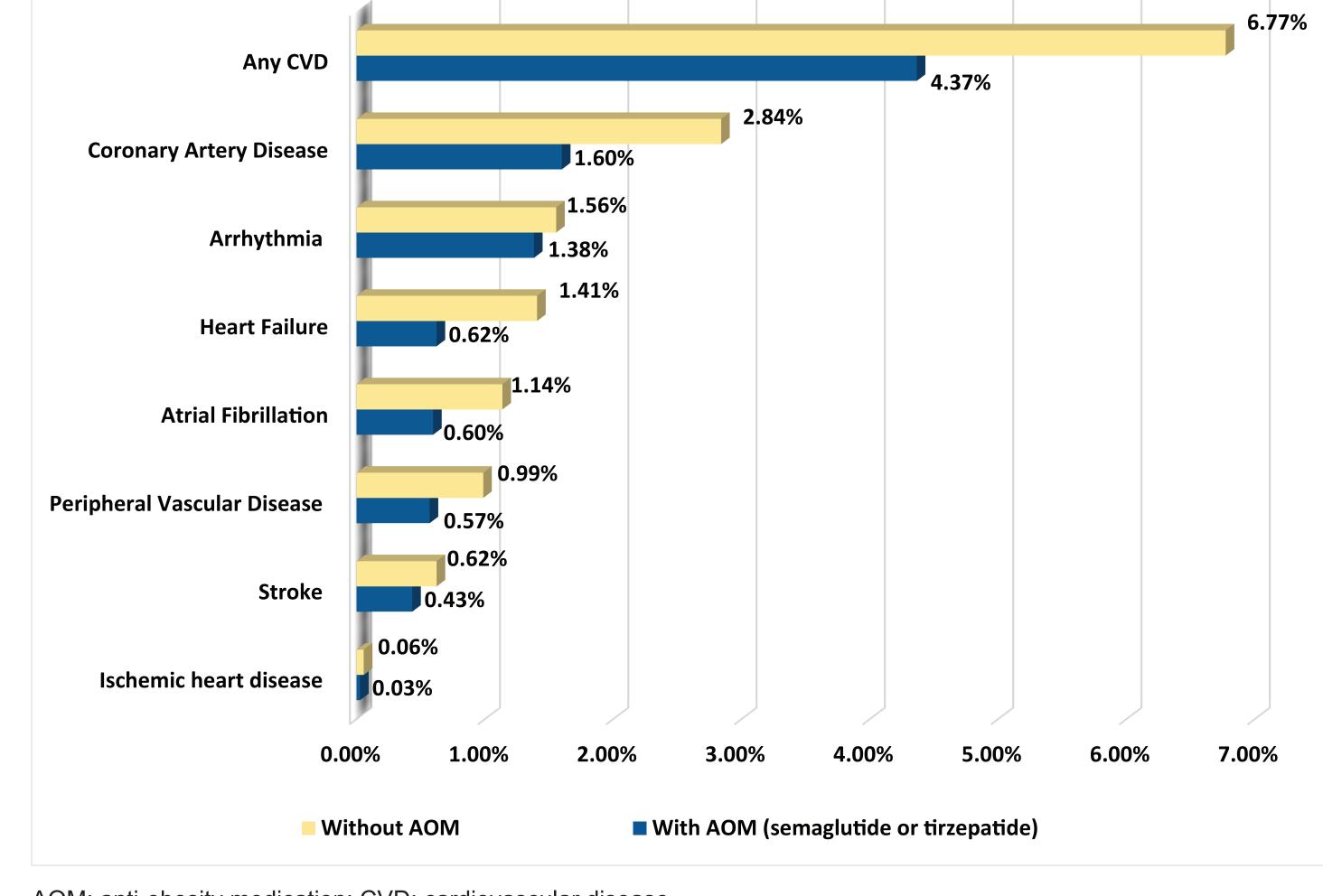
Table 1. Baseline characteristics for patients with vs without AOM use

| Characteristics                                       | With AOM<br>(semaglutide or tirzepatide)<br>(N = 3,687) | Without AOM<br>(N = 10,732) | P value |  |  |  |  |
|---|---|-----------------------------|---------|--|--|--|--|
| Age (years), mean (SD)                                | 47.96 (13.80)   | 53.20 (18.37)               | <.0001  |  |  |  |  |
| Age group, n (%)                                      |   |                             |         |  |  |  |  |
| 18-40 years   | 1,194 (32.38)   | 2,711 (25.26)               | <.0001  |  |  |  |  |
| 41-60 years   | 1,742 (47.25)   | 3,250 (30.28)               | <.0001  |  |  |  |  |
| 61-80 years   | 729 (19.77)   | 4,087 (38.08)               | <.0001  |  |  |  |  |
| 80+ years   | 17 (0.46)   | 517 (4.82)                  | <.0001  |  |  |  |  |
| Gender, n (%)   |   |                             |         |  |  |  |  |
| Male  | 649 (17.60)   | 4,396 (40.96)               | <.0001  |  |  |  |  |
| Female  | 3,038 (82.40)   | 6,336 (59.04)               | <.0001  |  |  |  |  |
| Comorbidity scores, n (%)                             |   |                             |         |  |  |  |  |
| CCI ≥2  | 475 (12.88)   | 1,753 (16.33)               | <.0001  |  |  |  |  |
| CDS ≥2  | 2,228 (60.43)   | 3,092 (28.81)               | <.0001  |  |  |  |  |
| Elixhauser Score ≥2                                   | 2,418 (65.58)   | 6,679 (62.23)               | 0.0003  |  |  |  |  |
| SES, n (%)  |   |                             |         |  |  |  |  |
| Low   | 1,166 (31.62)   | 3,481 (32.44)               | 0.3633  |  |  |  |  |
| Medium  | 1,159 (31.43)   | 3,483 (32.45)               | 0.253   |  |  |  |  |
| High  | 1,284 (34.83)   | 3,502 (32.63)               | 0.0147  |  |  |  |  |
| Baseline cardiovascular disease-related comorbidities |   |                             |         |  |  |  |  |
| Hypertension  | 1,369 (37.13)   | 4,670 (43.51)               | <.0001  |  |  |  |  |
| Hyperlipidemia  | 726 (19.69)   | 2,477 (23.08)               | <.0001  |  |  |  |  |
| Type 2 diabetes                                       | 663 (17.98)   | 1,861 (17.34)               | 0.3766  |  |  |  |  |
| COPD  | 69 (1.87)   | 365 (3.40)                  | <.0001  |  |  |  |  |
| Smoking history                                       | 167 (4.53)  | 666 (6.21)                  | 0.0002  |  |  |  |  |
| Alcohol use disorder                                  | 32 (0.87)   | 157 (1.46)                  | 0.0061  |  |  |  |  |
| Chronic kidney disease                                | 22 (0.60)   | 144 (1.34)                  | 0.0003  |  |  |  |  |
| Any CVD-related comorbidities                         | 1,893 (51.34)   | 6,051 (56.38)               | <.0001  |  |  |  |  |

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

Unadjusted analysis showed no significant differences in CVD between AOM and non-AOM cohorts for arrhythmia, stroke, and ischemic heart disease (p>0.05 for each outcome). However, the non-AOM cohort was more likely to have any CVD, coronary artery disease, heart failure, atrial fibrillation, or peripheral vascular disease. (Figure 2).

#### 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 demographics and socioeconomic and clinical factors, the use of obesity medication was linked to a 16% decrease in cardiovascular risk (Table 2). No significant disparities in cardiovascular risk were observed between tirzepatide and semaglutide users (HR=1.07; confidence interval=0.77-1.49).

|                        |      | Confidence interval |       |         |
|------------------------|------|---------------------|-------|---------|
|                        | HR   | Lower               | Upper | P value |
| Treatment              | 0.84 | 0.71                | 0.99  | 0.0401  |
| No treatment           | 1    | 1                   | 1     |         |
| Age group (years)      |      |                     |       |         |
| 18-40                  | 0.2  | 0.15                | 0.26  | <.0001  |
| 41-60                  | 0.37 | 0.3                 | 0.46  | <.0001  |
| 61-80                  | 0.75 | 0.61                | 0.91  | 0.0033  |
| 80+                    | 1    | 1                   | 1     |         |
| Sex                    |      |                     |       |         |
| Female                 | 0.79 | 0.7                 | 0.89  | <.0001  |
| Male                   | 1    | 1                   | 1     |         |
| Comorbidity Scores     |      |                     |       |         |
| CCI (≥ 2)              | 1.66 | 1.43                | 1.92  | <.0001  |
| CDS (≥ 2)              | 1.29 | 1.14                | 1.45  | <.0001  |
| Elixhauser Score (≥ 2) | 1.64 | 1.36                | 1.97  | <.0001  |
| SES                    |      |                     |       |         |
| Low                    | 1.01 | 0.88                | 1.16  | 0.9154  |
| Medium                 | 1.06 | 0.92                | 1.22  | 0.3967  |
| High                   | 1    | 1                   | 1     |         |
| Comorbidities          |      |                     |       |         |
| Hypertension           | 1.5  | 1.3                 | 1.73  | <.0001  |
| Hyperlipidemia         | 1.15 | 1.02                | 1.3   | 0.0266  |
| Type 2 diabetes        | 0.94 | 0.81                | 1.08  | 0.3847  |
| COPD                   | 1.56 | 1.28                | 1.91  | <.0001  |
| Smoking history        | 1.24 | 1.03                | 1.49  | 0.0224  |
| Alcohol use disorder   | 0.86 | 0.52                | 1.41  | 0.5459  |
| Chronic kidney disease | 1.02 | 0.72                | 1.45  | 0.9131  |

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

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

This study found that anti-obesity medications, tirzepatide and semaglutide, reduce cardiovascular risk by 16% in active US military personnel with obesity, with no significant difference between the two drugs. Age, gender, and comorbidities also influenced outcomes, suggesting the need for personalized care. These findings highlight the potential cardiovascular benefits of AOMs in this population, warranting further research.

## REFERENCES

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- 2. Cho YK, La Lee Y, Jung CH. The cardiovascular effect of tirzepatide: A glucagon-like peptide-1 and glucose-dependent insulinotropic polypeptide dual agonist. J Lipid *Atheroscler*. 2023;12(3):213-222.
- 3. Ryan DH, Lingvay I, Deanfield J, et al. Long-term weight loss effects of semaglutide in obesity without diabetes in the SELECT trial. Nature Med. 2024;30(7):2049-2057.