

Cost-effectiveness of Routine Provider-Initiated Testing and Counseling for Children With Undiagnosed HIV in South Africa

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Background. We compared the cost-effectiveness of pediatric provider-initiated HIV testing and counseling (PITC) vs no PITC in a range of clinical care settings in South Africa.

Methods. We used the Cost-Effectiveness of Preventing AIDS Complications Pediatric model to simulate a cohort of children, aged 2–10 years, presenting for care in 4 settings (outpatient, malnutrition, inpatient, tuberculosis clinic) with varying prevalence of undiagnosed HIV (1.0%, 15.0%, 17.5%, 50.0%, respectively). We compared “PITC” (routine testing offered to all patients; 97% acceptance and 71% linkage to care after HIV diagnosis) with no PITC. Model outcomes included life expectancy, lifetime costs, and incremental cost-effectiveness ratios (ICERs) from the health care system perspective and the proportion of children with HIV (CWH) diagnosed, on antiretroviral therapy (ART), and virally suppressed. We assumed a threshold of \$3200/year of life saved (YLS) to determine cost-effectiveness. Sensitivity analyses varied the age distribution of children seeking care and costs for PITC, HIV care, and ART.

Results. PITC improved the proportion of CWH diagnosed (45.2% to 83.2%), on ART (40.8% to 80.4%), and virally suppressed (32.6% to 63.7%) at 1 year in all settings. PITC increased life expectancy by 0.1–0.7 years for children seeking care (including those with and without HIV). In all settings, the ICER of PITC vs no PITC was very similar, ranging from \$710 to \$1240/YLS. PITC remained cost-effective unless undiagnosed HIV prevalence was <0.2%.

Conclusions. Routine testing improves HIV clinical outcomes and is cost-effective in South Africa if the prevalence of undiagnosed HIV among children exceeds 0.2%. These findings support current recommendations for PITC in outpatient, inpatient, tuberculosis, and malnutrition clinical settings.

Keywords. cost-effectiveness; HIV; pediatric; PITC.

Worldwide, nearly 150 000 children under age 15 acquired HIV in 2019, and about 1.8 million children under age 15 were living with HIV at the end of 2019, of whom 95 000 died due to HIV-related causes [1]. The past decade has witnessed unprecedented improvements in pediatric HIV prevention and care. Prevention of vertical transmission is possible, and HIV testing

and prompt initiation of antiretroviral therapy (ART) can allow children who acquire HIV to live long and healthy lives [1–3]. Despite these successes, pediatric HIV care and treatment still lag behind those for adults; only half of children under the age of 15 with HIV (CWH) are on treatment [1]. Although the World Health Organization (WHO) recommends early infant diagnostic testing (EID) at age 6 weeks for all HIV-exposed infants (ie, born to women with HIV), only about half of them are tested in the first 2 months of life [3, 4]. This is partly because knowledge of HIV exposure is lacking due to a range of factors, including stigma, lack of disclosure to male partners, absence of mother–baby pair longitudinal tracking mechanisms, and insufficient integration of HIV care within maternal, newborn, and child health services [5, 6]. Infants born to mothers with unknown HIV status face higher risks of HIV transmission and missed opportunities for infant diagnosis.

Received 20 August 2021; editorial decision 23 November 2021; accepted 3 December 2021; published online 5 December 2021.

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Open Forum Infectious Diseases® 2022

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After the WHO-recommended infant testing at 6 weeks to 18 months of age, there are limited opportunities for routine pediatric HIV testing [7]. Family index case testing may be a high-yield strategy to identify children, and it does not depend on children presenting to health facilities with illness [8]. The WHO recommends coupling this approach with additional efforts to identify CWH through provider-initiated HIV testing and counseling (PITC) in pediatric care settings, such as malnutrition clinics, tuberculosis (TB) clinics, inpatient wards, and outpatient services [9]. However, in many clinical settings, routine PITC—offered to all children regardless of symptoms or diagnosis—is rarely fully implemented [9]. This is partly due to competing priorities in overloaded health care facilities and concerns about the cost of testing programs, particularly in settings with anticipated low HIV prevalence [8].

In South Africa, national guidelines suggest the provision of facility-based PITC for all children as a standard component of HIV care [10, 11] and for index case testing to be provided to partners of people with HIV and their biological children [12]. South Africa has experienced a steep decline of 60% in under-5 mortality rates during the last 2 decades, accompanied by a 55% decrease in annual incidence of HIV among children between 2010 and 2018 [13, 14]. However, South Africa still lags behind UNAIDS 95-95-95 goals. In 2019, only 59% of 0–15-year-olds with HIV knew their status, and only 67% of these were virally suppressed. These figures are suboptimal compared with 90% and 54%, respectively, for adults with HIV in South Africa in 2019 [15]. Although there has been an emphasis on HIV testing of infants in South Africa, HIV testing in children after infancy has lagged behind and may miss children who were not eligible for infant testing because they were not known to be exposed to HIV or were born into settings where access to infant testing was limited [16, 17]. The objective of this study was to assess the cost-effectiveness of a routine PITC strategy compared with no PITC in various pediatric care settings in South Africa.

METHODS

Analytic Overview

We used the Cost-Effectiveness of Preventing AIDS Complications Pediatric (CEPAC-P) model to simulate a cohort of children aged 2–10 years (mean age, 6.29 years), presenting to a range of clinical settings in South Africa [18]. We compared the cost-effectiveness of 2 strategies: (1) a routine provider-initiated pediatric HIV testing and counseling (PITC) program, consisting of a rapid HIV test routinely offered to children who visit 1 of the clinical settings, with confirmatory testing per national guidelines in case of a positive test result, and (2) a comparator strategy without PITC in each setting, which included only existing testing practices in the general pediatric population in South Africa (eg, testing of some children presenting with clinical illness suggestive of HIV). We simulated 4 clinical settings:

outpatient (for management of illness only), inpatient, TB, and malnutrition clinics. The PITC strategy included a 1-time HIV test at simulation start to reflect testing at initial presentation to each health care setting. In both strategies, CWH who were not diagnosed at the initial health care visit for any reason (eg, lack of test offer, lack of result return) could be diagnosed later, either by presenting to care after an opportunistic infection (OI) or through a modeled testing probability derived from annual testing rates in the general population in South Africa [19].

Population

We simulated a pediatric cohort not previously known to have HIV and seeking care at each care setting. The primary modeled difference between the 4 care settings was prevalence of undiagnosed HIV among children presenting for care, derived from published reports of PITC program outcomes: outpatient departments 1.0% (South Africa), malnutrition clinics 15.0% (Sub-Saharan Africa), inpatient wards 17.5% (Sub-Saharan Africa), and TB clinics 50.0% (South Africa) (Table 1; Supplementary Table 2) [20–32]. In the absence of specific data about the characteristics of children receiving care in each setting, we modeled a cohort of children of aged 2–10 years, based on data from CWH receiving care in the IeDEA network Sub-Saharan African region [18], and assumed the same age distribution of children presenting to care in all 4 care settings. The lower bound of 2 years was chosen to reflect a population mostly no longer at risk for postnatal infection through breastfeeding, beyond the age range of most EID programs, and entirely eligible for testing with rapid diagnostic (serologic) tests [33, 34].

Model Structure

The CEPAC-P model is a first-order Monte Carlo simulation model of pediatric HIV acquisition, disease progression, diagnosis, and treatment, reported in detail and validated for children in South Africa in previous publications (Appendix) [35–37]. Previous model validation and calibration analyses were conducted to match observed mortality and OI rates for children off and on ART and rates of switch from first-line to second-line ART [35, 36]. In the model, children who are diagnosed with HIV via PITC have a probability of linking to HIV care and ART. Once on ART, children are assigned an age-dependent probability of suppressing HIV RNA to <400 copies/mL by 24 weeks on ART; after this initial suppression, there is a monthly risk of “late failure” for the duration of the ART regimen. Children face a monthly probability of being lost to care and, subsequently, a monthly probability of returning to care. CWH experience monthly risks of OI- and HIV-related mortality, stratified by age and CD4% (<60 months) or absolute CD4 count (>60 months), and monthly risks of non-HIV-related mortality. Full details of the CEPAC-P model structure are available at: <https://www.massgeneral.org/medicine/mpec/research/cpac-model>.

Table 1. Model Input Parameters for Newly Tested Children 2–10 Years of Age With Undiagnosed HIV in South Africa

Variable	Base Case Value	Range Examined ^a	Reference
I. Clinical input parameters			
Ia. Pediatric cohort characteristics			
Age, mean (SD), y	6.29 (2.64)	0.5x–1.2x	[18]
Male, %	48.84		[38]
Prevalence of undiagnosed HIV, %	1.0	0.1–50.0	[8, 20–32]
HIV incidence, %	0		Assumption
Ib. Clinical data, undiagnosed HIV-infected children			
CD4 at diagnosis, mean (SD) ^b		0.25x–2x	[18]
2–4 y, %	22 (11)		
5–8 y, cell count, cells/μL	638 (452)		
9–10 y, cell count, cells/μL	449 (348)		
HIV RNA distribution at diagnosis, %			[39]
>100 000 copies/ml	42		
30 000–100 000 copies/mL	28		
10 000–30 000 copies/mL	18		
3000–10 000 copies/mL	8		
500–3000 copies/mL	2		
20–500 copies/mL	1		
II. HIV testing characteristics			
Background testing (standard of care)			
Monthly background test frequency, %	2		[22]
Rapid HIV test cost, \$	1.47		[40]
Sensitivity/specificity of rapid HIV test, %	99/98	85–100	[43]
Linkage to HIV care and ART, %	71		[41]
Routine PITC testing (intervention)			
Rapid HIV test cost, ^c \$	4.7	0–35	[40, 42]
Sensitivity/specificity of rapid HIV test, %	99/98	85–100	[43]
Test acceptance probability, %	97	60–100	[44, 45]
Linkage to HIV care and ART, %	71	50–100	[41]
Variable	Base Case Value	Range Examined	Reference
III. ART regimen			
	ABC + 3TC + DTG	ABC + 3TC + LPV/r	
ART outcomes			
Probability of initial suppression, ^d %	79.1/67.0	82.7	[47, 48]
Probability of failure, % (monthly)	0.2	0.2	[49]
Monthly loss to follow-up after ART initiation, %	0.2		[50]
Cost by age, \$ (monthly)		0.1x, 0.5x, 2x	[51–53]
1–2 y	8.51	26.61	
3–4 y	10.95	34.22	
5–7 y	9.21	32.31	
≥8 y	6.25	26.60	
Order of ART regimens	First-line DTG regimen, second-line LPV/r regimen		[46]
IV. Care costs, US\$			
Acute OI event costs			
OIs, age >60 mo	220–740	0.1x, 0.5x, 2x	[54, 55]
OIs, age ≤60 mo	870–1540		[56]
Death costs, all causes	549.25		[54]
Routine care costs (on/off ART, male and female), all ages	18.07–140.13	0.1x, 0.5x, 2x	[54, 56, 57]

Abbreviations: 3TC, lamivudine; ART, antiretroviral therapy; DTG, dolutegravir; LPV/r, lopinavir/ritonavir; OI, opportunistic infection; PITC, provider-initiated HIV testing and counseling.

^aSelected values within this range were used to perform univariate and multivariate sensitivity analyses.

^bThis cohort includes children who enrolled in care in 2018, were ART-naïve at enrollment, had CD4 measured <6 months before ART, and initiated ART between 2 and 10 years of age [7].

^cPITC program cost includes the cost of 2 concurrent rapid blood HIV tests, and the fully loaded cost component (ie, training, personnel, counseling, equipment, etc.).

^dDTG-based first-line ART with 79.1% probability of initial suppression was followed by 2 DTG-based re-suppression attempts with 67% probability of initiation suppression.

Model Input Parameters

For this analysis, we derived cohort characteristics, PITC offer and acceptance rates, linkage to care after a positive PITC test, disease progression, ART outcomes, and HIV-related health care costs from published trials and cohort studies in South Africa (Table 1; Supplementary Table 1) [18, 19, 38–57]. We assumed a 97% probability of PITC acceptance and used the published sensitivity (99%) and specificity (98%) of rapid HIV tests [43]. CWH who were detected through PITC had a 71% probability of linking to clinical care [41, 58]. Based on the current WHO pediatric guidelines, we modeled dolutegravir-based (ABC + 3TC + DTG) first-line ART and lopinavir/ritonavir-based (ABC + 3TC + LPV/r) second-line ART (Table 1) [46]. For CWH, we assumed the same absolute CD4 cell count or CD4% at the time of HIV diagnosis in all 4 care settings using data from CWH receiving care in the IeDEA network Sub-Saharan African region (Table 1) [7]. We varied all parameters in univariate and multivariate sensitivity analyses to investigate the impact on the cost-effectiveness results (Table 1).

PITC and HIV-Related Health Care Costs

South African costs were calculated from the health care system perspective. All costs were converted to 2019 US dollars, using South Africa-specific inflation and exchange rates [59]. The PITC program cost was modeled as fully loaded (base case: \$4.70/person tested) and included rapid antibody test kits, laboratory consumables, return of results to children/caregivers, and labor-related costs for laboratory technicians [40, 42]. Additional costs for the PITC program included telephone charges, electricity consumption, consumables such as paper forms, and building space for the program [42]. We used published South African health care costs for children with HIV, including costs for routine care, opportunistic infections, laboratory monitoring, and ART (Table 1; Appendix) [54–57].

Model Outcomes

Model outcomes for the PITC and no PITC strategies included 1-year survival, life expectancy, and lifetime per-person HIV-related health care cost. We projected these results both for the entire cohort of children presenting to each type of health care setting (with HIV prevalence depending on type of site) and for the subset of CWH. To put model results into perspective of the global progress toward the UNAIDS 95-95-95 targets [60], we modeled HIV care continuum outcomes at 1 year after the start of the simulation for both strategies, defined as the percentages of surviving CWH who know their status, who are on ART, and who are virally suppressed.

The incremental cost-effectiveness ratio (ICER) of PITC compared with no PITC was calculated as the difference in discounted lifetime cost between the 2 strategies, divided by the difference in discounted life expectancy (discount rate: 3%/year), for the entire cohort presenting for care [61]. In the absence of

clearly recommended cost-effectiveness thresholds (CETs) for South Africa, several approaches have been suggested: 1× per capita GDP/year of life saved (YLS) based on older WHO suggestions [36, 62], an estimate of \$550–870/YLS based on demonstrated willingness to pay in South Africa [63], and ~\$3200/YLS based on health opportunity costs [58]. Consistent with prior work, we used the health opportunity cost estimate to determine a cost-effectiveness threshold of \$3200/YLS, approximately equal to 0.5× per capita GDP [58, 59, 64, 65].

Sensitivity Analyses

To investigate the impact of uncertainty in model input parameters on cost-effectiveness results for each health care setting, we varied the PITC test acceptance rate, HIV rapid test sensitivity and specificity, linkage to care after a positive PITC test result, OI rates and death from OI (varied together), ART and HIV care costs (varied together), PITC program cost, and the undiagnosed HIV prevalence, as well as key combinations of these parameters (Table 1). Additional setting-specific parameter combinations can be evaluated in a decision support tool, available at: <https://www.who.int/publications-detail/paediatric-hiv-testing-strategy-decision-tool>. [66]

Finally, we simulated clinical characteristics that might reflect children with more severe underlying illness, for example, children presenting to care at TB and malnutrition clinics. In these scenarios, we varied presenting CD4/CD4%, age distribution, and risk of death from non-HIV causes.

RESULTS

Base Case

Among CWH presenting to care in any of the 4 settings (assuming age and initial CD4 did not vary by setting, due to lack of these setting-specific data), the PITC program led to a projected 1-year survival of 95% and undiscounted life expectancy (LE) of 32.7 years, compared with a 94% survival and LE of 31.2 years in the no PITC strategy (Table 2, section I). Projected 1-year care continuum outcomes for children presenting to care were markedly improved with PITC (Figure 1; Table 2). In the PITC strategy, 83% of surviving CWH were diagnosed, 80% were on ART, and 64% were virally suppressed; in the no PITC strategy, 45% of surviving CWH were diagnosed (via OI or background testing), 41% were on ART, and 33% were virally suppressed.

Among the entire cohort of children presenting to care, projected results varied by health care setting type, reflecting differences in undiagnosed HIV prevalence. In outpatient settings (undiagnosed HIV prevalence, 1.0%) with PITC, undiscounted LE was 61.97 years, discounted LE was 27.44 years, and discounted lifetime HIV-related cost was \$110/person. Without PITC, undiscounted LE was 61.95 years, discounted LE was 27.43 years, and discounted lifetime HIV-related cost was \$100/

Table 2. Clinical and Cost-effectiveness Results of PITC vs No PITC by Clinical Setting

I. Children With HIV: All Settings	PITC	No PITC
HIV care continuum at 1 y after the start of the simulation ^a		
% survival	95	94
% diagnosed	83	45
% on ART	80	41
% virally suppressed	64	33
Undiscounted life expectancy, y	32.68	31.21
II. Entire Cohort of Children Seeking Care: Setting-Specific Outcomes		
Outpatient setting (1.0% HIV prevalence)		
Entire cohort		
Undiscounted life expectancy, y	61.97	61.95
Discounted life expectancy, y	27.44	27.43
Lifetime discounted per-person cost, \$	110	100
Incremental cost-effectiveness ratio, \$/YLS ^b	1240	-
Malnutrition setting (15.0% HIV prevalence)		
Entire cohort		
Undiscounted life expectancy, y	57.83	57.61
Discounted life expectancy, y	26.03	25.96
Lifetime discounted per-person cost, \$	1460	1380
Incremental cost-effectiveness ratio, \$/YLS ^b	740	-
Inpatient setting (17.5% HIV prevalence)		
Entire cohort		
Undiscounted life expectancy, y	57.09	56.83
Discounted life expectancy, y	25.83	25.69
Lifetime discounted per-person cost, \$	1700	1600
Incremental cost-effectiveness ratio, \$/YLS ^b	730	-
TB setting (50.0% HIV prevalence)		
Entire cohort		
Undiscounted life expectancy, y	47.47	46.74
Discounted life expectancy, y	22.65	22.27
Lifetime discounted per-person cost, \$	4840	4570
Incremental cost-effectiveness ratio, \$/YLS ^b	710	-

Abbreviations: CWH, children with HIV; PITC, provider-initiated HIV testing and counseling; TB, tuberculosis; YLS, year of life saved.

^aThe denominator is the number of CWH alive at month 12.

^bIncremental cost-effective ratios are shown as rounded numbers to the nearest 10.

person. The ICER of PITC compared with no PITC in the outpatient setting was \$1240/YLS. In the other 3 settings, ICERs of PITC vs no PITC were \$710–740/YLS (Table 2, Figure 2; Supplementary Tables 3–6).

Sensitivity Analyses

For CWH, projected care continuum outcomes were most sensitive to varying the combination of test acceptance and linkage to care (Figure 1). An increase from the lowest to the highest published values of test acceptance and linkage to care led to markedly higher projected percentages of CWH who were diagnosed (a relative increase of 38%), on ART (+40%), and virally suppressed (+31%) at 1 year after diagnosis (Figure 1).

For the entire cohort of children presenting to care in each setting, the ICER of PITC vs no PITC was most sensitive to changes in the prevalence of undiagnosed HIV among children presenting to care (Figure 2). The threshold of undiagnosed

HIV prevalence below which the PITC was no longer cost-effective was between 0.2% and 0.3% (Figure 2). Considering that prevalence values in all settings in our analysis were above this threshold, PITC was considered cost-effective in all 4 settings. Above an undetected prevalence of 2%, the ICER remained fairly constant and <\$1000/YLS, driven primarily by the yearly cost of HIV care and ART.

For any setting, the cost-effectiveness of PITC compared with no PITC was most sensitive to variations in PITC program costs, ART and HIV care costs, initial CD4, and age distribution (example for outpatient setting: Figure 3; similar trends for other settings shown in Supplementary Tables 3–6 and Supplementary Figures 1–3). Cost-effectiveness results were less sensitive to changes in OI incidence and OI-related mortality rates, linkage to care after a positive test, test sensitivity, specificity, and acceptance rate (Figure 3; Supplementary Table 3). However, variation in these parameters had a substantial impact on clinical outcomes, particularly on the HIV care continuum (Supplementary Table 3).

In 3-way sensitivity analyses, varying the most influential parameters simultaneously, we identified combinations of PITC program costs, ART and HIV care costs, and undiagnosed HIV prevalence at which the ICER of PITC vs no PITC was <\$3200/YLS (Figure 4). When ART and care costs were lower, PITC program costs were lower, or both, the PITC program became cost-effective at lower undiagnosed HIV prevalence rates (Figure 4).

Varying mortality associated with underlying illness, up to 20-fold from base case for 2 years after presentation to care, did not change our model-based conclusions about the optimal strategy (Supplementary Table 3). Varying both mortality and CD4 at presentation to care had a larger impact, primarily due to variation in CD4 (Figure 3; Supplementary Tables 3–6).

DISCUSSION

We used a validated HIV simulation model to project clinical and economic outcomes of routine PITC offered to all children (aged 2–10 years) who present to pediatric care settings in South Africa. We observed 3 key findings. First, PITC markedly improved projected HIV care continuum outcomes for CWH, regardless of the type of health care setting (outpatient, malnutrition, inpatient, or TB). In the base case analysis, PITC increased the projected percentage of children with HIV who presented to care and knew their status from 45% to 83%, the percentage on ART from 41% to 80%, and the percentage virally suppressed from 33% to 64% at 1 year after the start of the simulation. The UNAIDS strategy to end the AIDS epidemic by 2030 includes the following targets: 95% of people with HIV will know their HIV status, 95% of people with diagnosed HIV infection will receive sustained ART, and 95% of people receiving ART will have viral suppression [67]. Our model results suggest

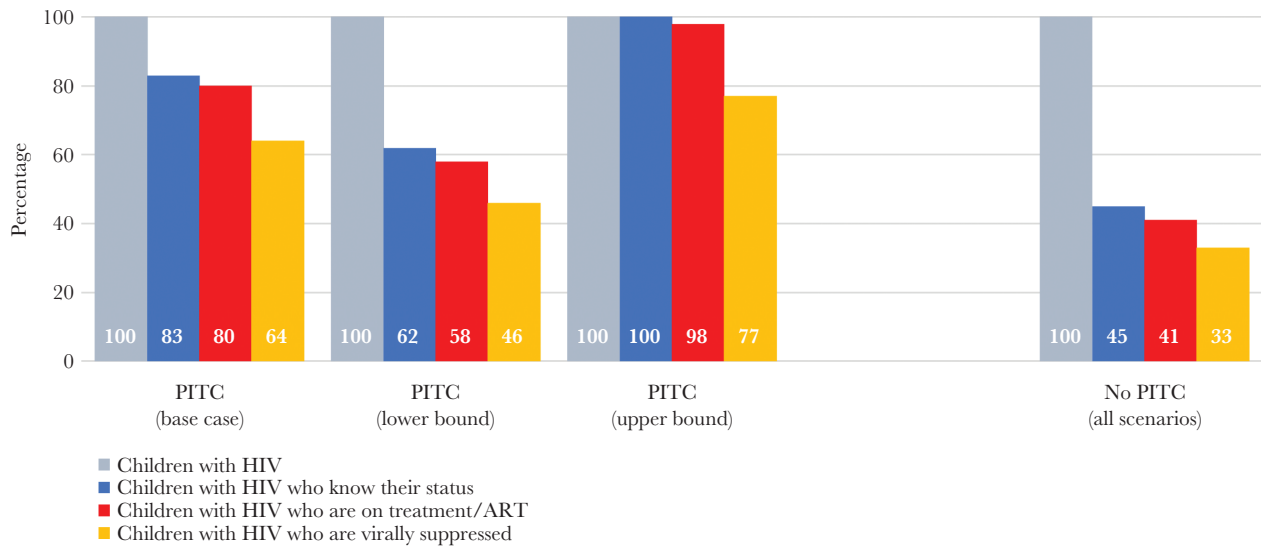


Figure 1. One-year cascade of HIV care in the base case and 2-way sensitivity analysis with varying PITC acceptance rate and linkage to care upon receiving positive test results. We used lower-bound values of 60% for test acceptance and 50% for linkage to care and an upper-bound value of 100% for both. The change of 38%, 41%, and 31% for children who know their status, are on ART, and are virally suppressed, respectively, represents the relative increase from the lowest to the highest value in the HIV care continuum. Abbreviations: ART, antiretroviral therapy; PITC, provider-initiated HIV testing and counseling.

that in all 4 health care settings, offering PITC can make substantial progress toward these targets among CWH who present with illness.

Second, a PITC program could be considered cost-effective as long as the prevalence of undiagnosed HIV among children presenting to a given health care setting exceeds ~0.2%. This finding should encourage countries to implement and strengthen routine testing in the 4 clinical settings evaluated in this analysis. At base case South African costs, the ICER of a PITC program, compared with no PITC program, was stable at ~\$1000/YLS with any prevalence of undiagnosed HIV >2%.

Third, the cost-effectiveness of the PITC program was sensitive to several key costs, including ART, HIV care, and PITC program costs, as well as clinical parameters such as monthly risks of disease progression and mortality. With lower ART and care costs, the undiagnosed HIV prevalence at which PITC was cost-effective became lower (Figure 4). Such lower costs will become more relevant over time; ART costs in particular are likely to decline in the future [53]. Published data on routine PITC program costs—including not only assays but also implementation costs—are limited for pediatric populations and vary widely, depending on the clinical setting and reported cost

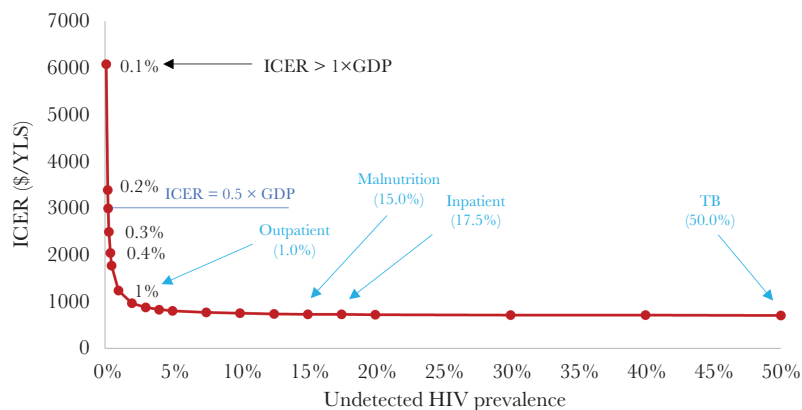


Figure 2. Effect of undiagnosed HIV prevalence on the ICER of the routine PITC strategy vs no PITC in the base case analysis. The blue arrows point to the values of undiagnosed HIV prevalence that correspond to specific clinical settings—1.0% prevalence in outpatient centers, 15.0% prevalence in malnutrition clinics, 17.5% prevalence in inpatient wards, and 50.0% prevalence in TB clinics. The data point labeled ICER = 0.5x GDP is the cost-effectiveness threshold. The data points labeled ICER > 1xGDP and ICER > 0.5xGDP represent the undiagnosed HIV prevalence values at which the ICER of the PITC strategy vs no PITC becomes greater than 1x or 0.5x of the GDP of South Africa, respectively. Abbreviations: GDP, gross domestic product; ICER, incremental cost-effectiveness ratio; PITC, provider-initiated HIV testing and counseling; TB, tuberculosis; YLS, years of life saved.

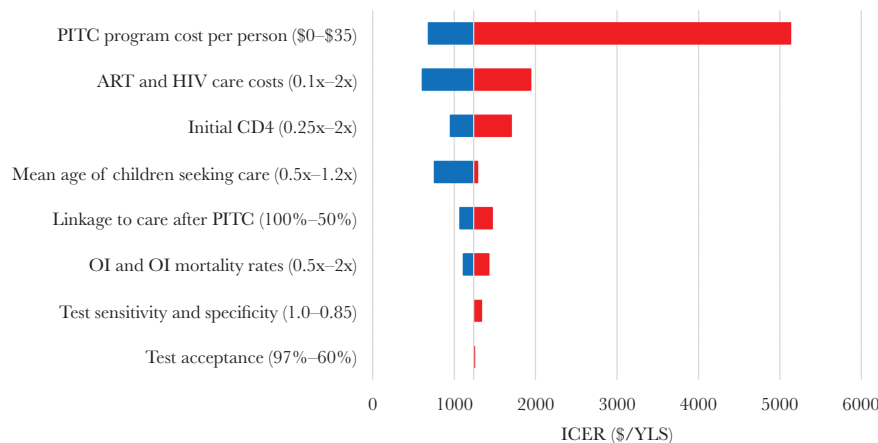


Figure 3. Univariate sensitivity analyses examining the impact of variation in individual input parameters on the ICER of the routine PITC program vs no PITC in the outpatient setting. Key parameters varied in sensitivity analyses are shown on the left. Values in parentheses indicate the range examined (from the value leading to the lowest ICER to the value leading to the highest ICER). The vertical line between the blue and red bars indicates the base case ICER value in the outpatient setting (\$1240/YLS). Blue bars indicate values of parameters at which the ICER is lower than in the base case, and red bars indicate values of parameters at which the ICER is higher than in the base case. Longer bars indicate parameters to which cost-effectiveness results were more sensitive. Abbreviations: ICER, incremental cost-effectiveness ratio; PITC, provider-initiated HIV testing and counseling; YLS, year of life saved.

components [68]. For this analysis, we included the costs of personnel, counseling, and equipment for the PITC program and found that variations in the total delivery cost for the program markedly impacted cost-effectiveness results [40].

This study was subject to several limitations. First, we excluded children age <2, who may account for substantial HIV-related mortality and health care utilization; although young children eligible only for virologic assays are beyond the scope of the current study, they have been the focus of previous CEPAC work [37]. Second, there is a lack of current, South Africa-specific data for each of the 4 clinical settings about age of presentation to care, prevalence of undiagnosed HIV, and CD4/CD4% among children with HIV seeking care. We therefore derived HIV prevalence data from multiple countries in Sub-Saharan Africa (ie, South Africa, Zimbabwe, Malawi, Cameroon, Botswana); we derived age and CD4/CD4% data from the IeDEA consortium; and we assumed that the 4 health care settings differed only with respect to undiagnosed HIV prevalence. In reality, these settings likely differ in the age and CD4/CD4% of children presenting to care, costs of implementing PITC, and test acceptance rates. For example, children in TB clinics may present with lower CD4, but may also have higher HIV test acceptance and linkage to care, compared with children in outpatient settings. To address these limitations in clinical data, we varied all uncertain model parameters over a broad range of values in sensitivity analyses. We found substantial impact of varying CD4/CD4%, but minimal impact of varying non-HIV mortality on the ICER of PITC vs no PITC. Third, although many of our clinical inputs are likely to be generalizable across settings and thus were derived from several Sub-Saharan African countries, we deliberately used only South African health care costs. South African data

are limited in the CD4- and OI-stratified structure needed to fit the CEPAC-P model; more recent data encompassing all care components suggest very similar annual HIV-related health care costs to those generated by the CEPAC-P model (\$700–800 per child receiving HIV care) [56, 62, 63]. Additionally, costs of training and mentorship to ensure good uptake of PITC were not included in PITC program costs, as they vary significantly and are not consistently defined in the literature. We varied all cost parameters widely in sensitivity analyses; we found that if HIV-related health care costs were reduced 10-fold compared with the base case, PITC would likely be cost-effective even in general population settings.

There are several policy implications from this work. We simulated cohorts of children in 4 clinical care settings and across a range of HIV testing conditions. A decision support tool that accompanies this analysis can help to apply these results to settings with different characteristics (<https://www.who.int/publications-detail/paediatric-hiv-testing-strategy-decision-tool>). A systematic assessment of pediatric HIV prevalence in different clinical care settings over time (ie, sentinel surveillance studies, as done for malaria) [69] may help to guide use of resources and provide an opportunity to critically review testing strategies at the national, subnational, and facility levels. This will enable a more tailored approach to optimizing case finding in the context of the evolving pediatric epidemic. Additionally, our simulation of universal testing in each setting can easily be used to estimate the impact of pediatric HIV risk-based screening tools, which are being increasingly adopted in a number of countries with the goal of decreasing the number of children needing testing and improving PITC yield [8, 70–72]. The pre- and post-test probabilities of HIV generated by clinical screening tools can be used as inputs to the decision support

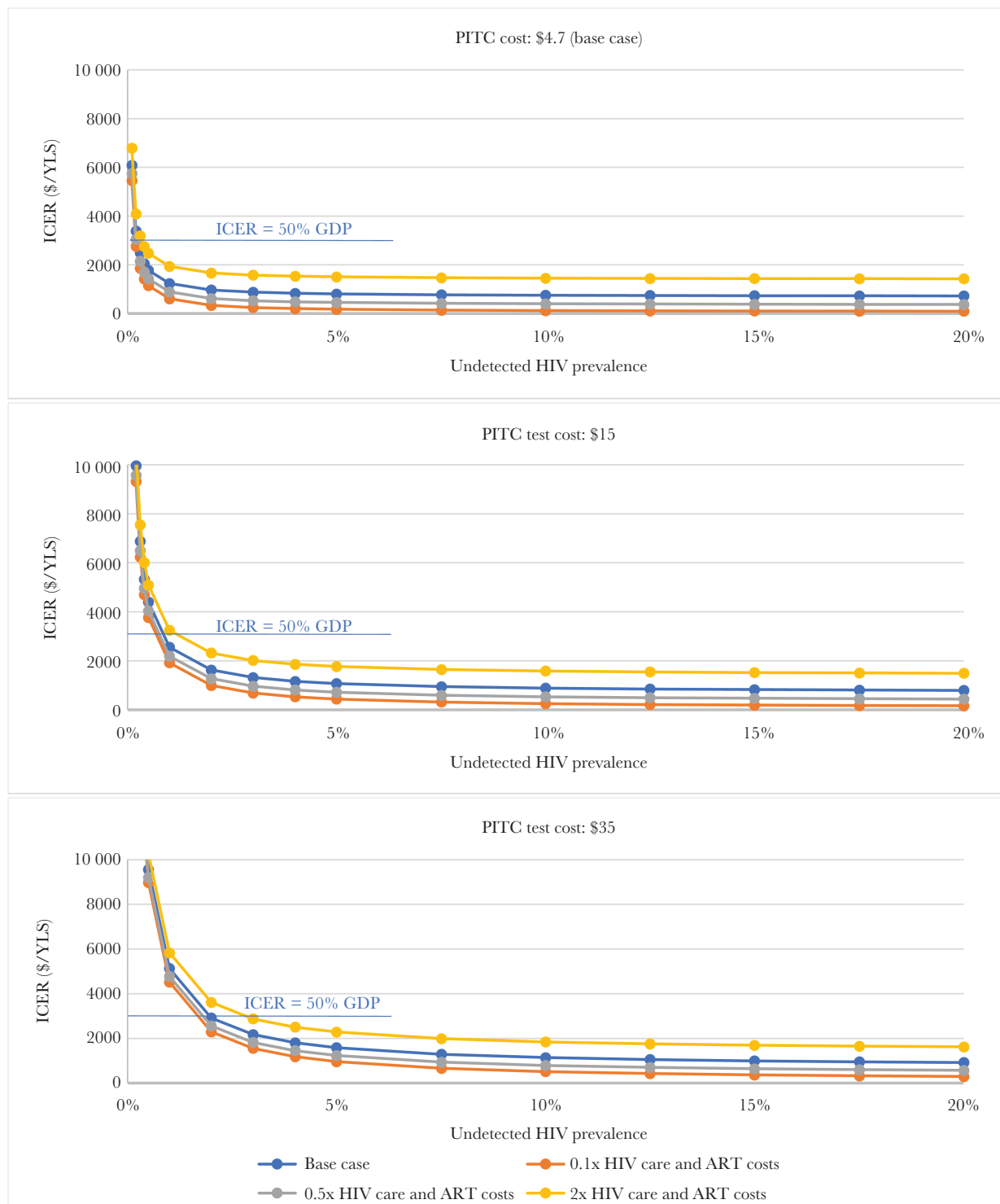


Figure 4. Effect of undiagnosed HIV prevalence on the ICER of the routine PITC program vs no PITC in a 3-way sensitivity analysis. Varying prevalence of HIV (0.1%–20%) is displayed on the x-axis, and the ICER corresponding to each prevalence value is displayed on the y-axis. PITC test costs are shown in the base case (\$4.70) and in sensitivity analyses (\$15 and \$35). The blue line indicates base case values of HIV care and ART costs. Orange, gray, and yellow lines indicate HIV care and ART costs at 0.1x, 0.5x, and 2x of the base case values, respectively. Abbreviations: ART, antiretroviral therapy; ICER, incremental cost-effectiveness ratio; PITC, provider-initiated HIV testing and counseling; YLS, years of life saved.

tool (<https://www.who.int/publications-detail/paediatric-hiv-testing-strategy-decision-tool>) to estimate the clinical benefit and costs of the screening tools, compared with testing no children or testing all children in a given setting.

In conclusion, routine PITC for children presenting to outpatient, inpatient, malnutrition, and TB health care settings in South Africa will markedly improve HIV care cascade outcomes and enable substantial progress toward the 95-95-95

targets [67]. Routine PITC testing of children in these settings will be cost-effective in South Africa if the undiagnosed HIV prevalence exceeds 0.2%. These findings support current recommendations to implement and expand routine PITC for children in outpatient, inpatient, tuberculosis, and malnutrition clinical settings.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Financial support. This work was supported by the World Health Organization. Additional support for model development was provided by the US National Institutes of Health (NICHD R01 HD079214).

Disclaimer. The content is solely the responsibility of the authors and does not necessarily represent the official views of the World Health Organization or the National Institutes of Health.

Potential conflicts of interest. The authors have declared that no conflicts of interest exist. All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Patient consent. This study does not include factors necessitating patient consent.

Acknowledgments

The authors gratefully acknowledge the WHO/CEPAC Pediatric Testing Collaboration Steering Committee members, including Ravi Bhairavabhotla, Jeannie Collins, Helen Dale, Sophie Desmonde, Landon Myer, Marie-Louise Newell, Andrew Phillips, Gayle Sherman, Emilia Rivadeneira, and Paul Revill, as well as the CEPAC-Pediatric Research Team.

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