Potential Risks and Benefits of Low-Barrier HIV PrEP:A Modeling Study

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BACKGROUND

- The population-level impact of HIV PrEP in the US has been limited by structural barriers to access.
- Low-barrier delivery strategies for PrEP, such as over-the-counter (OTC) availability, could substantially improve access.
- This strategy could increase risks associated with reduced monitoring, including antiretroviral resistance, renal toxicity, and hepatitis B virus (HBV) reactivation.

METHODS

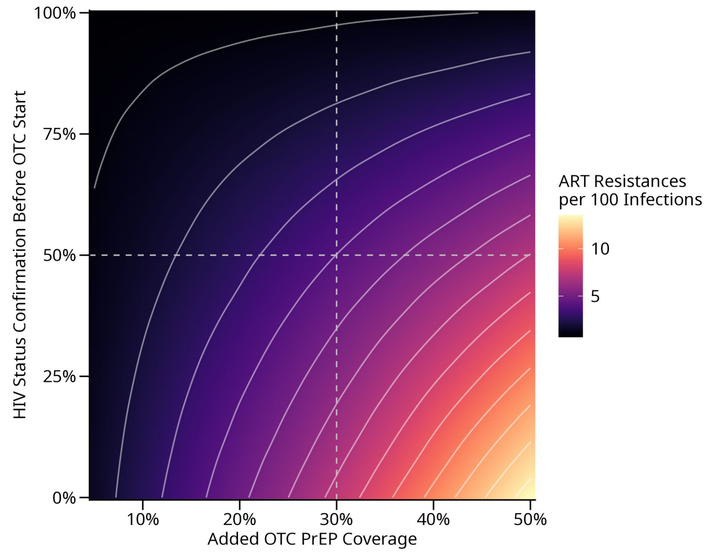
- A stochastic network-based mathematical model of HIV, gonorrhea, and chlamydia transmission among gay, bisexual, and other men who have sex with men (MSM) in the Atlanta metropolitan area.
- The model incorporated dynamic sexual networks, HIV/STI natural history, and two PrEP delivery pathways: standard-of-care prescription PrEP (Rx PrEP) and OTC PrEP with simplified initiation and reduced monitoring.
- We simulated increases in OTC PrEP uptake corresponding to 10–50% increases in total PrEP coverage over a 10-year horizon.
- Outcomes included percent of HIV infections averted, renal risk (exposure to TDF/FTC with GFR < 60 mL/min/1.73 m²), HBV-related reactivations, and antiretroviral resistance.
- Sensitivity analyses evaluated key OTC implementation parameters, including HIV testing at initiation, PrEP persistence, screening frequency, and renal monitoring.

Low-Barrier PrEP could be impactful as an entry point for people currently unable or unwilling to engage with PrEP

RESULTS

- Introducing OTC PrEP increased overall PrEP coverage and reduced HIV incidence across all scenarios. A 10% increase in total PrEP coverage averted 3.2% of HIV infections over 10 years, while a 50% increase averted 15.4%.
- These benefits were accompanied by increases in clinical risks.
- The proportion of PrEP users exposed to TDF/FTC with GFR < 60 rose from 2.5% in the Rx-only reference scenario to 4.8% at 50% higher PrEP coverage.
- HBV-related reactivations increased from zero to 2.27 per 100 person-years following PrEP discontinuation among individuals with HBV infection.
- Antiretroviral resistance increased with OTC PrEP uptake, with FTC resistance rising from 0.68 to 8.40 events per 100 HIV infections.
- Sensitivity analyses showed that increasing HIV-negative status confirmation at OTC PrEP initiation could reduce ART resistance by >90%, while more frequent renal monitoring substantially reduced renal risk.

	HIV Percent of Infection Averted	PrEP user with GFR < 60	HBV reactivations OTC IR100 PY	ART Resistances per 100 Infections
Rx PrEP Only	-	2.5% (2.4%, 2.7%)	-	0.68 (0.51, 0.91)
OTC PrEP + 10%	3.2% (-0.1%, 6.9%)	3.1% (3.0%, 3.3%)	0.44 (0.24, 0.71)	2.36 (1.99, 2.76)
OTC PrEP + 20%	6.4% (3.2%, 10.3%)	3.6% (3.4%, 3.9%)	0.91 (0.58, 1.25)	3.98 (3.49, 4.56)
OTC PrEP + 30%	9.4% (6.4%, 13.1%)	4.1% (3.9%, 4.3%)	1.36 (0.95, 1.83)	5.52 (4.91, 6.06)
OTC PrEP + 40%	12.4% (9.4%, 16.1%)	4.4% (4.2%, 4.6%)	1.83 (1.35, 2.41)	7.01 (6.35, 7.77)
OTC PrEP + 50%	15.4% (12.2%, 18.4%)	4.8% (4.5%, 5.0%)	2.27 (1.69, 2.95)	8.40 (7.64, 9.23)



CONCLUSIONS

- OTC PrEP could produce meaningful population-level HIV prevention benefits if it expands PrEP coverage beyond clinic-based care
- Net public health impact depends on implementation choices that preserve key safety functions without undermining access gains.
- HIV testing at PrEP initiation and targeted renal monitoring should be be easily accessible and actively promoted.

ADDITIONAL KEY INFORMATION

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PLAIN LANGUAGE SUMMARY

A Low Barrier PrEP could prevent more HIV infections by reaching people who don't access it. But safeguards like HIV testing before starting and kidney monitoring must be promoted to prevent resistance and side effects.