# Determinants of Steatotic Liver Disease Among People with HIV in Europe and Australia

RESPOND International Cohort Consortium of Infectious Diseases

No. 762

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## BACKGROUND

- Steatotic liver disease (SLD) affects close to 50% of people with HIV (PWH), but longitudinal data are lacking
- We investigated the prevalence and incidence of SLD and described the progression to liver fibrosis in RESPOND

## METHODS

- We assessed SLD and liver fibrosis in RESPOND participants from January 2012 to December 2022 using serological scores validated for PWH in Europe *
- Participants of black ethnicity, those with viral hepatitis, and pregnant women were excluded
- The Hepatic Steatosis Index (HSI) was calculated using sex, BMI, AST, ALT, and diabetes; the Fibrosis-4 (FIB-4) Index using age, AST, ALT, and platelet count
- Presumed SLD was indicated by a HSI of ≥36, and liver fibrosis by two consecutive FIB-4 scores of ≥3.25
- We used multivariable logistic regression to evaluate factors associated with HSI ≥36 at first assessment
- Incidence rates (IRs) of HSI ≥36 per 100 person-years of follow-up (PYFU) were calculated for participants with an initial HSI <36, and IRs of two consecutive FIB-4 ≥3.25 for those with HSI ≥36

**Table 1. Participants characteristics at time of first HSI**

| *Characteristics* | **N= 14,449** |
|---|---|
| **Baseline date** | Oct 2012 (Apr 2012, Nov 2015) |
| **Median age, years (IQR)** | 45 (37-53) |
| **Female sex (%)** | 2766 (19.1) |
| **Race/ethnicity (%)** | |
| White/Caucasian | 12112 (83.8) |
| Asian | 433 (3.0) |
| Other | 429 (3.0) |
| Data collection prohibited | 1284 (8.9) |
| Unknown | 191 (1.3) |
| **MSM HIV acquisition risk (%)** | 8343 (57.7) |
| **Body mass index ≥25 kg m² (%)** | 5433 (37.6) |
| **Diabetes (%)** | 716 (5.0) |
| **Dyslipidemia (%)** | 10236 (70.8) |
| **Hypertension (%)** | 6805 (47.1) |
| **Median CD4+ count, cells/µl (IQR)** | 554 (381-748) |
| **HIV viral load < 200copies/mL (%)** | 10691 (74.0) |
| **ART duration, years (IQR)** | 6.7 (2.3-13.7) |
| **Recent exposure to NNRTIs (%)** | 5054 (35.0) |
| **Recent exposure to PIs (%)** | 4598 (31.8) |
| **Recent exposure to InSTI (%)** | 1431 (9.9) |
| **Recent exposure to TDF (%)** | 6379 (44.1) |
| **Recent exposure to TAF (%)** | 620 (4.3) |

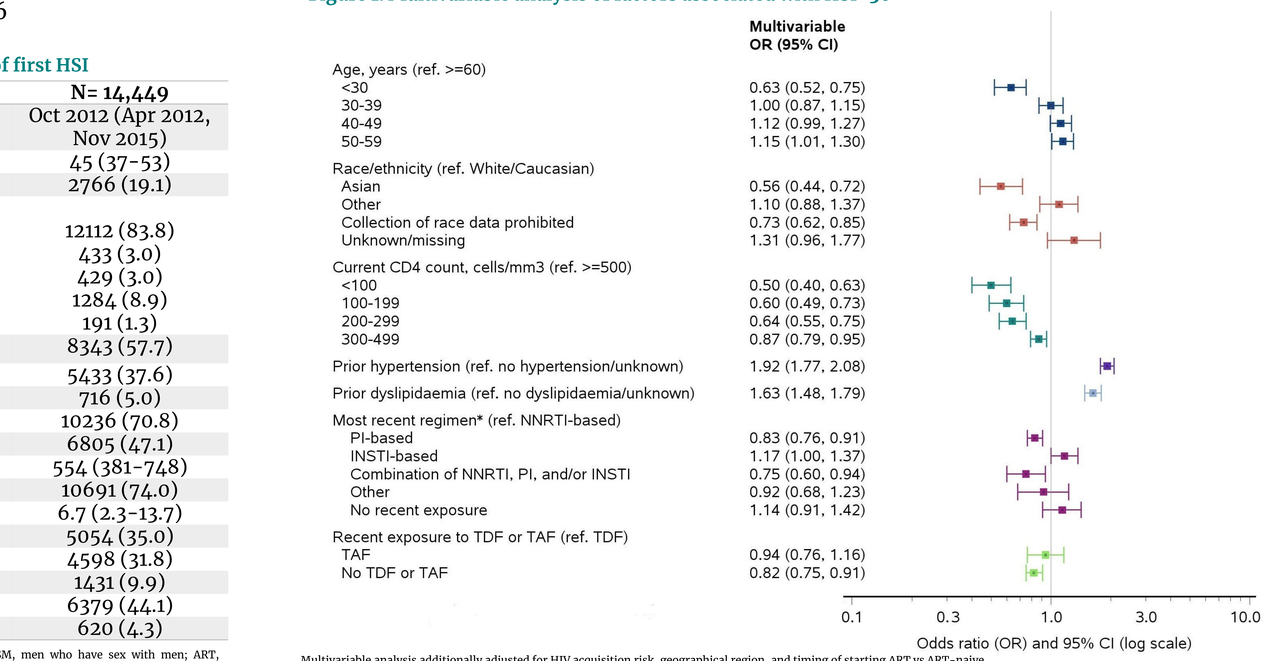
Abbreviations: HSI, hepatic steatosis index; IQR, interquartile range; MSM, men who have sex with men; ART, antiretroviral therapy; NNRTI, Non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor; InSTI , integrase strand transfer inhibitor; TDF, Tenofovir disoproxil fumarate ; TAF, tenofovir alafenamide

- At their first assessment, one third of eligible RESPOND participants had an HSI ≥36
- The prevalence of HSI ≥36 was highest in participants aged 50-59 years, those with high CD4 counts or metabolic comorbidities, and was slightly higher with exposure to InSTI versus NNRTI (Figure 1)
- Among participants with HSI ≥36, progression to liver fibrosis was rare

## RESULTS

- Of 14,449 participants included (Table 1), 4,445 (**30.8%**) had HSI ≥36 at first assessment
- In the remaining 10,004 participants with HSI <36 at first assessment:
  - The median follow-up was 8 years (IQR 4.1-10.0), and the median time between assessments was 6 months (IQR 4.1-8.0)
  - During 58,717 PYFU, the IR for HSI ≥36 was **12.9 per 100 PYFU (95% CI 12.7-13.2)**
  - Figure 1 shows the factors associated with HSI ≥ 36, with hypertension and dyslipidaemia being the most important risk factors
- Among 8,555 participants with HSI ≥36 at the first or a subsequent assessment:
  - The median follow-up was 7 years and 1.3% had FIB-4 ≥3.25 at the time of first HSI ≥36
  - During 50,285 PYFU, the IR of subsequently having two consecutive FIB-4 ≥3.25 was **0.5 per 100 PYFU (95% CI 0.5-0.6)**

**Figure 1. Multivariable analysis of factors associated with HSI≥36**

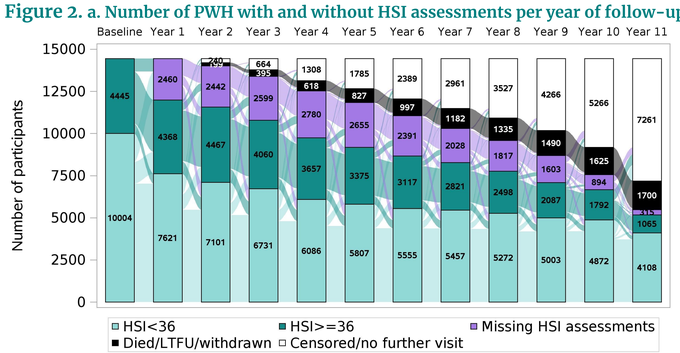



Multivariable analysis additionally adjusted for HIV acquisition risk, geographical region, and timing of starting ART vs ART-naive.
*Received within past 3 months and for a duration of at least 30 days.
NNRTI, Non-nucleoside reverse transcriptase inhibitors; PI, protease inhibitor; InSTI , integrase strand transfer inhibitor; TDF, Tenofovir disoproxil fumarate ; TAF, tenofovir alafenamide

## RESULTS (cont.)

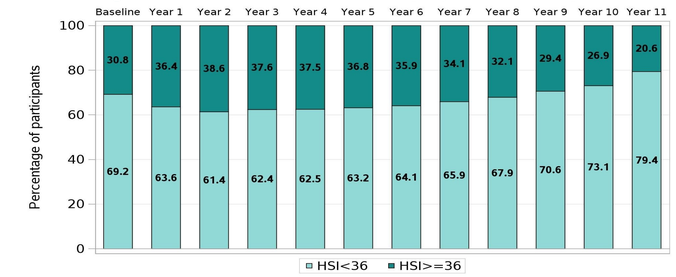
- Figure 2a shows the number of PWH with and without HSI each year, along with annual changes in HSI category for those assessed
- Figure 2b shows that the prevalence of HSI ≥36 remained stable for each year of follow-up

**Figure 2. a. Number of PWH with and without HSI assessments per year of follow-up**




If >1 HSI assessment during year, category is based on maximum HSI score. Censored/no further visit category includes those recruited later with less than maximum number of years follow-up available

**b. Percentage of PWH with HSI <36 and HSI ≥ 36 per year of follow-up**




If >1 HSI assessment during year, category is based on maximum HSI score. All PWH still under follow-up with HSI available are included.

## CONCLUSION

- The prevalence of HSI ≥36 was similar to previous studies in PWH
- Participants aged 50-59 years, those with higher CD4 counts, or metabolic comorbidities were more likely to have HSI ≥36
- A slight increase in the odds of HSI ≥36 was observed with exposure to InSTI versus NNRTI, showing borderline significance
- In participants with HSI ≥36, over a median follow-up of 7 years, progression to liver fibrosis was rare

**References**

*Riebensahm, C., et al., External Validation of Serologic Scores for the Detection of Liver Steatosis Among People With HIV. Open Forum Infect Dis, 2024.

**ADDITIONAL KEY INFORMATION**

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**The RESPOND Study Group** https://www.chip.dk/Studies/RESPOND/Study-Group
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