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Cost-Effectiveness of Voluntary HIV Testing Strategies in a Very Low-Prevalence Country, the Republic of Korea

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ABSTRACT

Background: The Republic of Korea has a very low prevalence of human immunodeficiency virus (HIV) infection, but the number of new HIV diagnoses has steadily risen, strongly indicating a large number of undetected HIV infections. Thus, it is important for Korean public health authorities to adopt and encourage cost-effective HIV detection tools, such as rapid HIV screening tests. In this study, we aimed to evaluate the cost-effectiveness of enzyme-linked immunosorbent assays (ELISA) and rapid tests in a public health center (PHC) setting.
Methods: We developed a decision analytic model to assess the per-examinee cost and the cost-effectiveness of identifying HIV patients in a PHC setting using two HIV testing strategies: conventional HIV screening by ELISA versus rapid HIV testing. Analysis was performed in two scenarios: HIV testing in an average-risk population and in a high-risk population.
Results: Compared to the ELISA, the rapid test was cost-saving and cost-effective. The per-examinee cost was USD 1.61 with rapid testing versus USD 3.38 with ELISA in an average-risk population, and USD 4.77 with rapid testing versus USD 7.62 with ELISA in a high-risk population. The cost of identifying a previously undiagnosed HIV case was USD 26,974 with rapid testing versus USD 42,237 with ELISA in an average-risk population, and USD 153 with rapid testing versus USD 183 with ELISA in a high-risk population.
Conclusion: Rapid testing would be more cost-effective than using conventional ELISA testing for identifying previously undiagnosed HIV-infected cases in Korea, a country with extremely low HIV prevalence.

Keywords: HIV Screening Test; Cost-effectiveness Analysis; Korea

INTRODUCTION

Since its peak in 1997, the global incidence of human immunodeficiency virus (HIV) infection has decreased.[1] However, in the Republic of Korea—where the prevalence of HIV/AIDS has been very low of 0.02% (10,000 of the total population)[2] in contrast to 0.8% (36.7 million people) globally in 2016[3]—the number of newly diagnosed HIV patients has continuously

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The authors have no potential conflicts of interest to disclose.

Author Contributions
Conceptualization: Lee YH, Bang JH, Park SM, Kang CR. Formal analysis: Lee YH. Methodology: Lee YH, Park SM, Kang CR. Writing - original draft: Lee YH. Writing - review & editing: Bang JH, Park SM, Cho SI, Oh MD, Lee JK.

risen.[4] The majority of newly diagnosed HIV patients in Korea receive antiretroviral treatment (ART) and exhibit good compliance.[5] Since patients with good treatment compliance rarely transmit HIV to others, the increasing number of HIV diagnoses in Korea may indicate a large population of undiagnosed HIV patients.[6-8] Thus, it is important for Korean public health authorities to adopt and encourage cost-effective HIV detection tools.

Public health centers (PHCs) in Korea provide anonymous and free voluntary counseling and testing (VCT). The majority of PHCs use conventional HIV enzyme-linked immunosorbent assays (ELISA). However, PHCs in the metropolitan city of Seoul, as well as some regional PHCs outside of Seoul, have adopted rapid finger-stick HIV screening tests.

To our knowledge, no study has compared the cost-effectiveness of the rapid test versus the ELISA in a country with a very low HIV prevalence, such as Korea. Thus, in our present study we aimed to evaluate the cost-effectiveness of the two different HIV testing strategies in the PHC setting.

METHODS

Testing procedure

The ELISA HIV testing procedure involved phlebotomy, and submission of a serum specimen to a PHC laboratory for processing. Specimens with positive ELISA results were re-tested, and repeatedly reactive samples were subjected to confirmatory western blot analysis. If the second ELISA yielded negative results, no further analysis was performed. The examinee was notified of the results within 1 week via telephone.[9]

Rapid HIV testing was performed using a finger-stick kit (SD BIOLINE HIV-1/2 3.0; Standard Diagnostics, Inc., Yongin, Korea). After blood sampling via finger-stick, the test result could be read within 20 minutes. Staff informed examinees of their results in a face-to-face meeting or via telephone. Examinees with positive rapid test results were asked to submit to ELISA testing. If ELISA results were positive, confirmatory western blot analysis was performed.

Examinees confirmed to have HIV infection were referred for further counseling at a PHC.[9] Both the ELISA and rapid tests were performed anonymously and free of charge.

Strategies and scenarios

In Strategy 1, ELISA testing was performed to detect HIV in all examinees. In Strategy 2, HIV detection was performed by rapid testing using a finger-stick kit. Since the examinees' risk level was unknown, analyses were performed in two different scenarios: one assuming that examinees belonged to an average-risk population, and the other assuming a high-risk population, such as men who have sex with men (MSM). In both scenarios, we determined the total cost of identifying a previously undiagnosed HIV infection in a PHC setting.

Decision tree

A decision tree model was developed to assess the cost-effectiveness of voluntary HIV testing at PHCs (**Fig. 1**). The decision tree structure represented both HIV testing strategies and both scenarios. Analyses were performed using TreeAge software (TreeAge Software Inc., Williamstown, MA, USA). For example, if a HIV-infected case underwent ELISA or rapid testing, the probability of a positive result being positive reflected the sensitivity, and the

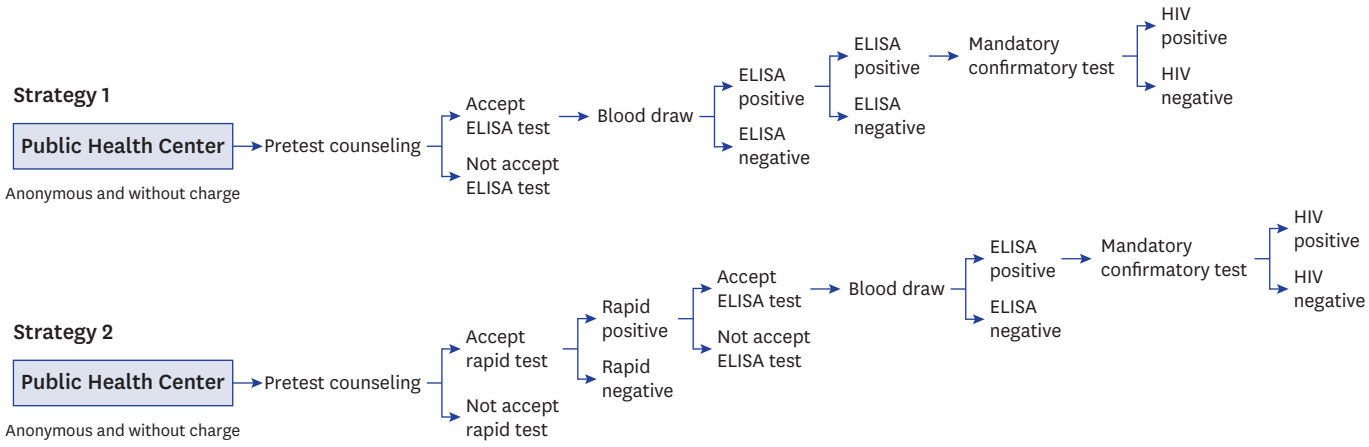

Fig. 1. Summary of HIV testing protocols.
HIV = human immunodeficiency virus, ELISA = enzyme-linked immunosorbent assays.

probability of it being negative would be 1 – sensitivity. Meanwhile, if a non-infected case underwent ELISA or rapid testing, the probability of the test result being negative would reflect the specificity, while the probability of it being positive would be 1 – specificity.

Input variables

Table 1 shows the input variables for each procedure. The listed baseline probabilities for estimating the cost per identified HIV-infected case using the two testing methods correspond to the chance nodes in **Fig. 1**. The HIV prevalence among the average-risk population in Korea was obtained from a UNAIDS report.[10] The HIV prevalence among the high-risk population was acquired from a study of HIV infection global epidemiology among MSM in the Asia-Pacific region.[11] Since there are no domestic reports on this subject, we assumed the test acceptance rate suggested by Farnham et al.[12] The utilized sensitivities

Table 1. Summary of input parameters for the HIV testing cost-effectiveness analysis

Parameters	Base value (range)	Ref. No.
Probabilities that the examinee is HIV-infected		
Average-risk population	0.0001 (0.00024–0.0004)	10
Men who have sex with men	0.052 (0.049–0.056)	11
Test acceptance rate		
ELISA[a]	0.80 (0.67–1.0)	12
Rapid test	0.80 (0.67–1.0)	12
Sensitivity and specificity of testing		
ELISA sensitivity	1.00 (0.977–1.0)	13
ELISA specificity	0.997 (0.0981–1.0)	14
Confirmatory procedure (western blot) sensitivity	1.00	[b]
Confirmatory procedure (western blot) specificity	1.00	[b]
Rapid test sensitivity	1.00 (0.992–1.0)	22
Rapid test specificity	0.999 (0.992–1.0)	22
Acceptance rate of confirmatory test after rapid test	0.747	15
Cost, USD[c,d]		
ELISA kit	4.2 (3.5–5.0)	
Rapid test kit	2.0 (1.8–2.5)	
Confirmatory procedure (western blot) test kit	98.0 (77.0–110.0)	

HIV = human immunodeficiency virus, ELISA = enzyme-linked immunosorbent assays.
[a]Conventional HIV screening test by enzyme immunoassay; [b]A confirmatory test procedure was assumed to have no false-positive or false-negative results, as is typically assumed in the literature; [c]Exchange rate: 1,000 KRW for one USD; [d]Data obtained by interviews with laboratory staff and test kit manufacturers.

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and specificities of the ELISA, western blot, and rapid test, and the acceptance rate for the confirmatory test after the reactive rapid test, were found in the literature.[13-15]

Our analysis included only additional costs. Fixed costs, such as wages, were not considered because the examinees' choice of ELISA or rapid testing did not influence the monthly pay of the PHC staffs, or the number of laboratory technicians required. Costs were estimated from the provider perspective. All costs were reported in 2017 US dollars, assuming an exchange rate of KRW 1,000 for USD 1. The cost data for each HIV testing procedure—including the price of reagents, test kits, and laboratory supplies—were obtained from estimates provided by the test kit manufacturers and from the laboratory staff of the Seoul Research Institute of Public Health and Environment.

Outcome measures

Outcome measures were the average per-patient cost of completing the entire ELISA or rapid testing procedure, and the additional cost per identified and previously undiagnosed HIV-infected case. The latter was the key measure of cost-effectiveness, and was calculated by dividing the former average cost by the HIV infection detection rate per examinee. The detection rate was the product of HIV prevalence, the testing tool sensitivities, and the test acceptance rate.

Sensitivity analysis

Sensitivity analysis was performed using the input probabilities and cost variables that affected the cost per identified HIV-infected case. The HIV prevalence ranged 0.00024–0.0004 in the average-risk population, and 0.049–0.056 in the high-risk population. The acceptance rate for the ELISA and rapid test ranged 0.67–1.0, and the acceptance rate for western blot analysis after a reactive rapid test ranged 0.5–1.0. Test costs ranged from USD 3.5 to USD 5.0 for the ELISA, from USD 1.8 to USD 2.5 for the rapid test, and from USD 77.0 to USD 110.0 for the western blot kits.

Ethics statement

The present study protocol was reviewed and approved by Institutional Review Board (IRB) of Seoul National University (IRB No. E-1608-113-786).

RESULTS

Average cost of the HIV testing procedure

Table 2 summarizes the average costs per examinee completing the conventional ELISA and rapid test procedures. The average costs were higher for HIV-infected examinees than for uninfected examinees, since a positive result required confirmation with a second ELISA and western blot analysis. The overall average costs were consistently lower for the rapid testing procedure compared to ELISA because the rapid test kit was cheaper than the ELISA kit. The average per-examinee cost was USD 3.38 for ELISA and USD 1.61 for rapid testing in

Table 2. Average cost per examinee for HIV testing strategies[a]

Strategies	Scenario 1: average-risk population	Scenario 2: high-risk population
Strategy 1: ELISA	USD 3.38	USD 7.62
Strategy 2: rapid test	USD 1.61	USD 4.77

HIV = human immunodeficiency virus, ELISA = enzyme-linked immunosorbent assays.
[a]In 2017 dollars.

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Table 3. Cost-effectiveness of HIV testing strategies[a]

Strategies	Scenario 1: average-risk population	Scenario 2: high-risk population
Strategy 1: additional cost per HIV-infected patient detected using ELISA	USD 42,237	USD 183
Strategy 2: additional cost per HIV-infected patient detected using rapid test	USD 26,974	USD 153

HIV = human immunodeficiency virus, ELISA = enzyme-linked immunosorbent assays.
[a]In 2017 dollars.

scenario 1 (average-risk population), and USD 7.62 for ELISA and USD 4.77 for rapid testing in scenario 2 (high-risk population).

Cost-effectiveness of HIV testing strategies

Table 3 presents data regarding the additional cost per newly identified HIV patient among all examinees, as well as the cost-effectiveness of the two scenarios. In scenario 1, the additional cost was USD 42,237 with ELISA and USD 26,974 with the rapid test. In scenario 2, the additional costs were USD 183 and USD 153, respectively.

Sensitivity analysis

In scenario 1, the cost of the rapid test kit was the variable having the largest effect on the average cost per identified HIV-infected individual. One-way sensitivity analysis revealed that the rapid test's cost-effectiveness was best at USD 24,292, with the lowest-priced rapid test (USD 1.80), and worst at USD 33,682, with the highest-priced rapid test (USD 2.50). On the other hand, the cost-effectiveness of the ELISA was consistently USD 42,237.

In scenario 2, the acceptance rate of ELISA testing after a reactive rapid test was the variable with the largest effect on cost-effectiveness. One-way sensitivity analysis revealed that the rapid test's cost-effectiveness was best at USD 141 with the highest ELISA acceptance rate (100%), and worst at USD 179 with the lowest ELISA acceptance rate (50%). In contrast, the cost-effectiveness of ELISA was consistently USD 183. In both scenarios, the rapid test was more cost-effective than the ELISA.

In a setting with higher HIV prevalence, the costs would be increased for both strategies in both scenarios. However, the cost-effectiveness for detecting previously undiagnosed HIV cases would be improved due to the lower the additional cost per HIV patient detected. Likewise, in a lower prevalence setting, the cost-effectiveness would be decreased.

All sensitivity analyses indicated that the rapid test had a consistent cost advantage over the ELISA, with regards to both the average cost per-examinee and the additional cost per identified HIV-infected case.

DISCUSSION

The results of the present study demonstrated that the rapid HIV test is less expensive and more cost-effective compared to the conventional ELISA, even in Korea, which has a very low HIV prevalence. The average per-examinee costs of the rapid test (USD 1.61 in scenario 1 and USD 4.77 in scenario 2) were less than half the costs of the ELISA (USD 3.38 in scenario 1 and USD 7.62 in scenario 2). Moreover, the additional cost per newly identified HIV case using the rapid test (USD 26,974 in scenario 1 and USD 153 in scenario 2) was lower than the additional cost with ELISA testing (USD 42,237 in scenario 1 and USD 183 in scenario 2).

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No previous study has compared the cost and cost-effectiveness of the ELISA versus the rapid test in an anonymous voluntary screening setting. However, a study from the United States reports that the cost of HIV-infected cases receiving their test results was lower with rapid testing than with conventional ELISA. In that study, although the rapid test had a higher per-patient cost, the cost per HIV-infected patient receiving test results (i.e., the cost-effectiveness) was about 25% lower with the rapid test compared to ELISA.[12]

Since the rapid test results could be provided within 20 minutes, wider adoption of rapid testing could reduce barriers to testing, and increase the number of voluntary participants in HIV screening programs. Participants who chose the rapid test were also more likely to receive their test results than those who chose a conventional test.[16] Overall, use of the rapid test could increase the detection of previously undiagnosed HIV infections.[17,18] This is in agreement with the results of a pilot project implemented in Korea in 2014.[15]

There are several challenges associated with conducting the rapid test. Notably, the rapid test may be inappropriate for patients in an early stage of HIV infection, as its window period is longer than that using the ELISA.[19,20] Additionally, the test results may be affected by the skill level of the testing staff.[21] Nevertheless, the rapid test is useful, having the advantages of greater cost-effectiveness and a higher acceptance rate.

Our present study had several limitations. Importantly, we lacked more detailed data—such as the HIV prevalence and acceptance rate for each HIV testing procedure—therefore, we cannot be certain that this study reflects the exact HIV-related environment in Korea. Furthermore, our analysis did not include fixed costs—such as laboratory staff wages, the cost per examinee completing the HIV testing procedure, or the cost of identifying each additional HIV-infected case—therefore, the results cannot be used to simulate the budget of any national HIV screening program. Despite these limitations, this is the first study to demonstrate the cost-effectiveness of a rapid HIV test compared to the conventional ELISA in a country with a very low HIV prevalence, in which voluntary and anonymous screening is being implemented.

In conclusion, our present results suggest that use of a rapid test rather than the conventional ELISA would save costs and confer greater cost-effectiveness for the identification of previously undiagnosed HIV-infected cases in Korea, where the HIV prevalence is extremely low. Based on these results, we propose widespread adoption of the rapid test in PHCs throughout Korea.

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