ASSOCIATIONS BETWEEN ANTIRETROVIRAL THERAPY AND CARDIOVASCULAR EVENTS IN PEOPLE WITH TREATED HIV

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BACKGROUND

- Several antiretroviral therapy (ART) agents are associated with increased risk of cardiovascular disease, but less is known about the safety of contemporary ART.
- We sought to compare the risk of major adverse cardiac events (MACE) between different ART regimens.

METHODS

- We used the Merative™ MarketScan® Commercial (2008-2020) and Multistate Medicaid (2011-2020) databases to identify adults between 18-64 years of age who newly initiated a stable ART regimen.
- Nucleoside reverse transcriptase inhibitor (NNRTI)-based regimens were compared to protease inhibitors (PI) and integrase inhibitors (INSTI) at class-level as well as to individual INSTI drugs.
- We used propensity score-weighted Kaplan-Meier functions to estimate the 6, 12, 18, 24, 36, and 48-months risks and risk differences (RD) for MACE. NNRTI-based regimens served as the reference group.
- Baseline covariates including age, sex, type of insurance, cardiovascular medications, and comorbidities were identified using all available claims.

Table 1. Selected Baseline Characteristics of Participants by Initial Antiretroviral Therapy Class.

Characteristic n=37,935	NNRTI-based regimens n=14,692 (39%)	PI-based regimens n=6,136 (16%)	INSTI-based regimens n=17,107 (45%)
Age in years (median, IQR)	41 (32, 49)	42 (33, 49)	38 (28, 49)
Male	11,852 (80.7)	4,144 (67.5)	13,347 (78.0)
Medicaid insured	2,419 (16.5)	1,962 (32.0)	5,592 (32.7)
Hypertension	2,034 (13.8)	916 (14.9)	2,980 (17.4)
Diabetes	783 (5.3)	373 (6.1)	1,194 (7.0)
Obesity	705 (4.8)	376 (6.1)	1,954 (11.4)
Chronic Kidney Disease	94 (0.6)	109 (1.8)	279 (1.6)
Tobacco use	570 (3.9)	329 (5.4)	2,738 (16.0)
Lipid lowering therapy	1,740 (11.8)	703 (11.5)	2,758 (16.1)
Drug use	750 (5.1)	605 (9.9)	1,944 (11.4)
Hepatitis B infection	23 (0.2)	21 (0.3)	280 (1.6)
Hepatitis C infection	65 (0.4)	44 (0.7)	576 (3.4)
Depression	826 (5.6)	488 (8.0)	1,965 (11.5)

Protease- and integrase inhibitor-based regimens are associated with higher risk of cardiac events compared to non-nucleoside reverse transcriptase inhibitors-based regimens after antiretroviral initiation

RESULTS

- The proportion of INSTI-based ART initiation increased dramatically from 2008(5%) to 2020(97%) (**Figure 1**).
- MACE occurred in 418 individuals (1.1%) over the study period [INSTI, n=199 (1.2%); PI, n=87 (1.4%); NNRTI, n=132 (0.9%)]. The highest risk of MACE occurred with PI-based regimens followed by INSTI- and NNRTI-based regimens (**Figure 2**).
- Compared to NNRTI initiators, the risk of MACE was higher at 12 months [RD 0.50, 95% CI (0.14, 0.99)], 18 months [RD 0.53, 95% CI (0.11, 1.06)] and 24 months [RD 0.62, 95% CI (0.04, 1.29)] for the PI-group, and at 12 months [RD 0.20, 95% CI (0.03, 0.37)] and 18 months [RD 0.31, 95% CI (0.06, 0.54)] for INSTI initiators. The precision of estimates was limited in later months of follow-up. The risk of MACE did not differ by individual INSTIs (**Figure 3**).
- Secondary analysis accounting for tenofovir disoproxil fumarate, tenofovir alafenamide or abacavir use were performed and no significant differences were observed in the risk of MACE.

Figure 2. Propensity score-weighted cumulative risk and risk difference estimates of MACE by major ART classes.

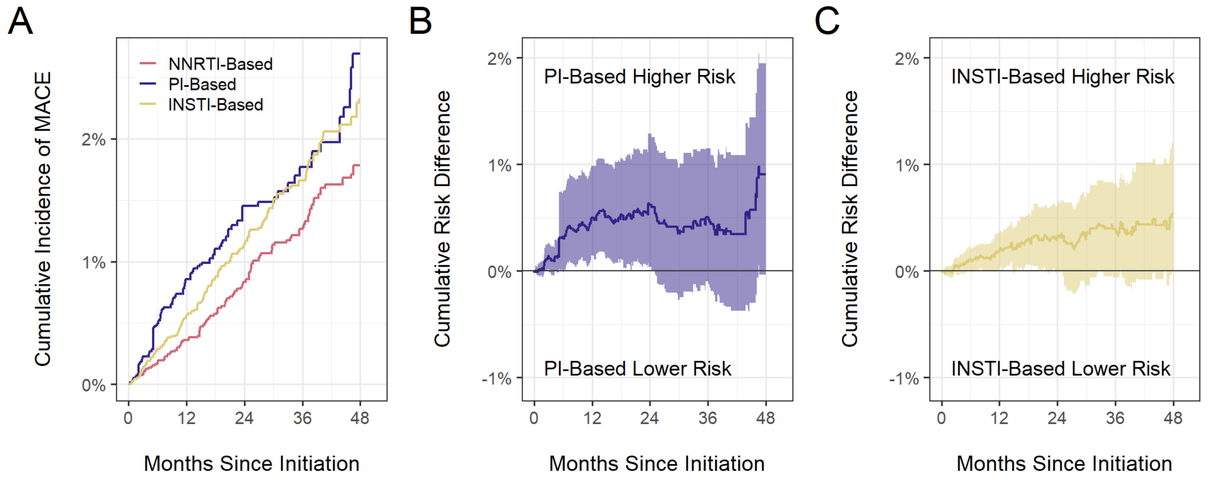


Figure 1. Proportion of new ART users initiated on INSTIs between 2008 and 2020

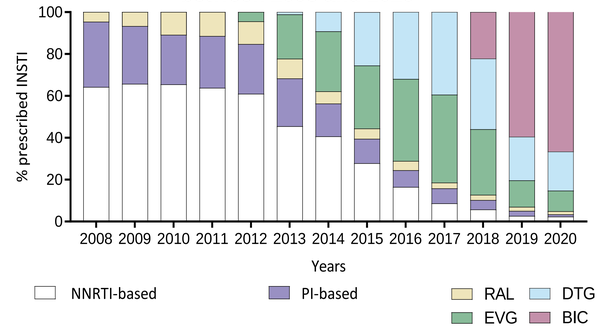
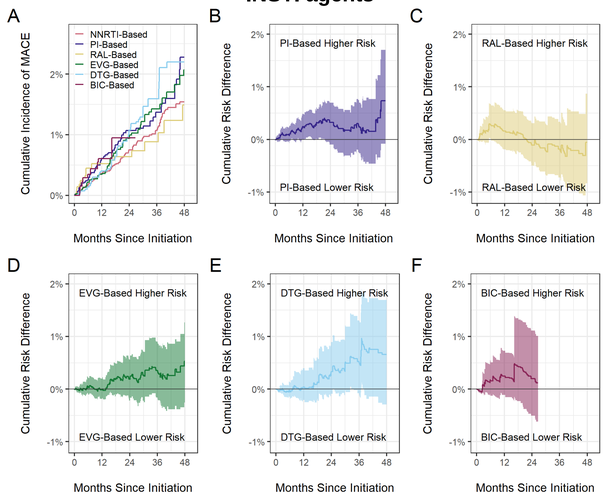


Figure 3. Propensity score-weighted cumulative risk and risk difference estimates of MACE by ART classes and individual INSTI agents



CONCLUSIONS

- In this active comparator, new-user study among people with HIV using U.S. claims databases, PI- and INSTI-based regimens were associated with higher risk of MACE compared to NNRTI-based regimens after ART initiation.
- We did not observe a difference in risk of MACE between INSTI and PI initiators. The risk was also similar by individual INSTI drugs, tenofovir, or abacavir use.

CONTACT INFORMATION

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