SHORT COMMUNICATION

Assessment of Extrinsic Validity of HIV Oral Self-Test in A Low-Prevalence Population: A Bayesian Approach

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ABSTRACT

Background: HIV oral self-test (HIVOST) is used for screening, particularly in diverse populations. While these tests offer convenience and privacy, their accuracy in low-prevalence settings remains a concern. A key measure of test reliability is extrinsic validity, which considers test sensitivity, specificity, and disease prevalence to determine the probability of true positivity given a positive test result. This statistical investigation aimed to evaluate the extrinsic validity of an HIVOST in a low-prevalence population.

Methodology: We applied Bayes' theorem to calculate the extrinsic validity of the HIVOST, incorporating test sensitivity, specificity, and the prevalence of HIV infection.

Important Findings: The analysis yielded an extrinsic validity of 7.70% (95% CI: 1.8% to 25%), meaning that in this low-prevalence setting, the probability of an individual truly having HIV after testing positive was relatively low. The participant who tests negative has a 99.97% (95% CI: 99.94% to 99.98%) chance of truly not having HIV, indicating high reliability of a negative result in this low-prevalence setting. Sensitivity analysis shows that PPV increases with prevalence, while NPV remains high, confirming the reliability of negative results across scenarios.

Conclusions: Although a positive HIVOST result strongly suggests HIV infection, the low extrinsic validity underscores the need for confirmatory testing, particularly in low-prevalence settings.

Keywords: Bayes, HIV self-test, Sensitivity, Specificity, Extrinsic Validity

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INTRODUCTION

The accurate diagnosis of HIV infection is critical for effective management and prevention of the disease. In recent years, self-test for HIV has gained importance as a convenient and confidential method for individuals to determine their HIV status. The World Health Organization (WHO) published HIVOST guidelines in 2016, recommending its use as a screening test.[1]

The original study that this work is based on, involved a small group of 100 individuals, across different clinics of the institute, located in the district of Pune in the Western State of Maharashtra. Half of the individuals were HIV sero-positive, and the other half HIV sero-negative. The study aimed to test how well a new HIVOST works and to see its acceptability. During the study, both the doctors and the participants read the HIVOST results after 20 minutes. The performance of the HIVOST kit was compared to the results of a confirmatory blood test for HIV, following the national testing guidelines.[1] The study reported a sensitivity of 83.3% and a specificity of 98% of HIVOST.[2]

However, the reliability of these tests depends on their sensitivity and specificity, as well as the prevalence of HIV within the tested population. Sensitivity measures the ability of the test to correctly identify true positives (HIV-infected individuals), while specificity measures how well true negatives are identified (HIV-negative individuals).

The study aimed to assess the extrinsic validity of an HIVOST using Bayesian approach, considering its sensitivity and specificity against blood-based tests, and considering HIV prevalence as prior probability.

METHODOLOGY

Bayes' Theorem is useful in determining the post-test probability, or the positive predictive value (PPV) and negative predictive value (NPV) of a diagnostic test.[3-4] The theorem incorporates the sensitivity (true positive rate) and specificity (true negative rate) of the test with the prevalence (prior probability) of the disease in the population. Bayes' theorem adjusts the probability of a true HIV infection based on test performance and disease prevalence, accounting for false positives.

Extrinsic validity refers to the test's performance in a real-world context, where disease prevalence can vary significantly. While sensitivity and specificity remain constant for a given test, Bayes' Theorem allows us to calculate how changes in prevalence affect the likelihood that a positive or negative result is accurate. This is particularly important for self-tests in public health, where individuals using the test may come from populations with differing levels of HIV prevalence.

We utilized Bayes' theorem[5-6] to calculate the extrinsic validity of the HIVOST. Bayes' theorem incorporates the sensitivity and specificity of the test, along with the prevalence of HIV infection, to determine the probability of having HIV given a positive HIVOST.

For the Bayesian analysis, we used secondary data on sensitivity (83.3%) and specificity (98%) extracted from the article published by the team from our institute.[2]

The probability that a person has HIV infection given a positive test result, can be calculated using Bayes' theorem and is expressed as:

$P(H|+) = P(+|H) \times P(H) / P(+)$

Where H to represent having HIV infection, and + to represent a positive test result.

In this context P(H|+) is the probability of having HIV infection given a positive test result; P(+|H) is the sensitivity of the test (the probability of getting a positive test result given that the person has HIV infection); P(H) is the prevalence of HIV infection; and P(+) is the probability of getting a positive test result, calculated using the law of total probability.

Prior probability is the initial probability of an event occurring before any new data is taken into account.

What prior probability should be assigned to a participant of having HIV infection?

We have used the national HIV prevalence of 0.2% (0.002) as the prior probability for a participant having HIV infection[7].

P(HIV) or P(H) = 0.002

Posterior probability is the updated probability of an event after considering new information.

When a participant undergoes HIV screening through self-test there can be two possible scenarios: either the participant has HIV infection or does not have HIV infection as illustrated in Figure 1. If HIVOST yields a positive result, what is the probability that the participant has HIV infection?

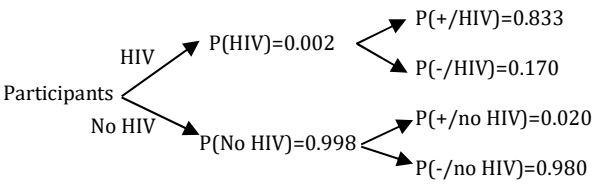

Figure 1: Tree Diagram for Estimating Posterior Probability of HIV Infection

Caption: *Bayesian probability tree diagram illustrating the relationship between HIV status and test outcomes. The tree shows prior probabilities of HIV infection (P(HIV) = 0.002) and no infection (P(No HIV) = 0.998), along with the conditional probabilities of testing positive or negative based on true HIV status.*

Table 1: Parameters Used in Bayesian Analysis

Parameter	Value	Reference Number
Prevalence P(H)	0.002	7
Sensitivity P(+|H)	0.833	2
Specificity P(−|−H)	0.980	2

To calculate the extrinsic validity of the HIVOST, considering the prevalence of HIV infection and other key parameters (Table 1), we can use Bayes' theorem.

First, to calculate P(+), the probability of a positive test result:

$$P(+) = P(+|H) \times P(H) + P(+|-H) \times P(-H)$$
$$P(+) = 0.833 \times 0.002 + (1-0.980) \times (1-0.002)$$
$$P(+) = 0.021626$$

Putting all the above information in to the following Bayes' formula

$$P(H|+) = P(+|H) \times P(H) / P(+)$$

Now, the probability of having HIV infection given a positive test result is

$$P(H|+) = 0.833 \times 0.002 / 0.021626$$
$$P(H|+) \approx 0.07703$$

So, the extrinsic validity of the HIVOST, considering the given prevalence, is 7.70% (95% CI: 1.8% to 25%). Step-by-step Calculation of PPV Using Bayes' Theorem is provided in *appendix I*. This represents the probability that a participant actually has HIV infection given a positive test result.

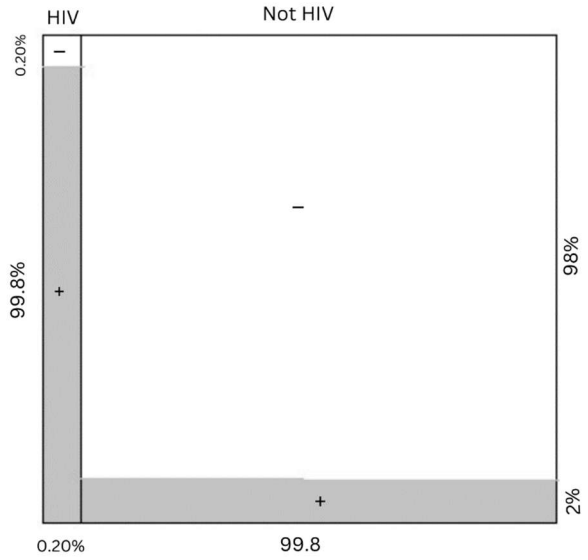

Figure 2: Geometric Representation of Bayes' Theorem in Low HIV Prevalence

*Caption***:** *Geometric representation of Bayes' theorem showing the proportion of true positives (shaded area) among all positive HIV test results in a low-prevalence population (0.2%). The figure highlights how false positives can outnumber true positives when disease prevalence is low.*

The low probability might seem unexpected, but it becomes clearer when we consider the problem visually (Figure 2). In the diagram below, we have divided the participants based on whether they tested positive for HIV infection and whether they used the HIVOST. The shaded part shows everyone who tested positive for HIV infection by HIVOST. Those who truly positive for HIV infection are those that were confirmed sero-reactive based on the national algorithm. This means false positive results outnumber true positive results by a significant margin.

Calculating Negative Predictive Value (NPV): NPV is the probability that a person who tests negative for a disease truly does not have the disease.

Mathematically, it is defined as:

NPV = P(Negative Disease | Negative Test Result)

$$NPV = P(-H/-) = P(-/-H) \times P(-H) / P(-)$$

Where:

$P(-H/-)$ = Specificity = 0.980

$P(-H) = 0.998$

$P(-)$ = Total probability of a negative test

Step-by-step Calculation of NPV Using Bayes' Theorem is provided in *appendix II*

$$NPV \approx 99.97\%$$

This suggests that a participant who tests negative has a 99.97% (95% CI: 99.94% to 99.98%) chance of truly not having HIV, indicating high reliability of a negative result in this low-prevalence setting.

Sensitivity Analysis: To account for uncertainty in parameters and assess the robustness of our findings, we performed a sensitivity analysis by varying the prevalence of HIV from 0.1% to 1%, which reflects the range typically observed in low-prevalence settings like India (Table 2).

RESULTS

Our analysis revealed that the extrinsic validity of the HIVOST, considering a prevalence of HIV infection of 0.002, was 7.70% (95% CI: 1.8% to 25%). This indicates the probability that a participant actually has HIV infection given a positive test result. In other words, if participant receives a positive test result using the HIVOST, there is an 7.70% chance that they truly have HIV infection. The PPV of 7.7% (95% CI: 1.8% to 25%) reflects uncertainty in test performance and prevalence estimates. The NPV result indicate that HIVOST has a very high NPV, suggesting its effectiveness in correctly identifying HIV-negative participants (99.97%).

This sensitivity analysis demonstrates how changes in prevalence influence the Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of the HIVOST. While PPV increases with higher prevalence, NPV remains consistently high, indicating the reliability of negative results across a range of varying prevalence (Table 2).

Table 2: **Sensitivity Analysis of PPV and NPV Across Varying HIV Prevalence with 95% Confidence Intervals**

Prevalence	PPV	95% CI (PPV)	NPV	95% CI (NPV)
0.001	0.04	0.009 – 0.140	0.9998	0.9996 – 0.9999
0.002	0.077	0.018 – 0.250	0.9997	0.9994 – 0.9999
0.003	0.111	0.026 – 0.323	0.9995	0.9991 – 0.9998
0.004	0.143	0.035 – 0.385	0.9993	0.9988 – 0.9997
0.005	0.173	0.043 – 0.438	0.9991	0.9985 – 0.9996
0.006	0.201	0.051 – 0.484	0.999	0.9983 – 0.9995
0.007	0.227	0.058 – 0.525	0.9988	0.9981 – 0.9994
0.008	0.251	0.066 – 0.561	0.9986	0.9979 – 0.9993
0.009	0.274	0.073 – 0.593	0.9985	0.9977 – 0.9992
0.01	0.296	0.080 – 0.621	0.9983	0.9975 – 0.9991

Discussion

The findings of this statistical exercise highlight the importance of considering both the sensitivity and specificity of HIVOST in combination with the prevalence of HIV infection when assessing extrinsic validity of HIVOST.

While a positive test result is highly indicative of HIV infection, the relatively low extrinsic validity highlights the potential for false-positive results, especially in low-prevalence settings.

The high NPV implies that the self-test is highly effective in ruling out HIV in participants who are truly HIV negative. These values are reliable in reassuring individuals about their HIV status, reducing anxiety, and preventing unnecessary follow-up testing for those who test negative. The 7.7% PPV suggests that HIVOST should be integrated into screening programs with robust confirmatory testing protocols to avoid unnecessary anxiety or misdiagnosis.[8] While HIVOST can help overcome testing barriers, there are concerns about potential unintended harms, including psychological, social, and medical effects.[9] False positives can be emotionally distressing, and appropriate counselling services should be available to help participants cope with the uncertainty and stress.[10-12]

Bayes' method enhances decision-making by clarifying test reliability across prevalence settings and guiding resource allocation to maximize the effectiveness of self-testing programs.

In low-prevalence settings, HIVOST programs should prioritize timely linkage to confirmatory testing and use strategic information and communication campaigns to set realistic expectations about test reliability. Public health messaging must emphasize that a positive self-test is preliminary and requires confirmation, reducing anxiety and inappropriate actions. Programs should provide clear, community-based or facility-linked follow-up services to minimize delays and loss to care.[13] Integrating psychosocial support and peer navigation can strengthen care linkage and emotional well-being for individuals receiving positive results.

Limitations

The wide interval for PPV (95% CI:1.8% to 25.0%) reflects the impact of low disease prevalence and the potential variability in test accuracy (sensitivity and specificity) on the reliability of a positive result. The Bayesian model assumes constant sensitivity and specificity, which may not hold in diverse populations with varying test administration conditions. The variations in HIV prevalence across different populations may influence the calculated extrinsic validity, emphasizing the need for further studies on larger sample size to confirm these results in diverse settings.

Conclusion

Larger studies are needed to validate these findings and improve HIVOST generalizability. This analysis underscores the need for confirmatory testing in low-prevalence settings, with public health programs ensuring clear pathways for follow-up and counselling. HIVOST kits should offer contextual result guidance, while clinicians must inform users of limitations and arrange prompt confirmatory tests. Future research should assess the impact of these strategies on testing outcomes and care linkage.

Availability of Data: This research is based on secondary data and the required data is available within the manuscript.

Author's contributions: AN was responsible for conceptualization, methodology, and statistical analysis. The investigation and evaluation were conducted by **AN**, **AR**, and **SP**, who also contributed to writing the original draft. Supervision, review, and editing were carried out by **MM**, **MK**, and **UM**. Validation and statistical analysis were performed by **AN**, **MK**, and **UM**.

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Appendix

Appendix I: Step-by-step Calculation of PPV Using Bayes' Theorem for HIVOST

Step	Description	Formula / Calculation	Result
1	Prevalence of HIV (Prior Probability)	P(H)	0.002
2	Probability of not having HIV	P(−H) = 1 − P(H) = 1 − 0.002	0.998
3	Sensitivity (True Positive Rate)	P(+ | H)	0.833
4	Specificity (True Negative Rate)	P(− | −H)	0.980
5	False Positive Rate	P(+ | −H) = 1 − Specificity = 1 − 0.980	0.020
6	Probability of a positive test result (P(+))	P(+) = P(+ | H) * P(H) + P(+ | −H) * P(−H) = 0.833 * 0.002 + (1-0.980) * (1-0.002) = 0.833 * 0.002 + 0.020 * 0.998 = 0.001666 + 0.01996	0.021626
7	Posterior probability of HIV given a positive result	P(H | +) = [P(+ | H) * P(H)] / P(+) = 0.833*0.002 / 0.021626 =0.001666 / 0.021626	0.0770

Appendix II: Step-by-step Calculation of NPV Using Bayes' Theorem for HIVOST

Step	Description	Formula / Calculation	Result
1	Prevalence of HIV	P(H) = 0.002	0.002
2	Probability of not having HIV	P(−H) = 1−P(H) = 0.998	0.998
3	Sensitivity (True Positive Rate)	P(+|H) = 0.833	0.833
4	Specificity (True Negative Rate)	P(−|−H) = 0.980	0.980
5	False Negative Rate	P(−|H) = 1−Sensitivity = 1−0.833 = 0.167	0.167
6	Total probability of a negative test result P(−)	P(−) = P(−|H)*P(H) + P(−|−H)*P(−H) = 0.167*0.002+0.980*0.998 = 0.000334+0.97804	0.978374
7	Apply formula for NPV	NPV = P(−|−H) * P(−H) / P(−) = 0.980 *0.9980 / 978374 = 0.97804 / 0.978374	0.9997