Is a Study of PrEP Adverse Events in Adolescents Needed? Value of Information and Implementation Analyses

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BACKGROUND

- Incomplete bone mineral density recovery is reported in adolescent males prescribed tenofovir-disoproxil-fumarate/emtricitabine (TDF-FTC) for HIV pre-exposure prophylaxis (PrEP). Lifelong fracture risk is uncertain in this age group which is yet to accrue peak bone mineral density.
- Increased hypertension risk is reported for tenofovir-alafenamide/emtricitabine (TAF-FTC) vs. TDF-FTC in adults.
- 37% of US providers prescribe TAF-FTC over TDF-FTC, despite substantially higher price, potentially due to differences in adverse event profiles.
- Objective: Apply value of information (VOI) and value of implementation (VOM) frameworks to estimate the potential value associated with a clinical study on HIV PrEP adverse events among adolescents.

METHODS

Using the CEPAC model, we simulate young men who have sex with men (YMSM) aged 15-22 years in the US to compare two daily oral PrEP strategies:1) TDF-FTC vs. 2) TAF-FTC
10-year and lifetime model-projected outcomes include:
1) Quality-adjusted life-years (QALYs), 2) Costs (2023 USD),
3) ICER: Incremental cost-effectiveness ratio
= Δ cost / Δ QALYs between strategies,
4) NMB: Net monetary benefit
= QALYs × willingness-to-pay − cost,
5) EVPI: Expected value of perfect information
= Δ between expected value of a decision made with perfect versus current knowledge about uncertainties
6) EVM: Expected value of implementation
= [value of optimal decision with current information] - [value of current decision taken with the same information]
Base-case willingness-to-pay = $100,000/QALY

Table 1. Select microsimulation model input parameters

Input parameter	Value	PSA range	Source
Age, median (years, IQR)	19.2 (3.9)	N/A	Assumption
TDF-/TAF-FTC efficacy, %	82	95% CI, 70 – 94	[1]
TDF-/TAF-FTC adherence, %	46	95% CI, 39 – 52	[2,3]
HIV incidence, n/100 person-years, by age			
Off-PrEP[a]	0.7 – 10.2		[2,3]
On-PrEP	0.5 – 6.4	95% CI, 0 – 10	[2,3,4]
PrEP adverse events excess incidence, n/1,000 person-years			
TAF-FTC hypertension	0.37	95% CI, 0.23-0.58	[5]
TDF-FTC bone fracture	71	95% CI, 24 – 185	[6]
PrEP drug + program costs, USD/month			
TDF-FTC / TAF-FTC	269 / 1,781	N/A	[7]
Pre-/post-study uptake, %	TDF-FTC=63/94, TAF-FTC=37/6		Assumption

[a] HIV incidence on PrEP/(1-PrEP efficacy*PrEP adherence)
CI: confidence interval; IQR, interquartile range; PSA, probabilistic sensitivity analyses.

When accounting for the possible impact of TDF-FTC on bone mineral density, TAF-FTC would not be cost-effective compared to TDF-FTC for HIV PrEP among YMSM in the US. Aligning prescriptions with available data could yield substantial health system value.

RESULTS

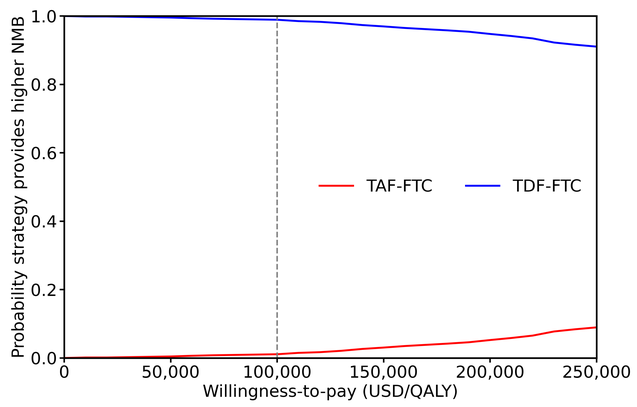
Table 2. 10-year model-projected outcomes of oral PrEP options for young MSM in the US

Strategy	Percent acquiring HIV	QALYs, per person		Costs, per person (2023 USD)		ICER,[a] $/QALY
		Undiscounted	Discounted[b]	Undiscounted	Discounted[b]	
TDF-FTC	21.1	9.62	8.35	48,000	42,000	–
TAF-FTC	20.6	9.69	8.41	96,000	86,000	730,000

[a] Incremental cost-effectiveness ratio: difference in total healthcare-related costs divided by the difference in total QALYs compared with the next most expensive strategy, rounded to the nearest 1,000. [b] Discount rate=3%/year.

- TAF-FTC would not be cost-effective compared to TDF-FTC with an ICER of $730,000/QALY.

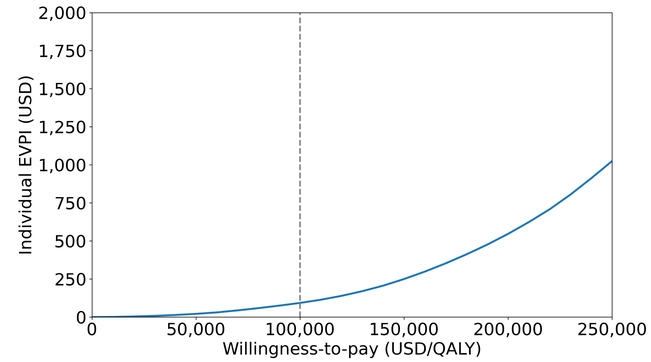
Figure 1. Cost-effectiveness acceptability curve



- When accounting for data uncertainty and using lifetime projected outcomes, TDF-FTC would provide greater NMB compared to TAF-FTC in 99% of PSA simulations.

RESULTS

Figure 2. Expected value of perfect information



- EVPI is $90 per individual.
- EVM for improving TDF-FTC uptake from 63% to 94% would yield a value of implementation of $33,500 per individual.

CONCLUSIONS & FUTURE DIRECTIONS

- Considering the uncertainties, TAF-FTC would not be cost-effective compared to TDF-FTC for HIV PrEP among YMSM in the US.
- The maximum expected value of information from a study of oral HIV PrEP adverse events among YMSM in the US that eliminates uncertainties is $90 per individual.
- The value of such a study could lie in scaling up TDF-FTC implementation, potentially creating value of $33,500 per individual even when accounting for uncertainties in fracture risk.
- Limitations: Only first bone fracture (TDF-FTC) and lifelong hypertension (TAF-FTC) were modeled.

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PLAIN LANGUAGE SUMMARY: Decreased bone mineral density has been observed in adolescents on TDF-FTC. It is unclear how clinically or economically important this is. Based on available data, TAF-FTC would not be cost-effective compared to TDF-FTC.

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