Cost-effectiveness and budget impact of immediate ART initiation in Côte d'Ivoire

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BACKGROUND

- In sub-Saharan Africa, HIV antiretroviral therapy (ART) is often initiated in patients with advanced disease, leading to high mortality.
- While timing of ART initiation has been a major debate in HIV clinical care and policy, in 2015, the Temprano and START trials independently demonstrated the clinical benefit of early ART initiation, regardless of CD4 count.
- In response to these two trials, the WHO modified its guidelines in 2015 to recommend immediate ART initiation for all HIV-infected individuals.

OBJECTIVE

- To project clinical and economic outcomes of immediate ART initiation in Côte d'Ivoire, the setting of the Temprano trial.

METHODS

- We used the CEPAC-International model, a state-transition, first-order Monte Carlo microsimulation model of HIV infection incorporating natural history, disease progression, and treatment.
- We simulated all persons living with HIV (PLWH) in care in Côte d'Ivoire (n=170,000) and evaluated three ART initiation strategies based on CD4 count criteria:
  1. **ART <350/µL**, the current standard of care (SOC) in Côte d'Ivoire
  2. **ART <500/µL**
  3. **Immediate ART** initiation upon linkage to care
- Yearly, we incorporated a newly-infected cohort. Transmission calculations, including from the initial prevalent cohort and all prior incident cohorts, determined the number of persons in this new yearly cohort.
- We populated the model with TB incidence from the Temprano trial and other Côte d'Ivoire-specific data. We simulated patients from initial distributions of age, sex, CD4 count, and HIV RNA level. Patients are at increasing risk for morbidity and mortality as CD4 declines; ART reverses this decline (Table 1).
- Outcomes included number of transmitted HIV cases, years of life saved, costs, and incremental cost-effectiveness ratios (ICERs) at 10 years.
- We varied model input parameters in one-way sensitivity analyses and then varied those most influential in multi-way sensitivity analyses.

Table 1. Model input parameters for a model-based analysis of immediate ART initiation in Côte d'Ivoire

Parameter	Base case value	Range explored	Reference
Age, mean (SD) years	37 (9)	18-55	Preco-CI
CD4, mean (SD) cells/µl (total cohort)	259 (198)	207-569	Preco-CI
CD4, mean (SD) cells/µl (newly-infected)	750 (100)	-	
Monthly TB rates/100 PY, range	0.06-0.66	-	Temprano, Anglaret *CID* 2012
ART initial virologic suppression at 6 months, %	80	50-90	Messou *JAIDS* 2011
ART virologic failure after 6 months, per 100 PY	15	8-30	Messou *JAIDS* 2011
Loss to follow-up, per 100 PY	9	4.5-18	Fox *Trop Med Int Health* 2010
Transmission rates (per 100PY), by viral load	0.16-9.03		Attia *AIDS* 2009
Costs, 2015 USD			
ART, annual			
1st-line ART	122	57-1,830	CHAI ARV price list 2013
2nd-line ART	391	166-497	
Laboratory monitoring, per test			
CD4 test	11	5-14	CeDReS
HIV RNA test	33	-	CeDReS
OI treatment costs (range by OI)	65-402	33-804	Anglaret *Lancet* 1999

ART: antiretroviral therapy; SD: standard deviation; USD: 2015 US dollars; PY: person-years; CeDReS: Centre de diagnostic et de Recherce sur le SIDA et les Affections Opportunistes at Treichville University Hospital, Abidjan, Côte d'Ivoire; OI: opportunistic infection

RESULTS

Table 2. 10 year clinical, economic and HIV transmission outcomes of persons in care in Côte d'Ivoire by ART initiation strategy

Strategy	Transmissions, 10y	Life expectancy (years)	Total life years, 10y	Total costs, 10y	ICER, 10y ($/YLS)
ART<350/µL (SOC)	70,500	26.5	1,489,000	860,988,000	-
ART<500/µL	66,700	26.8	1,501,000	867,680,000	Dominated
Immediate ART	64,200	27.0	1,506,000	870,518,000	550

Cost outcomes are reported in US dollars. All clinical and economic outcomes above, except transmissions, are reported discounted at 3%/year. Dominated: more costly and less effective than some combination of other strategies.

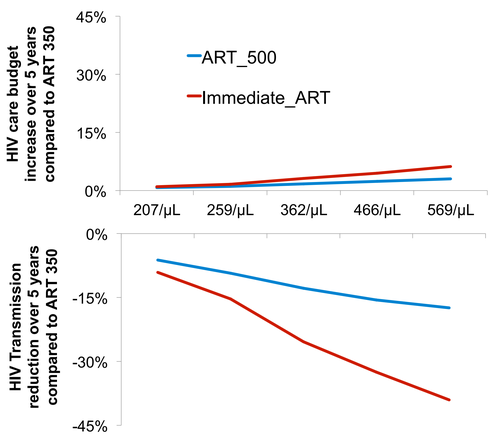
- The Immediate ART strategy averts 6,300 new transmissions from persons currently in care and persons infected from that cohort.
- ART <500/µL saves 12,000 years of life and Immediate ART saves 17,000 years of life over 10 years compared to ART <350/µL.
- Immediate ART is very cost effective ($550/YLS < 1x Côte d'Ivoire *per capita* GDP=$1500) compared to ART <350/µL. ART <500/µL is not an economically efficient use of resources in this setting (Table 2).

Table 3. 5-year budget impact by ART initiation criteria for PLWH in care in Côte d'Ivoire

Strategy	ART costs	Monitoring costs	Total costs	Budget increase compared to SOC, $ M (%)
ART<350/µL (SOC)	79.5	23.3	515.8	-
ART<500/µL	84.2	23.7	521.4	5.5 (1.1)
Immediate ART	87.1	24.0	524.3	8.5 (1.7)

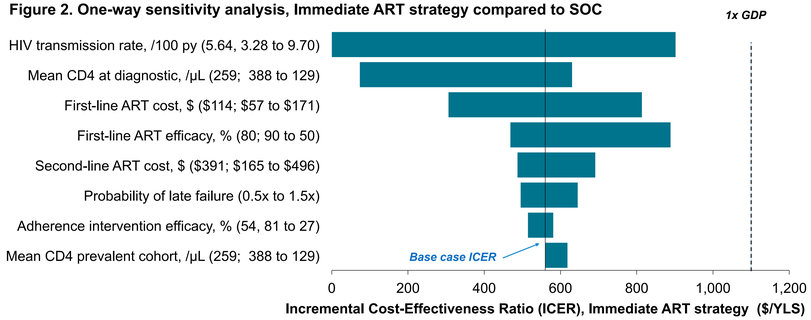
Cost outcomes are in US dollars, in millions. All clinical and economic outcomes are reported undiscounted.

Figure 1. HIV care budget increase and reduction in transmissions by ART initiation strategy and CD4 at diagnosis



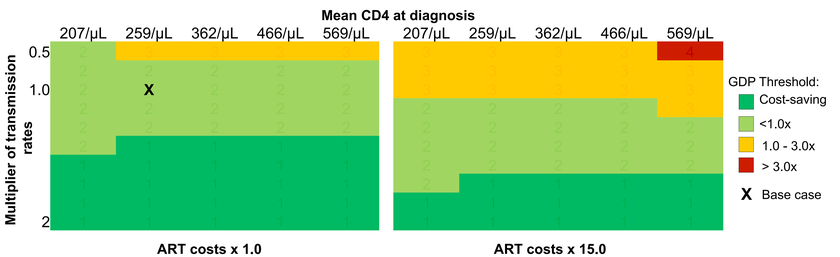
- Immediate ART would increase the 5-year budget by $8.5 million compared to the SOC, an increase of 1.7%.
- Across a wide range of CD4 count at diagnosis thresholds, the % reduction in transmissions far exceeds the % increase in budget for both the ART <500/µL and Immediate ART strategies (Figure 1).

Figure 2. One-way sensitivity analysis, Immediate ART strategy compared to SOC



- The ICER of the Immediate ART strategy was most sensitive to variations in HIV transmission rates, mean CD4 at diagnosis, and first-line ART costs.
- When transmission rates were increased to the upper bounds of the 95% confidence interval, Immediate ART became cost-saving.
- No plausible variation in input parameters produced an ICER that exceeded 1x the Côte d'Ivoire annual *per capita* GDP of $1,100 (Figure 2).

Figure 3. Multi-way sensitivity analysis on cost-effectiveness of immediate ART initiation in CI



- Only when transmission rates were multiplied by 0.5x, ART costs multiplied by 15.0x, and the mean CD4 at diagnosis increased to 569 cells/µL did the ICER of the immediate ART initiation strategy exceed 3x the *per capita* GDP (Figure 3).

CONCLUSIONS

- Immediate ART, regardless of CD4 count, would be very cost-effective in Côte d'Ivoire by international standards, with an ICER < 1x the annual *per capita* GDP.
- The cost-effectiveness findings are robust across a wide range of plausible input parameters, with no one-way sensitivity analysis range exceeding the 1x GDP threshold for Côte d'Ivoire.
- Immediate ART will reduce transmissions, increase survival, be very cost-effective and it is unlikely to increase the budget any more than ~2%.
- Over a wide range of estimates for CD4 count at diagnosis, transmission rates, and ART costs, Immediate ART was cost-saving.
- The results may be limited by the use of population level transmission data in the transmission calculations, the exclusion of persons out-of-care in the cost-effectiveness analysis, and the exclusion of non-HIV medical costs.
- Immediate ART should become the standard of HIV care in Côte d'Ivoire.