Use of tenofovir disoproxil fumarate shows weight loss vs placebo: a meta-analysis of 7 clinical trials in 19,359 HIV-negative individuals

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Introduction

Recent clinical trials have shown weight gain associated with newer antiretrovirals, in particular integrase inhibitors (1). It is unclear how the nucleoside reverse transcriptase inhibitor backbone affects weight. Recent evidence from phase 3 clinical trials suggests greater weight gain with tenofovir alafenamide (TAF) compared to tenofovir disoproxil fumarate (TDF) (1,2). However, it is not fully understood whether TDF contributes to weight suppression or weight loss. The objective of this study is to establish how TDF plays a role in weight changes. We analysed weight safety data from clinical trials in HIV negative individuals, eliminating the return-to-health effect that is seen in HIV trials.

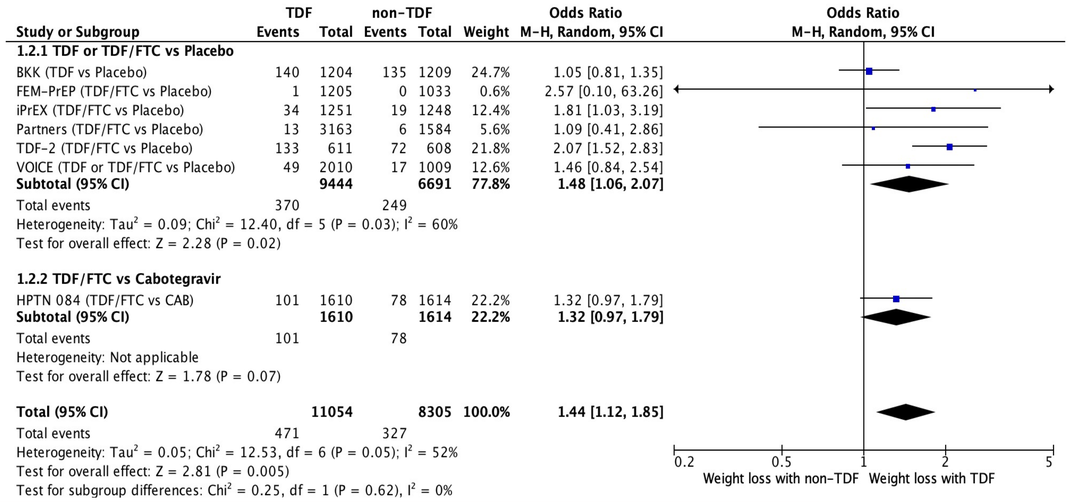
Methodology

A systematic search of PubMed, Embase and clinicaltrials.gov was conducted to identify all randomised control trials comparing TDF/FTC or TDF to control in HIV-negative individuals. The control group included participants taking placebo or cabotegravir. The primary endpoint included the number of events of '5% weight loss' or '≥grade 2 abnormal loss of weight'. The Mantel-Haenszel test with random-effects modelling was used to calculate the odds ratio (OR) and 95% confidence intervals (95% CI). A further safety analyses of gastrointestinal (GI) adverse events (AEs) were undertaken, including the number of reported adverse events of nausea, vomiting, loss of appetite and diarrhoea.

Results

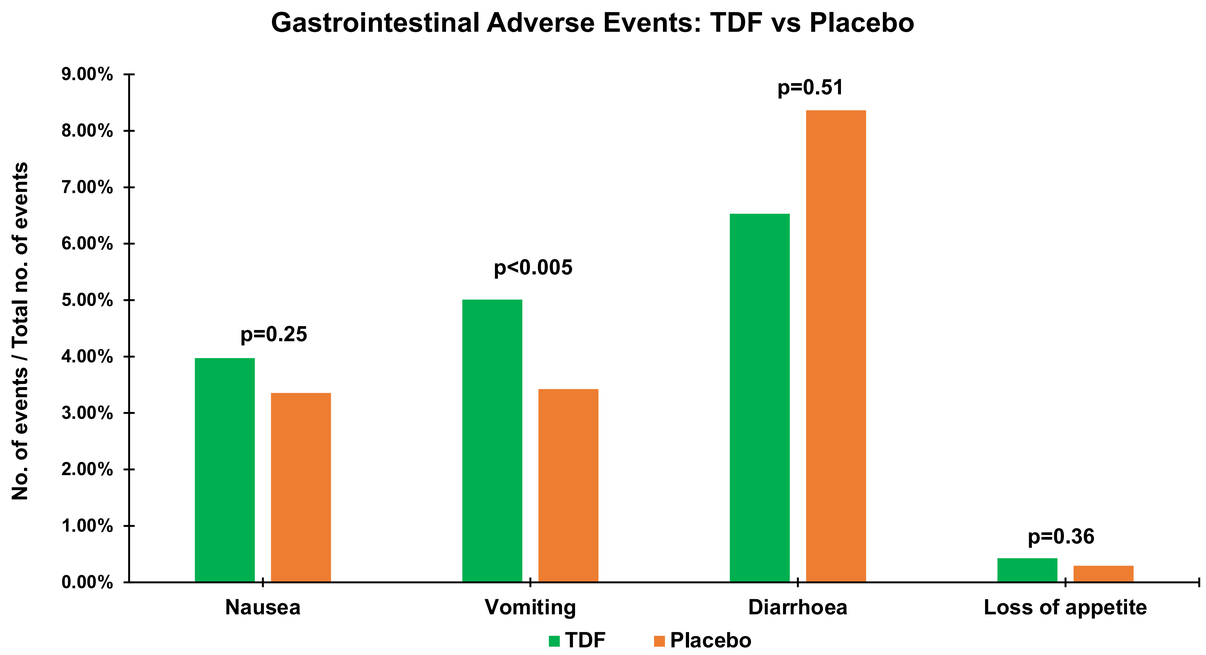
Weight loss

Seven PrEP trials: PARTNERS, VOICE, TDF-2, Bangkok PrEP, iPrEX, FEM-PrEP and HPTN 084 were included in the analysis of weight loss, with a total sample size of 19,359. One study (HPTN 084) compared TDF/FTC to cabotegravir (CAB). The remaining six trials compared either TDF or TDF/FTC or placebo. HIV-negative individuals taking TDF were more likely to experience weight loss compared to control (OR 1.44 95% CI 1.12 – 1.85 p = 0.005).



Gastrointestinal adverse events

In a separate analysis of GI AEs, exposure to TDF was also linked to greater odds of vomiting (OR 1.81 95% CI (1.20, 2.73) p <0.005). There were no increased odds of nausea, diarrhoea, or loss of appetite.



Conclusion

TDF is associated with greater odds of >5% weight loss when compared to placebo or control in HIV negative individuals. Further research should be carried out in HIV positive individuals, and clinical trials of TDF/FTC should publish weight data to widen the evidence base. The weight loss may be associated with gastrointestinal side effects, however, the evidence for this is limited. More research must be conducted to understand this effect. Long-term data is also required to establish whether weight loss is transient, or long-term.

References
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