**Supplementary Table 1**. Cohorts in the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) participating in the validation of end-stage liver disease and hepatocellular carcinoma diagnoses from 1996 - 2010.

|  |  |  |  |
| --- | --- | --- | --- |
| **NA-ACCORD Cohort** | **No. HIV/HBV Participants** | **Male, n (%)** | **Median Age (IQR)** |
| A | 1,719 | 1,409 (82.0%) | 42.5 (36.9-48.5) |
| B | 219 | 180 (82.2%) | 37.5 (31.5-42.2) |
| C | 355 | 342 (96.3%) | 40.3 (35.1-45.8) |
| D | 169 | 140 (82.8%) | 39.5 (34.5-44.6) |
| E | 84 | 70 (83.3%) | 43.0 (35.5-49.0) |
| F | 155 | 144 (92.9%) | 39.1 (33.8-44.8) |
| G | 160 | 135 (84.4%) | 39.4 (34.3-46.1) |
| H | 178 | 167 (93.8%) | 37.5 (33.0-42.7) |
| I | 199 | 178 (89.4%) | 38.0 (31.0-43.0) |
| J | 335 | 331 (98.8%) | 48.5 (42.5-53.5) |

Abbreviations: HBV=hepatitis B virus; HIV=human immunodeficiency virus; IQR=interquartile range

**Supplementary Table 2**.Unadjusted incidence rates of specified outcomes among HIV/hepatitis B virus coinfected patients within the North American AIDS Cohort Collaboration on Research and Design (1996 - 2010).

| **Outcome** | **No. Exposed** | **Median**  **Follow-up**  **(Years, IQR)** | **No. Events** | **Person-Years** | **Incidence Rate, Events/1,000**  **Person-Years**  **(95% CI)** |
| --- | --- | --- | --- | --- | --- |
| **Overall (1996-2010)** |  |  |  |  |  |
| Liver complications\* | 3,573 | 3.0 (1.8-5.0) | 111 | 13,790.1 | 8.0 (6.6-9.7) |
| End-stage liver disease | 3,573 | 3.0 (1.8-5.0) | 100 | 13,807.5 | 7.2 (5.9-8.8) |
| Hepatocellular carcinoma | 3,573 | 3.0 (1.8-5.0) | 21 | 13,947.1 | 1.5 (0.9-2.3) |
| **1996-2001** |  |  |  |  |  |
| Liver complications\* | 1,286 | 1.0 (1.0-2.8) | 27 | 2,574.6 | 10.5 (6.9-15.3) |
| End-stage liver disease | 1,286 | 1.0 (1.0-2.8) | 26 | 2,577.7 | 10.1 (6.6-14.8) |
| Hepatocellular carcinoma | 1,286 | 1.0 (1.0-2.9) | 2 | 2,598.7 | 0.8 (0.09-2.8) |
| **2002-2005** |  |  |  |  |  |
| Liver complications\* | 2,208 | 3.0 (2.0-4.0) | 35 | 6,101.2 | 5.7 (4.0-8.0) |
| End-stage liver disease | 2,208 | 3.0 (2.0-4.0) | 31 | 6,102.3 | 5.1 (3.5-7.2) |
| Hepatocellular carcinoma | 2,208 | 3.0 (2.0-4.0) | 5 | 6,129.2 | 0.8 (0.3-1.9) |
| **2006-2010** |  |  |  |  |  |
| Liver complications\* | 2,159 | 2.0 (1.4-3.0) | 49 | 5,114.3 | 9.6 (7.1-12.7) |
| End-stage liver disease | 2,159 | 2.0 (1.4-3.0) | 43 | 5,126.7 | 8.4 (6.1-11.3) |
| Hepatocellular carcinoma | 2,159 | 2.0 (1.5-3.0) | 14 | 5,153.2 | 2.7 (1.5-4.6) |

Abbreviations: CI=confidence interval; IQR=interquartile range

\* Liver complications included either end-stage liver disease or hepatocellular carcinoma.

**Supplementary Table 3.** Factors associated with liver complications, defined by first occurrence of end-stage liver disease or hepatocellular carcinoma, among HIV/hepatitis B virus-coinfected patients within the North American AIDS Cohort Collaboration on Research and Design (1996 - 2010; n=3,573), based on multivariable Cox regression analyses accounting for death as a competing risk.

|  |  |
| --- | --- |
| **Characteristic** | **Adjusted Hazard Ratio of Liver Complications\* (95% Confidence Interval)** |
| **Age** |  |
| <40 years | Ref |
| ≥40 years | 1.44 (0.99-2.09) |
| **Sex** |  |
| Female | Ref |
| Male | 1.83 (0.89-3.76) |
| **Race** |  |
| Black, non-Hispanic | Ref |
| Hispanic | 0.67 (0.28-1.63) |
| Non-black, non-Hispanic | 1.70 (1.13-2.54) |
| **Diabetes mellitus**†‡ |  |
| No | Ref |
| Yes | 2.02 (1.21-3.38) |
| **Hepatitis C virus coinfection**§ |  |
| No | Ref |
| Yes | 1.50 (0.98-2.28) |
| **Current HIV RNA**† |  |
| ≤500 copies/mL | Ref |
| >500copies/mL | 1.09 (0.75-1.59) |
| **Current CD4 cell count**† |  |
| ≥500 cells/mm3 | Ref |
| 200 – 499 cells/mm3 | 2.14 (1.23-3.69) |
| <200 cells/mm3 | 3.53 (2.02-6.17) |
| **History of heavy alcohol use||** |  |
| No | Ref |
| Yes | 1.98 (1.33-2.93) |
| **FIB-4 at start of follow-up**¶ |  |
| < 1.45 | Ref |
| 1.45 – 3.25 | 3.47 (2.07-5.81) |
| > 3.25 | 11.62 (7.13-18.94) |
| **Year of start of follow-up** |  |
| 1996 – 2001 | Ref |
| 2002 – 2005 | 0.82 (0.51-1.33) |
| 2006 – 2010 | 1.36 (0.70-2.65) |

Abbreviations: CI=confidence interval; FIB-4=Fibrosis-4 Index for Liver Fibrosis; HCV=hepatitis C virus; HIV=human immunodeficiency virus; HR=hazard ratio

\* Hazard ratios adjusted for all other risk factors and based on 10 imputations.

† Evaluated as a time-varying covariate.

‡ Diabetes mellitus was defined by: 1) hemoglobin A1c >6.5%, 2) prescription of anti-diabetic medication, or 3) record of a diabetes diagnosis plus the prescription of diabetes-related medication prior to start of follow-up.

§ Hepatitis C virus coinfection defined by detectable HCV RNA or available HCV genotype recorded at any time during observation.

|| History of heavy alcohol use was defined as ever having reported while under observation in the NA-ACCORD: 1) inpatient or outpatient International Classification of Diseases, Ninth Revision (ICD-9) diagnosis of alcohol dependence/abuse; 2) ≥3 drinks/day or ≥7 drinks/week for females; ≥4 drinks/day or ≥14 drinks/week for males on the self-reported Alcohol Use Disorders Identification Test-Consumption questionnaire; or 3) documentation of alcohol intoxication, dependence, or abuse identified during medical record review to confirm ESLD or HCC diagnoses.

¶ FIB-4 is a non-invasive score to estimate the amount of liver fibrosis, calculated by: (age [years] x aspartate aminotransferase [U/L]) / ((platelet count [109/L]) x (alanine aminotransferase [U/L])1/2). FIB-4 was estimated using aspartate aminotransferase, alanine aminotransferase, and platelet count measurements that were recorded as the closest values within 24 months before or after the start of follow-up.

**Supplementary Table 4.** Factors associated with liver complications, defined by first occurrence of end-stage liver disease or hepatocellular carcinoma, among HIV/hepatitis B virus-coinfected patients within the North American AIDS Cohort Collaboration on Research and Design (1996 - 2010), after exclusion of patients with an alanine aminotransferase or aspartate aminotransferase >1,000 U/L within +/-30 days of their qualifying hepatitis B virus laboratory test (n=3,478).

|  |  |
| --- | --- |
| **Characteristic** | **Adjusted Hazard Ratio of Liver Complications\* (95% Confidence Interval)** |
| **Age** |  |
| <40 years | Ref |
| ≥40 years | 0.83 (0.52-1.32) |
| **Sex** |  |
| Female | Ref |
| Male | 1.15 (0.52-2.53) |
| **Race** |  |
| Black, non-Hispanic | Ref |
| Hispanic | 1.01 (0.41-2.50) |
| Non-black, non-Hispanic | 1.96 (1.21-3.16) |
| **Diabetes mellitus**†‡ |  |
| No | Ref |
| Yes | 2.11 (1.18-3.79) |
| **Hepatitis C virus coinfection**§ |  |
| No | Ref |
| Yes | 1.27 (0.80-2.03) |
| **Current HIV RNA**† |  |
| ≤500 copies/mL | Ref |
| >500copies/mL | 0.95 (0.60-1.52) |
| **Current CD4 cell count**† |  |
| ≥500 cells/mm3 | Ref |
| 200 – 499 cells/mm3 | 1.60 (0.89-2.87) |
| <200 cells/mm3 | 2.68 (1.37-5.26) |
| **History of heavy alcohol use||** |  |
| No | Ref |
| Yes | 1.53 (0.99-2.37) |
| **FIB-4 at start of follow-up**¶ |  |
| < 1.45 | Ref |
| 1.45 – 3.25 | 3.85 (2.14-6.92) |
| > 3.25 | 11.21 (6.17-20.40) |
| **Year of start of follow-up** |  |
| 1996 – 2001 | Ref |
| 2002 – 2005 | 0.70 (0.42-1.14) |
| 2006 – 2010 | 1.60 (0.81-3.18) |

Abbreviations: CI=confidence interval; FIB-4=Fibrosis-4 Index for Liver Fibrosis; HCV=hepatitis C virus; HIV=human immunodeficiency virus; HR=hazard ratio

\* Hazard ratios adjusted for all other risk factors and based on 10 imputations.

† Evaluated as a time-varying covariate.

‡ Diabetes mellitus was defined by: 1) hemoglobin A1c >6.5%, 2) prescription of anti-diabetic medication, or 3) record of a diabetes diagnosis plus the prescription of diabetes-related medication prior to start of follow-up.

§ Hepatitis C virus coinfection defined by detectable HCV RNA or available HCV genotype recorded at any time during observation.

|| History of heavy alcohol use was defined as ever having reported while under observation in the NA-ACCORD: 1) inpatient or outpatient International Classification of Diseases, Ninth Revision (ICD-9) diagnosis of alcohol dependence/abuse; 2) ≥3 drinks/day or ≥7 drinks/week for females; ≥4 drinks/day or ≥14 drinks/week for males on the self-reported Alcohol Use Disorders Identification Test-Consumption questionnaire; or 3) documentation of alcohol intoxication, dependence, or abuse identified during medical record review to confirm ESLD or HCC diagnoses.

¶ FIB-4 is a non-invasive score to estimate the amount of liver fibrosis, calculated by: (age [years] x aspartate aminotransferase [U/L]) / ((platelet count [109/L]) x (alanine aminotransferase [U/L])1/2). FIB-4 was estimated using aspartate aminotransferase, alanine aminotransferase, and platelet count measurements that were recorded as the closest values within 24 months before or after the start of follow-up.

**Supplementary Table 5.** Adjusted hazard ratios of liver complications associated with increasing consecutive months of HIV suppression compared with persons with unsuppressed HIV among HIV/hepatitis B virus-coinfected patients who received HBV-active antiretroviral therapy within the North American AIDS Cohort Collaboration on Research and Design (1996 - 2010; n=3,385), based on multivariable Cox regression analyses accounting for death as a competing risk.

| **HIV RNA Suppression** | **Adjusted Hazard Ratio (95% CI) of Liver Complications\*** | |
| --- | --- | --- |
| **Model #1†** | **Model #2‡** |
| Unsuppressed | Ref | Ref |
| <6 months | 1.06 (0.60-1.87) | 1.06 (0.60-1.87) |
| ≥6 months | - | 0.56 (0.35-0.90) |
| 6-11 months | 0.49 (0.21-1.17) | - |
| 12-17 months | 0.37 (0.12-1.14) | - |
| 18-23 months | 0.35 (0.10-1.15) | - |
| ≥24 months | 0.72 (0.40-1.28) | - |

Abbreviations: HIV=human immunodeficiency virus

\* Analyses adjusted for age, sex, race, time-updated diabetes mellitus, hepatitis C virus coinfection, time-updated CD4 cell count, heavy alcohol use, FIB-4 at start of follow-up, and year of start of follow-up.

† test for trend p=0.06

‡ test for trend p=0.02