

**FHS PUBLIC ACCESS**

Author manuscript

J Adolesc Health. Author manuscript; available in PMC 2019 January 01.

Published in final edited form as:

J Adolesc Health. 2018 January ; 62(1): 22–28. doi:10.1016/j.jadohealth.2017.08.028.**The optimal age for screening adolescents and young adults without identified risk factors for HIV****Anne M. Neilan, MD, MPH^{1,2,3,6}, Richard Dunville, MPH⁷, M. Cheryl Bañez Ocfemia, MPH⁸, Joshua A. Salomon, PhD⁹, Jordan A. Francke^{1,4}, Alexander J.B. Bulteel^{1,4}, Li Yan Wang, MBA, MA⁷, Katherine K. Hsu, MD, MPH^{11,12}, Elizabeth A. DiNenno, PhD⁸, Rochelle P. Walensky, MD, MPH^{1,2,4,6}, Robert A. Parker, ScD^{1,5,6}, Kenneth A. Freedberg, MD, MSc^{1,2,4,6,10}, and Andrea L. Ciaranello, MD, MPH^{1,2,6}**¹Medical Practice Evaluation Center, Massachusetts General Hospital, 50 Staniford Street, Boston, MA 02114, USA²Division of Infectious Diseases, Massachusetts General Hospital, 50 Staniford Street, Boston, MA 02114, USA³Department of Pediatrics, Massachusetts General Hospital, 50 Staniford Street, Boston, MA 02114, USA⁴Division of General Internal Medicine, Massachusetts General Hospital, 50 Staniford Street, Boston, MA 02114, USA⁵Biostatistics Center, Massachusetts General Hospital, 50 Staniford Street, Boston, MA 02114, USA⁶Harvard Medical School, 25 Shattuck Street, Boston, MA 02115, USA⁷Division of Adolescent and School Health, Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA 30329, USA⁸Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, 1600 Clifton Road, Atlanta, GA 30329, USA⁹Department of Global Health and Population, Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Boston, MA, USA¹⁰Department of Health Policy and Management, Harvard T.H. Chan School of Public Health, 677 Huntington Avenue, Boston, MA, USA

Corresponding Author: Anne M. Neilan, MD, MPH, Division of Infectious Diseases, Massachusetts General Hospital, 50 Staniford Street, Floor 9, Boston, MA 02114, USA, Phone: 617-724-4790, Fax: 617-726-2691, aneilan@partners.org.

AUTHOR ROLES

All authors contributed substantively to this manuscript in the following ways: study design (all authors), data analysis (AMN, JAF, AJB, KAF, ALC), interpretation of results (all authors), drafting the manuscript (AMN, ALC), and critical revision of the manuscript (all authors) and final approval of submitted version (all authors).

CONFLICTS OF INTEREST AND FINANCIAL DISCLOSURES

The authors have no conflicts of interest or financial disclosures.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

¹¹Boston Medical Center, One Medical Center Place, Boston, MA 02118, USA

¹²Massachusetts Department of Public Health, 250 Washington Street, Boston, MA 02108, USA

Abstract

Purpose—To assess the optimal age at which a one-time HIV screen should begin for adolescents and young adults (AYA) in the United States without identified HIV risk factors, incorporating clinical impact, costs, and cost-effectiveness.

Methods—We simulated HIV-uninfected 12-year-olds in the US without identified risk factors who faced age-specific risks of HIV infection (0.6–71.3/100,000PY). We modeled a one-time screen (\$36) at age 15, 18, 21, 25, or 30, each in addition to current US screening practices (30% screened by age 24). Outcomes included retention in care, virologic suppression, life expectancy, lifetime costs and incremental cost-effectiveness ratios in \$/year-of-life saved (YLS) from the healthcare system perspective. In sensitivity analyses, we varied HIV incidence, screening and linkage rates, and costs.

Results—All one-time screens detected a small proportion of lifetime infections (0.1–10.3%). Compared to current US screening practices, a screen at age 25 led to the most favorable care continuum outcomes at age 25: proportion diagnosed (77% vs. 51%), linked to care (71% vs. 51%), retained in care (68% vs. 44%) and virologically suppressed (49% vs. 32%). Compared to the next most effective screen, a screen at age 25 provided the greatest clinical benefit, and was cost-effective (\$96,000/YLS) by US standards (<\$100,000/YLS).

Conclusions—For US AYA without identified risk factors, a one-time routine HIV screen at age 25, after the peak of incidence, would optimize clinical outcomes and be cost-effective compared to current US screening practices. Focusing screening on AYA ages 18 or younger is a less efficient use of a one-time screen among AYA than screening at a later age.

Keywords

Human immunodeficiency virus; HIV screening; HIV testing; Adolescence; Young adults

The US Centers for Disease Control and Prevention (CDC) estimate that 22% of new HIV diagnoses occur in adolescents and young adults (AYA) aged 13–24 years, and that nearly 61,000 AYA are now living with HIV in the US [1, 2]. In 2006, CDC recommended routine HIV screening at least once between the ages of 13–64, regardless of risk factors [3]. However, HIV screening rates among AYA remain low: 12% of US high school students reported ever being screened in 2005, increasing only to 13% by 2012 [4]. Among older youth aged 18–24, the proportion who had ever been screened declined over a similar period, from 37% reported in 2000 to 30% in 2010.

Of all AYA aged 13–24 living with HIV, 51% are estimated to be unaware of their HIV status, substantially higher than the 13% of HIV-infected US adults estimated to be unaware of their status [2]. People unaware of their HIV infection miss opportunities for treatment and improved individual health, as well as contribute disproportionately to HIV transmission [5]. CDC recommends that people at high risk for HIV infection, including people who have had sex with more than one partner since their last HIV screen, sexually active men who

have sex with men, and injection drug users, be rescreened at least annually [3]. For youth without identified risk factors, however, uptake of CDC guidelines for routine screening may be limited by differing recommendations among national professional organizations, as well as lack of evidence that 13 is the optimal age at which to initiate HIV screening in AYA [6, 7]. While many youth with unknown risk factors may be at higher risk of HIV infection than either they or their healthcare providers perceive [8], we hypothesized that offering a one-time screen at a younger age may cause harm by missing infections that occur later. Additionally, offering an HIV test to a 13-year-old without identified risk factors might take the place of potentially higher priority health considerations such as catch-up immunizations or assessing safety and counseling on injury prevention [9]. Our objective was to identify the age at which the CDC recommendation for one-time HIV screening should begin. We thus assessed the clinical impact, cost and cost-effectiveness of one-time HIV screening strategies for AYA aged 13–24 in the US without identified HIV risk factors.

METHODS

Analytic overview

We used the Cost-Effectiveness of Preventing AIDS Complications (CEPAC) microsimulation model to evaluate the cost-effectiveness of alternative strategies for routine one-time HIV screening in youth aged 13–24, in addition to current HIV screening and testing practices in the US (13% ever screened by age 18, and 30% by age 24) [4]. We simulated HIV-uninfected 12-year-olds without identified risk factors (Table 1). We modeled 5 screening strategies: a onetime *screen at age 15, 18, 21, 25 or 30* years; each one-time screening strategy was performed in addition to *current practice*. *Screens at age 25 and 30* were included to determine the value of screening after the AYA period. Model outcomes included CD4 cell count at diagnosis, life expectancy and HIV-related lifetime costs from the healthcare system perspective. In the base case, life expectancy was not quality-adjusted due to limited data among AYA [22]. To compare the marginal cost for an additional unit of health benefit when choosing between these different strategies, we report incremental cost-effectiveness ratios (ICERs) [23]. We calculated ICERs for each strategy compared to the next most costly alternative ($\text{cost} / \text{life expectancy}$), using outcomes for HIV-infected and HIV-uninfected people. Results were discounted at 3%/year to convert future costs and health outcomes [23]. We defined a strategy as “cost-effective” if its ICER fell below a willingness-to-pay threshold of \$100,000/year-of-life saved (YLS) [24]; we examine a range of ICER thresholds in sensitivity analyses.

Model structure, population, and data parameters

The CEPAC model is a patient-level simulation model of HIV infection, screening, disease progression, and treatment calibrated to clinical data with and without antiretroviral therapy (ART) in the US (<http://web2.research.partners.org/cepac>) [25]. Youth enter the model at age 12 without HIV infection, and are simulated through their lifetimes until death.

HIV incidence and diagnosis—Simulated patients face monthly risks of HIV infection, based on age-stratified incidence rates (Table 1 and online Appendix Table A1). For patients who become infected, diagnosis can occur via *current practice* of HIV detection (*e.g.* HIV

screening and testing already occurring in healthcare settings), or testing after presenting to care with an opportunistic infection (OI) or the one-time HIV screening program.

The model includes age-stratified monthly probabilities of detection under *current practice* HIV screening. *Current practice* screening rates were derived from Youth Risk Behavior Survey (YRBS) data for 13- to 17-year-olds (% ever tested) and the National Health Interview Survey (NHIS) for people >18 years (% tested within 12 months) (Table 1) [4]. We used National HIV Surveillance System (NHSS) data on stage of disease at HIV diagnosis during 2013, stratified by age, to calibrate these rates (Appendix Table A2) [11].

In addition to *current practice*, a one-time HIV screen was offered to both infected and uninfected patients (Table 1). In the base case analysis, for all one-time screening strategies, we assumed an 80.0% combined probability of being offered and accepting screening, 97.0% result return, 75.6% linkage to care and ART provision after a positive screen (based on data for AYA aged 13–24 when available), as well as screening costs of \$35.92 per screen plus an additional \$72.23 per completed reactive screen [13–15, 25, 26]. HIV screening was modeled as a fourth generation HIV immunoassay per CDC recommendations.

Disease progression and treatment—In the month of HIV infection, simulated patients are assigned a CD4 cell count and HIV RNA level from defined distributions (Table 1 and Appendix Table A1). ART is initiated in all patients who link to care, per US guidelines [27]. After ART initiation, simulated patients face a probability of virologic suppression and a resulting increase in CD4 cell count stratified by adherence [28]. Patients on suppressive ART experience a monthly probability of virologic failure after 48 weeks, also stratified by adherence [21, 29]. Monthly risks of OIs and mortality are determined by age, current CD4 cell count, and prior disease history. The model tallies time in each health state and associated costs, including clinical care, laboratory screening, and medications [25, 28].

HIV care continuum—The model also generates HIV care continuum outcomes (proportions HIV-diagnosed, linked to care, retained in care, and virologically suppressed). Monthly risks of becoming lost to follow-up and returning to care reflect movement within the care continuum (Table 1).

Sensitivity analyses and additional analyses

In sensitivity analyses, we first varied HIV incidence from 5- to 100-fold the base case inputs. The 5-fold increase approximated 2013 rates of new diagnoses reported among African American males (Appendix Figure A1) [11, 12]. We next shifted the age distribution of HIV incidence, ranging peak age from 15–28 (Appendix Figure A2), and varied rates of *current practice* HIV screening from 0.5- to 2-fold the base case. We also varied parameters of the HIV screening program, CD4 cell count at infection, loss to follow-up, virologic suppression, and HIV-related healthcare costs. We examined HIV screening and HIV care costs up to 5-fold the base case to understand where the ICER threshold was crossed. In multi-way sensitivity analyses, we varied the most influential of these parameters simultaneously, including costs of HIV screening and HIV care, and linkage.

Because of limited data in AYA, we excluded quality-of-life adjustments in the primary analysis. In sensitivity analysis, we used quality-of-life weights from adults, generating ICERs in \$/quality-adjusted life-year (\$/QALY), a more common unit for ICERs. We also calculated the proportion of one generation of HIV transmissions/100 person-years that would be averted by each strategy to estimate the impact on the optimal age for a one-time screen. The likelihood that a person will transmit HIV to others is modeled as a function of the HIV RNA level; HIV RNA-stratified transmission rates ranged from 0.16–9.03 transmissions/100 person-years, with higher rates for those within three months of infection and for those with advanced infection (Appendix Table A1). Further, we examined one-time screens at every age between 13–35 years to determine whether clinical and cost differences at similar ages were meaningful.

Base case results are reported according to cost-effectiveness convention, in order of increasing costs; ICERs are calculated comparing each strategy to the next most costly strategy after eliminating “dominated” strategies, which are strategies that are either more costly or less cost-effective than other strategies that produce greater benefits [23]. For sensitivity analyses, we report ICERs comparing the most effective strategy to *current practice* because of variation in the comparator strategies when calculating ICERs. Details of additional model parameters can be found online in the appendix.

RESULTS

Base case results: clinical outcomes

Among 12-year-olds in the US without identified HIV risk factors, the projected number of new HIV infections peaked at age 24, although more than 75% of lifetime infections were projected to occur afterwards (mean age: 37.3 years [SD 16.9 years] (Appendix Figure A1). Among AYA who became HIV-infected at any point in their lifetime, *current practice* led to a projected mean CD4 cell count at diagnosis of 324 cells/ μ L and an undiscounted life expectancy from age 12 of 585.05 months (48.75 years) (Table 2).

When projected for the entire cohort (including those becoming and never becoming HIV-infected), life expectancy from age 12 was 810.90 months (67.58 years) (344.49 months [28.71 years] discounted).

Any evaluated one-time screen in addition to *current practice* increased projected CD4 cell count at diagnosis and life expectancy among HIV-infected people. Of the one-time screening strategies, a *screen at age 25* led to the highest projected mean CD4 cell count at diagnosis (345 cells/ μ L) and the greatest gains in undiscounted HIV-infected life expectancy from age 12 (589.82 months, an increase of 4.8 months over *current practice*). The impact of any one-time screen on discounted life expectancy for the total population (HIV-infected and HIV-uninfected people) was very small (*current practice*: 810.90 months [344.49 months discounted]; additional *screen at age 25*: 810.97 months [344.52 months discounted]).

HIV detection

All one-time screening strategies identified a small proportion of total lifetime HIV infections (0.1–10.3%) (Figure 1a), because most infections occurred after age 25

(Appendix Figure A1). *Screen at age 25* provided the lowest proportions never diagnosed (10.6%) and diagnosed via OI (34.8%) (Appendix Figure A3a). Even a perfect *screen at age 25* (100% test offer and acceptance, result return, and linkage) would detect only 13% of lifetime infections. When limited to people infected before age 25, one-time screening strategies identified a larger proportion of HIV infections (0.4–33.8%), and results were still optimized with *screen at age 25* (Figure 1b, Appendix Figure A3b).

HIV care continuum outcomes at age 25 years and 11 months

Assessing outcomes at age 25 years and 11 months, *screen at age 25* led to the most favorable care continuum outcomes, with 77.3% diagnosed, 70.8% linked to care, 61.5% retained in care, and 51.4% virologically suppressed (Figure 2, Appendix Figure A4).

Base case results: cost and cost-effectiveness

Current practice led to the lowest projected HIV-related healthcare costs for the cohort, with lifetime discounted costs of \$2,860/person (Table 2, Appendix Figure A5). Lifetime HIV-related healthcare costs were greatest for the strategy with the most favorable clinical outcomes (*screen at age 25*: \$3,000/person). In cost-effectiveness analyses, *screens at age 15, 18 or 21* were dominated. The ICER of *screen at age 30* compared to *current practice* was \$62,500/YLS; the ICER of *screen at age 25* compared to *screen at age 30* was \$96,000/YLS.

Sensitivity analyses

The ICER of *screen at age 25* compared to *current practice* was most sensitive to linkage to care, increasing HIV screen costs, and HIV healthcare costs (Figure 3). A one-time *screen at age 25* optimized clinical outcomes over wide ranges in loss to follow-up, *current practice* screening, screen offer and acceptance, result return, screen sensitivity and specificity, CD4 cell count at infection and absolute increases in HIV incidence. If the one-time HIV screening program characteristics were much worse, the benefits of one-time screening strategies at any age were attenuated, and the cost-effectiveness ratios increased, but the optimal age for screening AYA remained after the peak of incidence. Cost-effectiveness outcomes improved with one-time screening at younger ages if the peak of HIV incidence was earlier and, conversely, with onetime screening at older ages if the peak of incidence was later (Appendix Table A3). Additional two-way sensitivity analyses of the most influential parameters are reported in the appendix (Appendix Figure A6).

Additional analyses

In the base case, using adult quality-of-life weights for AYA increased the ICER of *screen at 25* compared to *screen at age 30* to \$115,900/QALY. The greatest reduction in HIV transmissions/100 person-years occurred with a *screen at age 25* (3.8%) compared to *current practice* (range 0.05–3.8% for any one-time screen) (Figure A7). Evaluation of one-time screens between ages 13–35 revealed negligible differences in outcomes between specific consecutive yearly ages, and the policy conclusion favoring a test in the mid-20s was unchanged.

DISCUSSION

Our objective was to assess whether the CDC recommendation for one-time HIV screening between the ages of 13–64 should begin at age 13. We determined the value of one-time HIV screening, in addition to current screening practices, in AYA aged 13–24 without identified risk factors for HIV infection in the US. We had three principal findings. First, although an additional one-time screen at any age between 15–30 led to important gains in HIV diagnosis rates and life expectancy for HIV-infected people, a *screen at age 25* provided the most favorable clinical outcomes and the best value for money. Compared to *current practice*, an additional one-time *screen at age 25* led to a substantial gain in HIV-infected life expectancy of 4.8 months and was cost-effective in the US (ICER compared to a *screen at age 30*: \$96,000/YLS) [23, 24, 30]. These results align with other analyses which have found HIV screening to be cost-effective in the US in all but the lowest-risk populations [25, 31, 32]. CDC recommends screening for HIV infection at least once for all people aged 13–64 years [3]. Our results suggest that if a one-time screen is offered to AYA without identified risk factors, it would provide greater clinical benefit and economic value if offered later, in the mid-20s, than if offered in early adolescence. In this analysis, a *screen at age 18* or *21* was only superior to a *screen at age 25* if HIV incidence peaked at earlier ages. Diagnoses of new HIV infections among persons aged 13–29 years peaked between ages 22–25 from 2009–2013 [11]. While the timing of peak HIV incidence among persons aged 13–29 is unknown, it is unlikely that the population peak of HIV incidence in youth without identified risk factors occurs before age 18.

Second, while gains in life expectancy and the number of AYA detected by the one-time screen were small (because most infections occurred after age 24), a *screen at age 25* substantially improved care continuum outcomes for those who became HIV-infected by age 25. With a one-time *screen at age 25*, the proportion of HIV-infected youth diagnosed by age 25 increased markedly compared to screening at other ages (77% versus 51–53%); the proportion with virologic suppression also increased (51% versus 34–36%). These projections depend on data about rates of linkage and retention in AYA after routine screening, which vary by setting. Linkage to care rates for AYA, for example, range from 30% in Miami, FL to 92% in an emergency department in Bronx, NY (base case 76%) [13, 33, 34]. The *current practice* scenario projected more optimistic virologic outcomes than were reported in a recent review or in the CDC Medical Monitoring Project (80% versus 55% and 68% virologic suppression among those retained, respectively) [35, 36]. Our sensitivity analyses using lower rates of retention and suppression suggest that the benefits of an additional one-time screen are markedly attenuated if AYA are screened but subsequently do not remain in care and on ART. HIV-infected AYA have poorer outcomes compared to adults at every step of the HIV care continuum; interventions to support linkage and retention will therefore be critical to any HIV screening program for AYA [13, 37].

Third, any combination of *current practice* and an additional one-time screen among AYA without identified risk factors will detect only a small proportion of lifetime HIV infections, most of which occur after age 25. Even a perfect one-time *screen at age 25* would detect only 13% of lifetime infections, and in our less optimistic base case scenario, this value was 10%. Despite these modest contributions to HIV detection, a one-time *screen at age 25*

substantially improved clinical and cost-effectiveness outcomes compared to other one-time screening strategies. A *screen at age 30*, for example, led to lower CD4 cell count at diagnosis compared to a *screen at age 25* because those infected at young ages experienced substantial CD4 cell count decline by age 30. Combinations of routine HIV screening strategies for AYA, along with repeat screening in high-risk youth at appropriate intervals, will be needed to curb the rising epidemic of HIV in US AYA [37].

There are several limitations to this model-based analysis. First, incidence inputs were estimated from rates of new diagnoses, because the true number of new infections is unknown [38]. To address this uncertainty, we adjusted these values by age-stratified CDC-estimated proportions of infections that are undiagnosed, and then calibrated the model to NHSS data on CD4 cell count at diagnosis and total incidence rates. Second, *current practice* HIV screening inputs were derived from reported rates of HIV screening which likely do not capture barriers to HIV screening for all AYA (for example, the Youth Risk Behavior Survey only samples students in grades 9 through 12) [4]. Third, because of limited data in AYA, we assume HIV-related healthcare utilization was constant over the age group. We also excluded utility adjustments in the primary analysis. AYA aged 18–30 comprise only a small fraction of participants in HIV-specific health-related quality-of-life studies, and emerging data suggest that youth may attach different values to specific health states compared to adults [22]. When adult quality-of-life utility weights were applied to calculate ICERs with QALYs, all ICERs remained below \$150,000/QALY; ICER thresholds ranging from \$50,000–200,000/QALY have been recommended for use in the US [24]. We additionally used adult values when the rates reported in AYA seemed too extreme; for example, for test acceptance we used 80.0% instead of 95% reported among 13–21-year-olds, and varied this parameter in sensitivity analysis [34]. Fourth, we did not explore multiple generations of HIV transmission. The small (0.05–3.8%) proportion of primary HIV transmissions averted would likely make a one-time screen at all ages slightly more cost-effective; however, among AYA without identified risk behaviors, HIV prevalence by age 25 is so low that this impact is likely minimal.

Designed to assess routine one-time screening in AYA without identified HIV risk factors, this analysis did not examine the impact of repeat screening later in adulthood. Additionally, the results do not apply to AYA with identified risk factors. The peak HIV incidences (3.6/100PY and 7.2/100PY) examined in our sensitivity analyses mirrored that of higher risk populations (for example, Adolescent Trials Network study 110: 3.1/100PY; PROUD study 9.0/100PY), but we lacked data to derive age-specific incidence rates for these groups [39, 40]. Age-based, sexual identity- and orientation-based, racial/ethnic, and regional disparities have been described in both HIV screening and incidence [2, 4, 13, 33]. Risk factor assessment should be performed by health care practitioners and optimal screening strategies for known high-risk subgroups of AYA will be different than those presented in this analysis [41].

In summary, for AYA without identified HIV risk factors in the US, one-time routine HIV screening at age 25, shortly after the peak of HIV incidence, in addition to current screening practice, would improve clinical outcomes and be cost-effective compared to current US

screening practices alone. Focusing screening on AYA ages 18 or younger is a less efficient use of a one-time screen among AYA than screening at a later age.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

FUNDING

This research was funded by US Centers for Disease Control and Prevention National Center for HIV, Viral Hepatitis, STD, and TB Prevention (Epidemiologic and Economic Modeling Agreement number 6NU38PS004644). CDC co-authors roles are noted above. This research also received funding from the following organizations which had no role in this research: the National Institute of Allergy and Infectious Diseases, the Eunice Kennedy Shriver National Institute for Child Health and Human Development (NIAID T32 AI007433, R01 HD079214, R01 AI042006, R01 AI112340) and the Steve and Deborah Gorlin MGH Research Scholar Award.

ROLE OF THE FUNDING SOURCE

The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the U.S. Department of Health and Human Services or the National Institutes of Health or other funders.

All individuals other than authors and co-authors who contributed significantly to this work are listed in this section. The authors gratefully acknowledge Irene Hall, PhD, FACE, Chief, and Tianchi Zhang, MPH, Programmer, of the HIV Incidence and Surveillance Branch, US Centers for Disease Control and Prevention, for assistance with data. We thank Taige Hou, BS, who assisted with programming, and Milton Weinstein, PhD, and the Cost-Effectiveness of Preventing AIDS Complications (CEPAC)-US and -Pediatric research teams in the Medical Practice Evaluation Center at Massachusetts General Hospital for providing feedback on study design and interpretation. The findings in this manuscript were presented as a poster at the 2017 Conference on Retroviruses and Opportunistic Infections, and as an oral presentation for the Society for Adolescent Health and Medicine in April 2017.

ABBREVIATIONS

AIDS	Acquired Immunodeficiency Syndrome
ART	antiretroviral therapy
AYA	adolescents and young adults
CD4 cell count	measurement of the number of CD4 white blood cells
CDC	United States Centers for Disease Control and Prevention
CEPAC	the Cost-Effectiveness of Preventing AIDS Complications model
HIV RNA level	human immunodeficiency virus ribonucleic acid level
HIV	human immunodeficiency virus
ICER	incremental cost-effectiveness ratio
NHIS	National Health Interview Survey
NHSS	National HIV Surveillance System

OI	opportunistic infection
PROUD	PRE-exposure Option for reducing HIV in the UK
PY	person-years
QALY	quality-adjusted life-year
US	United States of America
USD	United States dollars
YLS	year-of-life saved
YRBS	Youth Risk Behavior Survey

References

- Centers for Disease Control and Prevention. HIV Surveillance Report. 2014; 26 [Accessed July 01, 2017] <http://www.cdc.gov/hiv/library/reports/surveillance/>. Published November 2015.
- Centers for Disease Control and Prevention. Monitoring selected national HIV prevention and care objectives by using HIV surveillance data - United States and 6 dependent areas, 2014. HIV Surveillance Supplemental Report. 2016; 21(4) [Accessed July 01, 2017] <http://www.cdc.gov/hiv/library/reports/surveillance/>. Published July 2016.
- Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR. 2006; 55(RR-14):1–17. [Accessed January 21 2017] Available at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5514a1.htm>.
- [Accessed July 03 2017] HIV testing trends in the United States, 2000–2011. Available at: http://www.cdc.gov/hiv/pdf/testing_trends.pdf
- Hall HI, Holtgrave DR, Maulsby C. HIV transmission rates from persons living with HIV who are aware and unaware of their infection. AIDS. 2012; 26:893–896. [PubMed: 22313960]
- Brown SR, Kenedy C. AAFP recommends universal screening for HIV infection beginning at age 18 years. Am Fam Physician. 2014; 89:614–317. [PubMed: 24784120]
- US Preventive Services Task Force. Screening for HIV: US Preventive Services Task Force recommendation statement. Ann Intern Med. 2013; 159:51–60. [PubMed: 23698354]
- Henry, J. Kaiser Family Foundation. [Accessed April 13 2017] Survey of Americans on HIV/AIDS. Available at: <https://kaiserfamilyfoundation.files.wordpress.com/2013/01/7522.pdf>
- Society for Adolescent Health and Medicine. Clinical Care Resources. 2017.
- [Accessed October 03 2016] Age and Sex Composition. 2010. Available at: <http://www.census.gov/prod/cen2010/briefs/c2010br-03.pdf>
- Centers for Disease Control and Prevention. HIV Incidence and Case Surveillance Report. 2013; 26 [Accessed July 1, 2017] <https://www.cdc.gov/hiv/pdf/library/reports/surveillance/>. Published November 2014. (Additional age stratifications released for this project.).
- Centers for Disease Control and Prevention. HIV Surveillance Report. 2013; 25 [Accessed October 03, 2016] <http://www.cdc.gov/hiv/library/reports/surveillance/>. Published February 2015. Available at: <http://www.cdc.gov/hiv/library/reports/surveillance/>.
- Hall HI, Frazier EL, Rhodes P, et al. Differences in human immunodeficiency virus care and treatment among subpopulations in the United States. JAMA Intern Med. 2013; 173:1337–1344. [PubMed: 23780395]
- Eggman AA, Feaster DJ, Leff JA, et al. The cost of implementing rapid HIV testing in sexually transmitted disease clinics in the United States. Sex Transm Dis. 2014; 41:545–550. [PubMed: 25118967]
- Schackman BR, Eggman AA, Leff JA, et al. Costs of expanded rapid HIV testing in four emergency departments. Public Health Rep. 2016; 131(Suppl 1):71–81. [PubMed: 26862232]

16. Walmsley SL, Antela A, Clumeck N, et al. Dolutegravir plus abacavir-lamivudine for the treatment of HIV-1 infection. *N Engl J Med*. 2013; 369:1807–1818. [PubMed: 24195548]
17. Cahn P, Fourie J, Grinsztejn B, et al. Week 48 analysis of once-daily vs. twice-daily darunavir/ritonavir in treatment-experienced HIV-1-infected patients. *AIDS*. 2011; 25:929–939. [PubMed: 21346512]
18. Yazdanpanah Y, Fagard C, Descamps D, et al. High rate of virologic suppression with raltegravir plus etravirine and darunavir/ritonavir among treatment-experienced patients infected with multidrug-resistant HIV: results of the ANRS 139 TRIO trial. *Clin Infect Dis*. 2009; 49:1441–1449. [PubMed: 19814627]
19. Healthcare T. [Accessed July 03 2017] Average wholesale price: Red Book. Available at: <http://sites.truvenhealth.com/redbook/index.html>
20. Levinson, D. Department of Health and Human Services. Medicaid drug price comparisons: Average manufacturer price to published prices. 2005.
21. Helleberg M, Engsig FN, Kronborg G, et al. Retention in a public healthcare system with free access to treatment: a Danish nationwide HIV cohort study. *AIDS*. 2012; 26:741–748. [PubMed: 22156974]
22. Griebisch I, Coast J, Brown J. Quality-adjusted life-years lack quality in pediatric care: a critical review of published cost-utility studies in child health. *Pediatrics*. 2005; 115:e600–614. [PubMed: 15867026]
23. Gold, MR, Siegel, JE, Russell, LB., et al., editors. Cost-effectiveness in health and medicine. New York: Oxford University Press; 1996.
24. Neumann PJ, Cohen JT, Weinstein MC. Updating cost-effectiveness - the curious resilience of the \$50,000-per-QALY threshold. *N Engl J Med*. 2014; 371:796–797. [PubMed: 25162885]
25. Paltiel AD, Weinstein MC, Kimmel AD, et al. Expanded screening for HIV in the United States—an analysis of cost-effectiveness. *N Engl J Med*. 2005; 352:586–595. [PubMed: 15703423]
26. Martin EG, Paltiel AD, Walensky RP, et al. Expanded HIV screening in the United States: what will it cost government discretionary and entitlement programs? A budget impact analysis. *Value Health*. 2010; 13:893–902. [PubMed: 20950323]
27. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1 infected adults and adolescents. Department of Health and Human Services; Available at: <https://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf> [Accessed June 25 2017]
28. Girouard MP, Sax PE, Parker RA, et al. The cost-effectiveness and budget impact of 2-drug dolutegravir-lamivudine regimens for the treatment of HIV infection in the US. *Clin Infect Dis*. 2015; 62(6):784–91. [PubMed: 26658053]
29. Fleishman JA, Yehia BR, Moore RD, et al. Establishment, retention, and loss to follow-up in outpatient HIV care. *J Acquir Immune Defic Syndr*. 2012; 60:249–259. [PubMed: 22531758]
30. Wright JC, Weinstein MC. Gains in life expectancy from medical interventions--standardizing data on outcomes. *N Engl J Med*. 1998; 339:380–386. [PubMed: 9691106]
31. Sanders GD, Bayoumi AM, Sundaram V, et al. Cost-effectiveness of screening for HIV in the era of highly active antiretroviral therapy. *N Engl J Med*. 2005; 352:570–585. [PubMed: 15703422]
32. Shah M, Risher K, Berry SA, et al. The epidemiologic and economic impact of improving HIV testing, linkage, and retention in care in the US. *Clin Infect Dis*. 2016; 62:220–229. [PubMed: 26362321]
33. Laffoon BT, Hall HI, Surendera Babu A, et al. HIV infection and linkage to HIV-related medical care in large urban areas in the US, 2009. *J Acquir Immune Defic Syndr*. 2015; 69:487–492. [PubMed: 25844695]
34. Calderon Y, Chou K, Cowan E, et al. Analysis of HIV testing acceptance and risk factors of an adolescent cohort using emergency department-based multimedia HIV testing and counseling. *Sex Transm Dis*. 2013; 40:624–628. [PubMed: 23859908]
35. Zanoni BC, Mayer KH. The adolescent and young adult HIV cascade of care in the United States: exaggerated health disparities. *AIDS Patient Care STDs*. 2014; 28:128–135. [PubMed: 24601734]

36. Bradley H, Mattson CL, Beer L, et al. Increased antiretroviral therapy prescription and HIV viral suppression among persons receiving clinical care for HIV infection. *AIDS*. 2016; 30:2117–2124. [PubMed: 27465279]
37. Wood SM, Dowshen N, Lowenthal E. Time to improve the global HIV/AIDS care continuum for adolescents: A generation at stake. *JAMA Pediatr*. 2015; 169:619–620. [PubMed: 25985061]
38. Hall HI, An Q, Tang T, et al. Prevalence of diagnosed and undiagnosed HIV infection—United States, 2008–2012. *MMWR Morb Mortal Wkly Rep*. 2015; 64:657–662. [PubMed: 26110835]
39. Hosek S, Rudy B, Landovitz R, et al. An HIV pre-exposure prophylaxis (PrEP) demonstration project and safety study for young MSM. *J Acquir Immune Defic Syndr*. 2016; 74:21–29.
40. McCormack S, Dunn DT, Desai M, et al. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. *Lancet*. 2016; 387:53–60. [PubMed: 26364263]
41. Van Handel M, Kann L, Olsen EO, et al. HIV testing among US high school students and young adults. *Pediatrics*. 2016; 137:1–9.

IMPLICATIONS AND CONTRIBUTION

This study found that for adolescents and young adults (AYA) without identified risk factors for HIV, a one-time routine HIV screen at age 25 would optimize clinical outcomes and be cost-effective. Focusing screening on AYA ages 18 or younger is a less efficient use of a one-time screen.

Figure 1a.

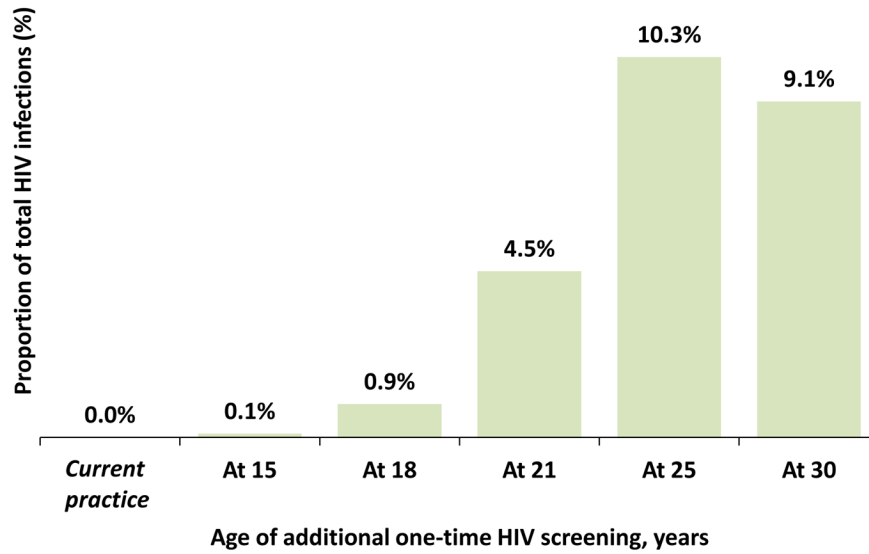


Figure 1b.

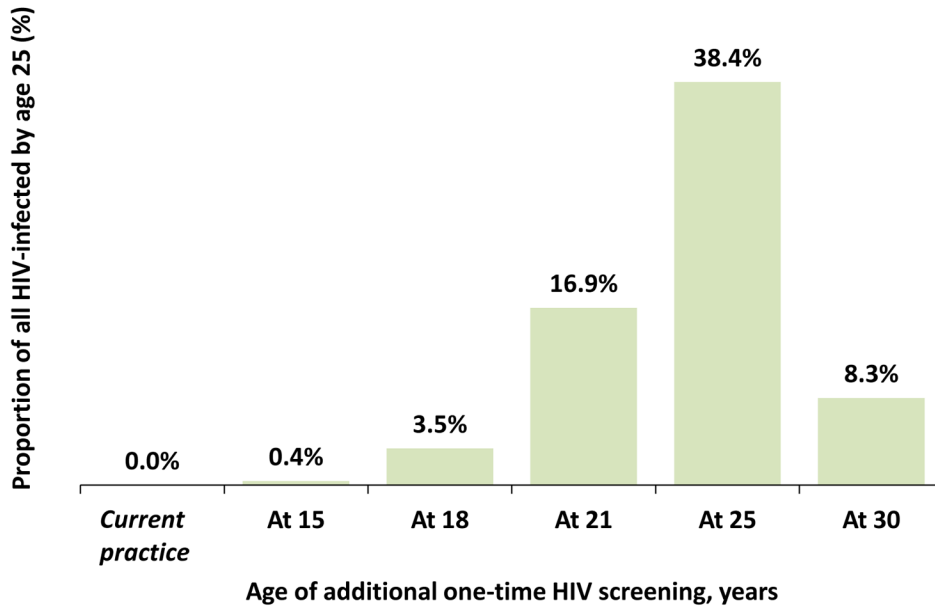


Figure 1.

Figure 1a. Proportion diagnosed by the HIV screening program for people HIV-infected at any age

This bar graph presents the proportion of people diagnosed by the HIV screening program for all HIV-infected people over their lifetime, regardless of the age of HIV infection. A one-time *screen at age 25* in addition to *current practice* screening will only detect 10.3% of infections, most of which occur after age 25.

Figure 1b. Proportion diagnosed by the HIV screening program for all people HIV-infected before age 25 years

This bar graph presents proportion of people diagnosed by the HIV screening program for all HIV-infected people over their lifetime, limited to those who were infected before age 25. A one-time *screen at age 25* in addition to *current practice* screening will detect 38.4% of infections.

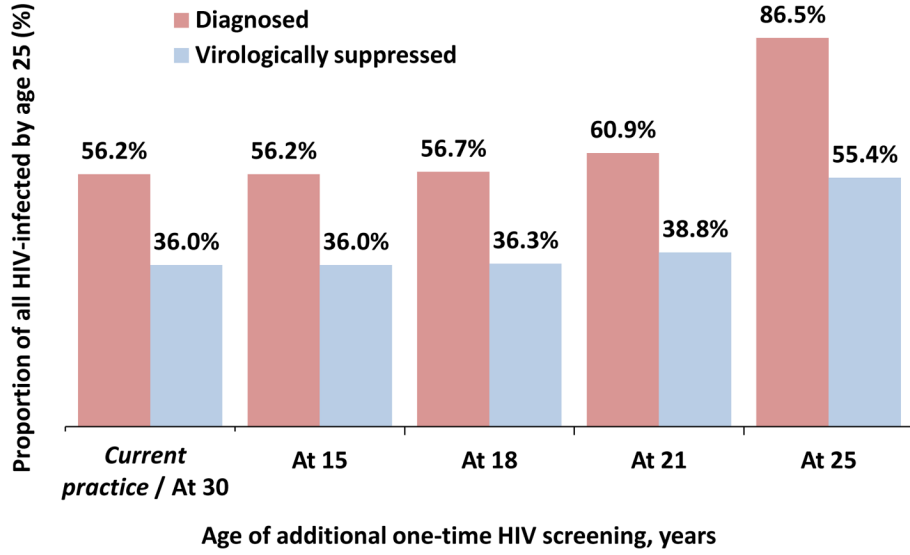


Figure 2. Proportions diagnosed and virologically suppressed, among people infected before age 25 years

This bar graph presents cross-sectional virologic suppression at age 25 years and 11 months for AYA infected before age 25 years. Among people HIV-infected by age 25 years, proportion diagnosed with HIV and proportion virologically suppressed are shown cross-sectionally at age 25 and 11 months. Compared to either *current practice*, or *screens at ages 15 or 18*, a *screen at age 25* substantially improved care continuum outcomes. A *screen at age 30* is equivalent to *current practice* when considering the care continuum at age 25 years. HIV screening occurs in the first month of the year, while HIV care continuum outcomes are calculated in the eleventh month of the year.

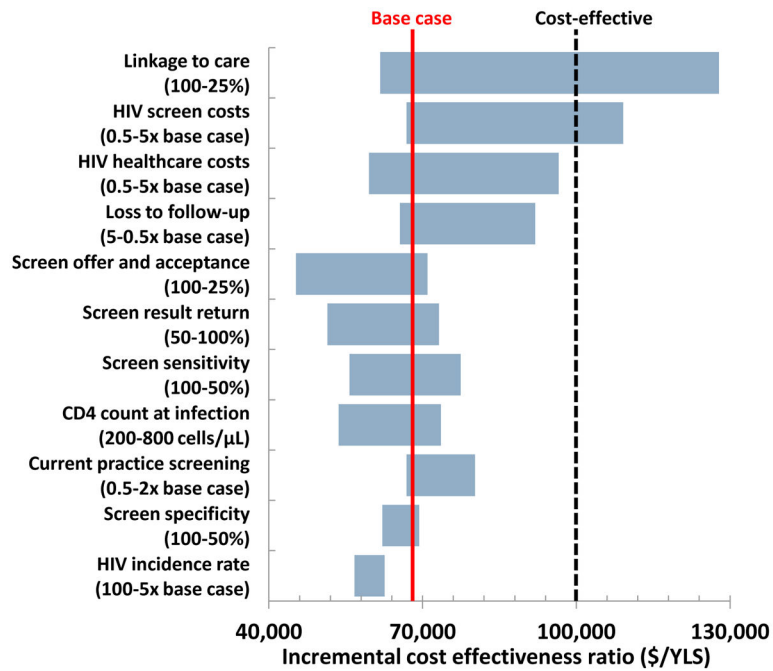


Figure 3. Sensitivity analyses: Screen at age 25 compared to current practice

Key parameters varied in model sensitivity analyses are shown on the left. Values in parentheses indicate the range examined. ICERs for the comparison of *screen at 25* vs. *current practice* are shown on the horizontal axis, in 2013 USD/YLS. The range of ICERs for each varied parameter is indicated by the blue horizontal bars. Longer blue horizontal bars indicate parameters to which the model results were more sensitive. The solid, red vertical line indicates the ICER for screen at 25 vs. current practice using all base case parameters: \$67,000/YLS. The dotted black vertical line indicates the “willingness-to-pay” threshold of <\$100,000/year-of-life saved (YLS) [23, 24]. This figure provides a framework for when decisions are made on cost-effectiveness grounds – the value within the horizontal bar indicates when one would favor an additional *one-time screen at 25* over current practice alone by this criterion. Bars extending to the far-right axis indicate scenarios in which screen at 25 results in an ICER of >\$100,000/YLS in comparison to current practice. For the base case, we reported results according to cost-effectiveness analysis convention, with results shown in order of increasing costs and ICERs calculated comparing each strategy to the next most costly strategy after eliminating dominated strategies (Table 2). Here, we reported ICERs comparing the most effective strategy to current practice because of variation in the comparator strategies. Given the co-linearity of ICERs of one-time testing strategies (Appendix Figure A5), small changes in population life expectancy and population costs resulted in variation in comparator strategies when comparing the most effective strategy to the next best strategy.

Table 1

Input parameters for a model of routine HIV screening in US adolescents and young adults

Population characteristics	General US population	Source
Age (years)	12	<i>Modeled population</i>
Male sex (%)	51.2	[10]
HIV prevalence at age <12 (%)	0	<i>Modeled population</i>
Annual HIV incidence by age, rate/100,000PY^a		
<13 years	0.6	[11, 12]
15	1.8	[11, 12]
18	22.9	[11, 12]
21	59.1	[11, 12]
24	71.3	[11, 12]
25	54.3	[11, 12]
26–30	46.3	[11, 12]
31–35	38.3	[12]
36–40	32.6	[12]
41–45	32.1	[12]
>45	8.6	[12]
Current HIV screening practice (annual probability)		
12–17 years	0.01	[4]
18–34	0.16	[4]
35–44	0.10	[4]
45–64	0.06	[4]
65	0.02	[4]
Probability of linkage to care (%)	75.6	[13]
HIV screening program costs (USD 2013)^c		
HIV screen	35.92	[14]
Completed positive screen	72.23	[14, 15]
Antiretroviral therapy (range, 1st through 6th available regimen)^d		
Efficacy (%)	93–81	[16–18]
Cost/month (USD 2013)	2,170–3,570	[19, 20]
Return to care (rate/100PY)	18.1	[21]

^aComplete age-stratified incidence rates are reported in Table A1 and Figure A1.

^bIncidence estimates presented incorporate rates of new diagnoses in 2013 from the National HIV Surveillance System (NHSS) and undiagnosed incidence. (See appendix Table A1.)

^cHIV screen cost was derived from an average of reported costs with and without counseling at sexually transmitted infection clinics [14]. The cost of completing a positive screen was based on average reported costs at hospitals [15]. Costs include costs of reagents and controls, laboratory equipment costs, specimen collection, transport and process, quality control, counseling and personnel time at national wage and fringe labor rates.

^dAntiretroviral efficacy is defined as the rate of suppression of HIV RNA <400 copies/mL at 48 weeks.

Additional references for inputs are noted in the appendix (Table A1).

PY: person-years; USD: US dollars

Modeled outcomes of 5 HIV screening strategies for US adolescents and young adults

Table 2

Age of one-time screening in addition to current practice, years	Mean CD4 at diagnosis (cells/ μ L)	Life expectancy (months from age 12)			Population (discounted) ^a	Lifetime per-person cost, population (\$) ^b	ICER (\$/YLS) ^{a, c}
		HIV-infected (undiscounted)	Population (undiscounted)	Population (discounted) ^a			
<i>Current practice</i>	324	585.05	810.90	344.49	2,860	--	
15	325	585.10	810.90	344.49	2,880	Dominated	
18	327	585.21	810.90	344.50	2,890	Dominated	
21	335	586.93	810.93	344.51	2,940	Dominated	
30	340	589.45	810.96	344.52	2,970	62,500	
25	345	589.82	810.97	344.52	3,000	96,000	

^aResults are discounted at 3 percent per year.

^bResults are rounded to the nearest \$10.

^cCost-effectiveness is the difference in cost divided by the difference in life expectancy for each strategy compared with the next most costly strategy. When comparing three or more strategies, if a strategy has a higher ICER than a competing strategy with a higher lifetime cost (as is the case here), then the strategy is said to be “dominated,” reflecting an inefficient use of healthcare resources, and the ICERs of all strategies are recalculated with that strategy omitted [23]. ICERs are calculated from unrounded model output and then rounded to the nearest \$100. Of note, an ICER with the same life expectancy and increased cost would also be dominated. ICERs are graphically represented in the appendix (Figure A5).

ICER: Incremental cost-effectiveness ratio; YLS: Year-of-life saved