Potential cost-effectiveness of availability of Community TLD for HIV prevention and treatment in sub-Saharan Africa: a modelling analysis

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BACKGROUND

We have proposed consideration of making tenofovir-lamivudine-dolutegravir (TLD) widely and freely locally available in communities without prescription (along with condoms, HIV self-test kits and emergency contraception), with community ownership and education ("community TLD"), to enable post-exposure prophylaxis (PEP) use within at most 24 hours of condomless sex. Giving unrestricted TLD access would mean some people might also use the drugs as pre-exposure prophylaxis (PrEP), or as treatment, without engagement in care, and hence the net effects on health outcomes are uncertain.

Potential beneficial effects include:

(i) higher PEP/PrEP prevention coverage for episodes of condomless sex in HIV negative people

(ii) greater likelihood of people living with HIV being on ART

Potential negative effects include:

(i) lack of initial / 3- monthly HIV testing in some PrEP and PEP users, meaning some have undiagnosed HIV and hence are taking TLD guided by sexual risk when it should be continuous, with a possible increased risk of resistance,

(ii) an increase in the proportion of people on ART who are not under care and not monitored with viral load testing or given adherence counselling, possibly leading to lower ART effectiveness

(iii) increased risk of immune response inflammatory Syndrome (IRIS) in people with advanced HIV and other concurrent infections starting ART without clinical assessment, and

(iv) some inappropriate use of TLD in people without HIV and without risk for HIV which results in drug wastage and possibly unnecessary drug toxicity.

We further developed an existing individual-based model (HIV Synthesis) to provide a framework for pilot implementation projects to quantify the net effects of such an approach at a population level.

METHODS

Each model run generates a simulated population of adults with variable values on each person updated every 3 months, including primary and non-primary condomless sex partners, HIV testing, VMMC, PrEP and PEP. In HIV-positive people, we model viral load, CD4 cell count, antiretroviral drugs, adherence, and drug resistance. Through sampling of parameter values we create 1000 "setting-scenarios" reflecting uncertainty in assumptions and a range of settings similar to those seen in SSA (**Table 1**). For each setting scenario, we compare outcomes from 2022 between policies of

(i) continuation of oral TDF/FTC PrEP availability at current levels and scale up of Cab-LA PrEP only, and

(ii) as (i) plus + community TLD.

Community TLD includes self-test kit access. We assume PrEP (and by definition PEP) would be used in a risk-informed way; there is an "indication" for PrEP in a 3-month period if person has condomless sex with at least one non-primary partner, or if the primary partner may have unsuppressed HIV. Cost of TLD, (incl supply chain) = $16 per 3 mths

Introduction of Community TLD, enabling enhanced PEP access, has a high chance of being cost-effective and hence leading to health benefits in sub-Saharan Africa.

RESULTS

The range of short term (3-year) effects of community TLD are shown in **Table 2.** Our assumptions on uptake and usage of community TLD result in 10% (90% range 5% - 16%) higher PEP/PrEP use amongst people with an indication for PrEP/PEP, and a mean 4% / 3% (men / women) increase in the % of PLHIV who are on ART (with a mean 13% of ART users using community available TLD rather than attending clinic (2% - 38%). **Table 2** also shows how these short-term effects translate into longer term outcomes, with a mean 4% increase in the % of PLHIV who have viral suppression of all PLHIV and a 36% (14% - 57%) reduction in HIV incidence over 20 years. There is not predicted to be a detrimental effect on prevalence of integrase inhibitor resistance. Considering DALYs, costs and cost-effectiveness (**Table 2**) over 50 years, overall costs are lower with community TLD in 97% of setting scenarios, with a $24.0 million (16% of the overall HIV budget) saving per year over 50 years as a result of less people requiring ART and lower ART-related clinic visits over the long-term (**Table 3**)

Table 1 Description of setting-scenarios in 2022. Based on n = 1000 setting-scenarios.

Characteristic	**Model** (median, 90% range)
HIV prevalence (women/men aged 15-49)	17.1% (7.5% - 34.1%) 9.5% (4.2% - 19.6%)
HIV incidence (/100 person years) (age 15-49)	0.62 (0.27 – 1.65)
Proportion of HIV positive people diagnosed	88% (79% - 95%)
Proportion of diagnosed HIV positive people on ART	93% (80% - 97%)
Of people on ART, proportion with VL < 1000.	94% (83% - 99%)

Table 2 Modelled implementation of community TLD and its effects across 1000 settings scenarios.

	No community TLD Mean (90% range over setting scenarios)	**Community TLD**	**Comparison**
Short term effects (3 years)			
% of people with a current PEP/PrEP indication who take PEP/PrEP	20 (10 to 33)	30 (18 to 43)	+10 (+5 to +16)
Percent of HIV negative adults aged 15-49 who are taking PEP or PrEP	0.9% (0.2% to 2.3%)	1.4% (0.4% to 3.5%)	+0.5% (0.1% to 1.3%)
Of people on TLD PEP/PrEP, % on PEP	-----	68% (48% to 89%)	+68% (+48% to +89%)
Proportion of PLHIV on ART (men / women)	76 (60 to 87) / 84 (72 to 91)	80 (68 to 89) / 86 (78 to 92)	+4 (+1 to +9) / +3 (+0 to +7)
Of PLHIV on ART,% not attending clinic	-----	13% (2% to 38%)	+13% (2% to 38%)
Outcomes over 20 / 50 years			
Of all people with HIV proportion with viral suppression (at 20 years)	78% (66% to 87%)	83% (72% to 91%)	+4% (-2% to +14%)
HIV Incidence age 15-49 (over 20 years)	0.51 (0.16 to 1.18)	0.32 (0.10 to 0.78)	36% reduction (14% incr to 57% redn)
Prevalence of INSTI resistant HIV among all adults (in 20 years)	0.6% (0.0% to 1.6%)	0.6% (0.0% to 1.7%)	+0.0% (-0.3% to +0.3%)
Deaths caused by HIV per year (over 50 years)+	21,800 (8,300 to 46,300)	20,400 (7,100 to 45,300)	-1,400 (-13,100 to +7,500)
Difference in DALYs per year over 50 years +	2,198,000	2,175,000	-23,300 (-108,000 to +28,000)
Difference in annual cost over 50 years+	$146.2M (64.5 to 273.4)	$122.2M (55.7 to 228.2)	-$24.0m (-60.4 to -1.6)
Difference in net DALYs per year over 50 years+	2,491,000	2,419,000	-71,000 (-183,000 to -9,000)
Percent of setting scenarios for which:			
Reduced HIV incidence	-----	-----	99%
HIV deaths averted	-----	-----	64%
DALYs averted	-----	-----	77%
Costs saved	-----	-----	97%
Community TLD cost-effective **	-----	-----	98%

*90% ranges reflect both uncertainty in assumptions and variability between settings in sub-Saharan ; + in context of an adult population of 10 million. ** based on a cost-effectiveness threshold of $500 per DALY averted.*

Community TLD is cost-effective in 98% of setting scenarios. This does not depend on high uptake: restricting to setting scenarios with low community TLD uptake of community TLD it is cost-effective in 99% of setting scenarios.

Figure Effect of community TLD on HIV incidence, given our assumptions on uptake and usage

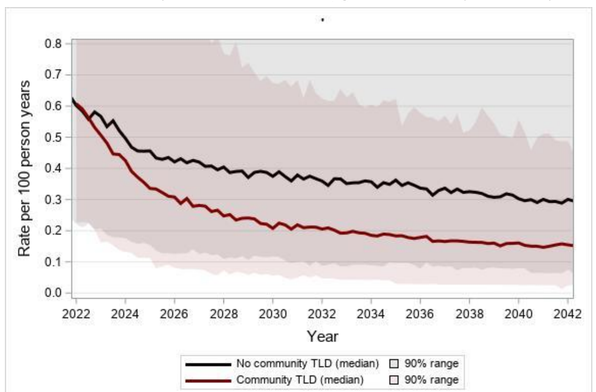


Table 3 Breakdown of costs

	No community TLD	**Community TLD**
	Mean ($ million per year) over 50 years	
Discounted annual cost over 50 years		
HIV testing (clinic-based)	13.8	12.8
HIV self-test kits	----	0.5
Oral PrEP / PEP drug	2.6 (oral PrEP TDF/FTC)	11.1 (oral PrEP / PEP is TLD)
Injectable PrEP drug	2.7	2.1
PrEP clinic visits	4.4	3.9
ART drug	51.4	44.6
Cotrimoxazole	3.6	2.1
ART clinic visits	36.4	21.0
Viral load tests	10.2	6.0
CD4 count tests	0.2	0.1
Treatment of WHO stage 3 / 4 conditions	10.7	10.0
VMMC	1.8	1.8
Care for children with HIV	4.8	3.5
Care for non-AIDS conditions pre-death	3.3	2.8
Total	**146.2**	**122.2**

DISCUSSION

Results suggest community TLD has clear potential to be cost-effective. While our results indicate a high impact of community TLD on HIV incidence this, unlike the cost-effectiveness, depends on the level of use of TLD attained. The main reason the substantial reduction in incidence does not translate to such a large reduction in deaths is due to the excellent outcomes of people with HIV, so many PLHIV do not die with HIV as the cause. There is not predicted to be any increase in overall levels of dolutegravir resistance, due to the decline in incidence balancing the small increase in resistance risk due to greater TLD use.

CONCLUSIONS

Introduction of community TLD, enabling greater PEP access, has a high chance of being cost-effective and hence leading to population health benefits. The approach can be tested in implementation studies and findings modelled.

* This correspondence was written by CG in her capacity as an USG employee, but the views expressed in this paper do not represent those of the Department of State or the Centers for Disease Control.

HIV Modelling Consortium