Background: Ritonavir (RTV) and cobicistat (COBI) significantly increase plasma AUC concentrations of tenofovir disoproxil fumarate (TDF), by 25-37%. Higher plasma tenofovir concentrations are associated with higher risks of renal and bone adverse events. When combined with RTV or COBI, the TAF dose is lowered from 25 to 10mg daily but the TDF dose is maintained at 300mg daily. Most recently published randomised trials of TAF versus TDF included RTV or COBI (e.g. with elvitegravir/COBI or darunavir/RTV). However, the most common use of TDF worldwide is unboosted, combined with FTC or 3TC and either efavirenz or dolutegravir.

Methods: A PubMed/Embase search identified 11 randomised head-to-head trials (8110 patients) of TDF versus TAF. Meta-analysis of absolute risks with Mantel-Haenszel methods compared TDF versus TAF using random-effects models, to show whether their relative efficacy and safety profiles were different when used boosted with RTV or COBI, versus unboosted.

Results: Nine clinical trials compared TAF and TDF for treatment of HIV-1 and two were for Hepatitis B treatment. The eleven clinical trials documented 4,574 patients with boosting RTV or COBI in both arms, covering 7,198 patient-years of follow-up. 3,537 patients received unboosted regimens, totalling 3,955 patient-years of follow-up. Boosted TDF-treated patients showed borderline lower HIV RNA suppression <50 copies/mL (p=0.05) more bone fractures (p=0.04), larger decreases in bone mineral density (p<0.001) and more discontinuations for bone events (p=0.03) or renal (p=0.002) adverse events. By contrast, there were no significant differences in HIV RNA suppression rates or clinical safety endpoints between unboosted TAF and unboosted TDF.

Conclusions:
- This meta-analysis included data from 8110 patients in 11 randomised trials. Patients were mainly young to middle age, with no pre-existing osteoporosis or kidney impairment.
- When boosted with ronitavir or cobicistat, TAF was associated with lower risks of bone and renal adverse events, and higher HIV RNA suppression rates, compared with TDF. However the use of combination treatments including ritonavir and cobicistat is declining in the UK.
- By contrast, when ronitavir and cobicistat were not used, there were no significant differences between TAF and TDF in safety or efficacy endpoints, after 3595 patient-years of follow-up.
- In the UK, TAF/FTC costs £4331 per person-year (BNF), versus under £600 per person-year for generic TDF/FTC.