# Pilot Study of the Use of Tests Designed for Self-testing of HIV Infection

NATIONAL INSTITUTE
OF PUBLIC HEALTH
PRAGUE 2022

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# Content

# 1. Introduction

One of the objectives of the HIV/AIDS National Programme in the Czech Republic for the period 2018–2022 within the framework of activities planned for prevention of HIV transmission was to conduct a pilot study of the tests designed for self-testing of HIV infection in the population at higher risk and to compare its results with the 4th generation of classic laboratory tests.

In order to meet these objectives, a study focusing on tests for self-testing of HIV infection was designed and implemented in cooperation with the National Institute of Public Health (NIPH) and the Czech AIDS Help Society; the clients were approached at the Lighthouse (a social and asylum centre of the Czech AIDS Help Society) and asked to participate. Between December 1, 2018 and June 30, 2019, three hundred clients tested themselves for HIV under the supervision of a trained staff member using five different tests designed for self-testing: Autotest VIH®, BioSURE HIV Self Test, EXACTO® PRO Test HIV, INSTI® HIV Self Test, HIV-1/2 OraQuick ADVANCE®. The study proved that Autotest and BioSURE tests are performed in the same way. Each of the tests was performed by sixty volunteers. At the same time, a venous blood sample was collected from the volunteers. Subsequently, the samples were tested with the EIA test ARCHITECT HIV Ag/Ab Combo, Abbott, at the National Reference Laboratory for HIV/AIDS (NRL). Self-tests were assigned randomly to individual participating clients. The opportunity to participate in the study was offered to all clients interested in anonymous testing at the Lighthouse, until the number of clients required to participate in the study was reached. This ensured a balanced sample of clients representing the whole population. Each of the tested clients completed a questionnaire designed for this study, in addition to the usual pre-test questionnaire used at the Lighthouse. A short questionnaire evaluating the participating client's procedure was also completed by the trained staff member – counsellor. Instructions for use were provided in the Czech language (translated by the contractor). The questionnaires were used to evaluate the usability and acceptability of the tests by the clients, including the clarity of instructions for use.

# 2. Objectives of the Study

The study pursued the following two objectives

1. to evaluate the practical use of the HIV self-tests from the user's point of view
2. to compare the test results based on pre-defined panels of patient sera.

# 3. Results

## 3.1 Evaluating the Practical Use of Self-tests

### Demographic Characteristics of Participating Clients

A total of three hundred persons participated in the study, 197 men (65.7%), 101 women (33.7%), 1 person of different gender and in 1 case the gender was not specified. The average age of the participating clients was 28.7 years, ranging between 15 to 68 years of age. Three-fifths of the participating clients (60.7%) were under the age of 30. In terms of nationality, 242 persons (80.7%) were from the Czech Republic, 27 (9.0%) from Slovakia and 31 (10.3%) from other countries (two from Belgium, one from Belarus, one from China, one from the Dominican Republic, one from France, one from Cameroon, four from Kazakhstan, two from Moldova, one from Mozambique, one from Portugal, eight from Russia, one from Turkey and seven from Ukraine). Prague (59.5%) was the most frequently mentioned place of permanent residence (temporary residence of foreigners), followed by Central Bohemia (12.0%). Other regions were represented from 0.3% to 3.0%.

Altogether, 54.3% of the tested participating clients identified their sexual orientation as heterosexual (163 persons), 38.7% as homosexual (116 persons) and 7.0% identified themselves as bisexuals (21 persons). In response to the question "Were any of your sexual partners a foreigner?", 47.7% of the participating clients (143 persons) answered positively. Money for sex was accepted by 2.7% of the participating clients and 8.0% had paid for sex or sexual services. A total of 31.7% of the participating clients (95 persons) reported use of alcohol or marijuana, 8.3% of the participating clients (18 persons) reported non-injecting drugs (tablets,

pills), 6.0% reported using a nasally shared sniff tube, and one participating client reported both injecting and non-injecting drug use.

Eight participating clients (2.7%) learned that one of their partners was HIV positive, and 4 persons (1.3%) had a present relationship with an HIV positive partner. Two participating clients did not answer this question. None of the participating clients were taking pre-exposure prophylaxis (PrEP). 56% of the participating clients (168 persons) had already been tested for HIV. The question **"What was the result of your last test?"** was answered as follows: 167 participating clients reported a negative result and one participating client reported a positive result. More than half of those tested (56.7%) reported having been tested for HIV by a routine laboratory test at least once (170 persons) and 120 persons (40.0%) reported having been tested repeatedly.

The question **"Have you had a hepatitis B or C infection?"** was answered as follows: 1.0% (3 persons) reported having had hepatitis B, 46.3% (139 persons) responded negatively and 52.7% (158 persons) reported having been vaccinated against hepatitis B. Regarding the question about other sexually transmitted diseases, 4.7% of the participating clients reported having had syphilis (14 persons, of whom 3 repeatedly), 8.0% of the participating clients having had gonorrhoea (24 persons, of whom 4 repeatedly) and 13.3% of the participating clients having had some other venereal disease or infection (40 persons).

A total of 21 participating clients (7.0%) reported donating blood, blood plasma or some other blood component, with 9 people during the last year.

## Evaluation of the Self-testing Process

### Evaluation by Participating Clients

12.4% (37 persons) of the participating clients reported previous experience with self-testing, 8 of them (2.7%) repeatedly.

**Regarding tests evaluated in the study,** 80.3% of **the participating clients reported they had understood the instructions for use** completely (241 persons), 17.7% partially experienced some difficulties (53 persons), and 2.0% of the participating clients answered they would not have been able to take the test without help (6 persons: 3 for the EXACTO test, 2 for the OraQuick test and 1 for the Autotest). If we evaluate the individual tests, full understanding was reported by 96.7% for the INSTI tests, 90.0% for the OraQuick test, 78.3% for the BioSURE and 75.0% for

the Autotest. In terms of the EXACTO test, only 61.7% of the participating clients had understood the instructions for use, 33.3% admitted difficulties and 5.0% of the participating clients reported that they would not have been able to perform the test without help.

In response to the question: **"Did you experience any difficulty while performing the test?"**, 25.0%, i. e. one quarter of the participating clients (75 persons) answered positively. Difficulties were reported by 45.0% of the EXACTO test users, by 25.0% of the BioSURE test users, by 25.0% of the Autotest test users, by 21.7% of the INSTI test users and by only 8.3% of the OraQuick test users. The incidence of difficulties was very similar for the clients who had no previous experience with HIV self-testing (25.9%) and those who had used the test once in the past (24.1%). Of the 8 participating clients who had repeated experience with self-testing, none of them reported difficulties. For the EXACTO and INSTI tests, the highest proportion of clients experiencing difficulties with performing the test (39.7% and 20.7% respectively) was found among those who reported full understanding of instructions for use.

More detailed questions focused on three types of difficulties: 11.7% of the clients experienced difficulties with **the test procedure** (35 persons), 14.7% of the clients experienced difficulties with the **finger prick** (44 persons) and 4.3% of the clients said they had faced difficulties with **understanding the test result** (13 persons). The participating clients were allowed to report more than one difficulty, twelve of them reported different combinations of two difficulties, and 3 persons reported a combination of all three difficulties. Table 1 shows that the prevalence of the reported difficulties varied between individual tests, being lowest for the OraQuick test and highest for the EXACTO. The participating clients experienced the most difficulties with test procedures, primarily with EXACTO and BioSURE tests, while a few of them experienced difficulties with the INSTI and OraQuick tests. The difficulties with the finger prick were mainly reported by the participating clients using EXACTO and INSTI, but not for OraQuick (saliva test). The difficulties with understanding the test result were most common for Autotest (12.0% or 5 people). A relationship between successful test performance and demographic characteristics, such as age and gender, was not identified.

In response to the question: **"Would you know how to proceed in the case of a reactive result?"**, 19.7% of the participating clients (59 persons) answered negatively. This means that **one fifth of the participating clients did not know how to proceed in the case of a reactive self-test result.**

Three quarters (75.7%) of the tested clients considered the HIV self-test to be beneficial and would recommend it to others, while 23.0% of the tested clients considered it beneficial but preferred the venous blood test. Two persons would not recommend it to others (both using Autotest in the study), and two persons did not answer this question.

## Evaluation by Counsellors

The sampling staff independently evaluated the client's performance of the test. They stated that 77.8% of the clients had no difficulties and performed the test independently (233 persons) and 19.3% of the participating clients performed the test with difficulties (58 persons). According to the counsellors, 3 persons failed to perform the test (1.0%). Evaluation of the test by counsellors was not performed for 6 participating clients (2.0%).

Difficulties with understanding **the instructions for use** were reported by the counsellors for 11.0% of the tested clients (33 persons). Difficulties **with the finger prick** were reported by the counsellors for 8.7% of the tested participating clients (26 persons). According to the counsellors, one person performed the test but was **unable to understand it**. Two participating clients experienced simultaneous difficulties with understanding instructions for use and with the finger prick.

The counsellors reported the following reasons for failure:

1. The lancet was activated before pricking (1× EXACTO).
2. Incorrect drip (1× INSTI).
3. Incorrect diluent squeeze (1× BioSURE).
4. Only one dot at the bottom (1× INSTI).
5. One test was defective, a new one was provided and it was OK (1× BioSURE).

Table 2 shows that the incidence of difficulties varied depending on the test used. The counsellors identified difficulties in performing the test or failure to perform the test for 58.3% of the EXACTO test users, followed by 25.0% of the Autotest users, 13.3% of the BioSURE test users, 10.0% of the INSTI test users and 5.0% of the OraQuick test users.

## Table 1 Evaluation of individual tests by participating clients

| Test | Difficulties while performing the test | Difficulties with the test | Difficulties with the finger prick | Difficulties with understanding the test result | Full or partial difficulties with understanding instructions for use | Lack of knowledge of the procedure in case of a reactive result |
|---|---|---|---|---|---|---|
| EXACTO | 27 | 14 | 17 | 5 | 23 | 7 |
| BioSURE | 15 | 10 | 7 | 2 | 13 | 11 |
| INSTI | 13 | 0 | 13 | 2 | 2 | 9 |
| OraQuick | 5 | 4 | 0 | 3 | 6 | 13 |
| Autotest | 15 | 7 | 7 | 1 | 15 | 19 |
| Total | 75 | 35 | 44 | 13 | 59 | 59 |

## Table 2 Evaluation of individual tests by counsellors

| Test | Test not performed | Test performed with difficulties | Difficulties with the finger prick | Difficulties with understanding the test result | Difficulties with understanding instructions for use |
|---|---|---|---|---|---|
| EXACTO | 1 | 34 | 16 | 0 | 20 |
| BioSURE | 1 | 7 | 2 | 0 | 5 |
| INSTI | 1 | 5 | 5 | 0 | 0 |
| OraQuick | 0 | 3 | 0 | 1 | 2 |
| Autotest | 0 | 9 | 3 | 0 | 6 |
| Total | 3 | 58 | 26 | 1 | 33 |

As the above results show, there were quite significant differences in the evaluation of test performance between the participating clients and counsellors. The difference in test evaluation by the clients and counsellors is demonstrated in Table 3, where three cases of failure to perform the test were classified as a full misunderstanding of the instructions for use, based on the counsellors' evaluation. In one of these three cases, the participating client believed that he/she had performed the test (INSTI) correctly, but the counsellor reported an incorrect drip. When we, for instance, directly compare evaluation by the counsellors vs. participating clients, we see that difficulties with understanding instructions for use were reported by the participating clients and counsellors in 24 cases, but in another 35 cases only by the participating clients and in another 9 cases only by the counsellors. Similarly, a difficulty was identified regarding the

finger prick: in 18 cases by both the participating clients and counsellors, in another 26 cases only by the participating clients, while in another 8 cases only by the counsellors.

The counsellors were also asked to evaluate the readability of the test result. Six times they evaluated it as "no result showed" and once "the result was weak and ambiguous". All these 7 cases relate to the INSTI test. The results were evaluated in 14 cases (5× EXACTO, 6× INSTI, 2× OraQuick, 1× Autotest) as "weakly readable but still unambiguous".

**Table 3 Differences in evaluation of the tests by participating clients and counsellors**

| Evaluated by | Difficulties with understanding instructions for use | | Difficulties while performing the test | | |
|---|---|---|---|---|---|
| | Partial | Complete | Difficulties with the procedure | Difficulties with the finger prick | Difficulties with understanding the test result |
| Client | 17.7% | 2.0% | 11.7% | 14.7% | 4.3% |
| Counsellor | 11.0% | 1.0% | 20.3% | 8.7% | 0.3% |

## 3.2 Comparison of Test Results Based on Pre-defined Panels of Patient Sera

A parallel examination and comparison of the results of the five self-tests for detection of antibodies to Human Immunodeficiency Virus type 1 (HIV-1) and type 2 (HIV-2) was performed in the National Reference Laboratory for HIV/AIDS (NRL), National Institute of Public Health. The basic specifications of the individual tests according to the Package Insert Leaflet are presented in Table 4.

All the tests used are based on the principle of immunochromatographic detection of antibodies against HIV-1 and HIV-2 antigens on nitrocellulose membranes. The used synthetic antigens come from the area of surface glycoprotein gp41, possibly also gp120 for HIV-1 and gp36 for HIV-2. The evaluation of the test is based on the presence or absence of coloured detection lines. The reading includes the detection of a specific test line for the presence of HIV-1/HIV-2 antibodies as well as a control line, which is used to verify the functionality of tests and to check the correctness of their performance.

A total of 20 plasma or serum samples were selected for the first testing panel, 16 of which were from HIV-1 positive patients after complete seroconversion, i.e., with a fully expressed antibody response. Eleven samples were also positive for p24 antigen. Four tested samples of plasma were HIV-1/HIV-2 negative. All samples, both positive and negative, were correctly identified by self-testing, although in some cases, the intensity of the test line was weaker. See Table 5 for results.

For the second testing panel, 14 samples of HIV-1 positive patients at a very early stage of infection were selected. For inclusion in this panel, the reactivity of the sample to antigens gp41 and gp120 in the Geenius HIV1/2 Confirmatory Assay (BIO-RAD) immunographic test, which always allows for the distinction of reactivity to a total of four HIV-1 antigens (p24, p31, gp41 and gp160) and two HIV-2 antigens (gp36 and gp140), was decisive. The result of the Geenius HIV1/2 reference test was HIV-1 positive in the first 9 patients (A–I). Reactivity in these samples was detected by all the self-tests, except for sample A, which reacted only in the EXACTO and INSTI tests. In patients J and K with unclear reference test results (i.e., they showed reactivity only to the gp41 antigen), sample J was determined to be HIV-1 reactive only by the EXACTO and INSTI tests; sample K was also reactive with the OraQuick test, in addition to the two above mentioned tests. Patients L–N had not yet developed antibodies; their HIV-1 positivity was confirmed by detection of the p24 antigen (L and M) or detection of HIV-1 RNA (sample N) – all the tests were negative, as expected. The results of testing in this panel are shown in Table 6.

Following the testing of the 300 clients participating in the study using self-testing, the National Reference Laboratory for HIV/AIDS (NRL) tested their sera from parallel venous blood samples with a 4$^{th}$ generation EIA test (HIV Ag/Ab Combo, Architect Abbott). The testing identified two reactive results in the previous self-test: one was also reactive in the EIA test and was subsequently confirmed as HIV-1 positive by confirmatory testing at the National Reference Laboratory for HIV/AIDS (NRL). In the second reactive sample, further testing identified a non-specific reactivity related to the Autotest VIH®.

For this reason, testing of the sample was extended to include four additional self-tests. Non-specific reactivity in this sample was also identified in the BioSURE HIV Self Test, which could be expected given the fact that this is an identical product, only with different distributors and trade names. The sample was negative in the other self-tests. The specificity of the Autotest VIH® and BioSURE HIV Self Test, stated in the

Package Insert Leaflet, is 99.8% and 99.9% respectively, which is not different from the other self-test manufacturers. The size of our sample was not large enough to confirm the claimed specificity of the tests.

### Table 4 Basic specification for the tested HIV antibody-based self-tests

| Name of the test | Manufacturer/ distributor, country of origin | Synthetic antigen | Material | Volume [µl] | Reading time [min] | Sensitivity [%] | Specificity [%] |
|---|---|---|---|---|---|---|---|
| Autotest VIH® * | AAZ Labs, France | gp41, gp36, gp120 | full blood | 2.5 | 15-20 | 100 | 99.8 |
| BioSURE HIV Self Test * | BioSURE, UK | gp41, gp36, gp120 | full blood | 2.5 | 15-60 | 99.7 | 99.9 |
| EXACTO® PRO Test HIV | Biosynex, France | gp41, gp36 | full blood, serum, plasma | 5.0 | 10-20 | 100 | 99.9 |
| INSTI® HIV Self Test | BioLytical Lab. Inc, Canada | gp41, gp36 | full blood | 50.0 | 0-60 | 100 | 99.8 |
| HIV-1/2 OraQuick ADVANCE® | OraSure Technologies, U.S.A. | not specified in details | full blood, plasma, saliva | 5.0 | 20-40 | 100 | 99.8 |

** The Autotest VIH® and BioSURE HIV Self Test products are identical and are manufactured by Chembio Diagnostics System, Inc., U.S.A., where they are distributed under the brand name SURE CHECK® HIV1/2 (see document UNITAID WHO – HIV rapid diagnostic tests for self-testing, 4th edition, 07/2018).*

## Table 5 Results of the first panel of tested samples

| Labelling of the sample | Confirmation result | Antigen p24 [pg/ml] | Autotest | BioSURE | EXACTO | INSTI | OraQuick |
|---|---|---|---|---|---|---|---|
| 1 | positive | 214.4 | + | + | + | + | + |
| 2 | positive | 39.0 | + | + | + | + | + |
| 3 | positive | 34.7 | + | + | + | + | + |
| 4 | positive | 27.4 | + | + | + | + | + |
| 5 | positive | 25.5 | +(s) | +(s) | + | + | + |
| 6 | positive | 21.3 | + | + | + | + | + |
| 7 | positive | 17.6 | + | + | + | + | + |
| 8 | positive | 14.5 | + | + | + | + | + |
| 9 | positive | 10.0 | + | + | + | + | + |
| 10 | positive | 5.7 | + | + | +(s) | + | + |
| 11 | positive | 5.1 | + | + | + | + | + |
| 12 | positive | negative | + | + | + | + | + |
| 13 | positive | negative | +(s) | +(s) | + | + | + |
| 14 | positive | negative | + | + | +(s) | + | + |
| 15 | positive | negative | + | + | + | + | + |
| 16 | positive | negative | + | + | + | + | + |
| 17 | negative | negative | - | - | - | - | - |
| 18 | negative | negative | - | - | - | - | - |
| 19 | negative | negative | - | - | - | - | - |
| 20 | negative | negative | - | - | - | - | - |

*Self-test result: + reactive, +(s) weakly reactive, -negative*

## Table 6 Results of the second panel of tested samples

| Labelling of the sample | Geenius HIV1/2 | | | Antigen p24 [pg/ml] | Autotest | BioSURE | EXACTO | INSTI | OraQuick |
|---|---|---|---|---|---|---|---|---|---|
| | Antibodies against antigen | | Evaluation | | | | | | |
| | gp41 | gp160 | | | | | | | |
| A | 1+ | 0 | positive | 128.7 | - | - | +(s) | + | - |
| B | 3+ | 1+ | positive | 24.5 | +(s) | +(s) | + | + | + |
| C | 3+ | 1+ | positive | 12.4 | + | + | +(s) | + | +(s) |
| D | 1+ | 1+ | positive | 6.3 | + | + | + | + | + |
| E | 1+ | 1+ | positive | 6.0 | + | + | + | + | + |
| F | 1+ | 1+ | positive | negative | +(s) | +(s) | + | + | +(s) |
| G | 1+ | 1+ | positive | negative | + | + | + | + | +(s) |
| H | 1+ | 1+ | positive | negative | + | + | + | + | + |
| I | 1+ | 1+ | positive | negative | + | + | + | + | + |
| J | 1+ | 0 | unclear | 242.0 | - | - | + | + | - |
| K | 1+ | 0 | unclear | 6.74 | - | - | + | +(s) | +(s) |
| L | 0 | 0 | negative | >400 | - | - | - | - | - |
| M | 0 | 0 | negative | 51.7 | - | - | - | - | - |
| N | 0 | 0 | negative | negative | - | - | - | - | - |

*Self-test result: + reactive, +(s) weakly reactive, -negative*

# 4. Conclusions of the Study

The evaluation by the clients participating in the study and the sampling staff – counsellors demonstrated that HIV self-tests are generally usable, however with some reservations. A quarter of the 300 participating clients reported that they had faced difficulties with performing the test and the counsellors identified difficulties in understanding the instructions for use in more than 10.0% of the participating clients. The availability of simple and clear instructions for use in the national language appears to be crucial.

The process of the finger prick and the use of the appropriate tool for this purpose also represented a source of difficulties. A very clear description of necessary manipulation is needed; an instructional video might help. It has been experimentally found that for some types of tests, without knowing the instructions for use, it is relatively easy to squeeze the stylus without pricking the finger. On rare occasions (in a few cases), the participating clients failed to perform the testing procedure successfully, and sometimes they were even not aware of the incorrect procedure.

A relatively large proportion of the participating clients (one fifth) did not know how to proceed in the case of a reactive self-test result, which indicates a potential problem. There were noticeable differences in the intensity of difficulties in different phases of the whole self-testing process. Overall, the greatest incidence of difficulties, both from the participating clients' and counsellors' perspective, was noted for the EXACTO test. In contrast, the OraQuick test showed the lowest incidence of difficulties. This method of testing does not seem to suit everyone; three-quarters of the participating clients would recommend the HIV self-test to others. The participating clients' and counsellors' evaluation for BioSURE and Autotest tests, which are identical (the same manufacturer with different distributors), was very similar, although the instructions for use were different. This is a positive message in terms of the value of the study.

The results of the laboratory part of the study within the first test panel demonstrated that serum samples from patients after complete seroconversion were reliably determined to be reactive by all the self-tests used.

Different results were seen in the second test panel, which contained serum samples from patients in the early stages of HIV-1 infection. Higher sensitivity was observed in tests based solely on detection of antibodies against gp41 (EXACTO® PRO Test HIV, INSTI® HIV Self Test) compared to a panel of tests using combined detection of antibodies against gp41 and gp120 (Autotest VIH®, BioSURE HIV Self Test).

Self-tests represent an alternative option to currently available laboratory screening for HIV infection; however, they remain an indicative test procedure with qualitative evaluation of the result by a lay person or a non-health professional and, therefore, all reactive results have to be confirmed. Self-tests are based on antibody detection only, leading to a risk of potentially false negative results if the risk behaviour occurred in a period shorter than last 3 months.

Manufacturers restrict the use of these self-tests to clients not taking antiretroviral agents as part of pre-exposure (PrEP) or post-exposure (PEP) prophylaxis.



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