Screening for HIV

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This report summarizes estimates of health impact and cost-effectiveness that were created to assess the relative value of most of the clinical preventive services recommended by the United States Preventive Services Task Force (USPSTF) and the Advisory Committee on Immunization Practices (ACIP). This ranking of clinical prevention priorities is guided by the National Commission on Prevention Priorities (NCPP).

A. USPSTF Recommendation

The USPSTF recommends screening for HIV in adolescents and adults aged 15 to 65 years and in younger adolescents and older adults who are at increased risk. This an A grade recommendation based on: high accuracy of both rapid and conventional testing; convincing evidence that identification and treatment of HIV infection is associated with a reduced risk of AIDS and AIDS-related events; evidence of the effectiveness of earlier initiation of combined antiretroviral therapy (ART); evidence of reduced HIV transmission; and evidence that harms of earlier treatment are frequently short-lived and that overall harms are small.[1]

The USPSTF did not find adequate evidence to recommend a specific screening interval, but notes that varied screening intervals, according to HIV risk status, may be appropriate. This may include one-time screening for the general population at low risk, screening every 3 to 5 years for those at increased risk, and annual screening or more frequent for those at highest risk.[1]

B. General Method

Rather than constructing a new infectious disease simulation model, we sought to derive estimates for clinically preventable burden (CPB) and cost-effectiveness (CE) based on an existing peer-reviewed modeling study that captured the impact of screening on disease transmission while estimating lifetime health consequences. To identify an analysis on which to base our estimates of CPB and CE, we reviewed health economic modeling studies of HIV screening that included (but were not limited to) screening for all U.S. adults who were not at increased risk of HIV infection.

To be consistent with USPSTF discussion of reasonable screening intervals, we identified studies with one-time or infrequent screening for the general population and more frequent screening for those at increased risk.[2-7] To help ensure the validity of a ranking of a wide variety of evidence-based clinical preventive services, several standards were employed to ensure consistency in the estimates of CPB and CE. The most fundamental of these standards is to estimate the value of each preventive service to a single U.S. birth cohort of 4,000,000 people. While a birth cohort analysis approach is common in health-economic modeling studies of clinical preventive services, it is not possible to model an infectious disease process in this manner because disease is transmitted between birth cohorts. A study needed to provide detailed reporting of methods and results to allow us to derive estimates of the health impact and cost-effectiveness of screening for single birth cohort among the multiple birth cohorts represented in the study's model.

We identified five analyses that report results with varying screening intervals for population groups with different risk levels. Among them, the 2010 analysis by Long et al. provided the best basis for

estimating the value of screening in a single birth cohort.[4] The authors estimated the impact of one-time screening for average-risk persons and annual screening for persons at increased risk.

Other studies had similar qualities but did not meet our needs for a variety of reasons. Hutchinson et al. (2010) and Long (2011) both focused their reporting on the incremental value of pooled NAAT testing rather than on varied screening intervals by risk status.[2,3] Paltiel et al. (2005) provided better discrimination of screening interval by risk group in their results but did not provide sufficient detail in reporting to allow us to use the results to estimate the impact of screening for a single birth cohort.[5] Paltiel et al. (2006), also offers an insightful analysis, but only brief results for population groups with alternate risk levels were reported,[6] though results are broadly consistent with this study's reported results. Lucas and Armbruster reported cost-effectiveness of varying intervals for low, medium and high risk groups as defined by HIV incidence rates. However their reporting focused on identifying optimal screening intervals based on the incremental cost-effectiveness of screening at variable intervals compared to a 20-year screening interval reference program and did not report the absolute value of screening at intervals that more closely aligned with USPSTF recommendations for lower-risk groups.[7] Finally, a study by Lin et al. was published after the analysis presented here was complete.[8] They found one-time screening for both high-risk and unselected populations to be cost-saving. We could not assess the relevance for a birth cohort with repeated opportunities for screening or other items related to consistency with our methods for the Prevention Priorities project at this time.

Our solutions for using the estimates of Long et al.[4] to estimate CPB and CE in a manner consistent with our estimates for other services in the prevention priorities ranking are described below in Sections C (Clinically Preventable Burden) and D (Cost-Effectiveness), and the primary limitations of our solutions are summarized in the final section.

C. CPB

We based our estimates on the results reported by Long et al. for screening low-risk adolescents and adults aged15-64 years once during their remaining lifetime and screening high-risk groups annually. Long et al. constructed a compartmental model of men and women in the general population, men and women injection drug users, men who have sex with men (MSM) and MSU injection drug users. In the model, asymptomatically screened individuals receive antiviral therapy earlier and derive benefit from reduced disease progression with reduced mortality and higher quality of life. In addition, using ART reduced infection probability from sexual contact by 90% and infection probability from injection drug use by 50%. In the model, tested patients receive counseling, and those patients identified to have HIV reduce their sexual partnerships by 20%.

Table 1 shows the summary calculations for CPB, reflecting adjustments we made to the reported QALYs saved of Long et al. to improve consistency with other services in the prevention priorities ranking. Most of the data points in Table 1 are either estimates from Long et al., from other literature, or are calculated from other data in the table. For data points taken from the literature, the "Data Source" column in Table 1 shows the reference numbers on which the estimate is based. For data points calculated within the table, the "Data Source" column shows the calculation formula. The letters in the formula refer to the row labels (a-y found in the left-most column of Table 1) for the data points from

which the calculation is made. Sources and calculations are described in text below. We created additional tables to summarize the evidence and perform supporting calculations but they are not shown due to multiple linking between tables that cannot be conveyed in a two-dimensional table. In the following text, we describe relevant content from those tables.

Key parameters from Long et al. that determine the effectiveness of HIV screening include a reduction in sexual partners by 20% among persons with HIV after post-test counseling, antiretroviral therapy reduces transmission through sexual activity by 90% and reduces transmission through injection drug use by 50%, and a reduction in quality of life of 0.07 when positive HIV status is identified. Readers who wish to develop a detailed understanding of the model and how its parameters may impact our final estimates are referred to the original paper by Long et al., including the technical appendix.[4]

C.1 Discounted QALYs saved scaled to a one-year birth cohort of 4,000,000

Long et al. estimated that 1.2 million discounted QALYs (row a) would be saved in a 20-year screening program for persons aged 15 to 64 years of age using one-time screening for low-risk persons and annual screening for those at increased risk (defined as men who have sex with men and intravenous drug users). This result was estimated in a much larger simulated population (203.5 million at model initiation; row b) than the number of individuals who would be alive at age 15 in a single birth cohort (3.8 million as tabulated from U.S. life tables, row c). Therefore, we scaled that result by the difference in population size to obtain an estimated 22,476 discounted QALYs saved in a 20-year program when estimated among a single birth cohort (row e).

This rescaling allows us to use the estimates that reflect transmission of disease among birth cohorts in the model of Long et al. while approximating the impact of the screening program for a single birth cohort. Some of the shortcomings of this approximation are discussed in the context of other adjustments in the next two sections.

C.2 Discounted QALYs saved scaled to lifetime screening program

The scaled discounted QALYs saved estimate in row e approximates the benefits of a 20-year screening program in a single birth cohort. The benefits of a lifetime screening program from ages 15-64 are likely larger among the high-risk population eligible for annual screening. We estimate that approximately 42% of infections that occur in a birth cohort between ages 15-64 would occur in higher-risk populations outside of the window of a 20-year program (row h). This estimate is based on separate estimates from CDC surveillance reports of cases that occur across a range of 20-year age bands (row f), and on the portion of infections that occur among the high-risk groups specified by Long et al. (row g). Row f is estimated by first calculating the portion of all cases that occur in seven overlapping 20-year bands (15-34, 20-39, 25-34 etc.). We then calculate an average across those overlapping age groups to approximate the portion of cases that occur on average in a 20-year period of a cohort between ages 15 and 64. Row f is the complement of that average percent. If it were available, a direct estimate based on infections by age group in high-risk persons alone would produce a more accurate estimate than the calculation in row h. However, more than 85% of infections occur in higher-risk groups and therefore the population-wide age-distribution of infection largely reflects the higher-risk population.

Some of the infections that would occur outside of the 20-year program estimated by Long et al. are already captured by the authors' estimates during the screen for prevalent infections in the first year of the program for a U.S. cross-section. In a birth cohort analysis, many of these infections would be detected in annual screening of the high-risk group closer to the time that the infections occurred. To reduce the amount of double-counting of infections already captured in the screen for prevalent conditions in Long et al.'s model, we reduced our adjustment for infections that occur outside the 20-year program by 20% (row i) as shown in the calculation for row k. Lacking data on the portion of cases outside the 20-year screening window that are already addressed by the initial screen for prevalent infections, we assumed this portion to be 20%.

Our adjustment to discounted QALYs saved for infections occurring outside a 20-year screening window assumes that discounted QALYs saved are proportionate to the portion of excluded infections (row j). Each additional infection prevented in a lifetime screening program may not produce the same number of QALYs as those prevented in a 20-year program. Differences in the average QALYs saved per infection could arise from differences in average age of infection, differences in timing of screen detection relative to symptomatic detection, or different impact on disease transmission. We vary the scalar in row j in sensitivity analysis to assess the impact of this assumption.

With these additional calculations and assumptions, our estimate of discounted QALYS saved for a single birth cohort in an ongoing program that covers all of their years between ages 15 and 64 is 29,954 QALYs (row k).

C.3 Other adjustments to discounted QALYs saved

As with other services in the prevention priorities project, we account for practical levels of patient adherence in estimating CPB. We identified 16 studies of acceptance of HIV screening when offered face-to-face that were published in the last 10 years.[9-23] These studies recruited patients from a variety of settings, including emergency departments (6 studies), outpatient clinics (3 studies), inpatient with or without additional recruitment from outpatient clinics (3 studies), dental clinics (2 studies), a community pharmacy (1 study), and college classrooms (1 study). There were not clear differences in acceptance rates based on and of the following: setting; whether or not those with recent prior screens were excluded; whether rapid testing or standard testing was offered; or whether an opt-in or opt-out strategy was employed. Across all studies, the mean acceptance rate was 62% (range 19% to 98%; median 60%). Most studies did not exclude individuals with prior screens; in the studies that had such an exclusion, individuals were only excluded when their prior screen was within the last 6 or 12 months. Therefore, the portion of the population who refuses screening included some who were already current with recommended screening. We estimated this to be an additional 16% among five studies that reported results in a way that allowed this calculation.[9,11,20,22,24] Therefore, we estimated that total portion of patients aged 15-64 years who would accept screening to be approximately 80% (row l), based on approximately 62% accepting screening in these studies and another 16% already being up to date, rounded to the nearest decile, given low precision of the estimate.

Other differences between the dynamic cross-section estimated by Long et al. and the birth cohort used to make estimates consistent across services in the prevention priorities ranking may cause our estimate

to be over- or under-stated. Our adjustments do not account for impact of starting the model in a cross-section as Long et al., and hence missing years of screening for all individuals in the model who were older than age 15 at model initiation, though some of these infections were detected prior to symptoms in the model's first year screening of prevalent cases. Our adjustments do not account for the fact that Long et al.'s dynamic cross section introduced new 15-year-olds into the model as they aged into the screening eligibility. In addition, Long et al.'s estimates are incremental to current testing, whereas our method for prevention priorities is to estimate the impact relative to zero utilization of the testing for asymptomatic screening. Long et al. used estimates of 23% of high-risk persons and 10% of low-risk persons having been screened in the previous 12 months. The original source does not contain information on the portion that were tested asymptomatically[25]. Because we lack data to make a reasonably accurate adjustment for these factors, our base case estimate implicitly assumes that they off-set. For sensitivity analysis, we introduce the adjustment scalar (row m; set to 1.0 in the base case), to explore sensitivity of the CPB scores to net under- and over-statement from these factors.

With these considerations, our estimated discounted QALYs saved for screening between ages 15-64 in a single year birth cohort is 23,963 (row n).

C.4 Undiscounted QALYs saved
Finally, while we do discount QALYs for the purpose of estimating cost-effectiveness, our estimates of CPB are not discounted. The typical ratio of undiscounted to discounted QALYs in the analysis of Long et al. was 1.53 to 1[26] (row o). Applying this ratio, our estimate of undiscounted QALYs saved is 36,663.

C.5 Sensitivity analysis of adjusted CPB estimate
We conduct sensitivity analysis for the purpose of informing the likelihood that each service's priority score may change by more than one point. When basing estimates on a journal article, we cannot conduct sensitivity analysis for each variable. Our approach is to apply a range to the main estimates coming from the published results and to explore sensitivity analysis related to our adjustments. We define a plausible range of values based on the combined impact of three variables moving to the end of the range used in sensitivity analysis in the same (favorable or unfavorable) direction. Two variables may be used rather than three when working with a published estimate if the "variables" represent an intermediate result reported by the article that embodies several variables, such as life years saved or medical costs saved across a number of conditions.

We found that the CPB of HIV screening is most sensitive in the favorable direction to changes to the combination of the published discounted QALYs saved (when increased by 40%), the scalar for net effect of adjustments not made (row m; when set to equal 1.25), and the ratio of discounted to non-discounted QALYs (when increased by 20%). In the unfavorable direction, CPB was most sensitive to the combination of the published discounted QALYs saved (when decreased by 40%), the scalar for net effect of adjustments not made (row m; when set to equal 0.75) and the acceptance rate of screening (when set to equal 50%). The range of CPB values that results from these changes is 10,000 to 77,000 QALYs saved.

D. Cost Effectiveness

Each of the adjustments made for CPB, other than the adjustment for discounting, are applicable to CE. However, they affect the number of people and years of screening represented in both the numerator and the denominator of the CE ratio (costs of screening, medical costs of treatment and health benefits of screening and early treatment), and therefore have little impact on the CE ratio itself. For example, factoring in non-acceptance of screening would proportionally reduce screening costs and the health and medical cost impacts of screening. To the extent that the extra or missing screens are not reflective of the average of a birth cohort, making adjustments to for these factors would impact the CE ratio; however, we lack the detailed information need to make adjustments at that level of accuracy. Adding or subtracting persons eligible for screening, or adding or subtracting years of screening, would affect both the costs and benefits of screening and, as a result, have less influence on the CE ratio than on CPB. Therefore the rough adjustments made above to calculate CPB very likely improved consistency with CPB estimates to other services in the prevention priorities ranking, but are not likely to markedly improve the comparability of the CE ratio reported by Long et al.

Instead of making adjustments that proportionally affect the numerator and denominator, we presume that the CE ratio estimated by Long et al. is representative of the experience of screening individuals in a single-year birth cohort from ages 15 to 64, and we focus our adjustments on two other issues to improve consistency with CE ratios for other services in the prevention priorities ranking. Each of these adjustments is to costs. Therefore we make adjustments to the discounted net costs reported by Long et al. for the dynamic cross-section and re-tabulate the CE ratio using their estimate of 1.2 million QALYs saved for the dynamic cross-section.

D.1 CE ratio adjusted for patient time costs and inflation
Following methods of the Panel and Cost-Effectiveness in Health and Medicine, we include patient costs for time and travel to receive preventive services and necessary follow-up. We make this adjustment by estimating the total number of screens included reflected in the estimates reported by Long et al. and add a per-screen cost for patient time and travel. Using the model's initial population size, population entrance and exit rates, and modeled screening frequency by risk group, we estimated the total number of screens in the screening program and in the baseline scenarios (rows q and r) based on the initial model population group sizes and model entry, exit and maturation rates reported by Long et al. We assumed that net follow-up visits with the screening program were zero (row s). This is a simplifying but plausible approximation grounded in a screening specificity being greater than 99% and the fact that follow-up from true positives from asymptomatic screening essentially replaces what would have eventually been follow-up after true positives with symptoms, therefore not contributing additional costs (though the effect of discounting does not make this an exact off-set).

We assign 50% of a 15-minute office visit is needed for streamlined counseling and testing.[23] Across preventive services, we assume that the equivalent of 2 hours of patient time is needed for time and travel for an office visit and we value that time at $62 using U.S. average earnings in 2012[27] (row t) and also attributed 50% of that time to counseling and testing and 50% to other services that would occur during a 15-minute visit. Therefore, $31 is allocated to patient time and travel costs for the portion of an office visit used for HIV counseling and testing. After discounting to present value at the first year of the

screening program, these costs add $8.7 billion (29%; row v) to the net costs estimated by Long et al. after adjusting to 2012 US dollars using the medical consumer price index (row w). Dividing the sum of patient time costs and net medical costs by the estimated 1.2 million QALYs saved in a U.S. dynamic cross-section yields a CE ratio of 31,983 $/QALY (row y).

D.2 Sensitivity analysis of adjusted CE ratio
When using the approach described above for sensitivity analysis of the CPB (Section C.5), we found that the CE ratio of HIV screening is most sensitive in both the favorable and unfavorable directions to changes to the combination of the published discounted QALYs saved (when changed by 40%) and the published estimate of discounted net costs (also changed by 40%). The range of CE ratios values that results from these changes is $16,000 to $70,000 per QALY saved.

E.   Limitations
Best estimates for this service would come from an agent-based model in which individuals in a single birth cohort interact with each other and with other cohorts while the outcomes for a single birth cohort are recorded. Because that level of modeling was not feasible for this update of the Prevention Priorities ranking, we chose to construct a literature-based estimate that required several adjustments to improve consistency with the estimates for other services in the ranking. Each of these adjustments is imperfect and adds to uncertainty of the base case estimates. Other adjustments that would have been ideal to include were not added due to data limitations. Although we expect the net impact of these excluded adjustments to be small, we cannot be sure of their combined impact on CPB and cost-effectiveness. There are also data limitations to the underlying model as discussed by Long et al. that may also impact the accuracy of our base-case estimate.

A more accurate estimate of HIV screening as described by the USPSTF might also come from stratifying the population into three risk categories that include a middle risk category screened every 3-5 years.[1] Our estimate is based on a single higher-risk group that is offered annual screening. Our estimates also do not include adolescents below age 15 and adults greater than 65 who are at increased risk for HIV as recommended by the USPSTF.

Finally, due to time limitations, we did not fully evaluate for applicability a recent study that found one-time screening to be cost-saving for both high-risk and unselected populations.[8]

Table 1. Clinically preventable burden and cost-effectiveness of HIV screening in a U.S birth cohort

Row	Variable	Value	Source or calculation
a	Discounted QALYs saved by screening low-risk individuals once and high-risk individuals annually as evaluated in a dynamic cross-section of the U.S. population	1,200,000	[4]
b	Size of model population at mode initiation	203,462,627	[4]
c	Average annual size of a U.S. birth cohort of 4,000,000 over years of age from 18-64	3,810,894	[28]
d	Approximate cohorts represented in initial model population	53.4	= b/c
e	Approximate discounted QALYs saved per single-year birth cohort	22,476	= a/d
f	Approximate portion of new cases not occurring in an average 20-year age span between 15 and 64 year of age	56%	[29]
g	Portion of infections in higher-risk compartments	74%	[29]
h	Portion of infections in a birth cohort potentially missed due to limited screening window	42%	= f x g
i	Portion of infections potentially missed that are captured as early stage prevalent infections in model first year	20%	assumption
j	Assumed association between missing infections and discounted QALYs saved	1.0	assumption
k	Discounted QALYs saved for full screening program, ages 15-65	29,954	=e*(1+h*(1-i)*j
l	Adherence (must assume = across all risk groups)	80%	[9-24]
m	Adjustment for other factors (net population model growth, baseline asymptomatic screening)	1.0	assumption
n	Discounted QALYs after adjustment for screening acceptance and other factors	23,963	= k*l*m
o	Ratio of undiscounted to discounted QALYs	1.53	[26]
p	**Clinically preventable burden (CPB), undiscounted QALYs saved**	**36,663**	= n*o
q	Approximate number of screens in screening scenario	402,740,147	see text
r	Number screened with no program	84,058,459	see text
s	Net diagnostic follow up	-	assumption
t	Patient time cost per entire visit	$62	[30]
u	Portion of 15 minute office visit for counsel and screen	50%	assumption
v	Patient time costs, discounted	$8,663,698,183	=q*t*u -r*t*u, discounting applied
w	Incremental discounted net costs from model, $2,012	$29,715,306,978	[4]
x	Incremental discounted QALYs	1,200,000	
y	**Inflation and patient-time-cost adjusted CE ratio***	**$31,983**	

* For CE, not making proportional adjustments to discounted QALYs and cost; implicitly assume that the relative costs and benefits of screening captured in the model are similar to a birth cohort

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