**SUPPLEMENT**

***Methodology details on the D:A:D replication analysis.***

Person-time and MI events were contributed by individuals from the time of study entry to study exit. Study entry was defined as the latter of, 1) enrollment into the NA-ACCORD, 2) the date of full capture of inpatient and outpatient laboratory and diagnosis data (MI observation start date), 3) ART initiation date or 4) January 1, 1999. Study exit was defined as the earliest date of, 1) incident MI, 2) death, 3) loss to follow-up (defined as one year after last CD4 or HIV RNA measurement) or 4) administrative censoring at the last date of the cohort full MI observation, or December 31, 2013. Participants with a validated MI at or prior to study entry were excluded. A discrete time-to-event approach was used with data summarized to the month level. Pooled logistic regression models were used to estimate crude hazard ratios (HR) and adjusted hazard ratios (aHR) and 95% confidence intervals ([,]). The effect of recent ABC use was adjusted for the same variables as in the D:A:D approach19 with the exception of family history of CVD, previous CVD disease, and BMI, which were not routinely available in the NA-ACCORD.

See Supplemental Figure S1, which depicts the selection of the study population for the D:A:D replication analysis. See Supplemental Table S1 for differences in the NA-ACCORD MSM approach and the D:A:D approach.

**Figure S1:** Selection of the two study populations from the NA-ACCORD: 1) the study population for the main analysisa, and 2) the study population for the replication of the D:A:D analysis

NA-ACCORD participants observed for myocardial infarctions

N=29,516 adults

(including n=605 MIs)

**D:A:D replication study population**

N=24,446 adults and 118,307 person-years

(including n=515 MIs)

n=809 adults not observed from 1 Jan 1999 to 31 Dec 2013

n=4,261 adults who were not observed to use ART

**Main analysis study population   
(for the marginal structural model approach)**

N=8,265 adults and 29,077 person-years

(including n=123 MIs)

n=148 adults not observed from 1 Jan 2001 to 31 Dec 2013

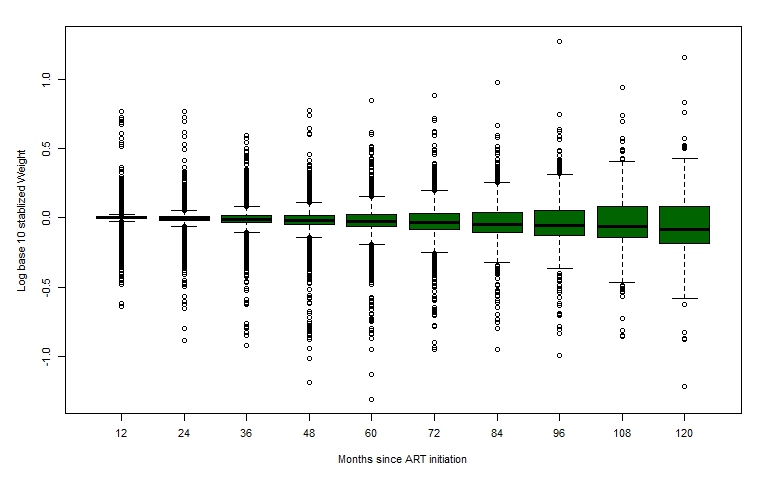
n=16,033 adults who were not observed to initiate ART

aThe “Main analysis study population” includes only those NA-ACCORD participants who were observed to initiate ART and were under observation for MI outcomes from 1 Jan 2001 to 31 Dec 2013. It is within this study population that marginal structural models were used to account for potential channeling bias and time-dependent confounding of the abacavir and MI relationship.

**Table S1:** Differences in the NA-ACCORD marginal structural model and D:A:D approach

|  |  |  |
| --- | --- | --- |
| **Characteristic** | **NA-ACCORD approach using marginal structural models** | **D:A:D approach (D:A:D, JID, 2010)** |
| Outcome (myocardial infarction [MI]) | Incident cases of MI were validated using an approach modeled off of MESA that included the Universal definition of myocardial infarction and experts in the field (Crane, AJE, 2014). Reviewers were blinded to ART use. | All incident cases of MI are reported to the study coordinating office for validation and coding using the WHO MONICA criteria. Reviewers are blinded to ART use. |
| Those with MI prior to study entry (i.e. prevalent MI cases) were excluded. | Those with previous MIs were included. This was accounted for via a variable of personal history of CVD (including MI). |
| Exposure (abacavir use in the last 6 months [ABC]) | Restricted to treatment-naïve individuals observed to initiate ART. Those that discontinue ABC are removed after 6 months with appropriate weights. | Individuals could have been ABC experienced at study entry. ABC use prior to study entry was accounted for using cumulative ABC exposure variable. |
| Study populations | Table 1: Differences in cardiovascular and HIV risk profiles comparing ABC users (characteristics measured at ABC initiation) to those who do not (characteristics measured at ART initiation) | Table 2 of DAD 2010: No differences in cardiovascular risk profiles of those exposed to ABC compared to those exposed to TDF. |
| Study period | January 2001 - December 2013 | December 1999 - February 2008 |
| Comparison group | Restricted to ART initiators | HIV treatment naïve individuals were included. |
| Confounders | Variables included in the weights for ABC initiation, ABC discontinuation, and censoring: Age, sex, race and ethnicity, HIV transmission risk, calendar year of ART initiation, cigarette smoking, hepatitis C infection, hypertension, diabetes mellitus, renal function, high LDL, TC: HDL ratio, high triglycerides, statin use, CD4 count, HIV viral load, history of clinical AIDS diagnosis, and initial HIV treatment regimen class.  Confounders included in the MSM model:  Age, sex, race and ethnicity, HIV transmission risk, calendar year of ART initiation), cigarette smoking, hepatitis C infection, hypertension, diabetes mellitus, renal function, high LDL, TC:HDL ratio, high triglycerides, statin use, CD4 count, HIV viral load, history of clinical AIDS and diagnosis. Note: only age was time-varying, all other variables were time-fixed at study entry (i.e. ART initiation). | Age, sex, HIV transmission group, ethnicity, cohort were time-fixed confounders. Calendar year, family history of CVD, previous CVD disease including MI, smoking status, BMI, cumulative ABC exposure, recent didanosine exposure, cumulative indinavir exposure, and cumulative lopinavir/ritonavir exposure were time-varying confounders. |
| Mediators | None. Covariates in the MSM model were time-fixed at ART initiation | Latest total cholesterol, HDL cholesterol, triglycerides, glucose level, systolic and/or diastolic blood pressure measurements, presence of lipohypertophy and/or lipoatrophy and diabetes mellitus. |
| Estimates | Hazard ratios using a discrete time-to-event approach with pooled logistic regression models | Incidence rate ratios using Poisson regression |
|  |  |  |

**Figure S2:** The stabilized weights for ABC initiation, censoring, and ABC discontinuation included in the marginal structural model



|  |  |  |
| --- | --- | --- |
|  | **Distribution of the stabilized weights before truncation** | **Distribution of the stabilized weights after truncation** |
| Mean | 1.008 | 0.998 |
| Median | 0.991 | 0.992 |
| 1st percentile | 0.422 | 0.422 |
| 99th percentile | 2.017 | 2.016 |

**Figure S3:** Trends in abacavir use in the NA-ACCORD

Abacavir use was defined as ≥1 month of abacavir prescription.

**Table S2:** Estimated crude (HR) and adjusted hazard ratios (aHR) and 95% confidence intervals (95% CI) from marginal structural models for the risk of myocardial infarction (MI), adjusted for Framingham Risk Score at ART initiation, N=8,265 and n=123 MIs (p-value for the interaction of ABC and Framingham Risk Group = 0.14; the *italic* point estimate is plotted in Figure 3)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **HR** | **95% CI** | | | **aHR** | **95% CI** | | |
| Prescription of ABC in the last 6 months |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- |  | 1.00 |  | -- |  |
| Yes | **2.48** | **1.66** | **,** | **3.71** | ***1.88*** | ***1.20*** | ***,*** | ***2.95*** |
| Framingham Risk Group |  |  |  |  |  |  |  |  |
| low (men <=9, women <=17) | 1.00 |  | -- |  | 1.00 |  | -- |  |
| Intermediate/high (men >9, women>17) | **2.87** | **1.66** | **,** | **3.71** | **2.23** | **1.50** | **,** | **3.32** |
| Missing | 1.27 | 0.65 | , | 2.47 | **1.39** | **0.72** | **,** | **2.70** |
| Age (years) |  |  |  |  |  |  |  |  |
| <40 | **0.18** | **0.11** | **,** | **0.30** |  |  |  |  |
| 40-49 | **0.47** | **0.31** | **,** | **0.71** |  |  |  |  |
| 50-59 | 1.00 |  | -- |  | Not included (in Framingham Risk Score) | | | |
| ≥60 | 1.69 | 0.89 | , | 3.21 |  |  |  |  |
| Sex |  |  |  |  |  |  |  |  |
| Male | 1.00 |  | -- | |  |  |  |  |
| Female | 1.12 | 0.73 | , | 1.70 | Not included (in Framingham Risk Score) | | | |
| Race and ethnicity |  |  |  |  |  |  |  |  |
| White | 1.00 |  | -- | | 1.00 |  | -- |  |
| Black | 1.39 | 0.91 | , | 2.10 | 1.19 | 0.80 | , | 1.78 |
| Hispanic | 0.59 | 0.28 | , | 1.26 | 0.65 | 0.31 | , | 1.38 |
| Other/unknown | 0.96 | 0.44 | , | 2.13 | 1.01 | 0.45 | , | 2.26 |
| HIV transmission risk |  |  |  |  |  |  |  |  |
| MSM | 1.00 |  | -- | | 1.00 |  | -- |  |
| IDU | **1.79** | **1.05** | **,** | **3.05** | 1.15 | 0.60 | , | 2.24 |
| Heterosexual | 1.02 | 0.65 | , | 1.59 | 0.89 | 0.55 | , | 1.42 |
| Other | 1.84 | 0.98 | , | 3.47 | 1.61 | 0.82 | , | 3.16 |
| Year of ART initiation | |  |  |  |  |  |  |  |
| 2001-2004 | **1.63** | **1.03** | **,** | **2.58** | 1.35 | 0.81 | , | 2.24 |
| 2005-2007 | 1.00 |  | -- | | 1.00 |  | -- |  |
| 2008-2013 | 1.20 | 0.72 | , | 2.01 | 1.33 | 0.82 | , | 2.18 |
| Cigarette smoking |  |  |  |  |  |  |  |  |
| Never | 1.00 |  | -- | |  |  |  |  |
| Ever | **1.78** | **1.09** | **,** | **2.90** | Not included (in Framingham Risk Score) | | | |
| Hepatitis C infection |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- |  |
| Yes | **1.76** | **1.17** | **,** | **2.65** | 1.29 | 0.76 | , | 2.20 |
| Hypertension |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | |  |  |  |  |
| Yes | **4.23** | **2.95** | **,** | **6.06** | Not included (in Framingham Risk Score) | | | |
| Diabetes mellitus |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- |  |
| Yes | **3.82** | **2.31** | **,** | **6.31** | **2.26** | **1.23** | **,** | **4.41** |
| Renal function |  |  |  |  |  |  |  |  |
| eGFR ≥60 | 1.00 |  | -- | | 1.00 |  | -- |  |
| eGFR <60 | **5.92** | **3.49** | **,** | **10.07** | **2.92** | **1.57** | **,** | **5.44** |
| High LDL |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- |  |
| Yes | 1.16 | 0.68 | , | 1.96 | 0.98 | 0.62 | , | 1.54 |
| TC:HDL ratio |  |  |  |  |  |  |  |  |
| <5.0 | 1.00 |  | -- | |  |  |  |  |
| ≥5.0 | **1.58** | **1.11** | **,** | **2.24** | Not included (in Framingham Risk Score) | | | |
| High triglycerides |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- |  |
| Yes | 1.34 | 0.88 | , | 2.05 | 0.98 | 0.62 | , | 1.54 |
| Statin use |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- |  |
| Yes | **3.27** | **1.97** | **,** | **5.43** | **1.96** | **1.01** | **,** | **3.78** |
| CD4 count (cells/mm3) |  |  |  |  |  |  |  |  |
| ≥350 | 1.00 |  | -- | | 1.00 |  | -- |  |
| 200-349 | 0.96 | 0.55 | , | 1.67 | 1.02 | 0.58 | , | 1.81 |
| <200 | **1.97** | **1.22** | **,** | **3.19** | 1.66 | 0.99 | , | 2.79 |
| HIV viral load (copies/mL) |  |  |  |  |  |  |  |  |
| ≤400 | 0.99 | 052 | , | 1.90 | 0.86 | 0.44 | , | 1.68 |
| >400 | 1.00 |  | -- | | 1.00 |  | -- |  |
| History of clinical AIDS diagnosis |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- |  |
| Yes | **2.41** | **1.67** | **,** | **3.46** | **1.60** | **1.07** | **,** | **2.39** |

Footnotes:

The model was adjusted for all the covariates seen here and cohort (time fixed).

Prescription of abacavir in the last 6 months is time-varying.,

Framingham risk score was measured at ART initiation (time-fixed).

Age was a time-varying variable.

Sex, race/ethnicity, and HIV transmission risk group were measured at enrollment into the NA-ACCORD.

Year of ART initiation was a time-fixed variable.

Cigarette smoking status was determined as ever having medical record information or substance survey information that denoted cigarette smoking.

Hepatitis C infection was defined as 1) a positive antibody test, or 2) a detectable HCV RNA, or 3) the presence of a genotype result. If an individual ever met this definition, they were considered HCV infected at all times under observation (a time-fixed variable).

Treated hypertension was defined as 1) a hypertension diagnosis, and 2) prescription for an antihypertensive medication. Treated hypertension was measured as close to study entry as possible, within the window of prior to study entry through 9 months after study entry and was time-fixed.

Diabetes was defined as 1) a diabetes diagnosis and prescription for diabetes-related medications, or 2) prescription for a diabetes-specific medication, or 3) hemoglobin A1C ≥6.5%. Diabetes was measured as close to study entry as possible, within the window of prior to study entry through 9 months after study entry and was time-fixed.

Renal function was estimated as estimated glomerular filtration rate (eGFR) calculated using the CKD-EPI study equation. Renal function was measured as close to study entry as possible, within the window of prior to study entry through 9 months after study entry and was time-fixed.

High low-density lipoprotein (LDL) was defined as LDL ≥130 mg/dL. If there was an LDL measurement ≥130 mg/dL within the window of prior to study entry through 9 months after study entry, then the individual was classified as having high LDL for the entire time they were under observation; otherwise they were classified as having LDL <130 mg/dL.

High triglycerides was defined as triglycerides ≥300 mg/dL. If there was a triglyceride measure >=300 mg/dl within the window of prior to study entry through 9 months after study entry, then the individual was classified as having high triglycerides for the entire time they were under observation; otherwise they were classified as having triglycerides <300 mg/dL.

Statin use included prescription of cerivastatin, fluvastatin, lovastatin, prvastatin, rosuvastatin, simvastatin, pravastatin & aspirin, atorvastatin & amlodipine, ezetimibe & simvastatin, pitavastatin, lovastatin & niacin. Statin prescription was measured within the window of prior to study entry through 9 months after study entry.

CD4 count and HIV RNA were measured at measured as close to study entry as possible, within the window of 9 months prior to study entry through 3 months after study entry.

History of clinical AIDS diagnosis was defined as those who had a first clinical AIDS diagnosis at, or prior to, study entry.

**Table S3:** Estimated crude (HR) and adjusted hazard ratios (aHR) and 95% confidence intervals (95% CI) for the risk of myocardial infarction (MI) after ART initiation (the “naïve analysis”), N=8,265 and n=123 MIs (the *italic* point estimate is plotted in Figure 3)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **HR** | **95% CI** | | | **aHR** | **95% CI** | | |
| Prescription of ABC in the last 6 months | |  |  |  |  |  |  |  |
| No | 1.00 |  | -- |  | 1.00 |  | -- |  |
| Yes | **2.54** | **1.79** |  | **3.90** | **1.76** | **1.15** | **,** | **2.68** |
| Age (years) |  |  |  |  |  |  |  |  |
| <40 | 0.19 | 0.12 |  | 0.32 | **0.33** | **0.19** | **,** | **0.59** |
| 40-49 | 0.48 | 0.32 |  | 0.73 | **0.60** | **0.39** | **,** | **0.92** |
| 50-59 | 1.00 |  | -- |  | 1.00 |  | -- |  |
| ≥60 | 1.69 | 0.89 |  | 3.21 | 1.17 | 0.57 | , | 2.38 |
| Sex |  |  |  |  |  |  |  |  |
| Male | 1.00 |  | -- | | 1.00 |  | -- | |
| Female | 1.16 | 0.77 |  | 1.75 | 1.27 | 0.77 | , | 2.09 |
| Race and ethnicity |  |  |  |  |  |  |  |  |
| White | 1.00 |  | -- | | 1.00 |  | -- | |
| Black | 1.37 | 0.94 |  | 2.00 | 1.08 | 0.71 | , | 1.63 |
| Hispanic | 0.59 | 0.28 |  | 1.25 | 0.81 | 0.38 | , | 1.73 |
| Other/unknown | 0.94 | 0.43 |  | 2.08 | 1.01 | 0.45 | , | 2.27 |
| HIV transmission risk |  |  |  |  |  |  |  |  |
| MSM | 1.00 |  | -- | | 1.00 |  | -- | |
| IDU | **1.78** | **1.08** |  | **2.95** | 0.80 | 0.40 | , | 1.59 |
| Heterosexual | 1.07 | 0.70 |  | 1.64 | 0.63 | 0.37 | , | 1.07 |
| Other | **2.05** | **1.12** |  | **3.75** | 1.39 | 0.70 | , | 2.75 |
| Calendar Year of HAART initiation (at entry into this study) | | | |  |  |  |  |  |
| 2001-2004 | **1.65** | **1.04** |  | **2.60** | **1.65** | **1.02** | **,** | **2.67** |
| 2005-2007 | 1.00 |  | -- | | 1.00 |  | -- | |
| 2008-2013 | 1.19 | 0.74 |  | 1.91 | 1.37 | 0.85 | , | 2.21 |
| Cigarette smoking |  |  |  |  |  |  |  |  |
| Never | 1.00 |  | -- | | 1.00 |  | -- | |
| Ever | **1.72** | **1.07** |  | **2.78** | 1.44 | 0.87 | , | 2.39 |
| Hepatitis C infection |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- | |
| Yes | **1.70** | **1.15** |  | **2.52** | 1.13 | 0.67 | , | 1.89 |
| Hypertension |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- | |
| Yes | **4.17** | **2.93** |  | **5.94** | **2.34** | **1.54** | **,** | **3.56** |
| Diabetes mellitus |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- | |
| Yes | **3.80** | **2.30** |  | **6.26** | 1.54 | 0.87 | , | 2.75 |
| Renal impairment |  |  |  |  |  |  |  |  |
| eGFR ≥60 | 1.00 |  | -- | | 1.00 |  | -- | |
| eGFR <60 | **6.02** | **3.56** |  | **10.20** | 1.73 | 0.93 | , | 3.20 |
| High LDL |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- | |
| Yes | **1.17** | **0.69** |  | **1.99** | 0.83 | 0.47 | , | 1.46 |
| TC:HDL ratio |  |  |  |  |  |  |  |  |
| <5.0 | 1.00 |  | -- | | 1.00 |  | -- | |
| ≥5.0 | 1.41 | 0.95 |  | 2.08 | 1.18 | 0.74 | , | 1.88 |
| High triglycerides |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- | |
| Yes | 1.37 | 0.89 |  | 2.10 | 0.93 | 0.57 | , | 1.51 |
| Statin use |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- | |
| Yes | 3.15 | 1.91 |  | 5.20 | 1.62 | 0.88 | , | 2.97 |
| CD4 count (cells/mm3) |  |  |  |  |  |  |  |  |
| ≥350 | 1.00 |  | -- | | 1.00 |  | -- | |
| 200-349 | 0.97 | 0.56 |  | 1.69 | 1.00 | 0.56 | , | 1.76 |
| <200 | **1.96** | **1.21** |  | **3.17** | 1.67 | 0.99 | , | 2.79 |
| HIV viral load (copies/mL) |  |  |  |  |  |  |  |  |
| ≤400 | 1.01 | 0.53 |  | 1.93 | 0.90 | 0.46 | , | 1.77 |
| >400 | 1.00 |  | -- | | 1.00 |  | -- | |
| History of clinical AIDS diagnosis |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- | | 1.00 |  | -- | |
| Yes | **2.33** | **1.62** |  | **3.33** | **1.67** | **1.13** | **,** | **2.45** |

Footnotes:

The model was adjusted for all the covariates seen here and cohort (time fixed).

Prescription of abacavir in the last 6 months is time-varying,

Age was a time-varying variable.

Sex, race/ethnicity, and HIV transmission risk group were measured at enrollment into the NA-ACCORD.

Year of ART initiation was a time-fixed variable.

Cigarette smoking status was determined as ever having medical record information or substance survey information that denoted cigarette smoking.

Hepatitis C infection was defined as 1) a positive antibody test, or 2) a detectable HCV RNA, or 3) the presence of a genotype result. If an individual ever met this definition, they were considered HCV infected at all times under observation (a time-fixed variable).

Treated hypertension was defined as 1) a hypertension diagnosis, and 2) prescription for an antihypertensive medication. Treated hypertension was measured as close to study entry as possible, within the window of prior to study entry through 9 months after study entry and was time-fixed.

Diabetes was defined as 1) a diabetes diagnosis and prescription for diabetes-related medications, or 2) prescription for a diabetes-specific medication, or 3) hemoglobin A1C ≥6.5%. Diabetes was measured as close to study entry as possible, within the window of prior to study entry through 9 months after study entry and was time-fixed.

Renal function was estimated as estimated glomerular filtration rate (eGFR) calculated using the CKD-EPI study equation. Renal function was measured as close to study entry as possible, within the window of prior to study entry through 9 months after study entry and was time-fixed.

High low-density lipoprotein (LDL) was defined as LDL ≥130 mg/dL. If there was an LDL measurement ≥130 mg/dL within the window of prior to study entry through 9 months after study entry, then the individual was classified as having high LDL for the entire time they were under observation; otherwise they were classified as having LDL <130 mg/dL.

High triglycerides was defined as triglycerides ≥300 mg/dL. If there was a triglyceride measure >=300 mg/dl within the window of prior to study entry through 9 months after study entry, then the individual was classified as having high triglycerides for the entire time they were under observation; otherwise they were classified as having triglycerides <300 mg/dL.

Statin use included prescription of cerivastatin, fluvastatin, lovastatin, prvastatin, rosuvastatin, simvastatin, pravastatin & aspirin, atorvastatin & amlodipine, ezetimibe & simvastatin, pitavastatin, lovastatin & niacin. Statin prescription was measured within the window of prior to study entry through 9 months after study entry.

CD4 count and HIV RNA were measured at measured as close to study entry as possible, within the window of 9 months prior to study entry through 3 months after study entry.

History of clinical AIDS diagnosis was defined as those who had a first clinical AIDS diagnosis at, or prior to, study entry.

**Table S4:** Estimated crude (HR) and adjusted hazard ratios (aHR) and 95% confidence intervals (95% CI) from marginal structural models for the risk of myocardial infarction (MI) after ART initiation, Estimated crude (HR) and adjusted hazard ratios (aHR) and 95% confidence intervals (95% CI) for the risk of myocardial infarction (MI), replicating the D:A:D approach (see D:A:D, JID, 2010), N=24,446 and n=515 MIs (the *italic* point estimate is plotted in Figure 3)

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **HR** | **95% CI** | | | **aHR** | **95% CI** | | |
| Prescription of ABC in the last 6 months |  |  |  |  |  |  |  |  |
| No | 1.00 |  | -- |  | 1.00 |  | -- |  |
| Yes | **2.05** | **1.69** |  | **2.49** | ***1.63*** | ***1.21*** |  | ***2.18*** |
| Cumulative exposure to ABC |  |  |  |  |  |  |  |  |
| risk per year | 0.88 | 0.84 |  | 0.92 | 1.03 | 0.96 |  | 1.10 |
| Age (years) |  |  |  |  |  |  |  |  |
| <40 | 1.00 |  | -- |  | 1.00 |  | -- |  |
| 40-49 | **2.47** | **1.95** |  | **3.12** | **2.18** | **1.71** |  | **2.77** |
| 50-59 | **4.59** | **3.56** |  | **5.90** | **4.02** | **3.11** |  | **5.20** |
| 60-69 | **5.95** | **4.03** |  | **8.78** | **5.26** | **3.54** |  | **7.82** |
| Sex |  |  |  |  |  |  |  |  |
| Male | 1.00 |  | -- |  | 1.00 |  | -- |  |
| Female | 0.82 | 0.65 |  | 1.02 | 0.92 | 0.71 |  | 1.20 |
| Race and ethnicity |  |  |  |  |  |  |  |  |
| White | 1.00 |  | -- |  | 1.00 |  | -- |  |
| Black | **1.26** | **1.04** |  | **1.54** | **1.38** | **1.13** |  | **1.69** |
| Hispanic | 0.48 | 0.31 |  | 0.75 | 0.67 | 0.43 |  | 1.06 |
| Other/unknown | 0.61 | 0.36 |  | 1.04 | 0.79 | 0.46 |  | 1.33 |
| HIV transmission risk |  |  |  |  |  |  |  |  |
| MSM | 1.00 |  | -- |  | 1.00 |  | -- |  |
| IDU | **1.69** | **1.33** |  | **2.16** | 1.27 | 0.98 |  | 1.65 |
| Heterosexual | 0.89 | 0.72 |  | 1.11 | 0.86 | 0.66 |  | 1.12 |
| Other | 1.11 | 0.77 |  | 1.61 | 1.03 | 0.71 |  | 1.51 |
| Cigarette smoking |  |  |  |  |  |  |  |  |
| Never | 1.00 |  | -- |  | 1.00 |  | -- |  |
| Ever | **1.52** | **1.20** |  | **1.92** | **1.34** | **1.05** |  | **1.71** |
| Years since ART initiation |  |  |  |  |  |  |  |  |
| risk per year | **0.94** | **0.91** |  | **0.96** | **1.03** | **1.01** |  | **1.06** |

Footnotes:

The model was adjusted for all the covariates seen here and calendar year (time varying) and cohort (time fixed). Unlike the D:A:D approach, measures of family history of CVD, previous CVD disease, and BMI were not available or included in the model.

Prescription of abacavir in the last 6 months was time-varying,

Cumulative exposure to ABC was a time-varying continuous variable defined as the number of moths prescribed ABC divided by 12 to allow us to estimate the risk per year.

Sex, race/ethnicity, and HIV transmission risk group, were time-fixed variables, measured at enrollment into the NA-ACCORD.

Cigarette smoking was a time-fixed variable.