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The price of tenofovir-emtricitabine undermines the cost-effectiveness and advancement of pre-exposure prophylaxis

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Pre-exposure prophylaxis (PrEP) is a promising preventive tool in the fight against HIV [1], but it remains expensive. In 2010, a year's worth of tenofovir-emtricitabine (TDF-FTC, or Truvada, the sole drug approved for this regimen in the United States) cost \$ 13 416 wholesale [2]. Insurance policies, Medicaid, and drug assistance programs have not responded to PrEP's emergence, so eligible patients must bear this cost in full. PrEP's large price tag abrogates its cost-effectiveness and is likely the biggest barrier to its widespread implementation.

Because the annual cost of a once-daily Truvada regimen will be a primary consideration for interested candidates, we investigated how local TDF-FTC costs may vary on the basis of where and how they are purchased. Several potential modes of purchasing were compared: four San Diego pharmacies, the AIDS Drug Assistance Program (ADAP), Medicaid, the San Diego Veterans Affairs Healthcare System, and Canadian online retailers. Prices ranged from \$ 1300 to 15 500 (Table 1) [3, 2], although some of these values are hypothetical. Although ADAP's reduced \$ 11470 reimbursement rate illustrates the potential power of negotiated pricing, online retailers (who may charge as little as \$ 1300 and may not require a prescription) provide the least expensive option by a wide margin.

Incremental cost-effectiveness ratios (ICERs) are well accepted indicators of a medical intervention's economic viability [4]. ICERs express the cost per quality adjusted life year (QALY) conferred by a given intervention, as compared to the status quo. Comparing ICERs for well established HIV interventions may provide a barometer for the socially-accepted value of HIV care in the United States [4].

Preliminary ICER data suggest that PrEP is unsustainably expensive. One math model predicted that, for a representative at-risk population (with an annual medication cost of \$ 9000, a 1.6% HIV incidence rate, and 50% PrEP efficacy), the corresponding ICER would be \$ 298000 per QALY gained [3]. In comparison, the cost per QALY for antiretroviral therapy, resistance testing, and the screening protocols endorsed by the Centers for Disease Control and Prevention (CDC) all fall below \$ 23000 [5–7]. Moreover, the \$ 298000 PrEP ICER is more than 2.5 times greater than what Americans are likely to spend on general health interventions (approximately \$ 113000 per QALY) [8].

This model also predicted how the age of the target population, the rate of incident infections, and varying drug costs can shift the cost—benefit ratio. Assuming a very high incidence rate of 2% and a target population of 34 years of age [9], the PrEP efficacy

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required to bring the ICER below \$ 50 000 per QALY exceeds 85% [3]. Even after reducing the price of TDF-FTC to \$ 2500 per year, PrEP would still need to be 55% efficacious to keep its ICER below \$ 50 000 per QALY. This level of success is ambitious, considering that the iPrEX trial achieved efficacy of only 44% [1]. These estimates suggest that the only cost-effective option may be to purchase TDP-PTC from Canadian online retailers.

Using a different model, some have estimated that given the 2.6% absolute risk reduction found in the iPrEX trial, the cost of preventing a single infection over the course of a year with PrEP would be nearly \$ 500000 [10]. In contrast, the lifetime costs of treating one person infected with HIV is approximately \$ 600000 [11]. These sorts of financial comparisons do not bode well for PrEP's future viability.

The CDC has endorsed preliminary guidelines for PrEP, but cost-reduction measures are necessary to translate these recommendations into clinical practice [12]. To expand PrEP's accessibility and cost-effectiveness, we recommend the following steps. First, the government should leverage reduced drug prices through programs such as Medicaid and ADAP. Second, Truvada's manufacturer, Gilead (Foster City, California, USA) must expand its patient assistance program to support financially eligible PrEP candidates. Unless low-cost purchasing routes are enabled, candidates who cannot afford full-cost PrEP may pursue unreliable substitutes, such as medication-sharing or online retailers. Third, clinics and clinicians must take the initiative to advocate for local at-risk communities and inform eligible patients of this developing preventive tool. PrEP programs will be most instrumental in populations with high incident rates of HIV, young at-risk populations, and well established risk-counseling programs [3].

Identifying these target communities and engaging their local health professionals should be a priority. Finally, further research must be performed in non-clinical trial settings to evaluate the 'real-world' efficacy and cost-effectiveness of a PrEP strategy. Delaying action on these cost-reduction and awareness measures is not only irresponsible from the standpoint of public health, but it also restricts important preventive care from those who need it most.

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Table 1

Approximate annual cost of tenofovir-emtricitabine on the basis of how it is purchased.

	Approximate annual cost of tenofovir-emtricitabine	Comments	Reference
National average in 2006	\$9000	Price factors in Medicaid reimbursement rates; expressed in 2006 dollars. Assuming 1.6% incident infection rate and 50% PrEP efficacy, this cost is associated with an ICER of \$ 298000 per QALY gained.	[3]
Average wholesale price (AWP) in 2010	\$13416		[2]
Medicaid reimbursement rate in California, 2010	\$11 135 ^a	Price calculated as AWP-17%.	[2]
Average out-of-pocket costs from four national drugstore chains in San Diego (2011)	\$15 500		Phone calls with pharmacy representatives
San Diego Veterans Affairs Healthcare System (2011)	\$6500 ^a		Correspondence with a VA staff pharmacist
Online search for generic formulation in Canada (2011)	\$1300-3 650	The quality of these websites cannot be verified and some websites do not require a prescription.	northdrugstore.com, northwestpharmacy.com
AIDS Drug Assistance Program of California (2011)	\$11 470 ^a	Data is not available to the public. Price cited is AWP-14.5%, but the final negotiated price likely includes further rebates.	Correspondence with ADAP representative

ADAP, AIDS Drug Assistance Program; AWP, average wholesale price; PrEP, Pre-exposure prophylaxis; QALY, quality adjusted life year; VA, veterans affairs;

^a Medicaid, Veterans Affairs, and ADAP do not subsidize the cost of tenofovir-emtricitabine for off-label regimens such as PrEP. These values represent reimbursement rates for conventional use of the drug.