Clinical and cost impact of long-acting ART in South African youth with HIV: a modeling analysis

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BACKGROUND

- Youth with HIV (YHIV, 15-24y) experience challenges to oral antiretroviral therapy (ART) adherence, leading to substantial short- and long-term morbidity and mortality.
- Long-acting injectable cabotegravir/rilpivirine (LA-ART) may improve outcomes but is unavailable outside research settings in South Africa.

METHODS

- We use the CEPAC microsimulation model to simulate YHIV in care and prescribed ART (All YHIV, n=223,500), including a hypothetical subset with oral ART adherence challenges (YHIV with low adherence, n=23,400).
- We compare two strategies:

(1) *SOC*: standard-of-care daily oral ART

(2) *LA-ART:* bimonthly injectable ART through age 25 (then transitioning to daily oral ART)

- Modeled outcomes include: life-years, costs, incremental cost-effectiveness ratios (ICERs) in $/life-year saved (LYS).
  - Base case willingness-to-pay threshold: <$3,000/LYS (0.5x South Africa per capita GDP).
- Sensitivity analyses include: retention characteristics, starting CD4, adherence patterns, and costs.

Table 1. Selected microsimulation model input parameters

Input parameter	All YHIV	YHIV with low adherence
Initial cohort characteristics		
Age, mean, years (SD)[1]	20.5 (2.8)	
Sex, male/female (%)[1]	30 / 70	
CD4, mean (SD) (cells/μL)[2,a]	447 (227)	159 (208)
Viremia (%)[3]	21	100
Oral ART adherence, mean (%)[4,a,b]	74	22
24-month retention in care (%)[5]	84	67
Additional inputs		
SOC (TLD) efficacy (%)[6-7,c]	95	
SOC annual drug prices (USD)[8]	30-280	
LA-ART efficacy (%)[9-12,c]	96	94
LA-ART annual drug price (USD)[8,d]	270	
HIV-related care, annual costs (USD)[13-14]	130-1,290	

Abbreviations: All YHIV: All youth with HIV in care and prescribed ART; YHIV with low adherence: a subset of All YHIV with previous oral ART adherence challenges; USD: 2024 United States dollars.

[a] YHIV with low adherence inputs are derived from model outputs.
[b] Adherence = % of pills taken/month.
[c] Efficacy = HIV RNA <50 copies/ml at 12 month with >85% adherence.
[d] LA-ART modeled as twice the cost of atazanavir/ritonavir.

LA-ART during adolescence would increase life expectancy and could be cost-effective for South African youth with HIV.

RESULTS

Table 2. Model-projected lifetime outcomes of *SOC* versus *LA-ART* for YHIV in South Africa

Strategy	Life-years beyond model start		Costs,[a] per person, discounted	Costs (discounted $ millions),[a] Population	ICER[b] ($/life-year saved)
	Undiscounted	Discounted			
All YHIV (n = 223,500)					
SOC	29.7	16.8	6,800	1,530	-
LA-ART	31.1	17.5	7,600	1,700	1,050
YHIV with low adherence (n = 23,400)					
SOC	10.4	6.8	5,600	130	-
LA-ART	15.3	9.6	6,800	160	400

Abbreviations: YHIV: youth with HIV, aged 15-24y; ICER: incremental cost-effectiveness ratio; *SOC*: oral TLD; *LA-ART*: long-acting injectable cabotegravir/rilpivirine.

[a] Costs in 2024 US dollars, rounded to the nearest hundred.
[b] ICERs are the difference in discounted healthcare-related costs divided by the difference in life-years saved (3%/y).

- *LA-ART* increased life expectancy compared to *SOC:* 1.4 life-years gained in All YHIV (31.1 years vs. 29.7 years), 5.0 life-years gained in YHIV with low adherence (15.3 years vs. 10.4 years).
- *LA-ART* ICERs were both less than the willingness-to-pay threshold of $3,000/LYS.

Plain language summary:

Using a microsimulation model, we found that long-acting injectable HIV treatment could help South African adolescents and young adults with HIV live longer than standard daily pills, especially those who struggle with adherence, and could represent a good value for money despite higher costs.

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2. Malaza PLoS One 2017
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6. Calmy N Engl J Med 2019 (NAMSAL)
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9. Overton Lancet 2020 (ATLAS-2M)
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RESULTS (CONTINUED)

Figure 1a. All YHIV cohort

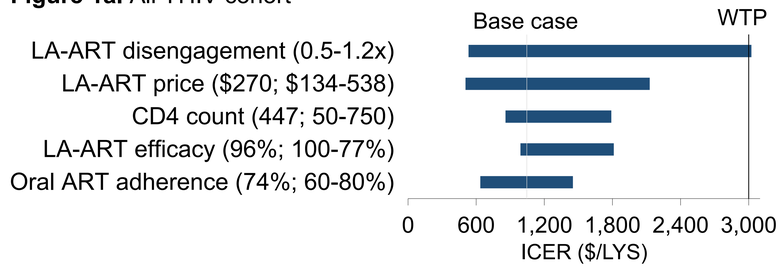
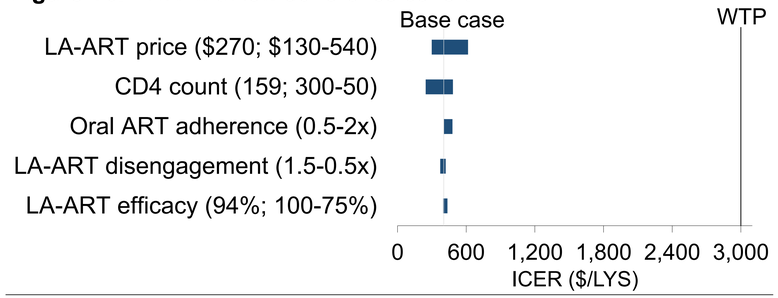


Figure 1b. YHIV with low adherence cohort



ICER of *LA-ART* vs *SOC*, in $/life-year saved.
WTP: The black vertical line at $3,000/LYS marks the willingness-to-pay threshold.

- For All YHIV, results were most sensitive to LA-ART care disengagement.
- For YHIV with low adherence, ICERs would remain well below the willingness-to-pay threshold across all scenarios.
- LA-ART would remain below the willingness-to-pay threshold if drug prices were <$760/year for All YHIV and <$3,580/year for YHIV with low adherence.

LIMITATIONS

- No sex-stratified analyses due to data availability.
- Limited long-term data on LA-ART, particularly among viremic individuals.

CONCLUSIONS

- Prioritizing access to LA ART during the critical developmental period of adolescence and young adulthood could markedly increase long-term survival for YHIV.
- Depending on pricing, LA ART could be cost-effective for South African YHIV, particularly those with adherence challenges.

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