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Risk of obesity, diabetes, hypertension, and MACE following a switch to an integrase inhibitor: a target trial emulation in REPRIEVE

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Background

Integrase strand transfer inhibitors (INSTIs) are highly effective anti-retroviral therapies and are linked to weight gain, but data on their effects on cardiovascular disease events (like heart attack and stroke) are limited.

Goals of the Study

We aimed to estimate the risk of obesity, diabetes, hypertension, heart attack, and stroke after switching to an INSTI among people with HIV (PWH) at low-to-moderate cardiovascular risk

REPRIEVE enrolled PWH between ages 40-75 with low-to-moderate traditional heart disease risk, randomized these participants to a cholesterol-lowering medication called pitavastatin or to placebo (a pill that contains no medication). Participants were followed for, on average 5 years, for heart disease events like a heart attack or stroke. Main findings from REPRIEVE were that [statin therapy reduced heart disease events among PWH by 36%](#), prompting guideline changes recommending statin use in PWH.

➤ The participants:

- 5114 REPRIEVE Participants on stable non-INSTI-containing ART regimen for atleast 6 months, with no previous INSTI exposure and no history of the events of interest
 - Low-to-moderate traditional heart disease risk
 - Emulated, or simulated trials were conducted

The Findings:

- There was a higher risk of obesity, diabetes, and hypertension among people who switched to an INSTI compared to non-switchers. We did not observe an effect on the risk of heart disease or stroke.
- Risk estimates were higher among females compared to males.
- Results persisted after taking into account the effects of other antiretroviral therapy regimens that REPRIEVE participants may take: tenofovir alafenamide, tenofovir disoproxil fumarate, prior efavirenz use, and change in BMI

In Summary: The increase in risk profile of obesity,, diabetes, and hypertension suggests long-term observation of PWH switching to INSTIs will be critical to ensure appropriate management of co-morbidities and to assess for future risk of heart disease and stroke.