Finding and treating early-stage HIV infections: A cost-effectiveness analysis of the *Sabes* study in Lima, Peru

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Summary

Background *Sabes*, a treatment-as-prevention intervention among men who have sex with men and transgender women in Lima, Peru, was developed to identify HIV during early primary infection (<3 months from acquisition) through monthly serologic assays and HIV RNA tests. Newly diagnosed individuals were rapidly linked to care and offered to initiate ART. In this study we sought to study the cost-effectiveness of *Sabes* compared to the standard of care (SOC) for HIV testing and initiation of treatment.

Methods We adapted a compartmental model of HIV transmission to evaluate the cost-effectiveness of the *Sabes* approach compared to the SOC using a government health care perspective, 20-year time horizon, and 3% annual discounting. We estimated the proportion of cases of HIV detected during early primary infection, reduction in HIV incidence and prevalence, incremental cost-effectiveness ratio (ICER), and net monetary benefit. We analyzed costs using data from the *Sabes* study, the Peruvian Ministry of Health, published literature, and expert consultation.

Findings The *Sabes* intervention is projected to identify 9294 early primary HIV infections in Lima, Peru over 20 years. The intervention costs $6,896 per early primary infection diagnosed and by 2038 is expected to decrease the fraction of early infections among prevalent infections by 62%. *Sabes* is expected to improve health, resulting in greater total discounted QALYs per person than the SOC (16·7 vs 16·4, respectively). *Sabes* had an ICER of $1431 (22% per capita GDP in Peru) per QALY compared to SOC.

Interpretation Our analysis suggests that in Lima, Peru the *Sabes* intervention could be a cost-effective approach to reduce the burden of HIV even under stringent cost-effectiveness criteria. This finding suggests that programs that use frequent HIV testing, rapid linkage to care and initiation of ART should be considered as part of a comprehensive HIV prevention strategy.

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Keywords: HIV prevention; Acute infection; Early primary infection; ART; Mathematical model; Cost-effectiveness

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Research in context

Evidence before the study

The use of antiretroviral therapy (ART) to achieve viral suppression and limit onward HIV transmission is an effective way to combine individual health and public health benefits. We reviewed the literature to identify studies which investigated the cost-effectiveness of HIV detection during early primary infection by searching the following terms on PubMed, between 2011 and October 2021, with no language restrictions: "HIV" AND ("acute" OR "early" OR "early primary") AND ("MSM" OR "men who have sex with men" OR "transgender" OR "transgender women") AND ("treatment" OR "antiretroviral therapy" OR "*ART") AND ("model") AND ("cost-effectiveness"). We identified four relevant cost-effectiveness studies. One study found that HIV screening and early treatment initiation is a cost-effective approach in the UK and that ICERs for MSM were well below the typical UK willingness to pay threshold. Another study among men who have sex witih men (MSM) in San Francisco found that high PrEP coverage in combination with earlier ART would produce the greatest reduction in new infections, but also incur the highest cost. Therefore, the authors proposed that without a substantial increase to San Francisco's HIV budget, the most advisable strategy is initiating ART earlier while maintaining current PrEP strategies in this population. A third study investigated the impact of HIV screening in STD clinics, emergency departments, and inpatient units and found that when the benefits of reduced transmission to partners from early diagnosis were included, screening in settings with less-advanced disease stages and initiating treatment with ART earlier in the course of infection was cost-saving compared to screening later in the course of infection. Another study found that symptom-based viral load testing to detect HIV during acute infection prevents more infections than annual antibody screening. We identified two additional studies from Lima, Peru that investigated the impact and cost-effectiveness of combined HIV prevention scenarios among transgender women (TW) and PrEP among MSM and TW. These studies found that strategic PrEP interventions could be a cost-effective addition to HIV prevention strategies, but that a considerable expenditure would be required to achieve substantial reductions in HIV incidence. They found that that investments in HIV services for TW in Lima would be cost-effective, even under stringent cost-effectiveness criteria and that increasing HIV testing rates and condom use, along with reducing PrEP costs will be key to reducing HIV incidence.

Added value of this study

Our study investigated the cost effectiveness of combining routine serologic assays and tests for HIV RNA with rapid linkage to care, and immediate initiation of antiretroviral therapy for newly diagnosed individuals in Lima, Peru. The intervention was utilized in the *Sabes* study and we found that rapid linkage to care was feasible, acceptable, and effective for MSM and male-to-female transgender persons (TW) at high risk for HIV acquisition in Lima. We found that early intervention (detection of HIV and rapid initiation of ART), especially during acute HIV infection when viral load is high, is cost-effective due to lower health care costs and reduced HIV transmission among MSM and TW in Lima, Peru. Our analysis suggests that the *Sabes* intervention may be a cost-effective approach to reducing the burden of HIV in vulnerable and high-risk populations in urban, epidemic hotspots such as Lima, Peru. Many upfront costs to deliver the intervention are offset by longer-term healthcare savings.

Implications of all the available evidence

Given the public health impact of the HIV epidemic, it is essential to capitalize on and scale-up interventions with known effectiveness to reduce onward HIV transmission in a cost-effective manner. Programs such as *Sabes* that implement frequent HIV testing for those at highest risk of HIV acquisition, rapid linkage to care, and immediate initiation of ART for those who test HIV-positive may offer a cost-effective approach despite its high upfront cost. This approach should be considered in combination with other HIV prevention approaches such as PrEP and future work should seek to determine the comparative cost effectiveness of various complimentary HIV interventions.

Introduction

Globally, current HIV testing and treatment programs are failing to effectively curtail the HIV epidemic. In Latin America specifically, HIV is concentrated in key populations of men who have sex with men (MSM) and transgender women (male-to-female transgender persons, TW) who are disproportionately impacted by the epidemic.[1] The prevalence and incidence rates in Lima, Peru are comparable to those observed in some heterosexual populations of sub-Saharan Africa.[2]

Early diagnosis in combination with rapid viral suppression is an effective way to combine individual and public health benefits. The approach of diagnosing HIV during acute or early primary infection and initiating early HIV treatment rapidly suppresses viremia resulting in improved clinical outcomes for the individual. It also benefits public health by limiting onward HIV transmission and has shown to be a cost-effective approach to HIV prevention.[3–7] The UNAIDS 90-90-90 guidelines set targets for scale-up of HIV treatment to reduce onward transmission, which rely on achieving undetectable viral loads in over 72% of people living with HIV (PLWH) by the year 2020.[8,9] It was estimated that only a small proportion (11-12%) of PLWH were virally suppressed shortly before the 2020 goalpost for the 90-90-90 target;[10,11] reaching the new UNAIDS 95-95-95 benchmark in Peru by 2030 will require both an expansion of existing programs, and new strategies for

diagnosing HIV, linking individuals to HIV care, and initiating ART.

Aggressive treatment as prevention (TasP) initiatives have been adopted by some national governments, including the United States in 2019, as part of programs to end the HIV epidemic.[12] They aim to diagnose all individuals infected with HIV as early as possible, and treat HIV infections rapidly and consistently to ensure sustained viral suppression. TasP interventions have the potential to severely limit HIV transmission, and although resource intensive, they are projected to be cost-effective in different heterosexual, MSM, and TW populations.[13–15]

We sought to assess the potential impact of a TasP approach among MSM and TW in Lima, Peru that detects HIV infection during acute or very recent (<3 months) infection and initiates ART rapidly to reduce onward transmission.[16] The *Sabes* study ("¿Sabes?" in Spanish means "Do you know?") aimed to intervene shortly after HIV acquisition, when the risk of onward transmission is thought to be highest, to decrease the period of time between HIV acquisition and viral suppression in order to prevent new infections.[17,18] This TasP intervention employed both frequent testing and the use of HIV RNA tests to identify HIV infections soon after acquisition, a more complex and costly approach than annual testing with serologic tests, which is often standard of care. The study was conducted by enrolling HIV-uninfected MSM and TW at high risk for HIV acquisition, using previously defined criteria. Participants attended monthly visits to test for HIV using serology and RNA, and newly diagnosed PLWH were rapidly linked to care using peer health navigators. Estimates show that, if this intervention were to be scaled-up in Peru to reach 50% of MSM and TW during early HIV infection, 40% of the expected HIV cases would be averted over a 20-year period.[19]

In this paper, we assess the potential economic impact of fully implementing the strategy used in the *Sabes* study in Lima, the capital city of Peru, which has the highest burden of HIV in the country. We estimate the costs, health outcomes, and cost-effectiveness of the *Sabes* approach compared to the standard of care from the perspective of the Peruvian Ministry of Health. To achieve this, we adapted a compartmental dynamic transmission model parameterized with epidemiological data representative of the HIV epidemic among MSM and TW in Lima.

Methods

Analytic overview

We developed a three-part model that included a mathematical model of HIV transmission, a costing analysis, and a cost-effectiveness analysis. The mathematical model compared HIV epidemic outcomes in Lima, Peru between the standard of care and the strategy employed in the *Sabes* study (Figure 1). The costing analysis estimated the costs associated with implementing both the standard of care and the *Sabes* approach. The cost-effectiveness analysis used a government healthcare sector perspective, 20-year time horizon (2018–2038), and 3% annual discount rate for outcomes. We followed recommendations from the ISPOR-SMDM Dynamic Transmission Modeling Task Force, World Health Organization, and the Second Panel on Cost-Effectiveness in Health and Medicine.[20]

Study population

The study population included MSM and TW with and without HIV infection between the ages of 15 and 49 years in Lima, Peru, who had an estimated HIV prevalence of over 10% in 2010.[21] The model was initiated with a population size of 127,100 in 2004. Population size was calculated based on 6% of Peruvian men ages 15-49 reporting sex with another male in 2010, a 95% gender ratio for MSM and TW, and the Peru age pyramid from 2007.[22,23]

HIV screening intervention efficacy

The *Sabes* study, led by the Asociación Civil Impacta Salud y Educación ("*Impacta Peru*") in Lima, Peru, screened patients between July 2013 and September 2015 (*Supplementary Appendix* 1.1).[16] HIV-uninfected individuals were enrolled into the *Sabes* cohort and re-screened monthly for incident HIV infection, for a maximum follow-up time of two years. Individuals who were newly diagnosed during early primary infection (defined as HIV detected within three months of a negative HIV RNA test) were eligible to enroll into a randomized study to assess the impact of the timing of ART initiation. Overall, 3337 participants were screened for HIV, 80% were HIV-negative and 2,109 began monthly HIV testing. Monthly testing identified 256 individuals within 3 months of acquisition of HIV and an additional 12 individuals with incident HIV detected during the acute phase were referred from a local STI clinic. *Sabes* enrolled people with acute infection (seronegative, RNA+) as well as recent infection (seropositive with a negative test within the past 3 months) - combined into one group referred to as "early primary" in this analysis.

HIV transmission model

We adapted a compartmental mathematical model with dynamic transmission that was previously developed to simulate HIV epidemics among MSM and TW in Peru to assess the benefits from the strategy implemented in the *Sabes* study (*Supplementary Appendix* 1.2).[19] The individuals in the simulated population are divided into groups by risk based on the number of male/TW partners in past year (high: ≥5 and low: <5), age (15

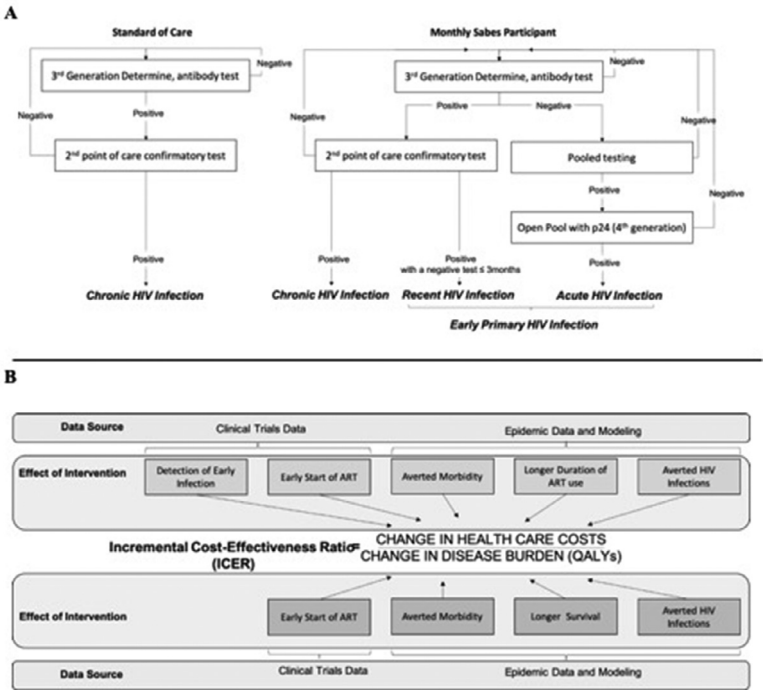

Figure 1. Conceptual diagram of (A) the designed mechanism of effect for the Sabes intervention approach to diagnose early primary infections among high-risk people in Lima, Peru and (B) the accumulation of costs and benefits considered in the cost-effectiveness analysis. Abbreviation: ART, antiretroviral therapy; QALY, quality adjusted life year.

−24 years, 25−34 years, and 35−49 years) and sexual positioning (insertive, receptive and versatile) (*Supplemental Figure* A1.1). The population is additionally stratified by HIV infection status and CD4 cells per mm^3 (early/acute HIV infection, CD4 > 500, CD4 350-500, CD4 200-350, and CD4<200). Infected individuals are assigned to compartments by treatment status (undiagnosed, diagnosed but not on ART, not virally suppressed on ART, and virally suppressed on ART).

The model is parameterized with epidemiological data representative of the HIV epidemic among MSM and TW in Lima. Demographic and sexual behavior characteristics including average number of partners per year, frequency of sex acts, proportion of acts protected by condoms, and lifetime duration of sexual activity are estimated from published data. The mixing between age and risk subgroups is informed directly from data collected in the *Sabes* study. We balanced the overall number of partnerships between population subgroups by continually updating the fraction of partners someone with a given risk, role and age has from the other subgroups. In order to calibrate the model, we fit its outputs to the HIV prevalence and the treatment cascade among MSM and TW in Lima with a calibration procedure described previously.[19]

The HIV epidemic was first simulated without intervention to provide a reference scenario for the evaluation of the impact of the intervention. In this base case scenario, we assumed that incident HIV infections will not be detected during early primary infection under the standard of care due to the use of antibody-based HIV tests and the infrequency of HIV tests. In contrast, intervention scenarios assume that 50% of early primary infections are diagnosed, linked to care, and initiate ART within 1 month of diagnosis.

Universal access to ART (i.e. initiation of treatment regardless of CD4 cell count) for all diagnoses after the year 2018 is assumed with stable rates of HIV diagnosis and constant ART initiation rates maintained until 2038. We also considered an alternative (optimistic) scenario with elevated rates of HIV diagnosis after 2018 to explore the influence of background epidemic conditions on the projected impact of the *Sabes* intervention.

Costing

To estimate the cost of implementing the *Sabes* program outside of the study setting, we first enumerated the types of resources required and gathered data on the local unit costs for each resource (Table 1). We created an annual visit schedule using the current HIV treatment guidelines in Peru, enumerated the healthcare resources required, and applied local unit costs for each product and service. Local costs were directly collected by the Impacta Peru Clinical Trials Unit staff and through interviews with HIV program staff at the Peruvian Ministry of Health central level and health care

Parameter	Value (Range)	Source
Discount rate, %	3% (0%, 5%)	Neumann[32]
HIV incidence rate per 100 person-years	2.4 (1·9–2·8)	Sabes Study
Probability of patient's monthly attendance	0·87 (0·78–0·96)	Sabes Study
Sensitivity of LIAT test	0·99 (0·89–1)	Package insert
Health State Utility*		
Acute infection	0·79 (0·63–0·95)	Expert consultation
CD4+ cells >500	0·73 (0·58–0·88)	Whitham,[33] ranges calculated
CD4+ cells 350-499	0·71 (0·59–0·85)	
CD4+ cells 200-349	0·70 (0·56–0·84)	
AIDS (CD4 <200)	0·67 (0·54–0·80)	
HIV testing costs (2017 USD $)		
Cost of routine monthly HIV test in Sabes	$14·29	Sabes Study
Cost of confirmatory test, early primary infection/seronegative in Sabes	$204·34	Sabes Study
Cost of confirmatory test, chronic infection in Sabes	$5·18	Sabes Study
Cost of routine monthly HIV test – Standard of Care	$3·71	Expert consultation
Cost of confirmatory HIV test – Standard of Care	$5·18	Sabes Study

***Table 1*: Key model inputs.**
Note: *Regional quality of life data with local estimates of health state utility weight values for HIV CD4-count defined health states in Peruvian men was not available and so we had to assume that data from a recent review of published studies was transferrable to this population.[34]

centers (*Supplementary Appendix* 1.3). Other data sources included the *Sabes* study budget and published literature. In order to project the fully scaled implementation costs, we calculated the incremental program cost for each additional HIV infection detected during the early primary infection period that would not have been detected until later with standard testing. A Markov model was developed to calculate the cumulative resources required for 24 months of *Sabes* implementation (study duration).

The analysis used multiple sources of cost information from different years, correcting for inflation with the Consumer Price Index from the Peruvian Central Bank.[24] Local cost data were collected in Peruvian Soles (PEN); the results are presented here in US Dollars (USD 2017). We used a fixed exchange rate of 3·24 PEN for 1 USD corresponding to the mean of the model calibration period (2004-2014).

Health outcomes and cost-effectiveness

The following metrics of effectiveness were evaluated for each scenario over 20 years of intervention: number of new HIV infections, proportion of cases of HIV detected within three months of HIV acquisition, cumulative number and fraction of HIV infections prevented, reduction in HIV incidence rate, changes in HIV prevalence due to the enhanced ART program, total quality adjusted life-years (QALYs), total healthcare costs, cost per HIV case averted, and incremental cost-effectiveness ratio (ICER [$/QALY gained]) (*Supplementary Appendix* 1.4). QALYs were calculated as the sum of person-time in each heath state adjusted for quality of life by multiplying person-time by the corresponding health-state defined utility value (Table 1). All metrics were compared in 100 simulations using the preselected sets of epidemic parameters identified in the calibration procedure with mean results being reported. Given the uncertainty surrounding the estimation of an appropriate incremental cost-effectiveness ratio (ICER) expressed by several authors,[25,26] we considered the historical threshold of one to three times the gross domestic product (GDP) per capita in Peru in 2017 ($6,572) per QALY gained,[27] as well as a more stringent estimate of 18–51% GDP per capita for middle-income countries.[26]

Sensitivity analysis

We performed a univariate sensitivity analysis by re-estimating the cost-effectiveness results with each of the following parameters at low and high reasonable ranges while holding all other parameters constant: utilities from all health states in the model, cost of non-early primary infection diagnosed, cost per case diagnosed during early primary infection, cost of treatment, and discount rate. A scenario analysis estimated the costs, outcomes, and cost-effectiveness of *Sabes* assuming optimistic improvements to the HIV care cascade over time.

Software

Mathematical models were developed as three connected modules using the following software: dynamic transmission in C++, costing in Tree Age Pro, and cost-effectiveness analysis in R version 3·4·2.

Role of the funding source

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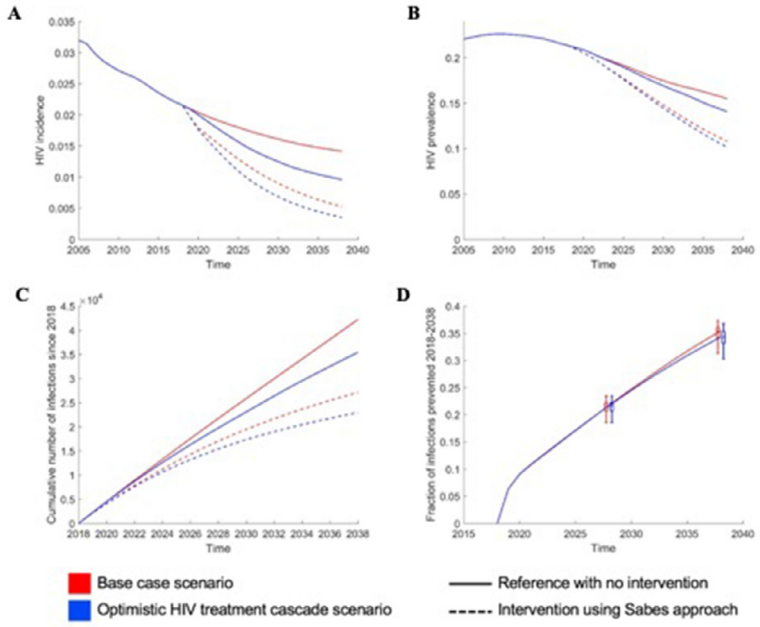

Figure 2. Epidemic projections among MSM and TW in Peru with and without intervention under (i) reference base-case cascade scenario (red lines) assuming with no changes in the calibrated rates of HIV diagnosis and constant ART initiation rates maintained until 2038 and (ii) optimistic cascade scenario (blue lines) assuming improved rates of HIV diagnosis after 2018. Dynamics of (A) HIV incidence (%) among MSM and TW; (B) HIV prevalence (%) among MSM and TW; (C) cumulative number of infections after 2018 and (D) cumulative fraction of infections prevented 2018–2038 calculated using the reference scenario without intervention as a baseline. The lines represent the median projections while box plots reflect estimated variation (interquartile range and 90% uncertainty interval) over 100 epidemic simulations selected in the calibration procedure.

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Results

We estimate that with existing HIV testing and treatment standards there will be 42,527 new HIV infections in Lima, Peru over the next 20 years (Figure 2c). While the overall incidence and prevalence of HIV among MSM and TW in Lima is expected to decline over time under the current SOC, from a prevalence 21·1% in 2018 to 15·5% in 2038, the implementation of the *Sabes* approach would speed the rate of decline to reach 10·9% in 2038. The addition of the *Sabes* strategy to the plethora of ongoing HIV prevention activities would markedly increase the proportion of cases detected during early primary infection and reduce HIV incidence. Our model estimates that the *Sabes* approach would reduce the total number of new HIV infections by 35% compared to the current SOC, to 27,608, in the same time period (Table 2).

The *Sabes* approach to HIV screening modestly improves the average length and quality of life for MSM and TW in Lima. Given the baseline population size of 133,500 MSM and TW in 2018, we estimate the next 20 years will accrue 2,190,000 QALYs in the base case scenario and 2,233,000 QALYs with implementation of the *Sabes* approach. This intervention gains a total discounted 43,000 QALYs in the population from 2018-2038, approximately 0·32 QALYs gained per person (Table 2).

Costs

We estimate that SOC HIV screening of MSM and TW in Lima, Peru cost the healthcare payer $2,057 on average per HIV diagnosis in the base case scenario and that the *Sabes* approach cost the healthcare payer $6,896 per early primary infection identified. These costs were integrated into the dynamic transmission model for calculation of total discounted healthcare payer costs from 2018-2038. The total discounted HIV-related healthcare costs for MSM and TW in Lima was $107·9 million in the base case scenario and $168·3 million with the *Sabes* approach. The incremental cost of *Sabes* is estimated to be $60·3 million over 20 years, averaging an incremental cost of $451 per MSM and TW person.

Cost-effectiveness

Implementation of the *Sabes* program in Lima, Peru is estimated to be cost-effective, with an ICER of $1,431

Result	Reference	Sabes Intervention	Incremental
Acute diagnoses over 20 years, total count	0	9294	9294
Proportion of infected MSM with undiagnosed acute infection in 2038 (%)	1.89%	0.91%	-1.185
Cost of Diagnosis			
Cost of diagnose an Early Primary HIV infection ($)	-	6896	6896
Cost of diagnose a non-Acute HIV infection ($)	2057	2057	0
HIV Infections, 2018-2038, total count	42,527	27,608	-14,919
Total QALYs, total count	2,191,248	2,233,394	42,146
QALYs per person	16.41*	16.73*	0.32*
Total Costs ($)	107,941,221	168,252,419	60,311,197
Costs per person ($)	808.55*	1260.32*	451.77*
ICER ($ per QALY gained)			1431**

***Table 2*: Summary of results.**
Note: Costs are presented in common currency of 2017 US$. Costs and QALYs discounted 3% annually. Time horizon of 2018-2038.
Abbreviations: QALYs, quality adjusted life years; ICER, incremental cost-effectiveness ratio.
*Rounded to 2 decimal positions.
**Results might vary due to rounding. ICER: 1,431 = 451.7693/0.3157002.

per QALY gained compared to SOC (Table 2). This ICER estimate represents 22% of the Peruvian GDP per capita and therefore falls within the cost-effectiveness range defined by Woods et al.[26] for middle-income countries.

Sensitivity analysis

Our results were robust to plausible ranges of each parameter value used in our models assessed in one-way sensitivity analyses (Figure 3). If the rates of HIV diagnosis were doubled under the standard of care, we estimate that the *Sabes* approach would still reduce the estimated number of new HIV infections by 34%. The univariate sensitivity analysis found ICERs ranging from $1,149 to $1,730 per QALY gained, which would fall within various ranges considered to be cost-effective. The greatest drivers of cost-effectiveness were the HIV incidence rate and the cost of the HIV test. The *Sabes* approach was more cost effective in scenarios with higher HIV incidence; assuming an HIV incidence rate of 2.8 per 100 person-years reduces the ICER to $1,232 per QALY; decreasing the cost of monthly HIV testing to $11.40 reduces the ICER to $1,191 per QALY.

Discussion

An expanded HIV testing and treatment program based on the strategy employed in the *Sabes* study, which tests individuals frequently and initiates ART soon after HIV acquisition, was found to be cost-effective in a population of MSM and TW in Lima, Peru over a 20-year period. Implementation of the *Sabes* program was estimated to cost $6,896 per additional case of HIV diagnosed during early primary infection. We estimate that implementing the *Sabes* approach could decrease the fraction of undiagnosed new infections to less than half of what would be expected by 2038 under the current standard of care. Many of the upfront costs associated with implementation of the *Sabes* strategy result in healthcare savings several years in the future.

In recent years there has been much debate about the appropriate selection of thresholds, what the thresholds express, and how thresholds can be used in different settings for cost-effectiveness studies. In line with this body of literature we used two ICER thresholds, the historical threshold of 1 to 3 times the GDP per capita and the novel approach proposed by Woods et al.[26] for middle-income countries of 18-51% of the GDP per capita. This lower threshold aims to reflect the higher opportunity cost of intervention that decision makers face in resource-constrained settings. Although there is no consensus in the literature yet, the use of a lower threshold to determine cost-effectiveness allows for a more realistic and contextual-dependent assessment of feasibility. Using this alternative cost-effectiveness threshold range for Peru ($1,080 to $4,260 USD), the *Sabes* strategy, with an ICER of $1,431 per QALY gained, falls at the lower end of this more stringent threshold. Furthermore, in March 2022, the Peruvian Institute of Health approved an ICER range of $2,663 - $5,326 to determine cost-effectiveness in health-technology assessment.[28] However, as our scenario analysis suggests, a more targeted approach has the potential to reduce the ICER and increase the economic feasibility of the intervention.

We found that the biggest driver of cost-effectiveness of the *Sabes* program was HIV incidence. In a setting with higher incidence, fewer people need to be tested to identify an infection during the early primary stage. Conversely, lower incidence settings increase the number needed to test in order to identify one new case, increasing the cost per early primary infection identified. This suggests the *Sabes* approach may be especially

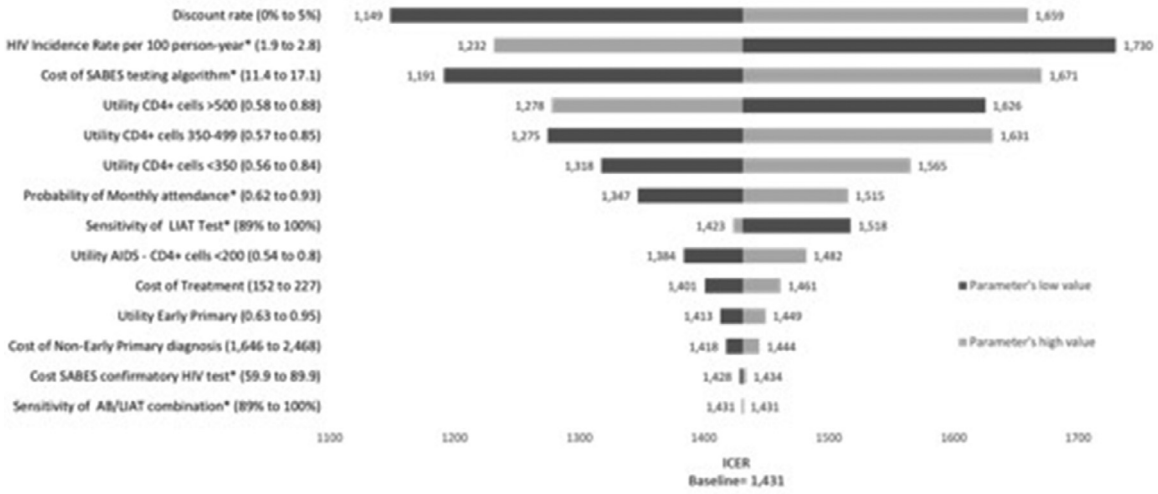

Figure 3. Univariate sensitivity analysis. Univariate Sensitivity Analysis. Costs are varied 20% in either direction; utilities range from their minimum to maximum, avoiding overlapping; HIV incidence rate takes plausible extreme values. The ICER per QALY varies from $1,149 to $1,730, maintaining a very cost-effective value at all extremes. Abbreviations: ICER, incremental cost-effectiveness ratio. QALY, quality adjusted life year.

worthwhile in areas experiencing an HIV epidemic with sustained rapid transmission. The second highest source of variation came from the cost of the HIV RNA test. A lower cost of the HIV RNA tests used in *Sabes* would reduce the total cost of the intervention and increase the cost-effectiveness of the intervention in Lima. Contrary to what was expected, the probability of a patient's monthly attendance for testing showed limited impact on cost-effectiveness.

As governments across the globe prioritize strategies to reduce new HIV infections, TasP interventions offer a cost-effective solution.[13,14,29] Since 2004, the Peruvian government through the Ministry of Health has invested in a national program delivering ART, and national HIV treatment guidelines have recently been updated to include universal treatment initiated at the time of HIV diagnosis. Nonetheless, there is still a testing gap; programs still use third generation serologic HIV tests, and linkage to HIV care is based on passive referral of individuals with HIV. The *Sabes* approach used PCR-based HIV RNA tests (Lab in a Tube: Liat®), which allowed for earlier diagnosis, but at a higher cost than the HIV antibody tests used in current standard of care. Although costly, this approach could provide a successful framework for testing and treatment guidelines for MSM, transgender women, sex workers and others at highest risk for HIV acquisition.

We found the ICER was very sensitive to the discount rate, suggesting the costs associated with the *Sabes* approach are experienced upfront, but lead to long-term benefits over a 20-year period. The cost-per-early primary infection diagnosed may be an appropriate real-time evaluation measure for monitoring program efficiency as the sustainability of the program is evaluated. Although changes in this value—assessed through a sensitivity analysis considering HIV incidence, cost of the Liat HIV test used in the *Sabes* study, and the probability of a patient's monthly attendance—did not meaningfully change the cost-effectiveness conclusions, we observed high variability relative to its original value: from $4,012 to $6,477 USD per HIV infection diagnosed during the early primary infection. A major increase in this cost could compromise the capacity of the Peruvian Health System to afford the intervention, and therefore disincentivize its implementation. Conversely, if the Liat and HIV confirmatory tests became point-of-care—allowing for real-time linkage to treatment—it may greatly increase affordability and incentivize the implementation of the *Sabes* frequent testing and immediate treatment intervention.

Our results do not necessarily imply this strategy is feasible for the Peruvian Ministry of Health, due to competing demands for government resources. The costs associated with monthly testing (the test itself and associated labor costs) are high; the tipping point for adopting this strategy will likely occur with (1) a decrease in HIV RNA test cost allowing the test to be performed on everyone without pooling, and (2) a point-of-care HIV RNA test which would both reduce the labor cost associated with laboratory testing and patient follow-up after an HIV-positive test and allow more timely and complete enrollment of individuals who test HIV-positive. Either, or both, would impact the complex HIV testing algorithm used in *Sabes* (serologic test, followed by pooled NAAT testing of seronegative specimens, followed by deconvolution of positive pools), and allow substantially quicker and cheaper testing algorithms using inexpensive HIV viral load and

qualitative HIV RNA/DNA assays. Hence, a budget impact analysis is recommended to provide a more comprehensive evaluation of the ability of the Peruvian Ministry of Health to adopt this approach as a standard for HIV control.

The results of our study should be interpreted with the following strengths and limitations in mind: first, the size of the MSM and TW population in Lima may be larger or smaller than the estimate we calculated, but we do not expect this will impact the efficiency of the *Sabes* approach. Second, there is always uncertainty projecting epidemic dynamics, but we selected a time horizon sufficiently long to capture longer-term health benefits. Third, pre-exposure prophylaxis (PrEP) was not available in Lima at the time of the *Sabes* study and therefore was not included in this model. Prior studies have found strategic PrEP interventions may be cost-effective but require a substantial expenditure to reduce HIV incidence among MSM and TW population in Lima and elsewhere.[30,31] Future studies may consider testing the efficiencies of expanded PrEP and the *Sabes* approach in combination. And finally, the utility weights for HIV may not be transferable to Peru, but our results are robust to a range of utility values. Our study is unique in that we used empirical parameter values for both the epidemic scenario and costs observed during roll-out of the *Sabes* study in the target population. We believe this makes our results generalizable to the target population of MSM and TW at high risk for HIV acquisition in Lima, Peru.

In summary, we found that implementation of the strategy used in the *Sabes* study, which includes monthly visits to test for HIV using serology and RNA, rapidly linking newly diagnosed PLWH to care using peer health navigators, and initiating ART immediately, is a cost-effective approach to address the HIV epidemic among MSM and TW in Lima, Peru.

Contributors

Study Design: AU, BA, ES, RG, DW, JB, JS, JL, DD, AD
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Interpretation of Results: AU, BA, ES, RG, JB, JS, JL, DD, AD
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Data sharing statement

All aggregated data are available either in the manuscript or appendix. Further requests might require ethical approval and should be discussed with the authors by contacting the corresponding author.

Declaration of interests

BA is an employee of Flatiron Health, an independent subsidiary of Roche. DW all work was completed prior to joining Amazon. For the remaining authors none were declared.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.lana.2022.100281.

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