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## Prevalence of Steatotic Liver Disease, MASLD, MetALD and Significant Fibrosis in People with HIV in the United States

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### Summary

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**Author's contributions:** Study concept, manuscript preparation (SG, NC, RL); data acquisition (All authors), statistical analysis (EV), data interpretation and critical review of manuscript (All authors)

**Background**—Metabolic dysfunction-associated steatotic liver disease (MASLD) has recently been proposed as a replacement term for NAFLD.

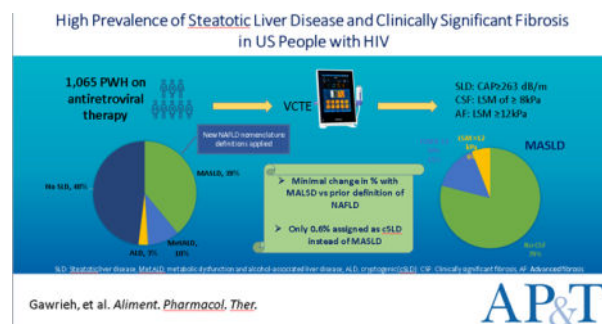
**Aims**—To assess the effects of this new nomenclature on the prevalence and distribution of different SLD categories in people with HIV (PWH) and identified factors associated with MASLD and clinically significant fibrosis (CSF)

**Methods**—PWH were prospectively enrolled from 9 US centres and underwent clinical evaluation and vibration-controlled transient elastography for controlled attenuation parameter (CAP) and liver stiffness measurement (LSM). SLD was defined as CAP  $\geq 263$  dB/m, CSF as LSM of  $\geq 8$  kPa, and advanced fibrosis (AF) as LSM  $\geq 12$  kPa. The prevalence of SLD, MASLD, metabolic dysfunction and alcohol-associated liver disease (MetALD), ALD, cryptogenic (cSLD), CSF and AF were determined. Uni- and multivariate logistic regression models were used to assess factors associated with MASLD and CSF risk.

**Results:** Of 1,065 participants, 74% were male, mean (SD) age  $51.6 \pm 11.9$  years, 46% non-Hispanic Black, and 74% with undetectable HIV RNA. The prevalence of SLD was 52%, MASLD 39%, MetALD 10%, ALD 3%, CSF 15% and AF 4%. Only 0.6% had cSLD. Black race was protective whereas obesity, ALT, and AST levels were associated with increased risk of MASLD and CSF in MASLD. HIV or antiretroviral therapy did not affect MASLD risk.

**Conclusions:** MASLD and MetALD are the dominant causes of SLD in PWH, affecting almost half. Application of the new nomenclature resulted in minimal change in the proportion of patients with MASLD who would have been diagnosed previously with NAFLD.

## Graphical Abstract



## Keywords

MASLD; NAFLD; stiffness; metALD; fibrosis; cirrhosis; CAP; prevalence

## Introduction

A major global effort was recently undertaken to address the scientific and civil communities' concerns about the adequacy of the terminology used to define fatty liver disease (FLD)<sup>1,2</sup>. A consensus emerged that the previously widely used term non-alcoholic FLD (NAFLD), did not capture the disease pathophysiology or allow optimal characterization of its subgroups, such as the group of patients that has hepatic steatosis,

metabolic risk factors, and consumed more alcohol than the definition “non-alcoholic” allowed<sup>1</sup>. There were also concerns the terms “non-alcoholic” and “fatty” were stigmatizing.

Using a Delphi process to guide the effort, a consensus emerged in support of using steatotic liver disease (SLD) as the overarching term to describe hepatic steatosis of any aetiology and to replace NAFLD with metabolic dysfunction-associated SLD (MASLD)<sup>1,3,4</sup>. The recently updated NAFLD Practice Guidance provides a framework for the definitions of NAFLD, nonalcoholic steatohepatitis (NASH), clinically significant fibrosis (CSF), and advanced fibrosis (AF)<sup>5</sup>. The new nomenclature calls for an adaptation of NAFLD to MASLD, and NASH to MASH.

Data have shown a heavy burden of SLD in people with HIV (PWH)<sup>6–8</sup>. Nearly half of PWH on suppressive antiretroviral therapy (ART) and without viral co-infections have SLD, 90% of which was attributed to NAFLD and 10% to alcohol<sup>9</sup>. Since the recent consensus changed both the name of NAFLD to MASLD and required the presence of at least one cardiometabolic risk factor for MASLD diagnosis, it is unclear how this impacts the prevalence of MASLD and distribution of different SLD categories in PWH.

The aims of this study were to characterise the prevalence of the different categories of SLD in PWH, including MASLD, as well as the frequency of CSF and AF in a large prospective multicentre study. We also identify factors associated with MASLD and CSF in this population.

## Methods

### Study participants

Participants from two National Institutes of Health funded cohorts were included in the analysis. Both cohorts prospectively enrolled consecutive adult PWH from outpatient HIV clinics after an informed consent process. Inclusion criteria were age ≥ 18 years, documented HIV defined by a positive HIV antibody assay and/or detectable HIV-1 RNA, and stable ART regimen for a minimum of three months prior to enrolment for those on ART at the time of study entry. Participants were excluded if they had evidence of hepatitis B or active hepatitis C co-infection (Hepatitis C prior infection allowable if three years from cure) or other liver diseases. The first cohort comprised eight sites (Duke University, Indiana University, Johns Hopkins University, University of Alabama-Birmingham, University of California-San Diego, University of California-San Francisco, University of Texas Health-Houston, and Virginia Commonwealth University) participating in R01 (NIDDK R01DK121378) HIV NASH CRN (HNC, [ClinialTrials.gov NCT05023044](https://clinicaltrials.gov/ct2/show/study/NCT05023044)). The second cohort comprised three sites (Indiana University, Massachusetts General Hospital, and University of Texas Health-Houston) participating in an R01 (NIDDK R01 DK112293)<sup>9</sup>. Data included in this study from some of the participants in the second cohort were previously published<sup>9,10</sup>. Attention was paid to removing duplicate data on the few participants who enrolled in both cohorts. A single Institutional Review Board (IRB) reviewed and approved the study protocol for the first cohort. Each site’s IRB reviewed and approved the study protocol for the second cohort.

## Study procedures

During the study visit, participants underwent clinical evaluation by a study physician and vibration-controlled transient elastography (VCTE) by Fibroscan® for controlled attenuation parameters (CAP) and liver stiffness measurement (LSM) by trained study staff. We prospectively collected data on demographic (including self-reported race/ethnicity), anthropometrics, medical history, laboratory, and HIV (HIV-1 RNA, CD4<sup>+</sup> T cell count) variables, in addition to ART regimen and classes (protease inhibitors [PIs], non-nucleoside reverse transcriptase inhibitors [NNRTIs], integrase strand transfer inhibitors [INSTIs], nucleoside reverse transcriptase inhibitors [NRTIs], and entry inhibitors). Acquired immunodeficiency syndrome (AIDS) was defined the presence of any AIDS-defining conditions or CD4 cell count <200 cells/mm<sup>3</sup>. Overweight was defined as body mass index (BMI) >25–29.9 kg/m<sup>2</sup> and obesity as BMI >30 kg/m<sup>2</sup>. All participants completed an Alcohol Use Disorders Identification Test (AUDIT) questionnaire to assess alcohol consumption in the past year<sup>11,12</sup>. AUDIT allows the quantification of alcohol intake as never, 1–2 standard drinks/day, 3–4 standard drinks/day, or higher intake levels. SLD was defined as CAP ≥263 dB/m<sup>9,13</sup>. We also performed a sensitivity analysis to examine the prevalence of SLD and its categories using different CAP cutoffs<sup>13</sup>. Cardiometabolic factors considered in MASLD definition included: 1) BMI ≥25 kg/m<sup>2</sup> (23 kg/m<sup>2</sup> for Asian individuals) or waist circumference ≥94 cm in males or 80 cm in females, or ethnically adjusted equivalent, 2) Fasting serum glucose ≥100 mg/dL or two hour post-load glucose level ≥140 mg/dL or haemoglobin A1C ≥5.7% or type 2 diabetes or treatment for type 2 diabetes, 3) Blood pressure ≥130 / 85 mmHg or specific antihypertensive drug treatment, 4) plasma triglycerides ≥150 mg/dL or lipid lowering treatment, 5) Plasma HDL-cholesterol <40 mg/dL for males and <50 mg/dL for females or lipid lowering agents per the recent multi-society Delphi consensus<sup>1</sup>. MASLD was defined as SLD with at least one cardiometabolic factor and low alcohol intake (<2 standard drinks/day), metabolic dysfunction- and alcohol-associated liver disease (MetALD) was defined as SLD, at least one cardiometabolic factor and moderate alcohol intake (3–4 standard drinks/day), alcohol-associated liver disease (ALD) was defined as SLD and excessive alcohol intake (>4 standard drinks daily), and cryptogenic SLD (cSLD) was defined as CAP ≥263 dB/m with no cardiometabolic risk factors or other causes of chronic liver disease<sup>1</sup>.

Fibrosis was assessed non-invasively with LSM<sup>13–15</sup>. CSF was defined as LSM of ≥8kPa and AF as LSM ≥12kPa<sup>5,9,16</sup>. We also performed a sensitivity analysis to examine the frequency of difference LSM cutoffs with a higher CAP cutoff to define steatosis.

## Statistical Methods

Baseline characteristics of participants were summarised by the five SLD subgroups (No-SLD, MASLD, MetALD, ALD, and cSLD). Categorical variables were summarised as percentages, whereas continuous variables as means and standard deviations or medians and interquartile range (IQR). We calculated the prevalence for each SLD category. Differences in means/medians or percentages of baseline characteristics among SLD categories were compared using One-way ANOVA or Kruskal–Wallis test (for data that does not follow a normal distribution), and categorical variables by chi-squared test or Cochran–Armitage trend test for ordered alternatives.

Univariate and multivariable logistic regression models were used to calculate ORs and 95% confidence intervals (Cis), to quantify the strength of the association of different variables with MASLD or those with MASLD and clinically significant fibrosis. Variables with a P value <0.10 at the univariate analyses and those with a recognised association with MASLD/CSF were included in the multivariable analyses. Covariates highly correlated ( $r>0.50$ ) with each other were included in different models to avoid collinearity issues. No missing value was recorded for our study outcomes or candidate predictors.

Stata version 16 (StataCorp, College Station, TX, US) was used for all analyses. Nominal p-values are reported and no adjustments were made for multiple comparisons. A two-sided  $P < 0.05$  indicated statistical significance.

## Results

### Cohort characteristics

A total of 1,065 participants were included in the analysis. The mean (SD) age was  $51.6 \pm 11.9$  years, 74% were male at birth, 46% identified as non-Hispanic Black, 28% as non-Hispanic White, and 22% as of Hispanic/Latino ethnicity, 84% reported high school or higher educational attainment, 35% were overweight and 43% had obesity (Table 1). Nearly half had hypertension, hypertriglyceridemia or abdominal obesity, and 18% had history of AIDS. The mean (SD) duration of HIV was  $17.3 \pm 10.1$  years, 74% had undetectable HIV RNA with median (IQR) HIV RNA 26 (20–40) copies/mL and CD4+ cell count 666 (513–919) (cells/mm<sup>3</sup>). The most commonly used classes of ART were NRTI in 90% and INSTI in 82%.

In the entire cohort, 555 (52%) had SLD, 412 (39%) MASLD, 106 (10%) MetALD, and 31 (3%) ALD (Figure 1). Only 6 (0.6%) participants had cSLD.

SLD was due to MASLD in 74%, MetALD in 19%, ALD in 6%, and cSLD in 1% of the participants. The clinical and laboratory characteristics of each group are shown in Table 1. The prevalence of SLD and distribution of its different categories using different CAP cutoffs are shown in Supplemental Table 1. As expected, using higher cutoffs for CAP to define steatosis results in lower estimates of SLD prevalence (40% with a CAP  $\geq 285$  dB/m, and 10% with a CAP  $\geq 353$  dB/m).

### Characteristics of participants with MASLD

Participants with MASLD were older than all other participants with or without SLD (Table 1). When compared to those without SLD, participants with MASLD were more frequently female at birth, White, Hispanic, and had larger waist circumference, higher body mass index (BMI) and greater frequency of obesity and other metabolic conditions (Table 1). They were also more commonly never smokers of cigarettes and more likely to have a history of AIDS and longer duration of HIV. There was no difference between the two groups concerning specific ART drugs classes. Participants with MASLD, also had higher levels of triglycerides, LDL, ALT, AST, alkaline phosphatase, creatinine and glucose, but lower HDL compared to those without SLD.

### Factors associated with MASLD

Table 2 shows the results of uni- and multivariable analyses of factors associated with MASLD. Of the independent factors associated with MASLD, obesity was associated with the highest risk [Adj OR 17.3, 95% CI (10.1–29.5),  $P < 0.01$ ], whereas Black race was associated with the lowest risk [Adj OR 0.45, 95% CI (0.29–0.70),  $P < 0.01$ ]. Older age, overweight, abdominal obesity, low HDL-C, ALT, AST and platelets levels were also independently associated with MASLD. No HIV-related factor or ART classes were associated with the risk of MASLD in the multivariable model.

### Prevalence of clinically significant and advanced fibrosis

In the entire cohort, 156 (15%) participants had CSF and 48 (4%) had AF (Table 1).

MASLD accounted for most [86/156 (55%)] cases of CSF in PWH with SLD followed by MetALD [21/156 (14%)] (Table 1). The same pattern is observed for AF. About a quarter of the cases of CSF and AF in PWH are observed in those without SLD (Table 1). In Supplemental Tables 2 and 3, the frequencies of different LSM cutoffs in those with CAP  $\geq 263$  dB/m and CAP  $\geq 285$  dB/m are shown.

CSF was present in 21% (86/412) of participants with MASLD, 20% (21/106) of those with MetALD and 8% (43/510) in those without SLD (Figure 2). The frequency of AF was highest in MetALD [9% (9/106)], followed by MASLD [6% (24/412)] then those without SLD [2% (11/510)] (Figure 2). The small number of participants with ALD and cSLD precluded accurate estimation of frequency of CSF and AF in these two SLD groups.

### Characteristics of participants with MASLD and MetALD who have clinically significant fibrosis

Compared to PWH with MASLD and CSF (Table 3), those with ALD and CSF were more frequently transgender females, Whites or Hispanic, but less likely to have low HDL levels or undetectable HIV RNA, had shorter duration of HIV, and higher ALT and AST levels. CD4+ cell count or exposure to different ART classes were not different between the two groups.

### Factors associated with CSF in participants with MASLD

Table 4 shows the results of uni- and multivariable analyses of factors associated with CSF in MASLD. Of the independent factors associated with CSF in MASLD, hypertension [Adj HR 2.7, 95% CI (1.4–5.0),  $P < 0.01$ ] and abdominal obesity [Adj OR 2.4, 95% CI (1.3–4.7),  $P < 0.01$ ] were associated with the highest risk, whereas Black race [Adj OR 0.45, 95% CI (0.23–0.87),  $P = 0.02$ ] and Hispanic ethnicity [Adj OR 0.36, 95% CI (0.17–0.79),  $P = 0.01$ ] were associated with the lowest risk. Other independent factors associated with increased risk of CSF in MASLD were time since HIV diagnosis and levels of ALT and AST. No other HIV-associated or ART-related factors were independently associated with the CSF in MASLD.

## Discussion

This large multicentre prospective cross-sectional study highlights the high prevalence of SLD and CSF in a cohort representative of the US population of PWH. In fact, 52% had SLD and 15% had CSF. The novelty of this study lies in the complete characterization of SLD in this prospectively recruited cohort of PWH. The application of the new nomenclature and SLD category definitions resulted in a more detailed understanding of the distribution of SLD categories: MASLD accounted for the majority (74%) of SLD cases, followed by MetALD (19%), ALD (6%), and cSLD (1%).

In an aging population of PWH that is largely on ART and treated for hepatitis B and C viral infections, NAFLD has emerged as the most common cause of liver disease<sup>6–8,17–25</sup>. In prior studies of persons with HIV mono-infection, NAFLD prevalence was reported in the range of 15–59%<sup>7,9,26–30</sup>. Clearly, case/phenotype definitions and alcohol use thresholds dictate the frequencies of each SLD category. The newer classification of SLD categories permits finer grouping based on the primary drivers of steatosis. Applying the new, more strict definition that requires the presence of at least one cardiometabolic risk factor in participant's with SLD in addition to non-significant alcohol consumption<sup>1</sup>, the prevalence of MASLD in this cohort is 39%. Incorporating the required cardiometabolic criteria for the definition of MASLD led to assignment of cSLD phenotype in only 0.6% of PWH, a subgroup with that would have been included under the umbrella of NAFLD previously. Thus, consistent with other studies from the US and China in non-HIV populations<sup>31,32</sup>, there is minimal discrepancy between NAFLD and MASLD assignment using the new nomenclature.

The prevalence rates of SLD and MASLD in this study of PWH (52% and 39%) are overall similar to SLD and MASLD rates in the US general population (SLD 50%, MASLD 42%), as reported in a recent study of the NHANES 2017–2020 cohort using a similar CAP cutoff ( < 263 dB/m) to that used in this study<sup>31</sup>. However, PWH seem to have slightly higher rates of MetALD and ALD (10% and 3%) than the general population (4% and 1%).

Since hepatic fibrosis is the major determinant of liver-related outcomes in these patients with SLD<sup>33,34</sup>, the observed burden of hepatic fibrosis in this population is significant. In each of the SLD groups except cSLD, approximately one in five participants had CSF. This is in line with previously reported rates of CSF in PWH and NAFLD<sup>7,8</sup>.

The synergistic interaction between the metabolic syndrome components and alcohol use is well established and increases the risk of severe liver disease<sup>35,36</sup>. The finding that the MetALD group had higher rate of AF (9%) than MASLD (6%) lends support to that hypothesis.

Older age, race/ethnicity and metabolic risk factors were the independent factors associated with the risk of MASLD and CSF in MASLD<sup>37,38</sup>. Interestingly, as PWH age, their risk factors for MASLD are influenced by similar factors as those affecting the risk of MASLD in the general population<sup>39,40</sup>. Similar to the general population, Black race is protective from MASLD in PWH<sup>41,42</sup>. HIV or ART class factors did not influence these risks. These findings are concordant with prior reports<sup>7,43–46</sup>.

An intriguing finding was that 8% of PWH without SLD had CSF and 2% had AF in absence of steatosis or other known liver diseases. These findings may be due to hazardous alcohol use as indicated by an AUDIT score 8 which was reported in 9% of this group of participants, or a prior history of poorly controlled HIV viremia that is known to impact liver fibrosis progression<sup>47</sup>.

This study has several limitations. It included PWH without viral hepatitis or other liver diseases thus may underestimate the total burden of SLD in PWH. Participants were on ART and achieved viral suppression, thus whether the findings apply to PWH not on ART or not virally suppressed is unknown. Biomarkers of alcohol use were not measured leaving the possibility of underreporting alcohol use by study participants. Lastly, despite the diversity and relatively large size of the cohort, precise estimates of different SLD categories rates in the racial and ethnic subgroups may not be possible given the relatively small number of participants in these subgroups and their frequencies of cardiometabolic conditions.

However, this study has several strengths including the large cohort, prospective enrollment, systematic questionnaire-based assessment of alcohol use, and protocolized phenotyping of participants. Another major strength is the racial and ethnic diversity of PWH we studied closely represent the diversity and proportions of these groups in PWH in the US reported in the recent Centers for Disease Control and Prevention survey 2015–2019<sup>48</sup>. Thus, our findings are probably generalizable to the US population of PWH.

In summary, MASLD and MetALD are the dominant causes of SLD and affect almost half of PWH who are on ART. Application of the new nomenclature resulted in minimal change in the proportion of patients with MASLD who would have been diagnosed previously with NAFLD. This population has a significant burden of CSF and AF. The risks of MASLD and CSF in MASLD in these patients are modulated primarily by demographic and metabolic factors. Efforts to screen for fibrotic SLD in PWH are justified based on these data. Future studies will be needed to evaluate whether the risk and severity of SLD can be modified with introduction of lifestyle and new pharmacological interventions targeting alcohol use and obesity in PWH.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Disclosures:

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Sciences and AbbVie and served as scientific advisory for Vir Bio (stock options/vested), Pardes Biosciences, Silverback Therapeutics, and served on event adjudication committee/DSMB for BMS/PRA and Personal Health Insights. **Dr. Sterling** declares none for this paper. For full disclosure, he has research support from Gilead, AbbVie, Abbott, and Roche, has served on a DSMB for Pfizer, AskBio, **Dr. Corey** serves on the scientific advisory board for Theratechnologies, Novo Nordisk and BMS and has received grant funding from Boehringer-Ingelheim, BMS and Novartis, **Dr. Cachay** has received unrestricted research grants paid to the University of California Reagents from Gilead Sciences for unrelated hepatitis C virus research project and has received payment or honoraria from Gilead Science (symposium, educational event November 2021) and THERATEchnologies), **Dr. Sulkowski** has served on scientific advisory boards for AbbVie, Aligos, Gilead, GSK, Precision Biosciences, and Virion, as a member of the Data Safety Monitoring Committee for Gilead related to HIV and COVID-19 and as an investigator for GSK, Janssen and Vir. **Dr. Chalasani** declares none for this paper. For full disclosure, he has had paid consulting agreements with Madrigal, GSK, Galectin, Zydus, Altimune, Foresite, Merck and Pfizer. He has research grants from DSM and Exact Sciences. He has equity ownership in Avant Sante Therapeutics, a contract research organization., **Dr. Loomba** serves as a consultant to Aardvark Therapeutics, Altimune, Anylam/Regeneron, Amgen, Arrowhead Pharmaceuticals, AstraZeneca, Bristol-Myer Squibb, CohBar, Eli Lilly, Galmed, Gilead, Glympse bio, Hightide, Inipharma, Intercept, Inventiva, Ionis, Janssen Inc., Madrigal, Metacrine, Inc., NGM Biopharmaceuticals, Novartis, Novo Nordisk, Merck, Pfizer, Sagimet, Theratechnologies, 89 bio, Terns Pharmaceuticals and Viking Therapeutics. RL has stock options in 89bio and Sagimet Biosciences. In addition his institutions received research grants from Arrowhead Pharmaceuticals, Astrazeneca, Boehringer-Ingelheim, Bristol-Myers Squibb, Eli Lilly, Galectin Therapeutics, Galmed Pharmaceuticals, Gilead, Hanmi, Intercept, Inventiva, Ionis, Janssen, Madrigal Pharmaceuticals, Merck, NGM Biopharmaceuticals, Novo Nordisk, Pfizer, Sonic Incytes and Terns Pharmaceuticals. Co-founder of LipoNexus Inc.

## Abbreviations

<b>ALD</b>	Alcohol-associated liver disease
<b>ALT</b>	Alanine aminotransferase
<b>ART</b>	Antiretroviral therapy
<b>AST</b>	Aspartate aminotransferase
<b>BMI</b>	Body mass index
<b>CAP</b>	Controlled attenuation parameter
<b>CI</b>	Confidence Intervals
<b>cSLD</b>	Cryptogenic steatotic liver disease
<b>FLD</b>	Fatty liver disease
<b>HIV</b>	Human immunodeficiency virus
<b>INSTI</b>	Integrase strand transfer inhibitors
<b>LSM</b>	Liver stiffness measurement
<b>MASLD</b>	Metabolic dysfunction-associated steatotic liver disease
<b>MetALD</b>	metabolic dysfunction- and alcohol-associated liver disease
<b>NAFLD</b>	Non-alcoholic fatty liver disease
<b>NNRTI</b>	Non-nucleoside reverse transcriptase inhibitors
<b>NRTI</b>	Nucleoside reverse transcriptase inhibitors
<b>PI</b>	Protease inhibitors

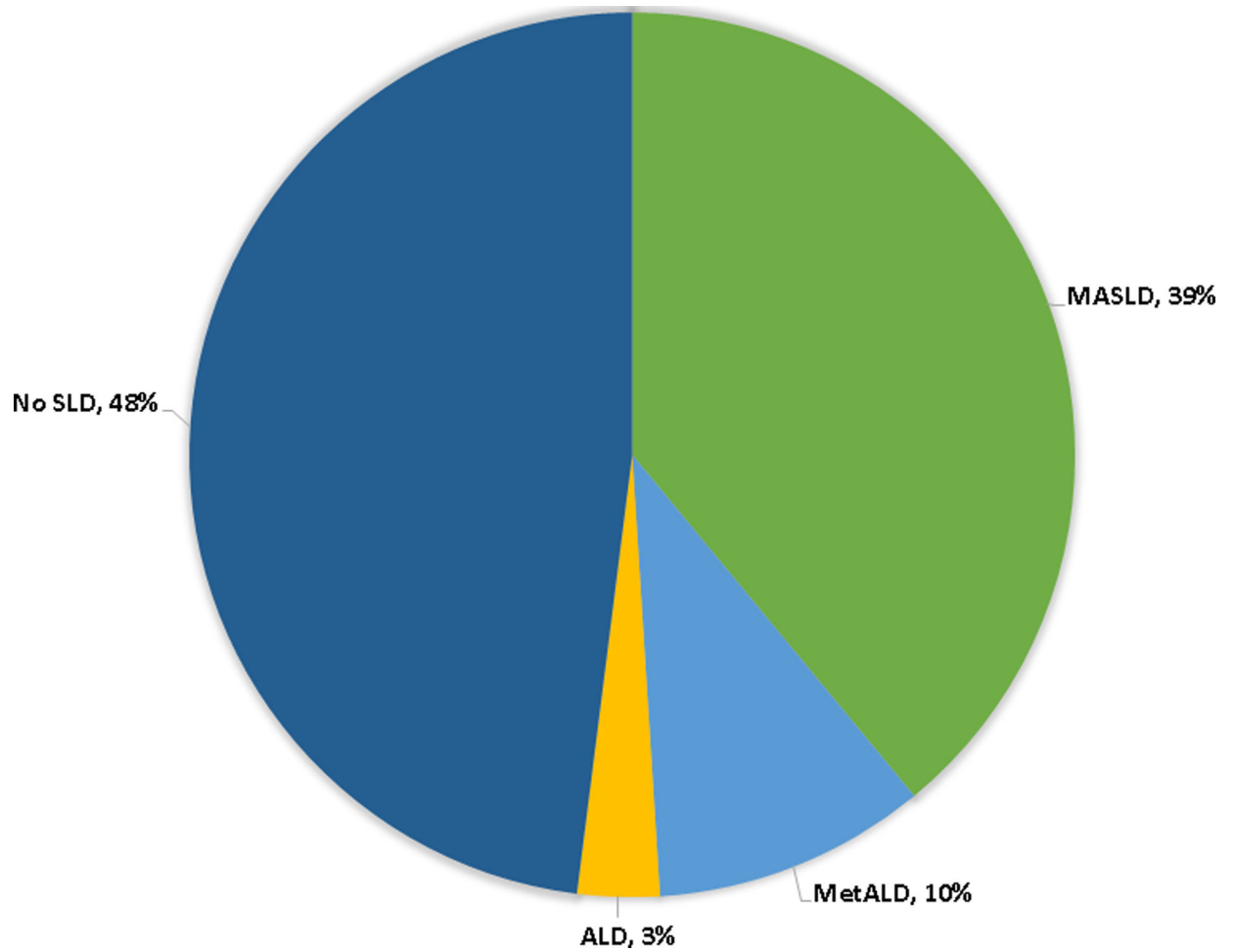
<b>PWH</b>	Persons or people with HIV
<b>SLD</b>	Steatotic liver disease
<b>VCTE</b>	Vibration-controlled transient elastography

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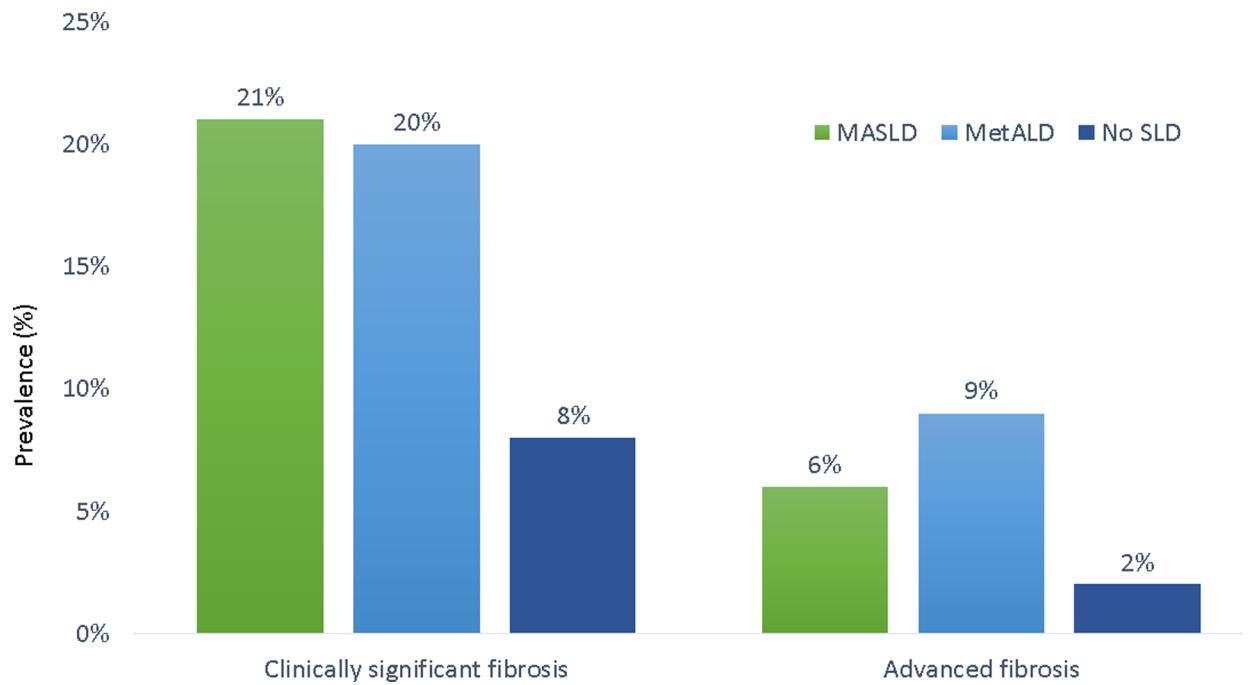
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**Figure. 1. Prevalence of steatotic liver disease and its categories.**

Abbreviations: SLD: steatotic liver disease, MASLD: metabolic dysfunction associated SLD, MetALD: metabolic dysfunction- and alcohol-associated liver disease, ALD metabolic alcohol-associated liver disease, cSLD: cryptogenic SLD.



**Figure 2. Frequencies of clinically significant and advanced fibrosis in participants with MASLD, MetALD, and no SLD.**

Abbreviations: SLD: steatotic liver disease, MASLD: metabolic dysfunction associated SLD, MetALD: metabolic dysfunction- and alcohol-associated liver disease, CSF: Clinically significant fibrosis (LSM  $\geq 8$  kPa), AF: Advanced fibrosis (LSM  $\geq 12$  kPa).

**Table 1.**

Baseline characteristics of study participants.

	Whole cohort Mean ± SD or n (%)	No SLD Mean ± SD or n (%)	MASLD Mean ± SD or n (%)	MetALD Mean ± SD or n (%)	ALD Mean ± SD or n (%)	cSLD* Mean ± SD or n (%)
<b>Number of participants</b>	1,065	510	412	106	31	6
Age, y	51.6 ± 11.9	50.5 ± 13.0	53.3 ± 10.8	50.9 ± 10.1	51.1 ± 9.2	49.4 ± 13.7
Sex at birth (male)	783 (74)	379 (74)	291 (71)	83 (78)	24 (77)	6 (100)
Transgender (female)	45 (4)	24 (5)	12 (3)	7 (7)	2 (7)	0 (0)
Race/ethnicity						
NH White	294 (28)	122 (24)	121 (29)	37 (35)	9 (29)	5 (83)
NH Black	489 (46)	276 (54)	175 (43)	29 (27)	9 (29)	0 (0)
Hispanic	240 (22)	89 (18)	99 (24)	39 (37)	12 (39)	1 (17)
Other/multiracial	42 (4)	23 (4)	17 (4)	1 (1)	1 (3)	0 (0)
Educational attainment						
Less than high school	172 (16)	89 (18)	62 (15)	15 (14)	6 (20)	0 (0)
High school or GED	283 (27)	136 (27)	101 (25)	31 (30)	12 (40)	3 (50)
College or above	596 (56)	276 (55)	246 (60)	59 (56)	12 (40)	3 (50)
BMI (kg/m <sup>2</sup> )	30.0 ± 6.6	26.8 ± 4.9	33 ± 6.8	33.5 ± 5.6	31.9 ± 6.0	23.9 ± 1.2
Classes						
<25	240 (22)	201 (39)	26 (6)	3 (2)	4 (13)	6 (100)
25–29.9	367 (35)	202 (40)	131 (32)	26 (25)	8 (26)	0 (0)
30	458 (43)	107 (21)	255 (62)	77 (73)	19 (61)	0 (0)
WC (cm)	101.1 ± 16.1	92.5 ± 12.4	108.8 ± 15.1	111.9 ± 15.0	106.7 ± 12.9	87.3 ± 7.6
High blood pressure <sup>b</sup>	517 (48)	214 (42)	232 (56)	56 (53)	15 (48)	0 (0)
Hyperglycemia <sup>c</sup>	221 (21)	63 (12)	124 (30)	29 (27)	5 (16)	0 (0)
Hypertriglyceridemia <sup>d</sup>	548 (51)	207 (41)	248 (60)	76 (72)	17 (55)	0 (0)
Abdominal obesity <sup>e</sup>	526 (49)	148 (30)	278 (68)	78 (77)	22 (71)	0 (0)
Low HDL-C <sup>f</sup>	359 (34)	135 (29)	183 (47)	30 (29)	11 (35)	0 (0)
Smoking status						

	Whole cohort Mean $\pm$ SD or n (%)	No SLD Mean $\pm$ SD or n (%)	MASLD Mean $\pm$ SD or n (%)	MetALD Mean $\pm$ SD or n (%)	ALD Mean $\pm$ SD or n (%)	eSLD* Mean $\pm$ SD or n (%)
Never	418 (39)	184 (36)	179 (44)	42 (40)	11 (36)	2 (33)
Former	396 (37)	177 (35)	169 (41)	37 (35)	10 (32)	3 (50)
Current	244 (23)	144 (29)	62 (15)	27 (25)	10 (32)	1 (17)
<b>HIV related features</b>						
History of AIDS	187 (18)	75 (15)	77 (19)	24 (23)	10 (32)	1 (17)
Time since HIV diagnosis (years)	17.3 $\pm$ 10.1	17.1 $\pm$ 10.4	18.3 $\pm$ 9.7	15.5 $\pm$ 9.9	15.3 $\pm$ 8.9	15.5 $\pm$ 11.3
HIV-RNA undetectable (yes)	789 (74)	372 (73)	321 (78)	67 (63)	24 (77)	5 (83)
HIV-RNA copies per-mL (median, IQR)	26 (20-40)	26 (20-35)	28 (20-45)	22 (20-40)	24 (20-29)	20 (20-25)
CD4+ cell count(cells/mm <sup>3</sup> ) (median, IQR)	666 (513-919)	644 (479-907)	687 (540-929)	688 (562-930)	813 (484-995)	852 (675-1035)
NRTI	958 (90)	449 (90)	378 (92)	96 (92)	29 (97)	6 (100)
NNRTI	184 (17)	88 (18)	71 (17)	20 (19)	5 (17)	0 (0)
PI/r	138 (13)	72 (15)	56 (14)	6 (6)	4 (13)	0 (0)
INSTI	868 (82)	411 (83)	342 (84)	87 (84)	22 (73)	6 (100)
Pharm-enhancer (cobicistat)	207 (19)	104 (21)	81 (20)	15 (14)	7 (23)	0 (0)
<b>VCTE features</b>						
CAP dB/m	267 $\pm$ 64	212 $\pm$ 36	316 $\pm$ 38	320 $\pm$ 37	321 $\pm$ 30	282 $\pm$ 19
263	555 (52)	-	-	-	-	-
LSM kPa	6.3 $\pm$ 5.7	5.6 $\pm$ 6.2	6.7 $\pm$ 4.2	7.8 $\pm$ 7.9	7.5 $\pm$ 5.0	5.4 $\pm$ 1.2
8	156 (15)	43 (8)	86 (21)	21 (20)	6 (19)	0 (0)
12	48 (4)	11 (2)	24 (6)	10 (9)	3 (10)	0 (0)
<b>Laboratory features</b>						
Total cholesterol (mg/dl)	175.8 $\pm$ 40.7	174.9 $\pm$ 42.1	175.9 $\pm$ 39.6	178.6 $\pm$ 41.1	177.5 $\pm$ 35.5	174.5 $\pm$ 25.6
Triglycerides (mg/dl)	145.4 $\pm$ 124.5	116.5 $\pm$ 61.1	170.4 $\pm$ 172.7	175.5 $\pm$ 89.2	179.8 $\pm$ 134.2	88.3 $\pm$ 37.9
HDL (mg/dl)	49.1 $\pm$ 16.7	52.7 $\pm$ 18.3	45.2 $\pm$ 14.7	46.9 $\pm$ 10.8	49.0 $\pm$ 18.8	59.2 $\pm$ 13.4
LDL (mg/dl)	100.3 $\pm$ 36.2	99.8 $\pm$ 34.9	101.9 $\pm$ 37.9	98.9 $\pm$ 38.0	92.9 $\pm$ 22.9	89.8 $\pm$ 39.4
ALT (U/L)	30.4 $\pm$ 25.4	24.4 $\pm$ 17.6	33.6 $\pm$ 26.4	44.3 $\pm$ 40.5	39.9 $\pm$ 28.9	28.5 $\pm$ 7.4
AST (U/L)	27.4 $\pm$ 18.3	25.1 $\pm$ 16.7	28.6 $\pm$ 19.7	31.6 $\pm$ 17.2	35.9 $\pm$ 22.5	27.5 $\pm$ 9.8
Albumin (g/dl)	4.29 $\pm$ 0.39	4.28 $\pm$ 0.38	4.29 $\pm$ 0.40	4.31 $\pm$ 0.37	4.25 $\pm$ 0.40	4.43 $\pm$ 0.19
Total bilirubin (mg/dl)	0.59 $\pm$ 0.53	0.59 $\pm$ 0.44	0.58 $\pm$ 0.62	0.59 $\pm$ 0.49	0.71 $\pm$ 0.63	0.56 $\pm$ 0.24

	Whole cohort Mean $\pm$ SD or n (%)	No SLD Mean $\pm$ SD or n (%)	MASLD Mean $\pm$ SD or n (%)	MetALD Mean $\pm$ SD or n (%)	ALD Mean $\pm$ SD or n (%)	cSLD* Mean $\pm$ SD or n (%)
Alkaline phosphatase (U/L)	79.8 $\pm$ 29.2	78.3 $\pm$ 30.6	81.4 $\pm$ 28.4	83.4 $\pm$ 25.7	78.1 $\pm$ 26.8	48.0 $\pm$ 8.6
Platelet x 10 <sup>9</sup> /L	241 $\pm$ 69	236 $\pm$ 67	248 $\pm$ 72	236 $\pm$ 67	223 $\pm$ 58	230 $\pm$ 61
Creatinine (mg/dl)	1.20 $\pm$ 3.30	1.14 $\pm$ 1.00	1.36 $\pm$ 5.2	0.96 $\pm$ 0.21	0.98 $\pm$ 0.19	0.98 $\pm$ 0.19
Glucose (mg/dl)	104.0 $\pm$ 39.8	95.6 $\pm$ 25.0	113.7 $\pm$ 52.8	108.3 $\pm$ 33.6	101.7 $\pm$ 27.7	91.7 $\pm$ 17.4

Abbreviations: SLD: steatotic liver disease, MASLD: metabolic dysfunction associated SLD, MetALD: metabolic dysfunction- and alcohol-associated liver disease, ALD: alcohol-associated liver disease, cSLD: cryptogenic SLD

<sup>a</sup> Continuous variables were compared using ANOVA or Kruskal–Wallis test when appropriate, and categorical variables by chi-squared test or Cochran-Armitage trend test for ordered alternatives.

<sup>b</sup> 130 mm Hg systolic blood pressure or 85 mm Hg diastolic blood pressure or drug treatment for hypertension.

<sup>c</sup> Fasting glucose 100 mg/dL or treatment for elevated glucose.

<sup>d</sup> Elevated triglycerides 150 mg/dL or drug treatment for hypertriglyceridemia.

<sup>e</sup> 102 cm in men or 88 cm in women. In non-Hispanic Asian waist circumference cut point: 90 cm in men and 80 cm in women.

<sup>f</sup> <40 mg/dL in men or <50 mg/dL in women or medications to treat reduced HDL-C.

**Table 2.**

Factors associated with MASLD in univariate and multivariable logistic regression models.

	No SLD <i>Mean ± SD or n (%)</i>	MASLD <i>Mean ± SD or n (%)</i>	P value	Adjusted OR (95% CI)	P value
Age, y	50.5 ± 13.0	53.3 ± 10.8	<0.01	1.03 (1.006–1.05)	0.01
Sex at birth (male)	379 (74)	291 (71)	0.21	-	-
Transgender (female)	24 (5)	12 (3)	0.17	-	-
Race/ethnicity			<0.01		
NH White	122 (24)	121 (29)		Ref (1)	
NH Black	276 (54)	175 (43)		0.45 (0.29–0.70)	<0.01
Hispanic	89 (18)	99 (24)		-	-
Other/multiracial	23 (4)	17 (4)		-	-
Educational attainment			0.13	-	-
Less than high school	89 (18)	62 (15)			
High school or GED	136 (27)	101 (25)			
College or above	276 (55)	246 (60)			
BMI (kg/m <sup>2</sup> )			<0.01		
<25	201 (39)	26 (6)		Ref (1)	
25–29.9	202 (40)	131 (32)		4.1 (2.4–6.8)	<0.01
30	107 (21)	255 (62)		17.3 (10.1–29.5)	<0.01
High blood pressure	214 (42)	232 (56)	<0.01	-	-
Hyperglycemia	63 (12)	124 (30)	<0.01	-	-
Hypertriglyceridemia	207 (41)	248 (60)	<0.01	-	-
Abdominal obesity	148 (30)	278 (68)	<0.01	4.3 (3.1–5.9)	<0.01
Low HDL-C	135 (29)	183 (47)	<0.01	1.8 (1.3–2.6)	<0.01
Smoking status			<0.01	-	-
Never	184 (36)	179 (44)			
Former	177 (35)	169 (41)			
Current	144 (29)	62 (15)			
<b>HIV related features</b>					
History of AIDS	75 (15)	77 (19)	0.11	-	-
Time since HIV diagnosis (years)	17.1 ± 10.4	18.3 ± 9.7	0.06	-	-
HIV-RNA undetectable (yes)	372 (73)	321 (78)	0.09	-	-
HIV-RNA copies per-mL	26 (20–35)	28 (20–45)	0.54	-	-
CD4+ cell count(cells/mm <sup>3</sup> )	644 (479–907)	687 (540–929)	0.07	-	-
NRTI	449 (90)	378 (92)	0.27	-	-
NNRTI	88 (18)	71 (17)	0.89	-	-
PI/r	72 (15)	56 (14)	0.73	-	-
INSTI	411 (83)	342 (84)	0.71	-	-
Pharm-enhancer (cobicistat)	104 (21)	81 (20)	0.68	-	-

	No SLD <i>Mean ± SD or n (%)</i>	MASLD <i>Mean ± SD or n (%)</i>	P value	Adjusted OR (95% CI)	P value
<b>Laboratory features</b>					
Total cholesterol (mg/dl)	174.9 ± 42.1	175.9 ± 39.6	0.72	-	-
LDL (mg/dl)	99.8 ± 34.9	101.9 ± 37.9	0.42	-	-
ALT (U/L)	24.4 ± 17.6	33.6 ± 26.4	<0.01	1.01 (1.003–1.02)	<0.01
AST (U/L)	25.1 ± 16.7	28.6 ± 19.7	<0.01	1.009 (1.0001–1.02)	0.04
Albumin (g/dl)	4.28 ± 0.38	4.29 ± 0.40	0.81	-	-
Total bilirubin (mg/dl)	0.59 ± 0.44	0.58 ± 0.62	0.74	-	-
Alkaline phosphatase (U/L)	78.3 ± 30.6	81.4 ± 28.4	0.12	-	-
Platelet x 10 <sup>9</sup> /L	236 ± 67	248 ± 72	<0.01	1.004 (1.001–1.006)	<0.01

Those variables with a P value <0.10 at the univariate analysis were included in the multivariable analysis. Covariates highly correlated ( $r>0.50$ ) between each other were included into different models to avoid collinearity issues.

**Table 3.**

Baseline features of participants with MASLD and MetALD who have clinically significant fibrosis.

	<b>MASLD</b> <i>Mean ± SD or n (%)</i>	<b>MetALD</b> <i>Mean ± SD or n (%)</i>	<b>P value<sup>a</sup></b>
<b>Number of participants</b>	86	21	
Age, y	54.8 ± 9.8	51.2 ± 8.5	0.06
Sex at birth (male)	64 (74)	18 (86)	0.27
Transgender (female)	1 (1)	3 (14)	<0.01
Race/ethnicity			<0.01
NH White	37 (43)	11 (52)	
NH Black	32 (37)	1 (5)	
Hispanic	13 (15)	9 (43)	
Other/multiracial	4 (5)	0 (0)	
Educational attainment			0.25
Less than high school	11 (13)	3 (15)	
High school or GED	27 (32)	10 (50)	
College or above	46 (55)	7 (35)	
Body mass index (kg/m <sup>2</sup> )	35.65 ± 7.9	34.5 ± 6.0	0.56
Classes			0.53
<25	4 (5)	2 (10)	
25–29.9	19 (23)	1 (5)	
30	62 (72)	18 (86)	
Waist circumference (cm)	116.5 ± 15.7	117.9 ± 13.5	0.71
High blood pressure <sup>b</sup>	64 (74)	13 (62)	0.25
Hyperglycemia <sup>c</sup>	40 (47)	6 (29)	0.14
Hypertriglyceridemia <sup>d</sup>	63 (73)	16 (76)	0.78
Abdominal obesity <sup>e</sup>	69 (81)	17 (85)	0.69
Low HDL-C <sup>f</sup>	42 (53)	3 (14)	<0.01
Smoking status			0.79
Never	30 (35)	9 (43)	
Former	42 (49)	9 (43)	
Current	14 (16)	3 (14)	
<b>HIV related features</b>			
History of AIDS	21 (24)	6 (29)	0.69
Time since HIV diagnosis (years)	21.1 ± 10.1	14.4 ± 8.8	<0.01
HIV-RNA undetectable (yes)	69 (80)	11 (52)	<0.01
HIV-RNA copies per-mL (median, IQR)	20 (20–42)	30 (20–71)	0.35
CD4+ cell count(cells/mm <sup>3</sup> ) (median, IQR)	662 (512–906)	614 (458–878)	0.67
NRTI	77 (90)	17 (81)	0.28

	<b>MASLD</b> <i>Mean ± SD or n (%)</i>	<b>MetALD</b> <i>Mean ± SD or n (%)</i>	<b>P value<sup>a</sup></b>
NNRTI	17 (20)	5 (24)	0.68
PI/r	14 (16)	1 (5)	0.17
INSTI	71 (83)	17 (81)	0.86
Pharm-enhancer (cobicistat)	17 (20)	3 (14)	0.56
<b>Laboratory features</b>			
Total cholesterol (mg/dl)	172.1 ± 36.7	176.8 ± 35.8	0.61
Triglycerides (mg/dl)	206.6 ± 290.9	187.3 ± 83.2	0.37
HDL (mg/dl)	42.5 ± 12.6	47.7 ± 8.5	0.08
LDL (mg/dl)	96.0 ± 30.5	92.2 ± 32.8	0.63
ALT (U/L)	41.7 ± 33.3	58.7 ± 31.6	<0.01
AST (U/L)	33.9 ± 21.4	45.1 ± 19.7	<0.01
Albumin (g/dl)	4.28 ± 0.38	4.20 ± 0.36	0.44
Total bilirubin (mg/dl)	0.61 ± 0.29	0.60 ± 0.25	0.95
Creatinine (mg/dl)	1.31 ± 1.45	0.94 ± 0.23	0.13
Glucose (mg/dl)	124.6 ± 61.4	109.2 ± 40.6	0.15
Alkaline phosphatase (U/L)	81.1 ± 27.6	83.3 ± 21.9	0.74
Platelet x 10 <sup>9</sup> /L	234 ± 62	213 ± 74	0.13

<sup>a</sup>Continuous variables were compared using ANOVA or Kruskal–Wallis test when appropriate, and categorical variables by chi-squared test or Cochran-Armitage trend test for ordered alternatives.

<sup>b</sup> 130 mm Hg systolic B.P. or 85 mm Hg diastolic B.P. or drug treatment for hypertension.

<sup>c</sup> Fasting glucose 100 mg/dL or treatment for elevated glucose.

<sup>d</sup> Elevated triglycerides 150 mg/dL or drug treatment for hypertriglyceridemia.

<sup>e</sup> 102 cm in men or 88 cm in women. In non-Hispanic Asian waist circumference cut point: 90 cm in men and 80 cm in women.

<sup>f</sup> <40 mg/dL in men or <50 mg/dL in women or medications to treat reduced HDL-C.

Note: Cryptogenic SLD is excluded from the analysis because only 1 patient had clinically significant fibrosis.

**Table 4.**

Factors associated with clinically significant fibrosis among people with HIV and MASLD (n=412)

	No CSF Mean $\pm$ SD or n (%)	CSF Mean $\pm$ SD or n (%)	P value	Adjusted OR (95% CI)	P value
<b>Number of participants</b>	326	86			
Age, y	52.9 $\pm$ 10.9	54.8 $\pm$ 9.8	0.14	-	-
Sex at birth (male)	227 (70)	64 (74)	0.39	-	-
Transgender (female)	11 (3)	1 (1)	0.28	-	-
Race/ethnicity			0.01		
NH White	84 (26)	37 (43)		Ref (1)	
NH Black	143 (44)	32 (37)		0.45 (0.23–0.87)	0.02
Hispanic	86 (26)	13 (15)		0.36 (0.17–0.79)	0.01
Other/multiracial	13 (4)	4 (5)		-	-
Educational attainment			0.20	-	-
Less than high school	51 (16)	11 (13)			
High school or GED	74 (23)	27 (32)			
College or above	200 (61)	46 (55)			
Body mass index classes (kg/m <sup>2</sup> )			0.09		
<25	22 (7)	4 (5)		Ref (1)	
25–29.9	111 (34)	20 (23)		-	-
30	193 (59)	62 (72)		2.6 (1.00–8.9)	0.05
High blood pressure <sup>b</sup>	168 (51)	64 (74)	<0.01	2.7 (1.4–5.0)	<0.01
Hyperglycemia <sup>c</sup>	84 (26)	40 (46)	<0.01	-	-
Hypertriglyceridemia <sup>d</sup>	185 (57)	63 (73)	<0.01	-	-
Abdominal obesity <sup>e</sup>	209 (64)	69 (81)	<0.01	2.4 (1.3–4.7)	<0.01
Low HDL-C <sup>f</sup>	141 (46)	42 (53)	0.25	-	-
Smoking status			0.17	-	-
Never	149 (46)	30 (35)			
Former	127 (39)	42 (49)			
Current	48 (15)	14 (16)			
<b>HIV related features</b>					
History of AIDS	56 (17)	21 (24)	0.12	-	-
Time since HIV diagnosis (years)	17.6 $\pm$ 9.5	21.2 $\pm$ 10.1	<0.01	1.03 (1.00–1.07)	0.04
HIV-RNA undetectable (yes)	252 (77)	69 (80)	0.56	-	-
HIV-RNA copies per-mL (median, IQR)	30 (20–48.5)	20 (20–42)	0.42	-	-
CD4+ cell count(cells/mm <sup>3</sup> ) (median, IQR)	708 (548–933)	662 (512–906)	0.43	-	-
NRTI	301 (93)	77 (90)	0.26	-	-
NNRTI	54 (17)	17 (20)	0.51	-	-
PI/r	42 (13)	14 (16)	0.43	-	-
INSTI	271 (84)	71 (83)	0.76	-	-

	No CSF <i>Mean ± SD or n (%)</i>	CSF <i>Mean ± SD or n (%)</i>	P value	Adjusted OR (95% CI)	P value
Pharm-enhancer (cobicistat)	64 (20)	17 (20)	0.99	-	-
<b>Laboratory features</b>					
Total cholesterol (mg/dl)	176.9 ± 40.2	172.1 ± 36.8	0.34	-	-
LDL (mg/dl)	103.4 ± 39.5	96.0 ± 30.5	0.13	-	-
ALT (U/L)	31.5 ± 23.9	41.7 ± 33.3	<0.01	1.01 (1.002–1.02)	0.02
AST (U/L)	27.2 ± 19.0	33.9 ± 21.3	<0.01	1.01 (1.00–1.03)	0.04
Albumin (g/dl)	4.29 ± 0.40	4.28 ± 0.38	0.66	-	-
Total bilirubin (mg/dl)	0.58 ± 0.69	0.61 ± 0.29	0.67	-	-
Alkaline phosphatase (U/L)	81.4 ± 28.6	81.1 ± 27.6	0.91	-	-
Platelet x 10 <sup>9</sup> /L	252 ± 75	233 ± 62	0.03	-	-

<sup>a</sup>Those variables with a P value <0.10 at the univariate analysis were included in the multivariable analysis. Covariates highly correlated ( $r>0.50$ ) between each other were included into different models to avoid collinearity issues.