A BOLD UNDERTAKING

It was spring 2006. The Centers for Disease Control and Prevention (CDC) estimated more than 1 million U.S. residents were infected with the human immunodeficiency virus (HIV), and approximately one-quarter of these individuals were unaware they were infected. In 2004, 39% of people diagnosed with AIDS had first tested positive for HIV infection less than 1 year prior to their AIDS diagnosis; a large majority of these individuals were already symptomatic by the time they learned that they were HIV infected. These two statistics illustrated vividly that HIV screening programs—directed at early detection among pregnant women, persons at high risk, and healthcare settings with high HIV prevalence—were not adequately reaching infected individuals.

A team of physicians and epidemiologists from the George Washington University (GW) Medical Center in Washington, DC, was focusing closer to home. Every day, their work reminded them that Washington’s AIDS incidence rate was higher than any other major metropolitan area in the United States. They were familiar with numerous studies demonstrating that individuals who know their HIV status and are able to receive counseling and treatment not only live longer (a personal health benefit), but also change their behavior, thereby reducing the likelihood of infecting others (a population health benefit).2,3

Because of the severe impact of HIV/AIDS in the District of Columbia, this team, led by Dr. Jeremy Brown, was contemplating a bold new undertaking—a project to test the feasibility of implementing near-universal opt-out HIV screening at the emergency department (ED) of The George Washington University Hospital. As safety net providers, emergency departments are the most likely source of medical services for low-income and indigent people who are also among those most at risk of acquiring HIV infection. The GW ED provided care to a diverse population of 60,000 patients annually, and many of its patients might not otherwise have a regular source of medical care where they could be screened for HIV.

Dr. Brown and his team members knew they faced numerous challenges if they were to get the proposed program off the ground in the fall of 2006, including:

- Convincing hospital administrators they should screen everyone, rather than just individuals who fit a high-risk profile
- Estimating the number of people who would assent to be screened
- Estimating the number that would screen positive, and of those, the number that would and would not be infected with HIV
- Deciding whether to conduct confirmatory testing in the ED or to refer people who screened positive to other providers for confirmatory testing
- Deciding whether they were comfortable with the ethical and civil liberties implications associated with omitting substantial pretest counseling and written informed consent from the HIV screening process
- Anticipating other challenges that might be encountered during the pilot project
A BRIEF HISTORY OF HIV

Researchers believe HIV-1 (the predominant strain of HIV in the developed world) originated in chimpanzees native to west equatorial Africa, and the virus entered humans in the mid-1900s via hunters exposed to infected blood. HIV first emerged in the United States between 1979 and 1981 among men who had sex with other men. The term acquired immunodeficiency syndrome (AIDS) was coined in 1982 to denote the spectrum of illnesses associated with advanced HIV infection; U.S. surveillance of AIDS cases began the same year. 5 HIV testing first became available in 1985; the incidence of HIV in the United States also peaked around that time. There was no effective treatment, but in 1987, the U.S. Public Health Service began to promote HIV counseling and testing as a means of preventing spread of the disease. Since 2000, the number of new cases per year in the United States has been relatively stable at 55,000 to 58,500.6

In 1996, with the advent of antiretroviral therapy, the progression of HIV infections to AIDS decreased markedly in the United States and other countries where antiretroviral therapies were available. With these new medications, HIV went from being a fatal disease to a chronic disease. Screening to identify HIV infection in asymptomatic individuals now enables a true delay in symptoms and improved survival.1

HIV SCREENING POLICY: THE NATIONAL AND LOCAL LANDSCAPE

Since 2001, CDC guidelines called for HIV screening among pregnant women, persons at high risk, and in healthcare settings with high HIV prevalence (defined as HIV seroprevalence rates of >1% or AIDS diagnosis rates of >1 per 1,000 discharges). Recommendations to screen pregnant women as a routine part of prenatal care had, for the 5 years leading up to the 2001 policy, incorporated streamlined pretest counseling and informed consent processes to reduce barriers for providers. However, screening in high-risk populations required more extensive pretest counseling and written informed consent. Because it can be difficult to identify high-prevalence healthcare settings and because of resource constraints, many healthcare providers did not introduce HIV screening programs as called for in the CDC guidelines.1

The CDC recognized that the effectiveness of risk-based HIV screening was limited, and throughout 2005 it engaged in a comprehensive evaluation of strategies to expand HIV testing. This process included broad input from healthcare providers, public health agencies, community organizations, people living with HIV, researchers, and clinicians. Dr. Brown and his GW colleagues were aware that the CDC was preparing to recommend, later in 2006, a major change in HIV screening policy—opt-out HIV screening for virtually all patients in virtually all healthcare settings.1

Specifically, the CDC was planning to recommend routine opt-out screening for all patients aged 13–64 years, unless the “prevalence of undiagnosed HIV infection in their patients has been documented to be < 0.1%.”1(p 7) Opt-out screening meant “performing HIV screening after notifying the patient that 1) the test will be performed and 2) the patient may elect to decline or defer testing. Assent is inferred unless the patient declines testing.”1(p 7) The CDC was further planning to specify that:

- “Separate written consent for HIV testing should not be required; general consent for medical care should be considered sufficient to encompass consent for HIV testing.”1(p 3)
- “Prevention counseling should not be required with HIV diagnostic testing or as part of HIV screening programs in healthcare settings.”1(p 3)

Meanwhile, the District of Columbia Department of Health was also aware of the upcoming changes in the CDC’s recommendations for HIV screening in healthcare settings. Because of the severe impact of HIV/AIDS in the District of Columbia, the DC Department of Health was planning to adopt a groundbreaking initiative that went even further: to encourage HIV screening for every District resident between the ages of 14 and 84 and to immediately refer those who test positive for counseling, medical care, and treatment. The Department of Health was working to launch its new program, “Come Together DC—Get Screened for HIV,” on June 27, 2006, National HIV Testing Day.7

So, in the spring of 2006, with HIV screening policy changes on the horizon at both the national and local levels, healthcare providers were weighing their options. On the one hand, universal HIV screening seemed like a positive public health move. On the other hand, many administrators grumbled that the upcoming policy changes constituted an unfunded mandate—yet another procedure requiring materials and personnel time without the promise of full cost recovery. This strain would be particularly evident in hospital emergency departments, whose primary mission was to care for urgently ill or injured patients—not to conduct public health programs.

HIV SCREENING TESTS

In March 2004, the U.S. Food and Drug Administration approved the OraQuick Advance HIV1/2 Antibody Test (also called the “HIV rapid test,” “rapid HIV test,” “rapid oral swab
test,” and “rapid test”) for use in screening both oral fluid and plasma for HIV antibodies. Previously, a whole blood specimen from either a finger stick or tube of blood was needed for testing.

With the HIV rapid test, the oral fluid specimen is collected via a gum swab and produces a result in 20 to 40 minutes. Interpretation is visual and no instrumentation is required.

The GW ED could obtain screening test kits at no cost from the DC Department of Health. A reactive (positive) rapid test result means that HIV-1 or HIV-2 antibodies have been detected in the specimen. Clinical studies by the manufacturer demonstrated a sensitivity of 99.3% and a specificity of 99.8%. Like other antibody tests for HIV, the rapid test is not able to detect recent infections; false negative results may occur within a window period of up to 3 months following infection with HIV. This is why CDC recommended that any individual who tests negative but who has had known or suspected exposure to HIV within 3 months should be instructed to obtain repeat screening 3 months after the exposure.

Although they are extremely accurate, rapid test results are not definitive; therefore confirmatory testing using either Western blot or immunofluorescent assay methods is necessary for all positive rapid HIV test results. The Western blot assay, more expensive and technically more difficult to perform than screening tests, is the gold standard, considered to be 100% accurate. It generally takes several days to obtain Western blot results.

**NAILING DOWN THE DETAILS: WHAT TO EXPECT?**

The GW Hospital is a tertiary care hospital serving a diverse group of patients, including residents of Washington, DC and nearby Maryland and Virginia, as well as tourists and visiting dignitaries. About 60,000 patients are treated annually in the ED, which is a level I trauma center.

Surveillance data from 2004 (the latest year with complete data) indicated at least 3% of Washington, DC residents had been diagnosed with HIV infection. However, Dr. Brown and his team did not know the prevalence of undiagnosed HIV infection among the GW ED patient population. They were also uncertain as to whether those who opted out of the routine screening program would have a different prevalence of infection from those who agreed to be tested.

In addition to not screening patients who already knew they were HIV-positive or had been given an HIV test in the previous 3 months, the research team made some up-front decisions about what, for this pilot study, they would exclude from screening. The exclusions included:

- Patients who did not speak English or Spanish (because the patient needed to give informed verbal consent)
- Patients who had an altered mental status (because they could not give informed consent)
- Patients who required urgent medical intervention (because their urgent medical needs took priority)

They also questioned the utility of screening older patients. Because of disproportionately low HIV prevalence among older adults, the CDC had called for screening through age 64 years. But the DC Department of Health, which was providing the HIV test kits free of charge, wanted to expand testing to persons up to age 84.

To inform their pilot program, the research team found it useful to model screening program results under varying scenarios. They enlisted their research assistant, a public health student named Priya who had recently completed her first epidemiology course. Eager to get some practical experience, Priya agreed to help with some calculations. For ease of comparing results, they asked her to base calculations on three scenarios, each involving 10,000 GW ED patients who would meet screening criteria and agree to be tested using the HIV rapid test (sensitivity 99.3%; specificity 99.8%).

**Scenario 1:** Ages 65 to 84
**Assumption:** Actual prevalence of undiagnosed HIV infection in screening population = 0.1%

**Scenario 2:** Ages 13 to 64—low estimate
**Assumption:** Actual prevalence of undiagnosed HIV infection in screening population = 1.0%

**Scenario 3:** Ages 13 to 64—high estimate
**Assumption:** Actual prevalence of undiagnosed HIV infection in screening population = 3.0%

Priya learned in her epidemiology class what to do next, so she got out her calculator and got to work. Follow Priya’s process to come up with projected screening program results under these three scenarios and present them to Dr. Brown. The formulas in Box 2-1 will be helpful for those who need a review of screening statistics.

**Question 1**

For each of the three scenarios, Priya constructed a two-by-two table to show the distribution of screening results. Dr. Brown reminded her to be sure to round all cell values to whole numbers.

Then, for each scenario, she calculated the predictive value positive (PVP) and the predictive value negative (PVN). She found that one decimal place was fine for PVP...
but she needed to use two decimal places to distinguish differences in PVN. Construct Priya’s three tables, and for each one, calculate PVP and PVN.

**Question 2** Priya met with Dr. Brown to summarize the key findings from the three sets of calculations. What would her important points have been?

**Question 3** Dr. Brown asked Priya to specifically detail the pros and cons for including individuals age 65 and over in this screening program. What pros and cons would she have likely identified?

**OPERATIONALIZING PILOT STUDY LOGISTICS**

Impressed by Priya’s ability to calculate and interpret screening statistics, Dr. Brown and his team invited her to also help develop the study’s operations manual. One section of the manual included scripts for communicating various test results to patients. The purpose of these scripts was for healthcare providers to describe in lay terms what the screening results meant for prototypical patients. In language that the average person can understand, the scripts were to explain what the test values indicate about the possibility of HIV infection and what the patient should do next.

**Question 4** In one script, Priya was to assume that HIV prevalence in the screened population was 3.0%, as in scenario 3. If an asymptomatic 23-year-old woman had a reactive (positive) HIV rapid test, what should the healthcare worker have told her?

**Question 5** Another script was based on scenario 1, with an HIV prevalence of 0.1%. If an asymptomatic 68-year-old man had a positive HIV rapid test, how should the script have been different for communicating his results?
Question 6 Finally, Priya assumed that the HIV prevalence was 1% as in scenario 2. A 31-year-old woman was being treated in the ED for symptoms of a sexually transmitted disease. How should the script have read for describing the results of her negative HIV rapid test?

A positive test result will ultimately lead to in-depth counseling. However, the GW ED protocol for patients who screened negative indicated they would only be given written materials about preventing HIV infection, regardless of whether a patient was in a high-risk group. This represented the loss of a potentially teachable moment, where some type of intervention may have prevented disease transmission. In fact, since 1994, CDC has recommended client-centered counseling for individuals with high-risk behaviors, focusing on the development of individualized prevention goals and strategies. Some states have detailed legal requirements for counseling. (See, for example, www.nccc.ucsf.edu/StateLaws/Index.html.)

Priya was aware that CDC’s upcoming recommendations would not recommend required prevention counseling as part of HIV screening programs in healthcare settings. This was a radical change from the way things had been done in the past, but she was particularly troubled that pretest counseling would not be required for someone like the 31-year-old woman with a possible sexually transmitted disease, and she questioned the ethics of this policy stance. (Requirements for pretest and posttest counseling vary widely from state to state. The District of Columbia had no legal requirements in 2006, nor do they as of 2011, although, of course, physicians use their discretion about the need for counseling.)

Question 7 This resulted in a vigorous debate among the project staff about whether the public health benefit of omitting pretest counseling outweighs the harms. Briefly outline the pros and cons the staff would likely have discussed.

TO CONFIRM OR NOT TO CONFIRM?

As mentioned previously, confirmatory testing would be necessary for any individual with a positive HIV rapid screening test. The ED did not have an infrastructure to support confirmatory Western blot testing and follow-up, although the hospital’s lab would be able to run the test if blood was drawn in the ED. The hospital’s division of infectious diseases did have the capacity to support confirmatory testing, as did local free clinics. As they planned the pilot study, Dr. Brown and his team debated whether to draw blood in the ED for confirmatory Western blot testing or to refer people who screened positive to other providers for confirmatory testing.

Question 8 It takes several days to get results back from confirmatory HIV testing, but the ED is organized for acute care. Dr. Brown asked Priya to think through the new process the team would need to put in place if they decided to conduct confirmatory testing in the ED as part of the pilot program. If you were Priya, what process would you recommend?

Question 9 Briefly describe key arguments that Dr. Brown’s team might have made for and against conducting confirmatory testing in the ED as part of this pilot study.

The research team concluded it was not feasible to conduct confirmatory Western blot testing in the ED, at least not for the pilot study. Given that the rapid testing program would produce some false positives and it would be useful to reduce these false positives before the patients left the ED, another idea was to screen all individuals whose first rapid test result was positive with a second test. The second test under consideration was the OraQuick Advance HIV1/2 Antibody Test utilizing a whole blood specimen from either a finger stick or venipuncture.

Dr. Brown asked Priya to work up the numbers for what the second round testing would look like using the OraQuick whole blood test. This test was reported to have a sensitivity of 99.6% and a specificity of 100%. For this projection, Priya went back to her highest risk assumption—scenario 3, which assumed an actual prevalence of 3% HIV infection in the screened population of 10,000. Further, she assumed all individuals with a reactive (positive) rapid test result would consent to be given a confirmatory Western blot test.

Priya was a little rusty on serial screening statistics, so she needed to review her epidemiology notes. “Ah yes,” she thought. “I need to start with the two-by-two table I created for the first round of testing.” [Question 1, scenario 3] “Then, to complete the second two-by-two table for projecting serial screening results, I need to take my entire positive row from round 1 and bring it down intact to form my total row for round 2.”

Question 10 What did Priya’s second-round two-by-two table look like? Calculate the positive predictive value for the second-round test.

Question 11 What is the actual prevalence of HIV infection in the group who would receive the second-round screening test?

Question 12 What is the net sensitivity of this serial testing program? The net specificity? (Refer to Box 2-2 for a primer on these definitions.)
Case 2
A Feasibility Study of Routine Screening for HIV in an Urban Emergency Department

Question 13 As the pilot project drew to an end, Dr. Brown and his team decided to extend the program. However, given the results described, they felt they could improve their screening program. Identify some key issues they were likely grappling with, and suggest possible solutions.

Early detection and treatment of HIV results in substantial increases in survival. In the CDC recommendations, Branson and colleagues concluded, “Even if only a limited fraction of patients who receive HIV-positive results are linked to care, the survival benefits per dollar spent on screening represent good comparative value.”1(p 8) Altogether, the 3-month pilot program at the GW ED cost approximately $44,000. Thus, each preliminary positive test result cost approximately $1700, while each confirmed case of HIV infection cost approximately $4900. Dr. Brown and his colleagues were happy to add more evidence relating to the cost-effectiveness of HIV screening, and stated, “This program is the first to demonstrate that compared with other methods of early detection, routine opt-out screening in the ED is also cost-effective.”14(p 400)

Priya Moves On . . .

Fast-forward 2 years. Priya received her public health degree and secured a research coordinator position with a major healthcare provider in her hometown. This healthcare provider had not previously implemented universal HIV screening, but was considering doing so. Knowing of her previous experience, Priya’s supervisor has asked her to think back on some lessons learned from the GW pilot program and to do some preliminary research to inform program design. Priya thought back to one of the first challenges confronting Dr. Brown’s team—how important it was to estimate the prevalence of undiagnosed HIV infection in the population that would be screened. Priya could see that any healthcare organization would want to characterize HIV/AIDS in its community before launching a screening program.

For insight into this, Priya could have looked at HIV/AIDS incidence, prevalence, or mortality data for her hometown, or she could have looked for surveillance data about demographic or behavioral risk factors for HIV/AIDS.

Question 14 Reproduce Priya’s investigation for your own hometown or any other location that interests you by choosing any health indicator relevant to population risk for HIV. Utilize a primary government source of surveillance data to characterize this health indicator for

THE PILOT PROGRAM LAUNCHES

The GW ED launched a 3-month pilot HIV screening program on September 12, 2006, 10 days before the CDC’s revised recommendations were published. All English- and Spanish-speaking patients aged 13–64 were eligible to be offered an HIV test. Patients with altered mental status, who needed urgent medical treatment, or who knew they were HIV positive were excluded. The triage nurse determined whether patients met screening criteria and informed those who did that free HIV screening was available and provided them with written materials about HIV disease and the importance of HIV testing.14

At an appropriate time during their ED evaluations, eligible patients were approached by specially trained screeners; the screeners were available in the ED between 8:00 am and midnight every day. The HIV screener explained that the ED was routinely offering HIV screening to everyone, and that the patient could opt out if he or she wanted to.14

During the 3-month pilot study, nearly 15,000 patients were treated in the GW ED—4,151 of whom met screening criteria and were offered rapid HIV screening. Of these, 2,476 (59.6%) accepted the test, and a rapid oral swab test was conducted. Twenty-six individuals tested positive, which was 1.1% of those tested. The proportion of patients testing positive differed significantly by sex (with males testing positive more often than females), and by race (with blacks testing positive more often than whites); no differences were seen by age.14

Of the 26 individuals with positive screening results, nine were confirmed by Western blot to be infected with HIV, and all but one of these individuals were linked to long-term care. Four individuals were confirmed to not have HIV. The remaining 50% of those who screened positive were lost to follow-up despite vigorous efforts to contact them.14

**Box 2-2 Net Sensitivity and Net Specificity for Serial Screening**

Net Sensitivity: The number of people who correctly screen positive on both tests (that is, the individuals in the TP cell for the second test) as a percent of all people with HIV infection.

Net Specificity: The number of people who correctly screen negative on the first test, plus people who correctly screen negative on the second test, as a percent of all people without HIV infection.
the population living in the town or region you specify. [Note that while there are many reputable sources of health status information, typically information from federal, state, or local government data sources would be considered most trustworthy.] If you prefer, you can zero in on a high-risk subgroup of interest rather than looking at population-wide characteristics. Summarize what you find, describing the following:

- Surveillance methods (Who do data represent? What was measured? When were the data collected? How were they collected?)
- What do the results show?
- Where you obtained the data (website reference, etc.)

The principles of good public health screening programs proposed by Wilson and Jungner in 1968 (see Box 2-3) are still used today to guide screening policy and practice. Priya’s supervisor asked her to consider these principles as she reviewed the surveillance data for their community, as well as all she knew about HIV screening in general.

**Question 15** Choose any six of these principles and evaluate healthcare-based HIV screening in your chosen setting against those principles. Base your evaluation on what you know from the *MMWR* article and this case. How does HIV screening stack up against these principles?

**About the Authors**

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**Jeremy Brown**, MD, is the director of clinical research and an associate professor of emergency medicine at The George Washington University Medical Center. He is a practicing emergency physician and the founding director of the ED HIV screening program. This program, which began in 2006 in response to the revised recommendations from the CDC, has screened over 30,000 patients in the ED at GW for HIV.

The clinical program has generated several research papers and presentations, which have been published in *JAIDS, Annals of Emergency Medicine, Academic Emergency Medicine, Public Health Reports, and The New York Times*. The program has also been highlighted in *American Medical News* and the *ADAP Report*, which described the GW program as a model for emergency room testing.
RECOMMENDED PREPARATORY READING


CDC HIV/AIDS website: http://www.cdc.gov/hiv/

REFERENCES


