EE534

Economic Evaluations of HIV-1 Disease in South Africa – a Targeted Literature Review

Angelina Addae, Cytel, Inc., Waltham, MA, USA; Mike Dolph, Cytel, Inc., Waltham, MA, USA; Lauren Ramjee, Cytel, Inc., Waltham, MA, USA; Gabriel Tremblay, Cytel, Inc., Waltham, MA, USA

Background

- Human deficiency virus 1 (HIV-1) is the principal causative agent of acquired immune deficiency syndrome (AIDS). HIV-1 infection results in the depletion of CD4+/CD8+T cells and alters the cytokine network in the infected individuals.[7] High incidence of HIV-1 infections are reported globally signifying a major global health crisis.[10]
- Due to the complex nature of the disease, multifaceted clinical pathway, and high number of treatment lines received over a HIV patient's life, developing economic models to assess HIV-1 is challenging. Clinically valid, and methodologically robust, methods should be used. Additionally, where possible, standardized approaches would be valuable when assessing HIV through economic models.

Objective

- This study investigates the methods and results of previously published economic models evaluating treatments for people with HIV-1 in South Africa to support the planning and development of future modelling studies.

Key Results

- Fourteen studies met the requirements for inclusion; 13 cost-effectiveness analyses and one comparative cost analysis. Within the cost-effectiveness analyses, microsimulations, markov models, and deterministic compartmental model types were used in 9 studies. In 4 studies, decision trees or other models were utilized. Efficacy (reported in 11 studies) and utility (reported in 5 studies) data were obtained from publicly available sources and costs were sourced from local healthcare agencies. 10 studies reported analyses from the healthcare payer perspective, 3 included societal perspective and one did not report any perspective. Health states reported were limited to two studies and were based on CD4 count (CD4 >500, 351 – 500, 201 – 350, < 200) and death. All research employed a 3% discount rate, but time horizons varied.

Conclusion

- Despite limited data available, the current literature review found an alignment on the parameters selected to model the economic evaluation of HIV treatments. The more predominant attributes were the following:
  - Model: Simulation.
  - Time Horizon: Lifetime.
  - Health States: CD4 > 500, CD4 351-500, CD4 201-350, CD4 < 200.
  - Perspective: Healthcare payer system.
- Evidence from the targeted literature review (TLR) suggests that HIV treatment regimens are cost-effective. The magnitude of their effectiveness is dependent on scenarios such as:
  - Prevalence of HIV.
  - The affordability of treatments.
  - The scale of HIV testing.
  - Type of population assessed.

Methods

Study design and search methods:

- Publications of interest were identified by searching databases available on the Ovid platform based on the targeted search strategy.
- The search was conducted on December 16, 2021, in the MEDLINE® ALL database.
- The search was restricted to studies in South Africa.
- Supplementary literature were obtained from PubMed, Google Scholar, Cochrane Library, and other databases. Key search terms used were: "HIV", "HIV-1", "South Africa", "economic evaluation", "cost effectiveness analysis", "cost benefit analysis", "cost-utility", "economic value".

Eligibility criteria

- The identified publications were reviewed for relevance against the inclusion and exclusion criteria, defined by the PICOS criteria listed in **Table 1**. Data from included studies were extracted into a pre-defined Excel-based extraction template, ensuring that data were extracted uniformly and were comparable across studies.

Table 1. Inclusion and Exclusion Criteria

PICOS	Criteria
Population	• Patients diagnosed with HIV-1 in South Africa
Intervention and comparator	• No restrictions
Outcomes	• Model summary (including perspective, time horizon, and discounting), model type (Markov, dynamic transition, decision tree, partition survival, microsimulation) and model structure • Sensitivity analysis (deterministic, probabilistic, scenario analysis) • Model outcomes (e.g., QALY, ICER)
Study design	• Cost-consequence • Cost-minimization • Cost-effectiveness • Cost-utility • Cost-benefit/Net-benefit approach
Other restrictions	• English Language, South Africa, Studies from 2010 to current

Abbreviations: HIV-1, human deficiency virus 1; ICER, incremental cost-effectiveness ratio; PICOS, patient/population, intervention, comparison and outcomes; QALY, quality adjusted life year.

Results

- The electronic database search yielded 12 studies. After screening through title and abstracts, 10 were excluded after title/abstract review as they did not meet the PICOS criteria. To ensure that the scope of literature has been covered, other databases were searched, and 12 additional studies were retrieved. A total of 14 studies were retained for extraction. A flow diagram of the selection process is illustrated in **Figure 1.**

Figure 1. Flow diagram of study inclusion

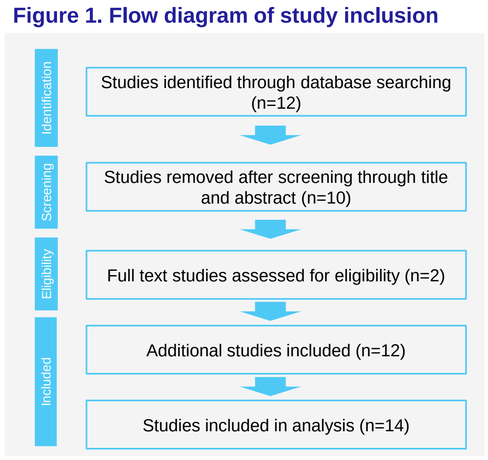


Figure 2. Interventions assessed

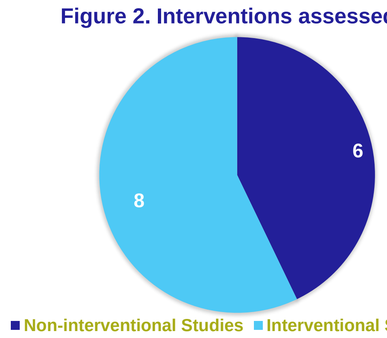
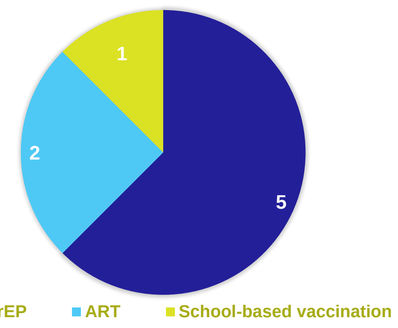


Figure 3. Interventions assessed

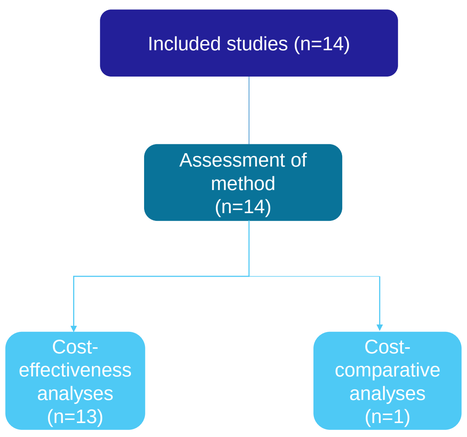


Abbreviations: ART, antiretroviral treatments; PrEP, Pre-Exposure Prophylaxis.

Intervention

- There were 8/14 therapeutic comparator studies that focused on various oral treatment regimens included.
- There were 6/14 non-therapeutic comparator studies such as HIV testing, HIV screening, and others included shown in **Figure 2**.
- Of the 8 therapeutic comparator intervention: Two studies assessed antiretroviral treatments (ART) regimens, five studies assessed PrEP treatments, one study assessed school-based vaccinations shown in **Figure 3**.
- **Model type:** The economic evaluations reported various model types:
  - The most common model types were Simulation model (whether cohort, dynamic, or micro) (4/14) and Markov/semi-markov model (3/14).
  - Followed by deterministic compartmental models (2/14), decision analytic model (1/14), static epidemiological and costing model (1/14), cross-sectional survey (1/14) and a micro costing analysis (1/14) were also reported. Results presented in **Figure 5.**
- **Time horizon:** (11/14) of the evaluations reported the time horizon:
  - (1/14) used a five-year horizon.
  - (1/14) used twenty-five-year horizon.
  - (1/14) used forty-year horizon.
  - (2/14) used an eleven-year horizon.
  - (2/14) used twenty-year horizon.
  - (4/14) used a lifetime horizon.
  - (2/14) did not report on time horizon used. Results presented in **Figure 6.**
- **Discount:** All (14/14) of evaluations reported the discount rate
- **Health states:** (5/14) studies presented health states. % (2/14) reported the same health states based on CD4+ count and death state (CD4 > 500, CD4 351-500, CD4 201-350, CD4 < 200). The infected state was often split into several sub-states to account for the varying degree of severity of symptoms experienced by infected persons.
- One other study (1/14) used health states based on the susceptible (S), infected (I), receiving treatment (R) transition.

Figure 4. Study Characteristics



Results (cont.)

Figure 5. Model type

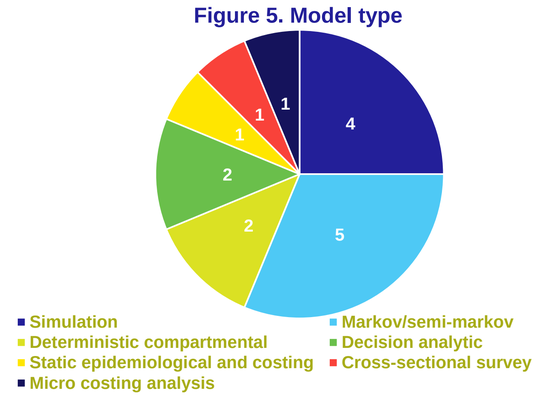


Figure 6. Time horizon

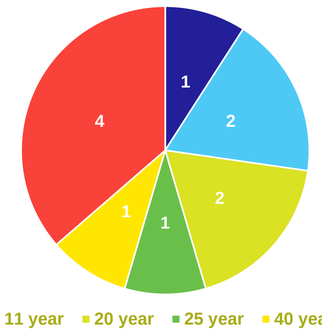
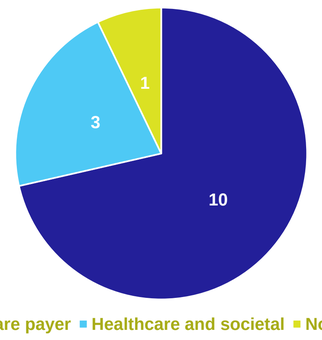


Figure 7. Perspective



- **Perspective:** (13/14) of evaluation reported the perspective:
  - (3/14) of studies presented both perspectives (societal and healthcare payer).
  - (10/14) of studies presented the healthcare payer perspective. Results presented in **Figure 7**.
- **Utility:** (5/14) of studies reported utilities. Only two reported utilities per health state. Other evaluations do not explicitly report the utilities used in the model.

Outcome

- Approximately (4/14) of evaluations used disability-adjusted life years (DALYs), while (5/14) used life years gained (LYs) and (2/14) used quality-adjusted-life years (QALYs). (2/14) did not use any life years but focused only on costs per testing or infection.
- (13/14) of the studies concluded that treatment was cost-effective as shown in **Table 3**. (1/14) of studies concluded that treatment was not cost-effective.
- (5/13) of studies indicated that cost-effectiveness was dependent on multiple conditions:
  - Access to affordable HIV testing and treatment.
  - Population subgroupings analyzed.
  - Prevalence of HIV-1 among couples.
  - Whether other treatment regimes are carried out simultaneously.

Table 3. Cost-effectiveness of Studies

Study	Economic endpoint	Cost-effectiveness
Vogelzang et al., 2020	Cost per DALY ICER: $1175 no PrEP intervention vs PrEP intervention	Not cost-effective
Moodley et al., 2016	Cost per LYG ICER: $5 HIV vaccination vs no HIV vaccination	Cost-effective
Glaubius et al., 2016	Cost per LYG ICER: <$1600 PrEP scale-up vs no PrEP	Cost-effective
Jewel et al., 2015	Cost per DALY ICER: 10,383 oral tenofovir-based PrEP vs no PrEP	Cost-effective
Granich et al., 2012	Cost per DALY averted: $9-$194 expanded ART scenarios vs unexpanded ART	Cost-effective with conditions
Walensky et al., 2012	Cost per LYG ICER: $2700 PrEP vs no PrEP	Cost-effective
Bendavid et al., 2012	Cost per QALY ICER: $5949 tenofovir/lamivudine/efavirenz vs tenofovir/lamivudine/nevirapine. Zidovudine/lamivudine/efavirenz	Cost-effective with conditions
Pretorius et al., 2010	Cost per infection averted: $12,500–$20,000 per infection averted	Cost-effective
Jamieson et al., 2021	Cost per LYS ICER: A (1 million HIVST kits (current)): $1394/LYS; B (6.7 million kits) : $4162/LYS vs no testing	Cost-effective
Simeon et al., 2019	Per patient cost: $26, $6, $3 of POC HIV viral load, CD4, and creatinine tests centralized laboratories, per-patient costs	Cost-effective with conditions
Larson et al., 2016	Overall cost: reflex cost $17,629 lower than provider-initiated screening strategy	Cost-effective
Li et al., 2015	Cost per QALY ICER: ZAR 81 978 HPV vaccine vs screening alone for HIV patients	Cost-effective with conditions
Tabana et al., 2015	ICER per client tested: $19	Cost-effective
Vickerman et al., 2011	Cost per LYG ICER: $1200 daily acyclovir vs ART provision	Cost-effective with conditions

Abbreviations: ART, antiretroviral treatments; DALY, disability-adjusted life years; HE, health economic; HIV, human immunodeficiency virus; HIVST, human immunodeficiency virus self testing; HPV, human papillomavirus; ICER, incremental cost-effectiveness ratio; LY, life-years, LYG, life years gained; PICOS, patient/population, intervention, comparison and outcomes; QALY, quality-adjusted-life-year; TLR, targeted literature review; POC, point of care; PrEP, Pre-Exposure Prophylaxis.

Limitations

- Considering the dynamic and complex nature of HIV, a TLR was considered a suitable approach. However, it must be noted that the methodology of TLRs are inherently not as rigorous as those of systematic literature reviews, leading to potential studies that might have been missed from the review.
- Each study is conducted in a different setting with different populations and cost-effectiveness may not be generalizable within and outside of South Africa.
- Therefore, limited conclusions can be drawn from this review and caution is needed in interpreting the data.

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Abbreviations:

AIDS, acquired immune deficiency syndrome; ART, antiretroviral treatments; DALY, disability-adjusted life year; HIV, human deficiency virus; HIV-1, human deficiency virus 1; LYs, life years gained; PICOS, patient/population, intervention, comparison and outcomes; QALY, quality-adjusted-life year; TLR, targeted literature review.

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