**Title page**

Title:

**A prospective observational study to evaluate the performance of the BioSure ® HIV Self-Test in the hands of lay users.**

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**Abstract:**

Objectives: In order to assess whether the BioSure® HIV Self-Test could be reliably performed by users at home, we carried out an evaluation study among attendees at a sexual health service, to determine whether they were able to perform and correctly interpret the test.

Methods: A prospective observational study of clinic attendees to determine their ability to follow the instructions, complete the test on themselves, and correctly interpret the results. The evaluation included interpretation of three dummy (contrived) devices, chosen at random from a sample of 12 devices, to ensure that a sufficient number of all possible test outcomes were included.

Results: 200 participants were recruited. 97.0% (95% CI 93.5-98.9) conducted the test so as to achieve a valid result. 99.5% correctly identified the test result. Participants correctly interpreted the result of 94.0% (95% CI 91.4-95.9) of 586 contrived devices.

Conclusions: The majority of participants were able to follow the instructions and perform the test in order to get a valid result. Interpretation of the test results was good and the majority of participants were able to correctly read the result of their own and contrived tests. The availability of HIV self-tests will provide another option to increase access to testing particularly for those who may not wish, or are unable to access clinical services.

**Key messages:**

* **In April 2014, the UK government revoked regulations preventing the sale of HIV self-testing kits directly to the public.**
* **To receive a licence to sell a self-test kit, a company must demonstrate correct use of the test by lay-users.**
* **The majority of participants (97%) were able to follow the instructions and perform the test in order to get a valid result.**
* **94% of the results of contrived devices were correctly interpreted by participants.**

**Background:**

Human immunodeficiency virus (HIV) continues to be a pressing issue for health care with an estimated 101,200 people living with HIV in the United Kingdom (UK) in 2015.1 However, around 13% of people living with HIV in the UK are unaware of their HIV status and two in every five new diagnoses occur in patients whose disease has progressed beyond the point at which treatment should have been started.1 Although the proportion of people unaware of their HIV infection has fallen, the consequent late diagnosis increases morbidity and health care costs, and increases the number of individuals at risk of onward transmission because they are not receiving effective antiretroviral therapy. By increasing access to testing options, it may be possible to help reduce the proportion of undiagnosed infections. HIV self-testing (HIVST) can be defined as when an individual performs a HIV rapid diagnostic test and interprets the result in private.2 This is distinct from HIV self-sampling (HIVSS) whereby a sample of blood or saliva is collected by an individual and sent to a laboratory for testing.

In April 2014, the UK government revoked the regulations that prevented the promotion and sale of HIV tests for self-testing. At the time of the change in UK self-testing regulations, the BioSure® HIV Self-Test was approved for professional use as SURE CHECK® HIV 1/2 Assay (manufactured by Chembio Diagnostics Systems, Inc.) but not for self-testing. It is a lateral flow device which detects HIV 1 and 2 antibodies. It requires a blood sample from a finger prick and the result is ready to read after 15 minutes.

The regulation of in vitro diagnostic devices is guided by a European Commission decision on common technical specifications for in vitro-diagnostic medical devices.3 Before the device can be sold to the public, there should be a lay user evaluation of the device to validate the operation of the device and the instructions for use.3 Once approved the device should display a “Conformité Européene” (CE) mark.

We report the findings of an observational study to assess the ability of lay users attending a sexual health service to perform the BioSure® HIV Self-Test and to correctly interpret the result of the self-test, and a number of dummy (contrived) devices, designed to mimic the appearance of all possible test outcomes.

**Methods:**

This was a prospective study recruiting attendees at a single, large sexual health clinic in London between November 2014 and March 2016. Participants were eligible if they were aged 16 years or over, reported having had a previous negative HIV test, or had never previously tested, and were able to read English sufficient to allow them to identify the kit as an HIV test and to have been able to purchase the item. Patients were excluded if they were known to be HIV positive, had a bleeding disorder, had needle phobia to an extent that they would be unable to perform the test, had received previous training in the use of the test kit, had significant visual impairment such that they could not read the test instructions, or the result. Potential participants were identified by clinic staff and referred to the research team for inclusion in the study.

The study was conducted in two parts. In the first part, the participant was given the test kit pack and asked to follow the instructions and complete the self-test by a researcher. The test kit included written instructions on how to perform and interpret the self-test; participants were not given any further verbal instructions or assistance by the researcher, in order to as closely replicate as possible a real-life self-testing situation. The participant was observed while they completed the self-test, and any deviation from the correct procedure, or other difficulty encountered was recorded by the researcher, who also verified the result. To complete the first part, the researcher undertook the clinic standard of care point-of-care test; the result was given to the participant but not until after they had interpreted their own self-test result.

The second part of the study assessed the ability of the participant to accurately interpret the results of three dummy (contrived) devices, chosen at random from a sample of 12 devices (6 reactive, 4 non-reactive and 2 invalid). These contrived devices mimicked the appearance of potential self-test results. There were three possible test outcomes: 1) “non-reactive” if a single control-line appeared but no other line was present; 2) “reactive” if two lines were visible, one control-line and a second test-line; or 3) “invalid” if no control-line was present after running the test.

The primary outcome measures were the percentage of participants conducting the test so as to achieve a valid result (for the first part of the study) and the percentage of correctly identified results on the contrived devices (the second part).

**Sample size:**

We originally planned to recruit 400 participants so as to provide 89% power to demonstrate (at 5% significance level) that the true percentage who achieve a valid result is at least 95%, assuming the true percentage is 98%. Recruitment was, however, halted at 200 participants when the manufacturer had enough evidence for CE mark submission.

**Statistical analysis:**

The primary outcomes were calculated with 95% confidence intervals for all participants. For the primary outcome in the first part of the study, the percentage of participants conducting the test so as to achieve a valid result, the association was tested with the key participant subgroup factor (Men who have Sex with Men (MSM), heterosexual men and women), measures of education and English language proficiency using a trend test or Fisher’s exact test as appropriate.

For the primary outcome in the second part of the study, the percentage of correctly identified results, we used the survey functions in Stata 14 to acknowledge the clustering of multiple outcome measures for each participant in the analysis. Associations with this outcome were tested for the key participant subgroup factor (MSM, heterosexual men and women), measures of education, English language proficiency, ethnicity and place of birth using the survey adapted chi-squared test. No multiple regression was planned due to the anticipated small number of incorrectly identified results.

**Ethics:**

The study was reviewed and ethical approval granted by the National Research Ethics Service (REC reference 14/LO/1666).

**Results:**

200 participants were recruited (median age 34.5 years, IQR 25.7 to 41.1) (Table 1). The majority were male (90%) and of white ethnicity (74%). Approximately half were born outside of the UK (53.5%), and for one third (32%) English was not their first language. Almost all (98.5%) participants had previously used the internet to purchase items.

Table 1: Demographic and behavioural characteristics of participants

|  |  |  |
| --- | --- | --- |
| **Characteristic** | **%** | **(n)** |
| Median age (IQR), years | 34.5 | (25.7-41.1) |
| Gender and sexual behaviour FemaleMen who have sex with menMen who have sex exclusively with women | 10.049.540.5 | (20)(98)(80) |
| Self-reported ethnicityWhiteBlackAsianOther | 74.018.35.212.5 | (142)(16)(10)(24) |
| Highest qualificationHigher degreeDegreeFurther educationSecondary schoolNone | 31.838.418.710.60.5 | (63)(76)(37)(21)(1) |
| Place of birthOutside UKUK | 53.546.5 | (107)(93) |
| English first languageNoYes | 32.068.0 | (63)(136) |
| Ever purchased from the internetNoYes | 1.598.5 | (3)(195) |

\*the numbers in categories may not add up to 200 due to missing data items

**Observed participant self-test**

Following informed consent, one participant decided not to complete the first part of the study. Of the remaining 199 participants, 193 (97.0%; 95% CI 93.5-98.9), conducted the test so as to achieve a valid result (Table 2). 99.5% of participants correctly identified the test result with a single participant interpreting their test as invalid when it was non-reactive. A single participant had a reactive test result which was confirmed on a second point-of-care test, and a laboratory test. No factors were significantly associated with the likelihood of an invalid result; all invalid results were among those who spoke English as a first language.

Table 2: Prevalence of a valid test result, and associated factors

|  |  |  |
| --- | --- | --- |
| **Characteristic** | **Valid result, % (n)** | ***p* value** |
| Total | 97.0 (193) |  |
| Gender and sexual behaviour FemaleMen who have sex with menMen who have sex exclusively with women | 95.0 (18)97.0 (95)97.5 (78) | 0.6821 |
| English spoken as first languageNoYes | 100.0 (63)95.6 (130) | 0.1801 |
| Highest qualificationHigher degreeDegreeFurther educationSecondary school/ None | 96.8 (61)98.7 (75)94.6 (35)95.5 (21) | 0.5352 |

1Fisher’s exact test; 2Trend test across ordered groups

Participants experienced few problems when performing the self-test (Table 3). The most common problem was not pushing the device far enough into the buffer solution container in order to allow the test to run (15.5%). This was noticed by the participants during the process, as the self-test instructions advise to check the test is running properly after a few minutes. At this point the device was inserted further into the buffer container and the tests ran as expected. Some participants had difficulty using the finger-prick lancet (3.0%), or expressing blood or collecting a sample (4.0%), although not to a degree that meant that the test was unable to be performed. A single participant did not read the self-test after the recommended time interval but did achieve a valid result.

Table 3: Prevalence of problems experienced when performing the self-test

|  |  |
| --- | --- |
| **Problem** | **N (%)** |
| Correct use of finger-prick lancetNoYes | 6 (3.0)193 (97.0) |
| Correct collection of blood sampleNoYes | 8 (4.0)191 (96.0) |
| Correct application of buffer solutionNoYes | 31 (15.5)168 (84.5) |
| Self-test read at recommended time pointNoYes | 1 (0.5)198 (99.5) |

Of the six participants with an invalid result, two experienced no difficulties performing the test. Two had difficulties applying the blood sample to the tip of the device but no other problems. One participant had difficulty using the finger-prick lancet and a further participant did not insert the device into the buffer solution correctly.

**Interpreting results of contrived devices**

196 participants went on to complete the second part of the study although two participants only read two contrived devices (total of 586 contrived devices read). The three participants who completed part one of the study but not part two, and the two participants who only read two contrived devices, stopped their participation due to time taken in clinic. Participants correctly interpreted the result of 551, 94.0% (95% CI 91.4-95.9), of the contrived devices (Table 4). Twenty-one participants misinterpreted a single device, seven misinterpreted two devices and no participants misinterpreted all three devices. Those of black ethnicity were more likely to misinterpret the contrived devices. There was also some evidence of greater misinterpretation of devices among those for whom English was not their first spoken language and among those born outside of the UK.

Table 4: Factors associated with correct interpretation of contrived devices

|  |  |  |
| --- | --- | --- |
|  | **Correct interpretation****% (95% CI)** | **p value** |
| Total, n=586 | 94.0 (91.4-95.9) |  |
| Contrived device resultNon-Reactive, n=229Reactive, n=197Invalid, n=90 | 93.3 (89.9-95.6)92.9 (87.3-96.1)98.9 (92.4-99.9) | *p*=0.114 |
| Gender and sexual behaviour Female, n=53MSM1, n=291MSEW2, n=236 | 90.6 (77.4-96.4)95.2 (91.6-97.3)93.2 (88.3-96.2) | *p*=0.442 |
| English spoken as first languageNo, n=182Yes, n=404 | 91.2 (85.0-95.0)95.3 (92.4-97.1) | *p*=0.092 |
| Highest qualificationHigher degree, n=186Degree, n=227Further education, n=107Secondary school/ None, n=66 | 93.0 (86.9-96.4)93.8 (89.0-96.6)95.3 (89.6-98.0)95.5 (87.4-98.5) | *p*=0.837 |
| Self-reported ethnicityWhite, n=419Black, n=47Asian, n=27Other, n=72 | 95.2 (92.4-97.1)83.0 (65.7-92.6)92.6 (76.7-97.9)94.4 (83.5-98.3) | *p*=0.030 |
| Place of birthOutside UK, n=307UK, n=279 | 92.2 (87.8-95.1)96.1 (92.8-97.9) | *p*=0.072 |

1Men who have sex with men; 2Men who have sex exclusively with women

**Conclusions:**

In this lay user evaluation of the BioSure® HIV Self-Test, 97% of participants were able to achieve a valid test result. 94% of contrived test devices were correctly interpreted. Incorrect interpretation of the contrived test results was associated with being of black ethnicity and born outside of the UK.

The majority of participants were able to follow the instructions and perform the test in order to get a valid result. Although many experienced some difficulty, these were not sufficient to prevent them obtaining a valid result. Errors in placing the test device far enough into the buffer solution were common and have also been observed in other self-testing studies.4 These findings are in keeping with other studies which assessed acceptability, feasibility and accuracy of HIV self-testing.5 6 For those who go on to use the test again, familiarity with performing the test may lessen the difficulties experienced. Participants did not have access to a video of how to perform the test, which is now available online to those who purchase the self-test kit.

Although overall interpretation of the test results was good and the majority of participants were able to correctly read the result of both their own and contrived tests, a number of participants experienced more difficulty in this task. This has also been seen in other self-testing studies with oral fluid-based and blood-based test kits.7-10 These difficulties were most commonly seen in those of black ethnicity, those born outside the UK, and those who do not speak English as a first language. The latter association suggests issues with how the instructions were displayed which could be overcome if supplied in another language. Therefore, those for whom English is not their first spoken language who attempt to use the self-test may benefit from the option of additional support and instructions. Making instructions available in languages other than English may be useful, especially as overcoming barriers to testing in non-English speaking populations is a potential benefit of this technology. This is of particular importance in addressing health inequalities and maximising testing in different risk groups.

The public and individual health impact of misinterpreting a result is perhaps of most concern if the test result is reactive but it is read as non-reactive. This would falsely reassure the individual. The number of misinterpreted contrived devices was low (35) which limited our ability to determine whether reactive results were more or less likely to be misread.

Performing a self-test too soon after a recent potential exposure may also lead to false reassurance of those testing. However, this study was not designed to address this issue and the test kit, which is now commercially available, has written advice regarding window periods.

Linkage to care after using rapid tests in a variety of settings is high, including after self-testing.11-14 Furthermore, HIVST kits offer access to rapid results which may help to encourage those who have never tested, test infrequently or have undiagnosed HIV infection to test.15-17 Individuals having clinic-based point of care tests are significantly more likely to receive their result.18 Users of self-tests are highly likely to read and correctly interpret their result, thereby allowing those users to know their status and manage their health accordingly.

To our knowledge, this is the first study to examine the ability of UK-based lay-users to correctly perform and interpret an HIV self-test device. There are a number of limitations to the study. Men and women attending sexual health services may be familiar with point of care tests and therefore may be more likely to be able to perform the self-test correctly.

The demographic characteristics of the study participants are not fully representative of those accessing HIV care during 2015 in the UK, which may limit wider applicability of the findings. Participants were younger than those accessing HIV care (median age 35 years vs. 45 years, respectively).19 Women (10%) and black and minority ethnic participants (26%) were also under-represented compared to those accessing HIV care (31% and 45%, respectively).20 However, the proportion of MSM (49.5%) and those born outside of the UK (53.5%) in our sample is broadly similar with those accessing care (45% and 48%, respectively).1 21 Study participants were highly educated with 70% holding a degree or higher degree. This data is not currently available for those accessing HIV care in the UK, however, 27% of English residents aged 16 years and over in the 2011 census data reported having a degree, higher degree or equivalent qualification.22 We did not collect any qualitative data to explore reasons for difficulties with performing the test nor to rate acceptability of the finger prick method, which may be important given that previous studies have shown some user preference for oral fluid-based tests to blood-based tests.23 Further work to explore user preference may be helpful. Finally, the relatively small sample size limited further exploration of factors associated with either difficulty conducting the test, or the interpretation of the result. The generalisability of our results may be limited as a result of these limitations.

To conclude, the majority of participants in this study were able to correctly perform the BioSure® HIV Self-Test without difficulty and interpret results. This is the first HIV self-test to be licensed in the UK since the relaxation of the regulations and currently retails for £29.95, approximately $39 US dollars.24 Self-testing offers individuals an additional option and may be attractive for some people. Providers of self-testing kits should ensure that instructions are clearly understandable by those who are likely to use them, and take into consideration those who do not speak English as their first language. Although this study identified a few technical issues that could be addressed by appropriate guidance to users, such as some failures to insert the device far enough into the buffer container, the test performed well overall and has now been granted a CE mark.

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**Contributorship statement:**

RG, AC, AM, GC wrote the protocol and secured funding for the study. AM managed the study. JS, MO, LP identified and recruited participants and managed data collection. NB and AC analysed data. JS led the writing of the manuscript with input from all authors.

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