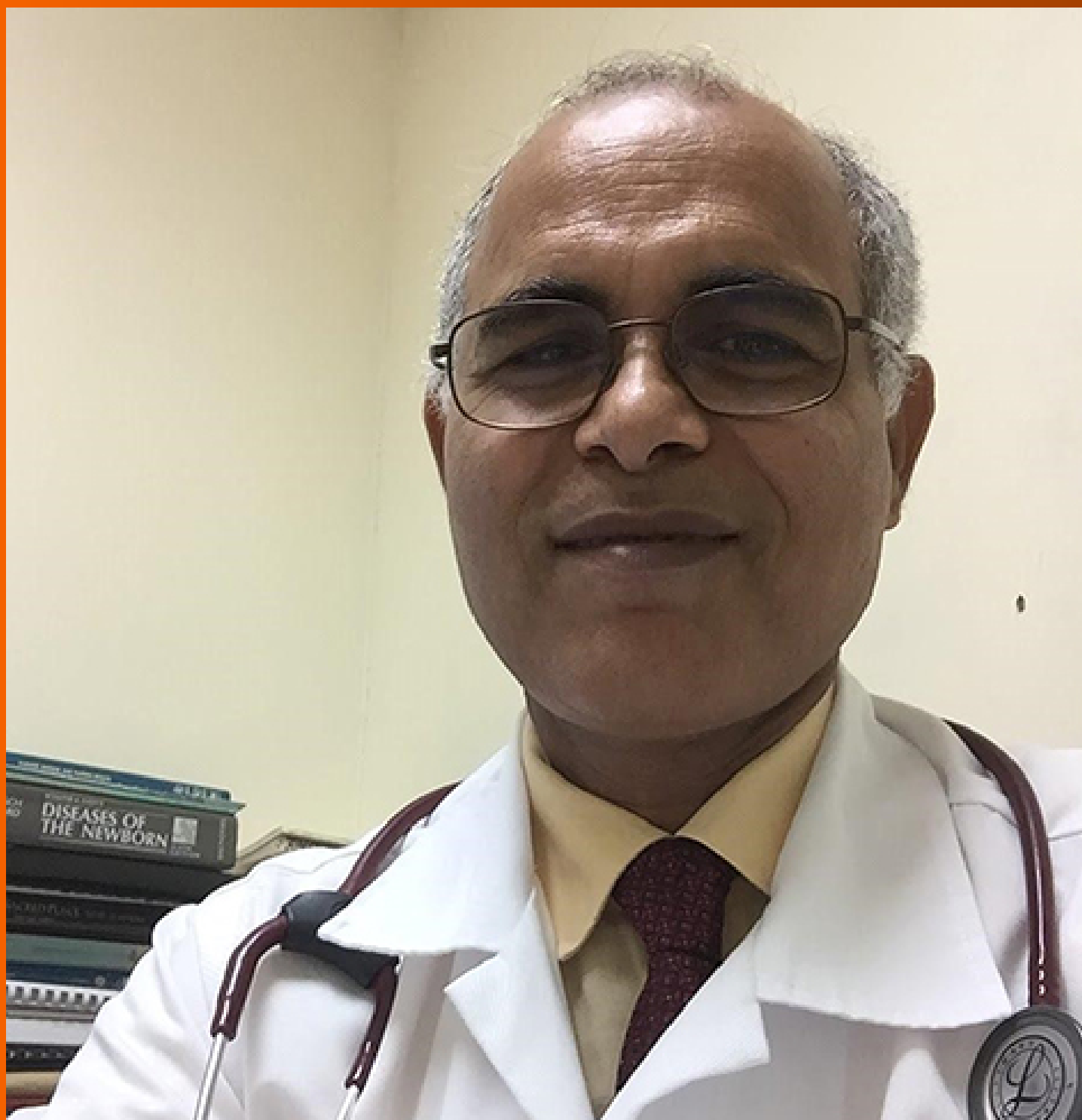


# World Journal of *Methodology*

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## Preferences for oral- vs blood-based human immunodeficiency virus self-testing: A scoping review of the literature

Victor Abiola Adepoju, Winifred Imoyera, Ali Johnson Onoja

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### Abstract

#### BACKGROUND

The evidence on preferences for oral- vs blood-based human immunodeficiency virus self-testing (HIVST) has been heterogeneous and inconclusive. In addition, most evaluations have relied on hypothetical or stated use cases using discreet choice experiments rather than actual preferences among experienced users, which are more objective and critical for the understanding of product uptake. Direct head-to-head comparison of consumer preferences for oral- versus blood-based HIVST is lacking.

#### AIM

To examine the existing literature on preferences for oral- vs blood-based HIVST, determine the factors that impact these preferences, and assess the potential implications for HIVST programs.

#### METHODS

Databases such as PubMed, Medline, Google Scholar, and Web of Science were searched for articles published between January 2011 to October 2022. Articles must address preferences for oral- vs blood-based HIVST. The study used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist to ensure the quality of the study.

#### RESULTS

The initial search revealed 2424 records, of which 8 studies were finally included in the scoping review. Pooled preference for blood-based HIVST was 48.8% (9%-78.6%), whereas pooled preference for oral HIVST was 59.8% (34.2%-91%) across all studies. However, for male-specific studies, the preference for blood-based

HIVST (58%-65.6%) was higher than that for oral (34.2%-41%). The four studies that reported a higher preference for blood-based HIVST were in men. Participants considered blood-based HIVST to be more accurate and rapid, while those with a higher preference for oral HIVST did so because these were considered non-invasive and easy to use.

## CONCLUSION

Consistently in the literature, men preferred blood-based HIVST over oral HIVST due to higher risk perception and desire for a test that provides higher accuracy coupled with rapidity, autonomy, privacy, and confidentiality, whereas those with a higher preference for oral HIVST did so because these were considered non-invasive and easy to use. Misinformation and distrust need to be addressed through promotional messaging to maximize the diversity of this new biomedical technology.

**Key Words:** Human immunodeficiency virus self-testing; Preferences; Oral human immunodeficiency virus self-testing; Blood-based human immunodeficiency virus self-testing

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**Core Tip:** We conducted a scoping review of the literature to determine the preferences for oral- vs blood-based human immunodeficiency virus self-testing (HIVST) and related factors. We searched PubMed, Medline, Google Scholar, and Web of Science databases for articles published between January 2011 and October 2022 that addressed preferences for oral- vs blood-based HIVST. The pooled preferences for blood- and oral-based HIVST were 48.8% and 59.8%, respectively. For male-specific studies, the preference for blood-based HIVST was higher than for oral. These results highlight the need to address misinformation and distrust through promotional messaging to maximize the diversity of this new biomedical technology.

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## INTRODUCTION

The Joint United Nations Programme on human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) (UNAIDS) has set 95:95:95 as a strategy to end HIV/AIDS by 2030. Although much progress has been made in achievement of the first 95 (*i.e.* 95% of individuals with HIV should test and know their HIV status), progress has been slow among hard-to-reach populations such as men, key populations, adolescents, and young persons. Men living with HIV perform less than women, with only 82% of men living with HIV knowing their HIV status[1]. Compared to women living with HIV, there are 740000 more men living with HIV who do not know their HIV status, 1.3 million more men who are not on treatment, and 920000 more men who are not virally suppressed[2]. The World Health Organization (WHO) released the first normative guideline on HIV self-testing (HIVST) in 2016[3]. WHO recommended HIVST as an additional approach to HIV testing services and recently added that both oral- and blood-based options should be provided. HIVST is safe, private, confidential, and convenient with the potential to improve access to testing for hard-to-reach populations such as men, adolescents, and young people as well as key populations. ST, being the first step in the care continuum, presents an enormous opportunity to close the HIV testing gap and achieve the global 95:95:95 fast track target set by UNAIDS. Self-testing empowers consumers to control when, where, and how they test for any of these diseases. Given the challenges in accessing traditional, provider-led testing services such as long distance from facilities, limited operating hours of conventional clinics, competing client priorities such as job and schooling, stigma, high cost, poor awareness, and dearth of culturally competent healthcare workers[4,5], ST as an alternative testing model, is a useful tool to expand access to testing for HIV, especially among vulnerable groups.

As of August 2022, six HIVST have been prequalified by the WHO (one using oral fluid and five using whole blood), *i.e.* Wondfo, Mylan, Insti, Check Now, Sure Check, and OraQuick[6,7]. However, evidence on preferences for oral- vs blood-based options has been heterogenous and inconclusive[8,9]. In addition, most evaluations have relied on hypothetical or stated use cases using discreet choice experiments[10,11] rather than actual use preferences from experienced end-users, which are more

objective and critical for uptake. Two main types of HIVST are available: oral- and blood-based tests. While both tests have demonstrated high sensitivity and specificity, the preferences of individuals for one test type over the other remain unclear. Understanding these preferences is crucial to promoting the widespread adoption and usage of HIVST.

The purpose of this scoping review is to provide a comprehensive overview of the literature on preferences for oral- vs blood-based HIVST, identify factors influencing these preferences, and explore the implications of these preferences for the promotion and implementation of HIVST programs. By synthesizing existing evidence, this review aims to inform policy-makers, healthcare providers, and other stakeholders involved in the design and implementation of HIVST programs, in order to maximize uptake and improve overall public health outcomes.

## MATERIALS AND METHODS

The scoping review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Figure 1). These reviews follow explicit, pre-specified and reproducible methods in order to identify, evaluate, and summarize the findings of all relevant individual studies (Grant and Booth, 2009)[12].

### Search strategy

One of the authors (Adepoju VA) searched for eligible studies between October 15 and 20, 2022. The Arksey and O'Malley[13] (2005) methodological framework guided the scoping of the published data. The scoping review conducted in this study was not registered in a registry such as PROSPERO. We chose not to register this scoping review, as registration is not a mandatory requirement for scoping reviews and our primary aim is to provide a broad overview of the literature rather than conduct a systematic assessment of the evidence. Although the Reference Citation Analysis tool was available for use, it was not utilized for this review. This decision was made based on the nature of the research question and the inclusion and exclusion criteria developed for the review, which ensured that all relevant studies were identified through the comprehensive search strategy described above.

### Data sources

Searched databases included PubMed, MEDLINE, Web of Science, and Google Scholar. For studies that may have been missed in the electronic search, we used reference lists of all the articles identified for cross-referencing. The first search took place between October 1 and 6, 2022, whereas the second took place between October 8 and 14, 2022. Detailed inclusion and exclusion criteria were developed with caution, to make sure that they matched the review questions and involved sufficient details to help point out all relevant studies and exclude irrelevant ones. The researchers then embarked on a two-stage process in which two reviewers independently screened the titles and abstracts for eligibility to be included in the final selection of papers. A combination of terms was used in the database searches; specifically: "HIV self-testing," OR "HIVST" OR "HIV self-screening" OR "HIVSS" AND "preferences" AND "values" AND "oral- and blood-based" OR "oral and fingerstick HIVST" OR Oral and capillary" OR "oral- vs blood-based." Specific keywords were combined with Boolean operators in the literature search (Table 1).

### Study selection

The systematic searches for eligible articles retrieved 2424 studies and 1454 duplicates were eventually removed. The authors (Adepoju VA, Imoyera W) independently screened the titles and abstracts for eligibility with the condition that if one or both authors identified the article as relevant, then the full-text review would be carried out. The researchers solved any disagreements *via* discussions and reached a consensus. After the title and abstract screening, two reviewers (Adepoju VA, Imoyera W) independently screened the full text of selected articles. Disagreements were resolved through discussions with a third reviewer (Onoja AJ) for final inclusion. The articles were selected in several parts, which allowed the reviewers to have a regular discussion of the eligibility criteria, ensuring the same understanding of the criteria, and the criteria remaining the same throughout the article selection phase. The researchers did not assess the risk of bias of the included studies. As in many scoping reviews, the goal was to describe preferences for oral- vs blood-based HIVST.

### Inclusion and exclusion criteria

Studies published in peer-reviewed journals between January 2011 and October 2022 and focusing on preferences of oral- vs blood-based HIVST among actual users were reviewed.

Inclusion criteria were: primary studies with participants aged 15 years or more with no geographic or population limitations; studies reporting on user preferences for HIVST with only two comparison groups (*i.e.* oral- vs blood-based HIVST); studies that adapted HIV Point of Care for HIVST for research purpose only; and studies that included actual users of oral- and blood-based HIVST. Exclusion criteria were studies comparing either oral- or blood-based HIVST with facility-based test or any other HIV



**Table 1** Search terms used in the literature search on preference for oral- vs blood-based human immunodeficiency self-testing in Nigeria

| Search terms       | OR                | AND                | AND                |
|--------------------|-------------------|--------------------|--------------------|
| HIVST              | HIV self-testing  | HIV self-screening |                    |
| HIV self-testing   |                   |                    |                    |
| HIVSS              |                   |                    | HIV self-screening |
| HIV self-screening |                   |                    |                    |
| Blood-based HIVST  | Fingerstick HIVST |                    | Capillary HIVST    |
| Fingerstick HIVST  |                   |                    |                    |
| Capillary HIVST    |                   |                    | Oral HIVST         |
| Oral HIVST         |                   |                    |                    |
| Preference         |                   |                    |                    |

Please note that the terms in the "OR" column are combined with an "OR" operator, whereas the terms in the "AND" columns are combined with an "AND" operator. The search strategy is designed to identify studies focusing on preferences for different HIV self-testing methods within the Nigerian context. HIV: Human immunodeficiency virus; HIVSS: HIV self-screening; HIVST: HIV self-testing.

testing approaches (*e.g.*, Voluntary Counselling and Testing, mail-in, Dry Blood Sample); studies evaluating user preferences for one type of HIVST only (*i.e.* oral- or blood-based specimen); studies where comparison group for preferences was not clear, not stated or measured qualitatively; and studies including hypothetical users rather than actual users of HIVST. Also excluded were articles published before January 2011, conference papers, books, studies with no full-text available, and magazines. This is because HIVST was not popular before this period and publications on this subject matter were either scarce or non-existent before this period. In accordance with PRISMA guideline 16b, we have cited and explained the exclusion of studies that appeared to meet the inclusion criteria but were ultimately excluded. The reasons for their exclusion are provided in the results and appendix section ([Supplementary Table 1](#)) ensuring transparency in the review process.

### Data extraction

The authors extracted relevant data using a standard excel-based template. Two authors (Adepoju VA, Imoyera W) independently extracted the data, and the results were reviewed and verified by both authors for quality and clarity. Two authors (Adepoju VA, Onoja AJ) separately and independently assessed the full text of the potentially eligible publications. Disagreements were resolved by consensus. Initial agreement was obtained on 90% of the items, and discrepancies were discussed between authors until 100% agreement was obtained. The following information was extracted from the included studies: author name and year of study, study design, type of specimen, product type, population and age, prevalence of preference for oral- and blood-based HIVST and major findings ([Table 2](#)). After extracting relevant information from the studies, the authors constructed a more specific classification for preferences of oral- vs blood-based HIVST.

### List of papers reviewed

The search results are shown in [Figure 1](#), along with a summary of the papers consulted (the PRISMA flow chart). Although 2424 research articles were retrieved initially from the databases, only 8 met the inclusion criteria for this scoping review.

## RESULTS

During the study selection process, we identified several studies that initially appeared to meet our inclusion criteria but were ultimately excluded upon closer examination and based on the predefined inclusion and exclusion criteria. We have provided a comprehensive list of these excluded studies and the reasons for their exclusion in the [Supplementary Table 1](#). By documenting this information, we aim to ensure transparency and reproducibility in our review and study selection process and to demonstrate compliance with PRISMA 16B.

### Geographic and population distribution of the included articles

The total number of participants across the 8 studies was 7129 (40-4496). Of the eight studies reviewed,



**Table 2 Summary of the included studies, *n* = 8**

| Ref.   | Country               | Study design                    | Type of specimen       | Product type              | Population, age in yr       | Preference for oral, % | Preference for blood, % | Other findings  |
|--|-----------------------|---------------------------------|------------------------|---------------------------|-----------------------------|------------------------|-------------------------|---|
| Tonen-Wolyec <i>et al</i> [14], 2020         | The Republic of Congo | Cross-sectional                 | Oral vs Fingerstick    | Oraquick, Exacto          | General population, 18-49   | 85.6                   | 78.6                    | Comparable accuracy. University education and higher risk increases BB preference   |
| Trabwongwitaya <i>et al</i> [15], 2022       | Thailand              | Cross-sectional                 | Oral vs Fingerstick    | Oraquick, INSTI           | Young adult KP, 18-24       | 34.4                   | 65.6                    | Performance and interpretation, O-93.3%, 100%; B-89.5%, 98%   |
| Cassell <i>et al</i> [19], 2022              | Cambodia              | Cross-sectional                 | Oral vs Fingerstick    | Oraquick, Combokit Abbott | KPs, 15+                    | 88.5                   | 11.5                    | Assisted-98.6%; Unassisted-1.4%   |
| Shapiro <i>et al</i> [20], 2020              | South Africa          | Cross-sectional                 | Oral vs Fingerstick    | Oraquick, Atomo           | Adult men, 18+              | 42                     | 58                      | 10% and 90% will prefer different and the same kit for repeat tests, respectively   |
| Lippman <i>et al</i> [17], 2018 <sup>1</sup> | South Africa          | Cross-sectional                 | Oral vs Fingerstick BB | Oraquick, Atomo           | MSM                         | 34.2                   | 64.6                    | 97% will use HIVST again if available in the future   |
| Lee <i>et al</i> [16], 2022                  | Australia             | Randomized Clinical Trial (RCT) | Oral vs Fingerstick    | Oraquick, Atomo           | MSM, 18+                    | 41                     | 58                      | O-not swabbing both gum, placing buffer on stand; BB-filling test channel, squeezing finger for blood drop                                |
| Ritchwood <i>et al</i> [18], 2019            | South Africa          | Qualitative                     | Oral vs Fingerstick    | Not stated                | Young adult, 18-24          | 80                     | 20                      | Post-test opinion change on ease of use and trust in result   |
| Gaydos <i>et al</i> [21], 2011               | United State          | Crosssectional                  | Oral vs Fingerstick    | Oraquick, Unigold         | Emergency department, 18-64 | 91                     | 9                       | 'Trust in result' O-similar for initial HCW-led and client ST (91%); B-client BBST result more (91.7%) than HCW provided HIV test (77.8%) |

<sup>1</sup>Indicates that it is a subsequent publication by the same author(s) in the same year. B: Blood; BBST: Blood-based self-testing; HCWs: Healthcare workers; HIV: Human immunodeficiency; KP: Key Population; MSM: Men who have sex with men; O: Oral; ST: Self-testing.

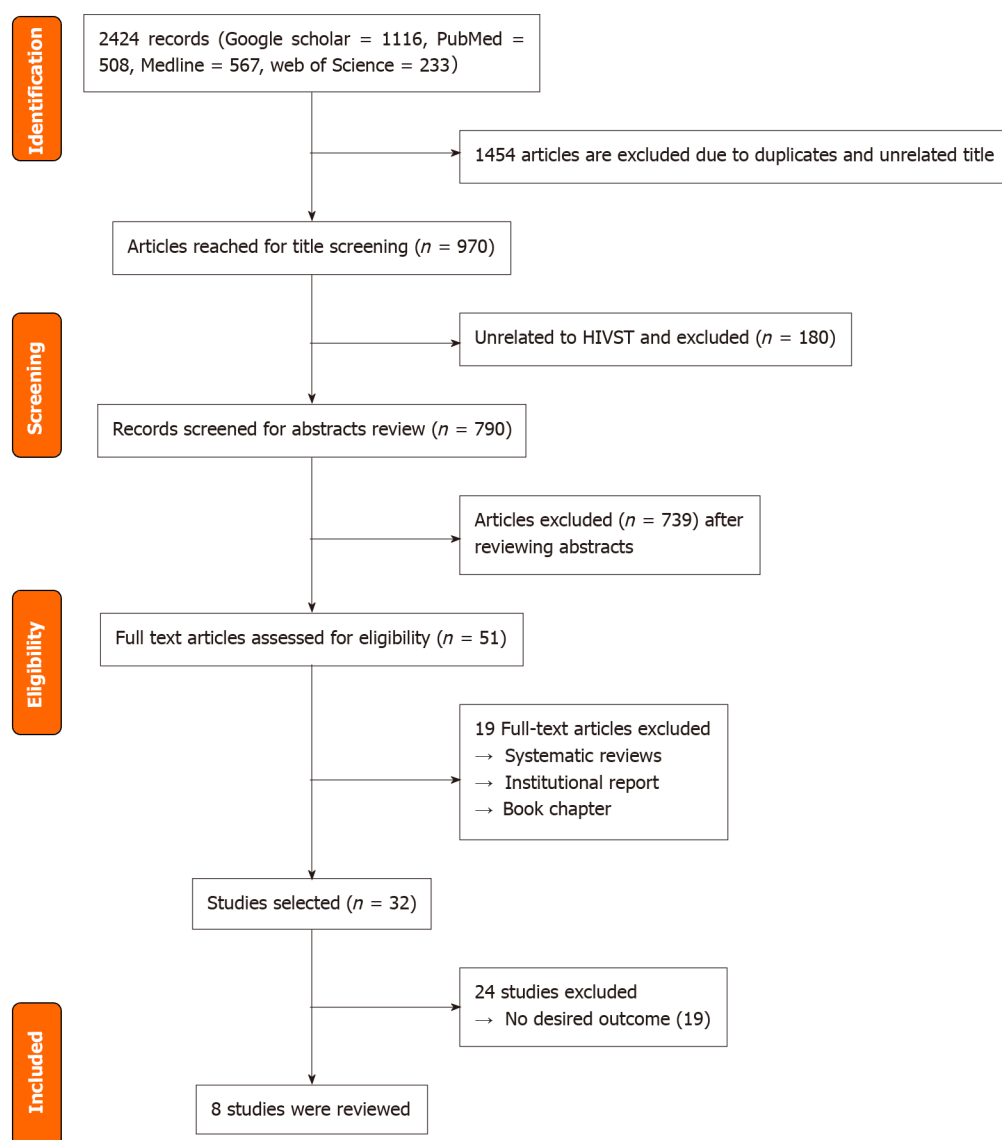
three studies were from South Africa and one each was from Cambodia, the United States, Thailand, Australia, and the Democratic Republic of Congo **Figure 2**. Three studies involved the general population (*n* = 3)[14-16], four involved the key population (*n* = 4)[14-17], and one involved young people (*n* = 1)[18]. A total eight studies, *i.e.* 6 quantitative studies[14,15,17,19-21], 1 randomized control trial[16], and 1 qualitative[18], were included in the study.

#### **Year of publication of included studies**

Out of the eight articles included, three were published in 2022[15,16,19], two in 2020[14,20], one in 2018 [17], one in 2019[18], and one in 2011[21] (**Figure 3**).

#### **Preference for oral- vs blood-based HIVST**

One hundred percent of the studies reported preference based on the actual use of HIVST, and 50% reported usability. Four of the eight studies (50%) reported a higher preference for blood-based HIVST [16,18-20], whereas four of the eight studies (50%) reported a higher preference for oral HIVST[14,15,17, 21]. Pooled preference for blood-based HIVST was 48.8% (9%-78.6%), whereas pooled preference for oral HIVST was 59.8% (34.2%-91%) across all studies. However, for male-specific studies[16,18-20], preference for blood-based HIVST (58%-65.6%) was higher than that for oral (34.2%-41%). The four studies that reported a higher preference for blood-based HIVST were in men, and participants considered blood-based HIVST to be more accurate and rapid whereas studies reporting higher preference for oral HIVST did so because they were considered non-invasive and easy to use with few false-negative results.



**Figure 1 Preferred reporting items for systematic reviews and meta-analyses flowchart: Study selection process for the scoping review on preferences for oral- vs blood-based human immunodeficiency virus self-testing.**

## DISCUSSION

Overall, the study observed a slightly higher preference for oral than fingerstick HIVST. Similar to this finding, in studies among pregnant women in India[22], primary healthcare attendees in South Africa [23], female sex workers in China[24], and young people in Nigeria[25], participants who chose oral HIVST (over blood-based) cited ease of use and ability to avoid needle prick as reasons for choosing oral HIVST. Those who did not choose oral HIVST distrusted its capacity to detect HIV in saliva specimens. The distrust in HIV detection in saliva may have stemmed from HIV messaging that has historically emphasized that HIV can neither be acquired nor transmitted through kissing and oral sex[26,27]; hence, clients have questioned the scientific basis for HIV detection in oral fluid.

Furthermore, a significantly higher preference for blood-based HIVST than oral HIVST was noted in male-specific studies in this scoping review. Consistent with this finding, preferences for blood-based HIVST in men who have sex with men (MSM) in the United Kingdom and heterosexual men in Singapore were higher due to its accuracy, rapidity of results, and minimal false-negative results[28-30]. Preferences were also associated with certain factors such as previous testing, type of product used for recent testing, and presence of high-risk sexual behavior, indicating that these factors may influence individual preferences[31-33]. For instance, a study previously highlighted that individuals reporting recent high-risk sexual behaviors (*e.g.*, unprotected sex, sex when drunk) were less likely to use oral HIVST[32], whereas the likelihood of using blood-based HIVST increased when offered with information on other sexually transmitted infections[33]. Men's greater preference for blood-based HIVST was influenced by perceived higher risk, desire for accuracy, and perception of having lesser

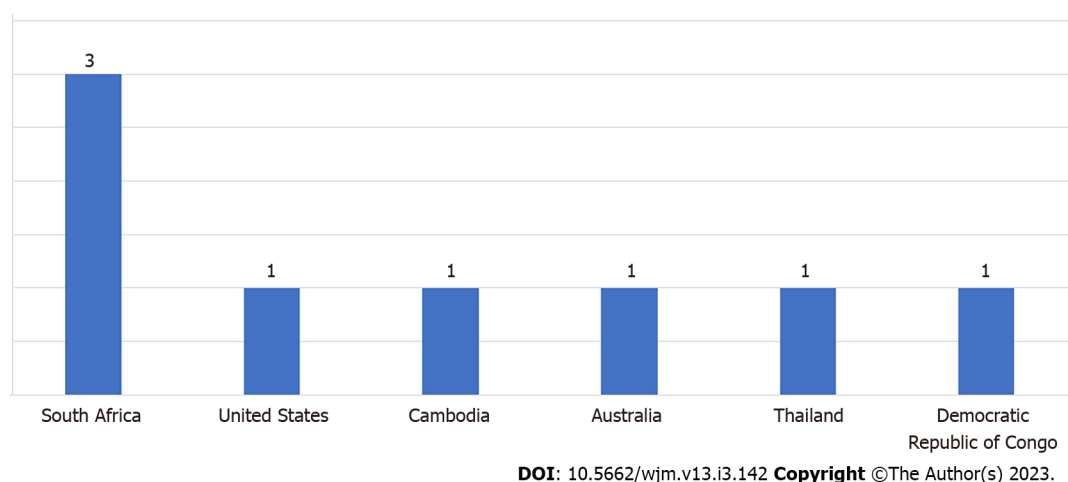


Figure 2 Number of included studies by country.

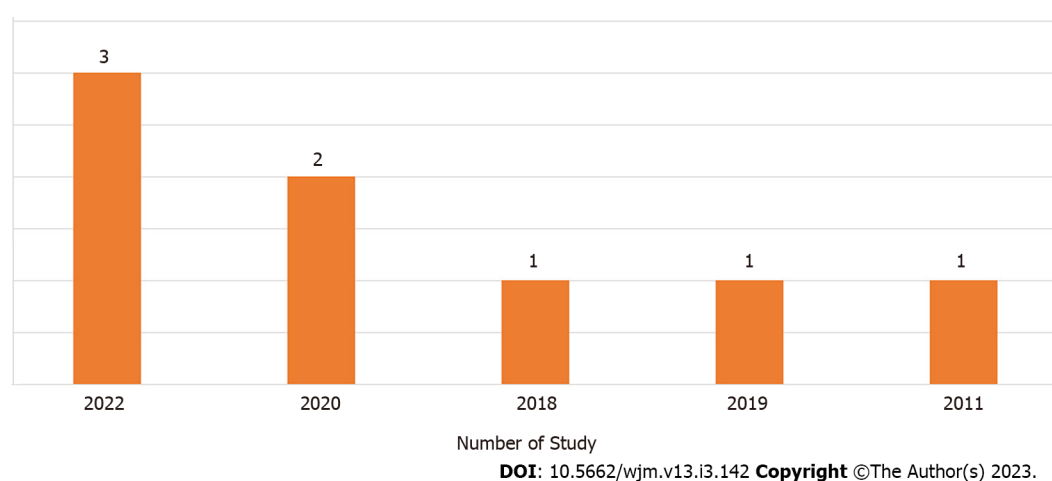


Figure 3 Number of included studies by year of publication.

false-negative results[30]. Previous studies have also suggested that the accuracy of blood-based self-tests is higher than that of oral-fluid self-tests due to the lower quantity of HIV antibodies in oral fluid compared with whole blood[34] and reduced sensitivity for oral fluid testing for antibody detection (compared with blood testing) when specimen was obtained early after HIV infection[35]. Moreover, evaluation report of the third-generation blood-based HIVST showed very high sensitivity of 100% and high specificity of 99.9% and the ability of this product to detect HIV infections 7 d sooner than second-generation tests (*i.e.* from day 21 of infection instead of 28 d associated with most second-generation oral- and blood-based HIVST)[36]. One would expect usability of blood-based testing to be a major barrier, especially among men where preference was high. By contrast, a usability index average of 92.8% (92.2%-95.5% for oral HIVST; 84.2%-97.6% for blood-based HIVST) was reported in a study that evaluated the usability of seven WHO Prequalified HIVST kits (five blood-based and two oral HIVST) in South Africa[37]. Since both oral- and blood-based HIVST are complementary, a choice-based approach is therefore needed to optimize HIV testing programs and close the gaps between HIV testing and treatment.

There are several limitations to consider when interpreting our findings. First, we only used four databases to search the literature and may have missed articles not embedded. That notwithstanding, these databases are the basic sources of public health literature. Also, by not including conference abstracts, more recent unpublished articles may have been missed. Moreover, by reviewing citations of scoping and systematic reviews, the chances of incorporating the full breadth of the research through our search strategies were increased. We are convinced of having reached saturation with our methods. The real strength of the study lies in the inclusion of studies that offered both oral- and blood-based HIVST to actual users in real-world situations rather than experimental studies. This has removed the generalizability bias often seen in studies that offer only one type of HIVST or measure preferences from an intention-to-use perspective[38,39].

## CONCLUSION

The scoping review consistently showed that men preferred blood-based HIVST than oral HIVST due to a higher risk perception and desire for a test that provides higher accuracy coupled with autonomy, rapidity, privacy, and confidentiality. The UNAIDS 2021 report showed a huge gap in knowledge of HIV status among general men and MSM, whereas AIDS-related death was higher in men than women due to late diagnosis, hence providing a blood-based HIVST option that can facilitate acceptability and the earlier diagnosis of HIV in men.

Similarly, the scoping review highlighted the diversity in preferences for oral- and blood-based HIVST and found that a single type of self-test kit is unlikely to cater for the preferences of diverse population and achieve high testing coverage. Integrating novel biomedical instruments into standard clinical and community procedures can occasionally prove difficult, as evidenced by the adoption of oral and injectable preexposure prophylaxis along with contemporary contraceptive methods. That notwithstanding, Ministries of Health and country programs should consider both blood and oral HIVST options. Offering choices among multiple kits may be the best way to maximize uptake and reach populations who may not otherwise test for HIV. Offering broader choices for HIVST could have a greater impact on testing uptake, but more research is needed to address misconceptions that drive HIVST and identify effective, population-specific dissemination channels needed to promote HIVST choices so people can make appropriately informed choices.

## ARTICLE HIGHLIGHTS

### Research background

Human immunodeficiency virus self-testing (HIVST) has been shown to increase testing rates and improve early HIV diagnosis. However, there are different testing modalities, including oral- and blood-based HIVST, and little is known about the preferences for these different types of HIVST.

### Research motivation

Identifying preferences for oral- *vs* blood-based HIVST is crucial for the development and implementation of effective HIVST programs. Understanding the factors that influence these preferences can also inform strategies for increasing uptake of HIVST.

### Research objectives

The main objective of this scoping review was to provide a comprehensive overview of the literature on preferences for oral- *vs* blood-based HIVST. Specific objectives included identifying factors that influence preferences, exploring the implications of these preferences for the promotion and implementation of HIVST programs, and highlighting gaps in the literature.

### Research methods

A scoping review methodology was used to identify and synthesize relevant literature on preferences for oral- *vs* blood-based HIVST. The review included studies published in English between 2011 and 2021 that focused on actual and not hypothetical users of HIVST.

### Research results

The search yielded 2424 records, of which 8 studies were included in the review. Across all studies, pooled preference for oral HIVST was 59.8%, whereas for blood-based HIVST, it was 48.8%. However, in studies specific to men, the preference for blood-based HIVST (58%-65.6%) was higher than oral (34.2%-41%). Men favored blood-based HIVST because of its perceived accuracy and rapidity, whereas oral HIVST was preferred for being non-invasive and easy to use.

### Research conclusions

Preferences for oral- *vs* blood-based HIVST are influenced by various factors, including user characteristics such as sex, testing context, and perceived test accuracy. Programs promoting HIVST should consider these factors when designing and implementing HIVST programs. Further research is needed to explore the impact of these preferences on HIV testing rates and to identify effective strategies for increasing the uptake of HIVST.

### Research perspectives

Future research should focus on identifying effective strategies for increasing the uptake of HIVST, particularly among populations that may have unique preferences or barriers to testing. Longitudinal studies could also help to explore the impact of these preferences on HIV testing rates and linkage to care. Additionally, studies should continue to explore the accuracy and feasibility of new HIVST techno-

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**Author contributions:** Adepoju VA conceptualized the study, designed the review methodology, conducted the initial literature search, contributed to the data analysis, and wrote the first draft of the manuscript; Imoyera W was involved in the study design, literature search, and data analysis, and contributed to writing and revising the manuscript including reviewing and synthesizing the data; Onoja AJ was involved in the literature search, data analysis, and manuscript revisions.

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