The Impact of Semaglutide on Depressive Symptoms Among People With HIV

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BACKGROUND

- Semaglutide, a glucagon-like peptide-1 receptor agonist, is now one of the most widely prescribed therapies for the treatment of type 2 diabetes and obesity
- Concerns have been raised about its psychiatric safety, including effects on depression and suicidality
- People with HIV (PWH) have high rates of depression and other mental health concerns, yet evidence on the mental health safety of semaglutide among PWH remains limited

Aim: To assess the **safety** of semaglutide among PWH in routine clinical care by evaluating changes in depressive symptoms after semaglutide initiation

METHODS

Setting: **Nine sites** from the Centers for AIDS Research Network of Integrated Clinical Systems **(CNICS) cohort**

- CNICS is a 10-site U.S. cohort of adults with HIV in care

Design: Within-person, pre-post, quasi-experimental observational study

Population: PWH initiating **semaglutide** in care for diabetes and/or obesity

Outcome: Average **change in depressive symptoms** after semaglutide initiation

- Depressive symptoms assessed using the **Patient Health Questionnaire-9 (PHQ-9)**

Statistical Analyses:

- Linear mixed models estimated average change in PHQ-9 scores after semaglutide initiation
- Adjusted for age, sex, race/ethnicity, and time
- Analyses stratified by baseline depression severity, sex, and clinical subgroups
- Baseline depression severity categorized as:
  - No/Minimal (PHQ-9 0–4)
  - Mild (PHQ-9 5–9)
  - Moderate (PHQ-9 10–14)
  - Moderately Severe to Severe (PHQ-9 ≥15)

RESULTS

Overall, depressive symptoms remained generally **stable** after starting semaglutide among PWH in routine clinical care

Figure 1. Study Design. PHQ-9 measurements were assessed up to 4 years pre-initiation. Follow-up continued until semaglutide discontinuation or October 2024.

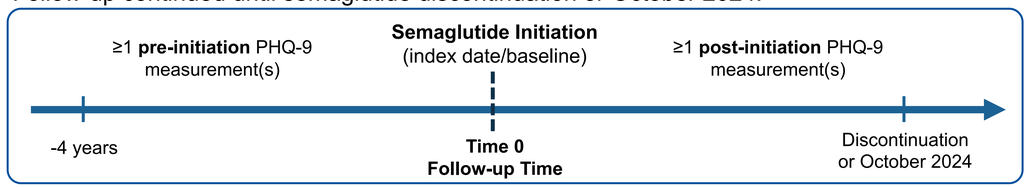
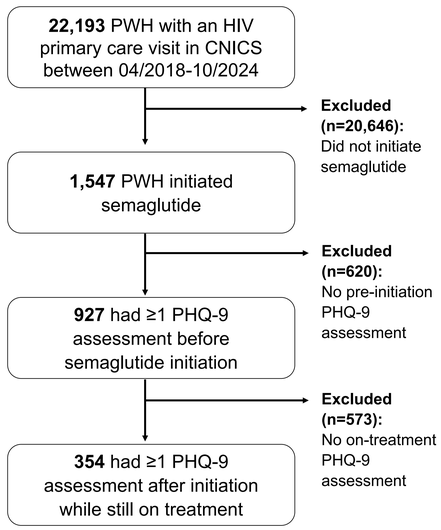


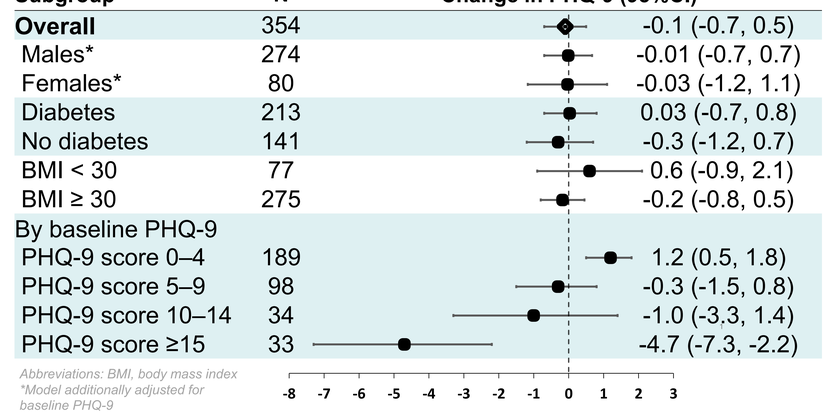
Figure 2. Flowchart for Cohort Selection



Baseline Characteristics of 354 PWH who initiated semaglutide

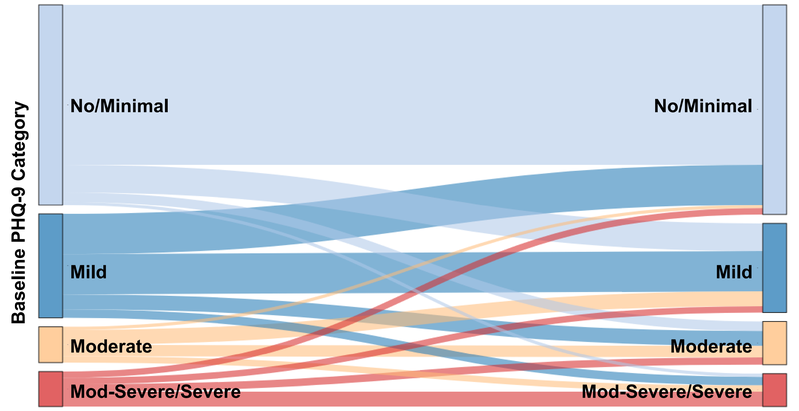
- Mean Age: 54 years (SD:10)
- 23% Female, 77% Male
- Race/ethnicity: 38% White, 32% Black, 26% Hispanic, 4% Other
- 53% had PHQ-9 0-4, 28% had PHQ-9 5-9, 19% had PHQ-9 ≥10
- Antidepressant use by baseline PHQ-9: PHQ-9 0–4: 64%, PHQ-9 5–9: 89%, PHQ-9 ≥10: 91%
- 78% had BMI ≥30, 60% had diabetes
- 97% had viral load <200 copies/mL
- Median follow-up: 9.4 months
- PWH had a median number of 1 follow-up PHQ-9 assessment (IQR 1–2) after semaglutide

Figure 3. Change in PHQ-9 After Semaglutide Initiation



Abbreviations: BMI, body mass index
**Model additionally adjusted for baseline PHQ-9*

Figure 4. Sankey Diagram Showing Transitions Between PHQ-9 Categories from Baseline to Last Follow-up After Initiating Semaglutide



Note: PHQ-9 depression severity categories: No/Minimal (PHQ-9 score of 0–4), Mild (5–9), Moderate (10–14), Moderately Severe to Severe (≥15).

CONCLUSION

- Semaglutide initiation was not associated with overall worsening of depressive symptoms in PWH
- Changes seen in subgroups with very low or high baseline PHQ-9 scores are likely due to floor/ceiling effects and regression to the mean, with no adverse mental health signal in PWH with higher baseline severity
- Interpretation is limited by small subgroup sizes, short follow-up time, and time-varying confounding; therefore, ongoing monitoring of depressive symptoms is recommended

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