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Cost-effectiveness of Frequent HIV Screening Among High-risk Young Men Who Have Sex With Men in the United States

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(See the Editorial Commentary by Schackman on pages e1936–7.)

Background. Of new HIV infections in the US, 20% occur among young men who have sex with men (YMSM, ages 13–24), but >50% of YMSM with HIV are unaware of their status. Using Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) data, we projected the clinical benefit and cost-effectiveness of frequent HIV screening among high-risk YMSM from age 15.

Methods. Using a mathematical simulation, we examined 3 screening strategies: Yearly, 6-monthly, and 3-monthly, each in addition to the Status quo (SQ, 0.7–10.3% screened/year, stratified by age). We used published data (YMSM-specific when available) including: HIV incidences (0.91–6.41/100PY); screen acceptance (80%), linkage-to-care/antiretroviral therapy (ART) initiation (76%), HIV transmission (0.3–86.1/100PY, by HIV RNA), monthly ART costs ($2290-$3780), and HIV per-screen costs ($38). Projected outcomes included CD4 count at diagnosis, primary HIV transmissions from ages 15–30, quality-adjusted life expectancy, costs, and incremental cost-effectiveness ratios (ICERs, $/quality-adjusted life-year saved [QALY]; threshold ≤$100 000/QALY).

Results. Compared to SQ, all strategies increased projected CD4 at diagnosis (296 to 477–515 cells/μL) and quality-adjusted life expectancy from age 15 (44.4 to 48.3–48.7 years) among YMSM acquiring HIV. Compared to SQ, all strategies increased discounted lifetime cost for the entire population ($170 800 to $178 100-$185 000/person). Screening 3-monthly was cost-effective (ICER: $4500/QALY) compared to SQ and reduced primary transmissions through age 30 by 40%. Results were most sensitive to transmission rates; excluding the impact of transmissions, screening Yearly was ≤$100 000/QALY (ICER: $70 900/QALY).

Conclusions. For high-risk YMSM in the US, HIV screening 3-monthly compared to less frequent screening will improve clinical outcomes and be cost-effective.

Keywords. Young men who have sex with men; adolescents and young adults; HIV; screening; cost-effectiveness.

Prompt HIV diagnosis and treatment improves individual health and reduces onward sexual transmissions [1]. New HIV diagnoses among young men who have sex with men (YMSM) continue to rise, accounting for 1 in 5 new HIV infections in the United States (US) [2]. Yet more than half of YMSM are unaware of their HIV infection [2]. Adolescent Medicine Trials Network for HIV/AIDS Interventions (ATN) studies 110 and 113 evaluated tenofovir disoproxil fumarate-emtricitabine-based HIV pre-exposure prophylaxis (PrEP) among 15–22-year-olds in the US [3, 4]. ATN 110 reported 4% HIV prevalence at screening among 18–22-year-olds. Despite facilitated access to and adherence support for PrEP use, HIV incidence in ATN 113 was 6/100 person-years among 15–17-year-olds: 10-fold higher than older MSM and 100-fold higher than all US youth [2, 5].

Despite the disproportionate impact of the HIV epidemic on YMSM, there is little evidence to guide how often HIV screening should occur in YMSM [6]. Although noting that some MSM might benefit from more frequent screening, the US Centers for Disease Control and Prevention (CDC) recently found insufficient youth-specific evidence to warrant changing their 2006 recommendation for annual HIV screening among all MSM [6]. We evaluated the clinical benefit and cost-effectiveness of frequent HIV screening strategies for YMSM at high risk of acquiring HIV.

METHODS

Analytic Overview

We used the Cost-Effectiveness of Preventing AIDS Complications (CEPAC) microsimulation model [7] to simulate self-identified, high-risk [3, 4], HIV-uninfected 15-year-old MSM in the US

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Table 1. Input Parameters for a Model of Frequent HIV Screening for High-risk Young Men Who Have Sex with Men in the United States

Population characteristics	Value	Range for sensitivity analysis	Source
Initial age (years)	15	14–30	[3, 4]
Male birth sex (%)	100	100	
HIV prevalence at age <15 years (%)	0	0–6.8	
Annual HIV incidence by age, rate/100PY			
15–17 years	6.41	0.64–12.82	[4]
18–22	3.29	0.33–6.58	[3]
≥23	0.91	0.09–1.82	[12]
Current HIV screening practice (annual probability of HIV detection by age) (%)			
14–15 years	0.7	0.4–3.5	[8, 9]
16–17	1.0	0.5–5	[8, 9]
18–20	10.3	5.2–51.5	[9, 10]
21–24	8.9	4.5–44.5	[9, 10]
25–29	7.6	3.8–38.0	[9, 11]
30–39	6.5	3.3–32.5	[9, 11]
≥40	5.9	3.0–29.5	[9, 11]
Mean CD4 at infection, cells/μL	667	200–800	[5]
Mean HIV RNA at infection, copies/mL	>100 000	-	[13]
Screen characteristics[a]			
Sensitivity (%)	99.6	50–100	[14]
Specificity (%)	99.7	50–100	[14]
Probability of screen offer and acceptance (%)	80	25–100	[15, 16]
Probability of result return (%)	97	50–100	[17, 18]
Probability of linkage to care (%)	76	25–100	[19]
HIV screening program costs (USD 2018)			
HIV screen	38.00	17.96–71.84	[20]
Completed reactive test[b]	76.42	36.12–144.46	[20, 21]
Antiretroviral therapy (range, 1st through 6th available regimen)			
Efficacy (%)[c]	93–81	-	[22–24]
Cost/month (USD 2018)[d]	2290–3780	0.5–2.0x base case	[25, 26]
Loss to follow-up (rate/100PY)			
Adherence >95%	0.1	-	[27]
Adherence <50%	84.5	41.5–498.6	[27]
Return to care (rate/100PY)	18.1	18.1–100	[28]
Onward transmission (rate/100PY), by disease stage and HIV RNA			
Acute infection, off ART[a]	86.1	0–262	[13, 29, 30]
Acute infection, on ART[a]	9.5	0–19	[29–31]
>100 000 copies/mL	16.5	0–33	[29]
>10 000–100 000 copies/mL	14.8	0–30	[29]
>3000–10 000 copies/mL	7.6	0–33	[29]
>500–3000 copies/mL	3.8	0–16	[29]
≤500 copies/mL[e]	0.3	0–0.6	[29]

Abbreviations: ART, antiretroviral therapy; PY, person-year; USD 2018, 2018 US dollars.

[a] Screen sensitivity and specificity were the same for both the acute and chronic phase. The duration of acute infection is 2 months in the base case (sensitivity analysis range: 0–6 months).

[b] Includes costs of confirmatory testing and counseling.

[c] Antiretroviral efficacy is defined as the rate of suppression of HIV RNA <400 copies/mL at 48 weeks.

[d] ART costs were based on averages for integrase-based regimens: $2290; protease inhibitor-based regimens: $2670; and salvage regimens: $3780.

[e] Although recent data from adults suggest 0 transmissions occurring from people with HIV with plasma HIV RNA durably suppressed to <50 copies/ml, we lack data to apply the same zero risk to adolescents and young adults, who often have less consistent virologic suppression. We therefore apply a transmission risk of 0.3/100PY to the lowest modeled RNA stratum based on the available data.

Additional details of inputs, including quality-of-life utility weights, may be found in Supplementary Table 2 [32, 33].

who faced age-stratified risks of HIV infection over their lifetimes (Table 1). High risk was defined based on ATN 110/113 enrollment criteria, including recent history of condomless anal intercourse, sexually transmitted infection, or multiple sexual partners. We modeled the *Status quo* (SQ), reflecting existing patterns of HIV screening for YMSM (screened at least once, with frequency ranging by age, Table 1 and Supplementary Table 1) [8–11]. We also modeled 3 more frequent HIV screening strategies performed in addition to SQ screening between ages 15–30 years: Yearly, 6-monthly, and 3-monthly.

We projected mechanisms of HIV detection, care continuum outcomes (proportions diagnosed, linked to care, retained in care, and virologically suppressed), clinical benefits, and costs. We report incremental cost-effectiveness ratios (ICER: difference in cost divided by difference in quality-adjusted life expectancy) for each strategy compared to the next least costly alternative, from a health-care sector perspective (see Supplementary Material). Clinical outcomes and costs are reported undiscounted and discounted at 3%/year, including health and economic benefits attributable to reduced primary transmissions. We defined a strategy as "cost-effective" if its ICER fell below a willingness-to-pay threshold of $100 000/QALY [34]. We report clinical outcomes for the following 4 groups: 1) Initial cohort, excluding primary transmissions from members of this cohort to others; 2) People who acquire HIV through age 30, a subset of the Initial cohort; 3) People who acquire HIV in their lifetimes, a subset of the Initial cohort; 4) Expanded cohort: the Initial cohort and one generation of primary transmissions from members of the Initial cohort to others. In the Expanded cohort, while we modeled HIV incidence, health outcomes, and costs occurring at all ages, we include HIV transmissions arising only from those aged 15–30 years. We report cost-effectiveness outcomes for the Initial and Expanded cohorts.

Model Structure

The CEPAC model is a validated Monte Carlo, state-transition microsimulation model of HIV disease and treatment [7]. Full details of the model, including graphical depictions, are available at https://www.massgeneral.org/medicine/mpec/research/cpac-model. YMSM enter the model at age 15 without HIV and are simulated in monthly cycles through their lifetimes until death.

HIV Disease and Screening

We define HIV incidence as new infections acquired by members of the Initial cohort. People who acquire HIV are assigned user-specified characteristics, including age, CD4 count, and HIV RNA. In the absence of effective antiretroviral therapy (ART), CD4 declines monthly. Each month, modeled patients face risks of opportunistic

infection and mortality, determined by current age and CD4 count. HIV diagnosis can occur via 1) SQ of HIV detection (ie, screening and testing currently occurring), 2) testing after developing an opportunistic infection, or 3) the more frequent screening strategy (Yearly/6-monthly/3-monthly), which is implemented from ages 15–30. Screen offer and acceptance are assumed to be conditionally independent [35] from previous and subsequent instances; test results are assumed not to impact behavior (ie, no change in condoms used after a negative screen).

Patients who link to care and are prescribed ART experience an initial modeled probability of virologic suppression, and an increase in CD4 count. Those with initial virologic suppression face monthly risks of later virologic failure. At any time (after screening or linkage to care), patients face monthly risks of loss to follow-up; those lost experience a monthly probability of returning to care or return after developing an opportunistic infection.

HIV Transmission

We define primary HIV transmission as one generation of new infections that are transmitted from members of the Initial cohort with HIV to people outside this group (the Expanded cohort). The rate at which a person transmits HIV to others is a function of plasma HIV RNA. HIV RNA levels and thus transmission rates vary by stage of infection (acute and chronic) and response to ART (see Supplementary Material).

Model Inputs

HIV Disease and Screening

Age-stratified risks of incident HIV infection were derived from ATN 110/113 and published sources (Table 1). All screening strategies used a fourth-generation HIV immunoassay (sensitivity/specificity: 99.6/99.7%) [14]. Age-stratified SQ screening rates were derived from survey studies [8, 10, 11] and calibrated to CDC data on stage of disease at diagnosis [9]; this resulted in a 0.7–10.3% annual probability of detection, varying by age (Supplementary Table 1). In the frequent screening strategies, we assigned an 80% conditionally independent, combined probability of being offered and accepting HIV screening at each opportunity [15, 16], 97% probability of receiving a result [17, 18], and 76% probability of linkage to care and ART receipt after a positive screen, based on YMSM-specific data when available [19]. For the annual, 6-monthly, and 3-monthly strategies this translates to 78%, 95%, and 99% annual probabilities of receiving a screening program test result, respectively, which are constant across age groups. Screening costs were $38.00 per screen, plus an additional $76.42 per completed reactive screen reflecting costs of confirmatory testing and counseling [20, 21]. ART costs ranged from $2290–$3780/month, depending on regimen (Table 1 footnote) [25, 26].

HIV Transmission

Transmission rates were 0.3–86.1 transmissions/100 person-years, varying by HIV RNA levels, with the highest transmission rates for those with acute infection and not yet taking ART (Table 1) [29–31]. Costs associated with averted transmissions included clinical care, laboratory monitoring, and ART (see Supplementary Material).

Sensitivity Analyses and Additional Analyses

To understand the robustness of our findings in the face of uncertainty in underlying data and assumptions, we undertook 1-way sensitivity analyses (varying single parameters through plausible ranges noted in Table 1) and multiway sensitivity analyses (varying the most influential parameters together) [36]. Additional analyses included scenarios in which: people enter the model at older ages, because a screening policy may be implemented starting at ages older than 15; 20–50% of the population proves "hard-to-reach," refusing screening despite additional $20/screen to offer screening; cost-effectiveness outcomes are examined over a 15-year horizon (vs lifetime in the base case); HIV screening intervals are as frequent as monthly; the age distribution of transmissions averted varies; and, given that youth may attach different values to preference-based health-state utilities than adults [37, 38] we report ICERs in $/year-of-life saved (YLS).

Additional details of methods (Supplementary Tables 1 and 2) and sensitivity analyses are provided in the Supplementary Materials.

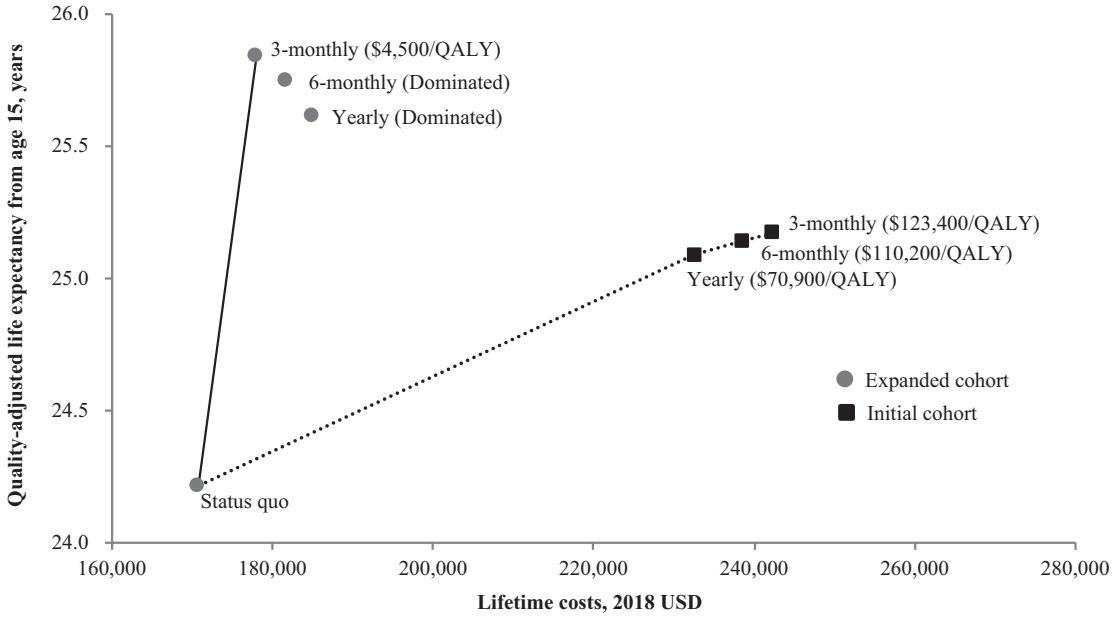
RESULTS

Clinical Outcomes for Initial Cohort

Among the Initial cohort, the median age of acquiring HIV was 22 years (IQR: 17–47); in this cohort, all frequent screening strategies increased undiscounted life expectancy compared to SQ (54.32–54.54 vs 52.06 quality-adjusted years) by 2.26–2.48 quality-adjusted years (Figure 1). Among people who acquired HIV (Supplementary Table 3), 3-monthly led to the shortest time spent with undiagnosed HIV (23.65 months, 40.48 months less than SQ), the highest CD4 count at diagnosis (515 cells/μL, an increase of 219 cells/μL over SQ), and the longest undiscounted quality-adjusted life expectancy (48.69 quality-adjusted years, an increase of 4.28 quality-adjusted years over SQ).

Mechanisms of HIV Detection and Care Continuum Outcomes: People Acquiring HIV over a 15-year Horizon

Over a 15-year horizon, compared to SQ, all more frequent screening strategies reduced the proportion of people with HIV detected via opportunistic infection (39% vs ≤3%) and the proportion not detected (22% vs ≤2%) through age 30 (Figure 2A). Frequent screening also increased the proportion diagnosed through age 30 from 82% (SQ) to 99% (3-monthly)



Screening strategy	Initial cohort			Transmissions averted		Expanded cohort	
	Quality-adjusted expectancy from 15, years [undisc]	Quality-adjusted expectancy from 15, years [disc]	Lifetime cost, $/ person [disc]	Quality-adjusted life-years saved/ person [disc]	Costs saved, $/person [disc]	Quality-adjusted life expectancy from 15, years [disc]	Lifetime cost, $/ person [disc]
Status quo	52.06	24.21	170,800[a]	--	--	24.21	170,800[a]
Yearly	54.32	25.09	232,600	0.52	47,600	25.61	185,000
6-monthly	54.45	25.14	238,700	0.60	57,000	25.74	181,700
3-monthly	54.54	25.17	242,300	0.67	64,200	25.84	178,100

YMSM: young men who have sex with men; ICER: incremental cost-effectiveness ratio; QALY: quality-adjusted life-year; Undisc: undiscounted; Disc: discounted

Initial cohort: self-identified, high-risk 15-year old MSM who face age specific risks of HIV infection (*i.e.* includes people with and without HIV infection; Expanded cohort: the Initial cohort and one generation of primary transmissions. Life expectancy and costs are discounted at 3%/ year. Costs and ICERs are rounded to the nearest $100 in 2018 USD.

[a] The lifetime cost of the Initial cohort and the Expanded cohort are the same for the Status quo. Costs in the screening strategies account for the impact of transmissions averted by frequent screening.

Figure 1. Efficiency frontiers: Cost-effectiveness outcomes, Initial and Expanded cohorts. The Initial cohort consists of self-identified, high-risk 15-year-old men who have sex with men who face age-specific risks of HIV infection (ie, people with and without HIV infection). The Expanded cohort consists of the Initial cohort and one generation of primary transmissions. The vertical axis shows discounted life expectancy, and the horizontal axis shows discounted per-person lifetime cost (USD 2018). Incremental cost-effectiveness ratios (ICERs) are shown next to the strategies which lie on the efficiency frontier (in parentheses, rounded to $100). Strategies below the line represent dominated strategies, or a less efficient use of resources. Cost-effectiveness outcomes including the impact of 15 years of transmissions are shown in circles (Expanded cohort) and outcomes excluding the impact of transmissions (Initial cohort) are shown in squares. Including the impact of transmissions, the ICER of 3-monthly screening remained ≤$100 000/QALY ($4500/QALY); excluding transmissions, the ICER of Yearly screening was ≤$100 000/QALY ($70 900/QALY). Comparing 3-monthly to the Status quo, the discounted gain in quality-adjusted life-years and costs saved per person attributable to averted transmissions was 0.67 quality-adjusted years and $64 200, respectively. Additional details of methods may be found in the Supplementary Materials.

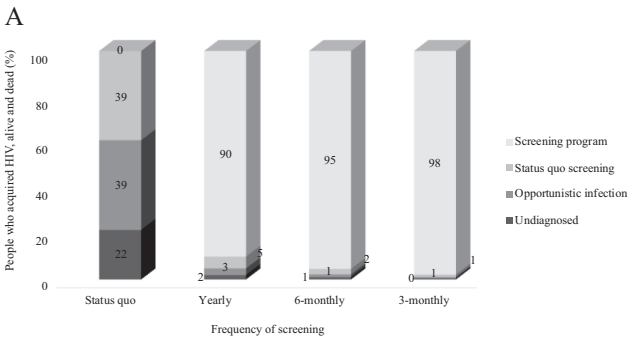


Figure 2A. Mechanisms of HIV detection for people who acquire HIV through age 30. This figure includes all people in the model simulation who ever acquired HIV through age 30, regardless of the age of diagnosis. Status quo screening reflects existing patterns of HIV screening. More frequent screening strategies were performed in addition to Status quo screening. All more frequent screening strategies identified a substantial proportion of YMSM (90%–98%). 3-monthly and 6-monthly screening resulted in the lowest proportions undetected (0%–1%) and diagnosed via opportunistic infection (1%).

and increased virologic suppression from 53% (SQ) to 62% (3-monthly; Figure 2B).

Transmissions

With SQ, the rate of transmissions attributable to the Initial cohort through age 30 was 2.3/100 person-years (PY), with peak transmissions from youth aged 17.9 years (2.9/100PY, Supplementary Table 4). Considering only a denominator of people with HIV over a 15-year horizon, the rate of primary transmissions was 12.6/100PY. Comparing 3-monthly to SQ, there was a 40% reduction in the mean cumulative number of primary transmissions at age 30 (0.58 vs 0.98/person with HIV; Figure 3).

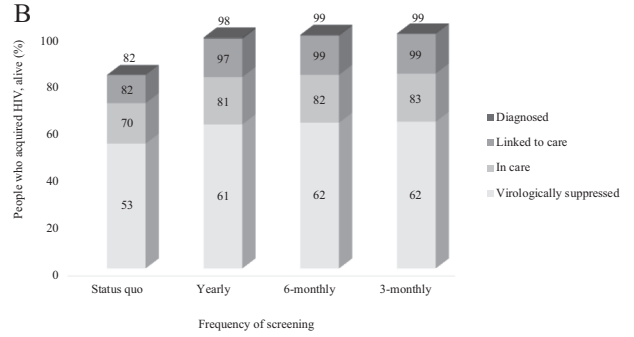


Figure 2B. Cross-sectional HIV care continuum outcomes for people acquiring HIV through age 30. Among people alive with HIV through age 30, the proportion diagnosed with HIV, linked to care, retained in care, and virologically suppressed are shown, assessed cross-sectionally at age 30 + 11 months. In the Status quo, we did not estimate a proportion diagnosed but unlinked to care. 3-Monthly screening led to the most favorable care continuum outcomes at age 30 + 11 months: 99% diagnosed, and 99% linked to care, 83% retained in care, and 62% virologically suppressed.

Cost-effectiveness Results: Expanded Cohort

Among the Expanded cohort, SQ led to the lowest projected HIV-related healthcare costs, with lifetime discounted costs of $170 800/person (Figure 1, circles, Supplementary Table 5). Lifetime population HIV-related costs were greatest for Yearly: $185 000/person. Due to the impact of transmissions, the Yearly and 6-monthly strategies were both more costly and less effective than 3-monthly (strongly dominated; Figure 1). SQ was both less costly and less effective than any of the frequent screening strategies; the ICER for 3-monthly compared to SQ was $4500/QALY. Considering only the Initial cohort (excluding the impact of transmissions; squares), the ICER for Yearly compared to SQ was $70 900/QALY.

Sensitivity and Additional Analyses

In one-way sensitivity analyses, ICERs for 3-monthly versus 6-monthly remained ≤$100 000/QALY despite wide ranges in linkage to care, screen offer and acceptance, screen test characteristics, and HIV care, ART, and screen costs (Figure 4). Up to a total cost per screen of $760/screen, the ICER of 3-monthly remained ≤$100 000/QALY (Supplementary Table 6). Rates of HIV transmission had the greatest impact on the ICER; however, only if the rate of HIV transmission was <0.05 times the base case rate did the ICER of 3-monthly exceed $100 000/QALY (Figure 4). In two-way sensitivity analyses, we varied transmission rates simultaneously with other parameters: In birth cohorts older than the base case (ie, model start at ages 18–28, when HIV incidence is lower), the ICER of 3-monthly remained ≤$100 000/QALY, except at ages >22 years and with transmissions less than or equal to half the base case (Supplementary Figure 1). When transmission rates were doubled and incidence rates were one quarter the base case, 3-monthly became cost-saving (Supplementary Figure 2). If there was no increased transmission risk during acute infection above chronic HIV infection, the ICER of 3-monthly remained ≤ $100 000/QALY even if subsequent transmission rates through chronic infection were one-twentieth base case values (Supplementary Figure 3).

In the "hard-to-reach" scenario analysis, even when 50% of the population refused any screen despite an additional $20/screen to offer screening, the ICER of 3-monthly remained ≤$100 000/ QALY (Supplementary Table 7). When even more frequent screening was examined, screening monthly was ≤$100 000/QALY (ICER: $2300/QALY); screening 2-, 3-, 4-, 5-, or 6-monthly was more costly and less effective than monthly screening (Supplementary Table 8). When cost-effectiveness outcomes were calculated over a 15-year horizon through age 30, the ICER of 3-monthly remained ≤ $100 000/ QALY ($11 700/QALY, Supplementary Table 9). Scenarios varying the age of people transmitted to

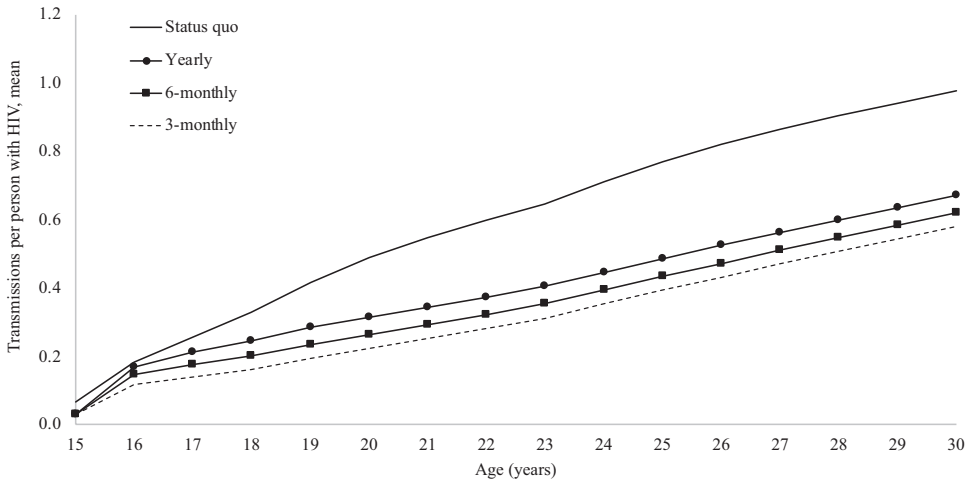


Figure 3. Mean primary transmissions per person among people who acquire HIV through age 30. Among people who acquire HIV by age 30, the graph presents the mean number of cumulative primary HIV transmissions by each year of age for each strategy. Comparing 3-monthly screening to Status quo, there was a 40% reduction (0.58 vs 0.98) in the mean number of primary transmissions at age 30. 3-Monthly screening led to the fewest projected transmissions.

in the Expanded cohort (Supplementary Table 10) or examining the potential impact of future, lower cost generic ART did not impact results; the ICER of 3-monthly remained ≤$100 000/QALY. Without quality-of-life utility weights, the ICER for 3-monthly versus 6-monthly was $4900/YLS (Supplementary Table 11).

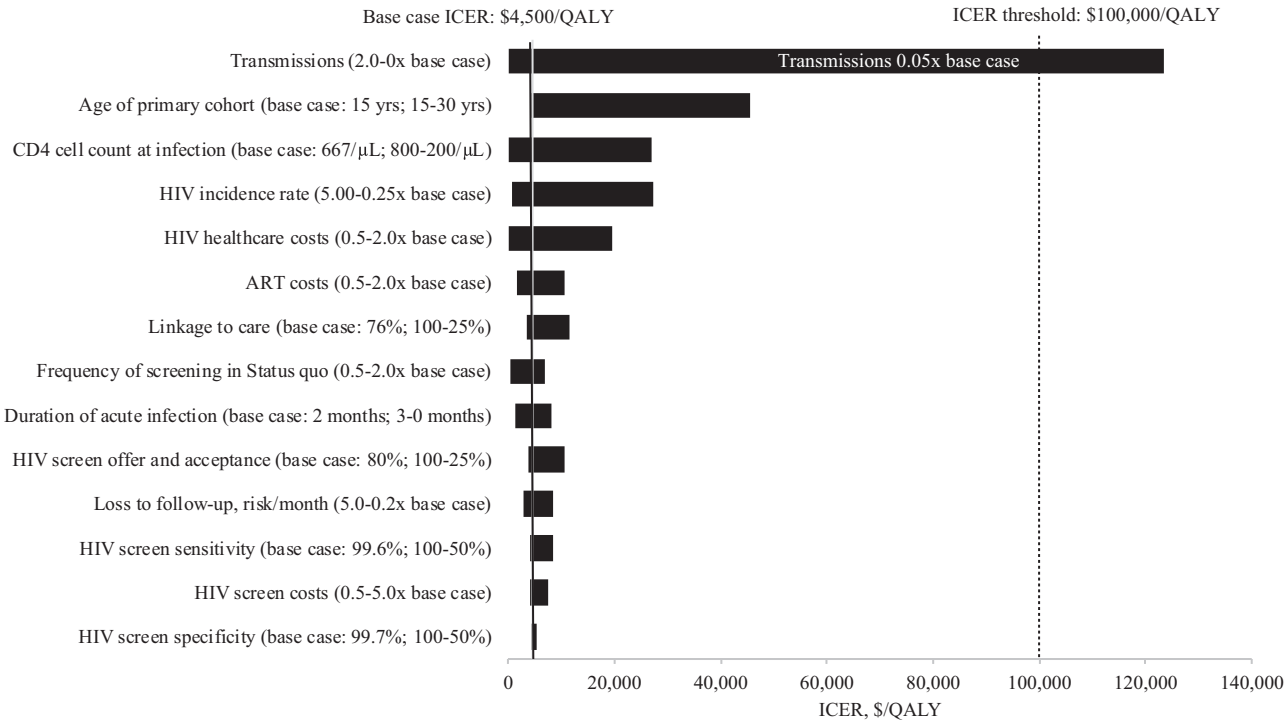


Figure 4. Sensitivity analyses: Incremental cost-effectiveness ratio of 3-monthly compared to the next least costly strategy, Expanded cohort. On the vertical axis, parameters and the ranges over which they are varied are shown. Incremental cost-effectiveness ratios (ICERs) for the comparison of 3-monthly vs 6-monthly are shown on the horizontal axis, in $/quality-adjusted life year (QALY). The range of ICERs for each varied parameter is indicated by the horizontal bars. Longer horizontal bars indicate parameters to which the model results are more sensitive. The black vertical line indicates the ICER for 3-monthly compared to 6-monthly in the base case ($4500/QALY). The vertical line indicates the cost-effectiveness threshold for this analysis, $100 000/QALY, and the white text within the bar indicates parameter values at which the threshold is crossed. 3-monthly compared to 6-monthly exceeds $100 000/QALY only if transmission rates are set to ≤0.05 times their base case values. Abbreviation: ART, antiretroviral therapy.

DISCUSSION

Current CDC guidelines recommend annual HIV screening for MSM and acknowledge that those at higher risk of infection may benefit from more frequent HIV screening [6]. Using a mathematical simulation model, we projected the value of more frequent HIV screening strategies, added to current screening practice, in 15-year-old YMSM in the US who self-report as being at high risk for HIV infection. We had four key findings. First, 3-monthly screening markedly increased life expectancy. Among people who acquired HIV, the projected life expectancy gain from 3-monthly screening was 4.28 quality-adjusted years compared to SQ (48.69 vs 44.41 quality-adjusted years, from age 15, Supplementary Table 3). When considering the entire population of high risk YMSM (both with and without HIV), 3-monthly screening increased life expectancy by 2.48 quality-adjusted years compared to SQ (54.54 vs 52.06). Screening 3-monthly also offered the best value for money, with an ICER of $4500/QALY compared to SQ, accounting for the life expectancy gained and costs averted due to reduced onward transmissions. If primary transmissions were excluded—limiting the clinical and economic benefits only to those accrued by the Initial cohort—the ICER of 3-monthly screening rose to $123 400/QALY (Figure 1). In this scenario, Yearly screening remained ≤$100 000/QALY (ICER $70 900/QALY).

Second, this analysis highlights opportunities for improved implementation of the current annual screening recommendations. If the current CDC guidelines for annual screening could be met among YMSM, we projected important gains compared to SQ in HIV care continuum outcomes, such as the proportion diagnosed (98% versus 82%) and the proportion virologically suppressed (61% versus 53%) by age 30. Implementing HIV screening for high-risk YMSM, similar to other sexual health interventions such as HPV vaccinations, however, relies on health care providers' accurate assessment of sexual histories and patients' disclosure. This may be difficult in practice: among CDC-funded programs serving youth in 2015, YMSM received only 28% of HIV tests despite comprising 83% of new HIV diagnoses in the US [39].

Third, the cost-effectiveness of the evaluated HIV screening strategies depends on reported high HIV incidence among the youngest high-risk MSM. In ATN studies 110/113, HIV incidence in the youngest MSM (ages 15–17) was twice that of older MSM (ages 18–22): 6.4 vs 3.3/100PY [3, 4]. Most participants lived at home and were enrolled in school [3, 4]; although incidence rates were high in ATN 110/113, this population may not represent the highest risk group of YMSM. While current HIV incidence rates are unknown for key subgroups (including by race/ethnicity, socio-economic status, or geographic location), our HIV incidence inputs and transmission rate outputs are similar to published reports for sexual minority males [1, 2, 40], and our conclusions remained robust to wide variations in these parameters.

Fourth, the cost-effectiveness of a specific frequent screening interval depends on onward HIV transmissions. Excluding transmissions, the ICER of Yearly screening was ≤$100 000/QALY. Including transmissions, screening very frequently generated the lowest ICERS (monthly, ICER: $2300/QALY; Supplementary Table 8). Because this finding depends on assumptions about transmissibility during acute infection, for which data are limited (see Supplementary Material), as well as the costs and life expectancy associated with those infections, aligning HIV screening guidelines with current CDC PrEP guidelines—which recommend 3-monthly HIV screening—may also be favorable from both patients' and clinical providers' perspectives. In practice, because healthy youth may interact infrequently with traditional healthcare sites, such as scheduled clinic visits, we interpret our results to suggest that self-identified high-risk youth should be offered HIV screening at virtually any opportunity when they present to care. Even if 3-monthly screening is costly ($760/screen), investments in innovative, effective screening approaches (eg, venue-based screening or mobile units [41]) are likely to provide excellent value for money (Supplementary Table 6).

This analysis has important limitations. First, we assumed constant, conditionally independent rates of screen offer and acceptance across serial screenings; in the base case, we also assumed that a change in policy could be implemented without substantial change in per-screen cost. However, in sensitivity analyses, accounting for increased costs incurred during efforts to reach a portion of the population who refuse testing, the ICER of 3-monthly versus 6-monthly remained ≤$100 000/QALY. Second, we modeled only newly-infected YMSM; we did not account for the added benefit of detecting people with undiagnosed HIV nor those who have fallen out of HIV care at the start of a screening program; this would increase the clinical benefit of all screening programs. Third, we derived HIV incidence rates from PrEP studies, but there are several factors that might lead to higher or lower HIV incidence rates and resulting onward transmissions over time. For example, community-level improvements in prevention, screening and treatment might reduce onward HIV transmissions at later ages over time (raising the ICERs of all screening strategies; Figure 4), whereas accounting for the chain effect of averting additional generations of HIV transmissions would lower the ICERs. Our policy conclusions, however, remained robust if transmission risks among YMSM were even 0.05 times of those in the base case, or if cost-effectiveness outcomes were considered only over a 15-year time horizon. This analysis will provide a foundation for future analyses examining the incremental benefit of PrEP in addition to screening in this population.

Our findings expand to YMSM similar conclusions from simulation model-based analyses of adult high-risk MSM. Three studies found 3-monthly screening to be cost-effective (range: cost-saving to $45 000/QALY) [42–44]. A fourth study found

that screening more often than annually was not cost-effective in all adult MSM [45]; our results would be expected to differ from this last study because we modeled a younger, higher-risk population as well as routine use of newer fourth generation immunoassays, and recent recommendations to start ART for all people with HIV.

Our updated findings should inform new CDC recommendations for more frequent screening in self-identified high-risk YMSM. For high-risk young men who have sex with men in the US, HIV screening every 3 months compared to less frequent screening will improve clinical outcomes and be cost-effective.

Supplementary Data

Supplementary materials are available at *Clinical 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.

Notes

Author contributions. All authors contributed substantively to this article in the following ways: study design (A. M. N., A. L. C.), data analysis (A. M. N., A. J. B., A. L. C.), interpretation of results (all authors), drafting the manuscript (A. M. N., A. J. B., A. L. C.), critical revision of the manuscript (all authors), and final approval of submitted version (all authors).

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