HIV pre-exposure prophylaxis study finds TAF has higher risk of hypertension than TDF

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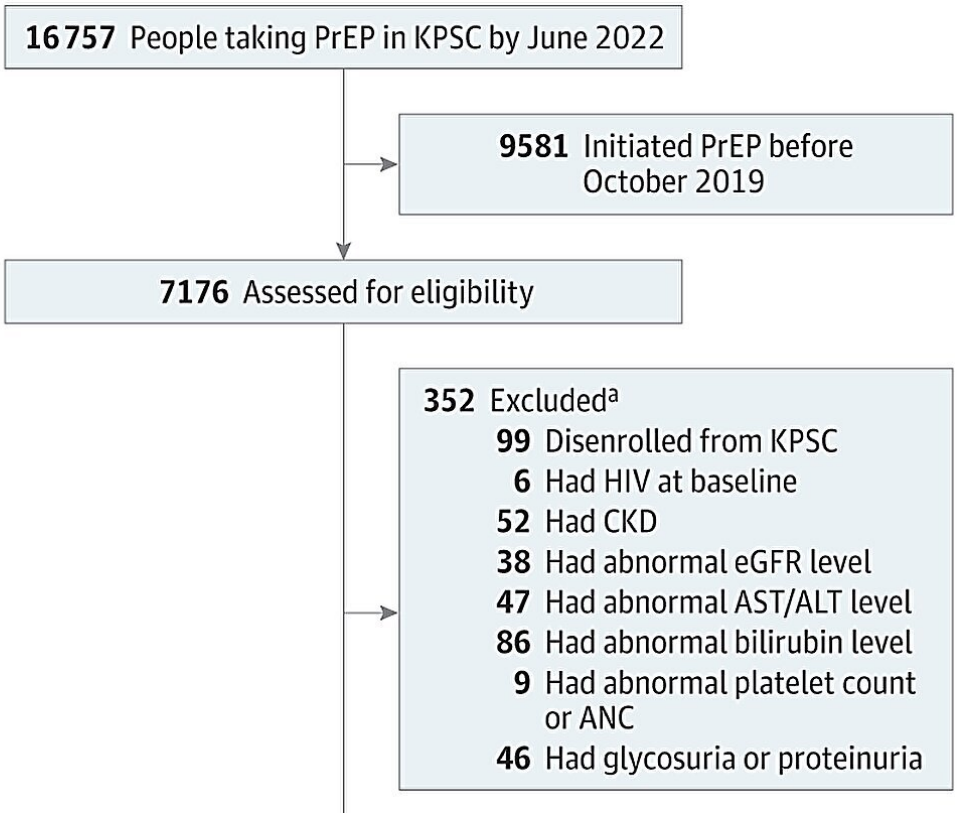

Identification of Eligible Pre-Exposure Prophylaxis (PrEP) Users, Kaiser Permanente Southern California (KPSC), October 2019-June 2022. ANC indicates absolute neutrophil count; AST/ALT, aspartate transaminase/alanine transaminase; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; TAF, emtricitabine/tenofovir disoproxil fumarate; TDF, emtricitabine/tenofovir disoproxil fumarate. Credit: *JAMA Network Open*

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Researchers at Kaiser Permanente Southern California, Pasadena, have found that in patients taking pre-exposure prophylaxis (PrEP), tenofovir alafenamide fumarate (TAF) use associated with higher incidents of hypertension and statin initiation compared with the alternative formulation tenofovir disoproxil fumarate (TDF), especially in those 40 years or older.

In a paper, "Use of Tenofovir Alafenamide Fumarate for HIV Pre-Exposure Prophylaxis and Incidence of Hypertension and Initiation of Statins," published in *JAMA Network Open*, the researchers detail a retrospective cohort analysis conducted using electronic health records from Kaiser Permanente Southern California database.

There is no cure for HIV, but the pathology can be held in check by controlling viral replication through a combination of drugs. Tenofovir is a nucleotide reverse transcriptase inhibitor with a prominent role in antiretroviral therapy drug combinations in part due to its superior performance and reduced side effects compared to earlier drug agents.

TDF and TAF are critical tools in antiviral HIV regimens as they are both effective and well-tolerated and are generally considered safe, though they each have a list of potential side effects.

TDF was the first version of tenofovir to market in 2001 and had an immediate impact. Not only was it more effective as a treatment, but because it greatly decreased ill effects over previous treatment agents, there was increased adherence by patients taking the treatment.

TAF is a more recent formulation of tenofovir, which reaches higher

intracellular levels of tenofovir at lower plasma levels, requiring just 10% of the active drug compared to TDF. The lower active drug ratio may be why it has a more favorable safety profile.

The study used propensity score matching and statistical techniques to assess the risk of cardiometabolic outcomes associated with TAF compared to TDF use. A total of 6824 eligible individuals were included in the study, primarily males with a mean age of 33.9 years. Those starting PrEP with TAF were older and more likely to be non-Hispanic White than those starting with TDF.

While not directly related to the current study, it is interesting that within the findings of a health care network's data, a disparity can be seen in the demographic of who receives which drug.

TAF is the newer, more expensive formulation, considered more effective with less potential side effects. Despite this, the researchers found that TAF use was associated with an elevated risk of incident hypertension (OR 1.64) and statin initiation (OR 2.33) compared to TDF use.

A study subgroup analysis for individuals 40 and older showed even more significant risk differences in statin initiation. Sensitivity analysis using a lower cutoff for hypertension also showed TAF use associated with a higher risk.

The authors conclude that "...TAF has been a welcome addition to the products for PrEP due to its benefits on kidney and bone health and smaller pill size. However, it may have an unwanted impact on cardiometabolic health."

More information: Adovich S. Rivera et al, Use of Tenofovir Alafenamide Fumarate for HIV Pre-Exposure Prophylaxis and

Incidence of Hypertension and Initiation of Statins, *JAMA Network Open* (2023). DOI: 10.1001/jamanetworkopen.2023.32968