

## Effectiveness Cost of HIV rapid tests in Italy and Europe

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### Abstract:

*In the United States, about a quarter of the estimated 1.1 million people living with human immunodeficiency virus (HIV) are not aware of their HIV status. HIV tests in communities with outreach settings can be an effective strategy to identify people with unidentified HIV infection. The spread of innovative rapid tests represents an additional opportunity in the field of HIV prevention. HIV rapid tests represent an excellent diagnostic tool to reach the rural or poor population where accessibility to test is limited or populations with high-risk infection. Cost-effectiveness point of view, this service always has the potential for early diagnosis by affecting lower hospital spending, preventing clinically aggravated cases with decreased CD4 and acquired immunodeficiency. The study analyses the characteristics of rapid tests by evaluating what can be used in Europe and Italy from case studies. The sensitivity, specificity and project needs are the main factors of choice in testing projects*

**Keywords:** Rapid Test, HIV, AIDS, Community based Service

### Introduction

More than 1.1 million people in the United States are infected by HIV, and the CDC estimates that one out of six does not know it (Kidder et al. 2008; Coates et al. 2008). These uninformed people cause 54-70% of the 56,300 new infections each year (CDC, 2005). 75% of HIV + people will change risky behaviors when they learn their status (Kalichman et al., 2005). It is estimated that in Italy, like other European countries, there is a significant proportion of people with HIV infection (about a third) who are unaware of being HIV-positive. Moreover, it has been shown that approximately 30% of HIV infection diagnoses are made in people who already reached an advanced stage of disease (CD4 <200 / MMC lymphocytes and / or pathologies indicative of AIDS) and nearly 60% of AIDS diagnoses is made in people with late recognition of HIV infection. This phenomenon leads to several negative consequences. First, the person with late-diagnosed HIV does not have the opportunity to start the antiretroviral therapy in best times and, on the one hand, has a higher risk of reaching full-blown disease and, on the other hand, a reduced probability of a full immunological recovery once pharmacological treatment has started. The lack of awareness of the infection condition may favour the further spread of the contagion. It has indeed been shown that people with HIV infection reduce, in part or completely, the behaviours at risk of transmitting the infection once informed of their status. In addition, there is evidence of the effectiveness of prevention interventions on the contagion spread addressed to people with known HIV infection. The antiretroviral therapy, reducing the viral load, can also help limit the spread of contagion. Indeed, a person aware of his / her serological status being ineffective therapy has a very limited risk of transmitting the infection to others. Finally, pregnant women aware of having HIV infection can access maternal-fetal prophylaxis programmes that drastically reduce transmission of the virus to the unborn child. In view of the high number of seropositive people still unaware of their serological status, it is considered strategic, priority and urgent to recognize the importance and to activate early detection actions that allow early contact and diagnosis of these people. Studies have shown that HIV counseling offer and tests on HIV in communities with outreach settings can be an effective strategy to identify people with unidentified HIV infection (CDC 2007). Effective HIV test mechanisms are already in use in the world, including some countries in Africa (Steen et al., 2007). The spread of innovative rapid tests, giving results in less than 30 minutes and over 99% in both sensitivity and specificity, represents a further opportunity in the field of HIV prevention (Branson et al., 2007; Doyle, 2005).

MSMs, drug addicts, and sex workers are the most vulnerable ethnicities, and all the studies conducted in the most industrialized countries focused their research on them, with the difference that in the USA studies were also aimed at African- Americans and Hispanics, given their wide presence in that country and their high percentages of infections (Biancone et al., 2018). The evidence of the literature regarding the benefits of using a rapid test, even in terms of cost-effectiveness, is growing (Bert et al. 2018). Some articles highlight the organizational characteristics, the cost and the effectiveness of some projects carried out towards high-risk populations in Italy (Tradori et al., 2017).

The data of the "Research project for the identification and the experimentation of intervention models apt to improve membership in HIV screening test" (funded by the Ministry of Health, coordinated by the National Institute of Health and realized with the contribution of the Associations that are part of the AIDS Fighting Consultation) highlight a situation of extreme heterogeneity of the HIV test offer today in Italy.

### **Medical devices and in vitro diagnosis in Italy and Europe**

The placing on the market and putting into service in the Italian and European territory of medical devices bearing the CE marking is permitted. This marking demonstrates compliance, respectively, with Legislative Decree 46/97 (implementation of Directive 93/42 / EEC). With the EC declaration of conformity, the manufacturer guarantees and declares that the products in question satisfy various provisions. The manufacturer prepares the required technical documentation. The manufacturer or the representative shall keep said documentation, including the declaration of conformity, a provision of national authorities for control purposes for at least five years from the date of manufacture of the last product. The documentation includes, in particular, a general description of the product, including the expected variations and the uses for which it is intended, the design schemes and manufacturing methods, the diagrams of the parts, the parts, the circuits, etc., the description and the explanations. necessary for understanding the schemes the results of the risk analysis and a list of the rules laid down, applied in full or in part, and a description of the solutions adopted to meet the essential requirements of this decree where the rules laid down have not been fully applied. in the case of products placed on the market in a sterile package, the description of the methods used and the validation report, the results of the design calculations, the checks carried out, etc. If a device is to be connected to one or more other devices for operate according to the intended purpose, the conformity of the first device with the essential requirements must be demonstrated in connection with at least one of the devices to which it is to be connected, which possesses the characteristics indicated by the manufacturer, the solutions adopted, the preclinical evaluation, the clinical evaluation and labeling and instructions for use. The clinical evaluation and related documentation are actively updated with data from post-sales surveillance. Where you do not consider Post-sale clinical follow-up within the surveillance plan is necessary after-sales applied to the device, this conclusion must be duly justified and documented. Not all the devices highlighted in the analysis meet the legal requirements and can be considered for use in Italy and in Europe.

### **Methodology**

The study group conducted a systematic review of the literature by identifying publications through TUTTO bibliographic database. This includes: Scopus (Elsevier), MEDLINE / PudMed, Science Citation Index (Web of Science), ProQuest Psychology Journals, ScienceDirect Journals (Elsevier), ProQuest Sociology, Sociological Abstracts, PMC PubMed Central), SpringerLink, Social Services Abstracts, Taylor & Francis Online - Journals, Informa - Taylor & Francis (CrossRef), Directory of Open Access Journals (DOAJ), JSTOR Archival Journals, Wiley Online Library, (BMJ Publishing Group), Wolters Kluwer - Ovid - Lippincott Williams & Wilkins (CrossRef), Lippincott Williams & Wilkins Journals (Wolters Kluwer Health). The words "community-based HIV test" were used both individually and in common for research, and only articles in English and Italian were selected, although the database identified only articles in English. The bibliography included revised periodicals, including articles and conferences. The research considered all the identifiable sources of the period between 2008 and 2017. The criteria identified in the research of literature were checked on the title and on the abstract. The initial results were 53,321, from a first analysis 31 articles with administration projects of the community-based test were selected. Subsequently, all magazines that did not have a result of the effectiveness of the HIV rapid testing project were excluded, highlighting those with the presence and the identification of the HIV TEST used, reducing the analysis to 12 articles. The characteristics relating to the product were conducted through market research and the request for estimates associated with the qualitative analysis of the observable characteristics conducted in the year 2017. The aim is to identify the effective cost of the various HIV rapid tests based starting from the best practices identified in the literature and the possibility to check the typologies and characteristics to be evaluated for prevention and diagnosis activities in Italy and Europe.

### **Discussion**

#### **Analysis of literature and projects of HIV early diagnosis**

For the purposes of the analysis, the following articles have been taken into consideration, of which a brief description is given for the sake of clarity.

1) *Implementation of Rapid Testing Programs in Community and Outreach Settings: Perspectives from Staff at Eight Community-Based Organizations in Seven U.S. Cities* (published in 2008 and realized between 2004 and 2006 in the cities of Boston, Chicago, Detroit, Kansas City [Missouri], Los Angeles, San Francisco, Washington).

Research based on the effectiveness of HIV rapid tests methods on the basis of MTU run by eight CBO. This research was conducted by surveying CBO staff. Among the positive aspects, there is the effectiveness of promotional activity and the ability to reach individuals at high risk of contracting the disease. Among the negative aspects, there are the high costs involved in staff training but above all the purchase and maintenance costs associated with MTU, which are also accompanied by logistical difficulties. Another challenging difficulty lies in the fact that many people, once having done the test within an MTU, are unapproachable if HIV-positive because contact information is often false (Clark, 2008).

2) *Cost-Effectiveness of Finding New HIV Diagnoses Using Rapid HIV Testing in Community-Based Organizations* (published in 2008 and realized between April 2004 and March 2006 in the cities of Kansas City [Missouri], Detroit).

Cost-effectiveness ratio in evaluating HIV tests in CBO. It turned out that in Kansas, where the clinic was also present, the HIV tests “conducted on the streets” brought higher costs. These costs have been found by dividing the total cost of the programme for the number of people who have been notified of new HIV diagnoses. Indeed, it has been found out that people who knew they had had sex at risk and therefore they contracted the disease, prefer to go to the clinic rather than to use mobile testing units (MTU) so that the percentage of people at risk is only 0.7% versus 2.2% of the clinic. In Detroit, however, where there are no clinics, costs are cheaper as MTU is a unique opportunity to conduct the test. Therefore, in Kansas, it is not advisable to continue investing in mobile units to conduct HIV rapid tests, while in Detroit it is and it is expected that, while continuing to invest, the results (costs-benefits) will only improve (Shrestha, 2008).

3) *Rapid HIV Testing in Transgender Communities by Community-Based Organizations in Three Cities* (published in 2008 and realized from January 2005 to December 2006 in the cities of Miami Beach (Florida), San Francisco, New York City).

Study of the demographic and behavioural characteristics of transgender people (TG) recruited through outreach strategies. It has emerged that among these people, the risk of contracting HIV is higher because of their behaviour and lifestyles (especially at-risk sex and injection of hormones and silicone). Therefore, efforts should be increased to develop new awareness and prevention strategies for these people, for example by encouraging them to do the test at least every year (Schulden, 2008).

4) *Number and timing of antenatal HIV testing: Evidence from a community-based study in Northern Vietnam* (published in 2011 and realized in Quang Ninh, a province north of Vietnam, between April and September 2007 among women who had given birth within 6 months from January, 1 to June 30, 2007). The study aims to document the absorption of HIV test among pregnant women in order to analyze the timing and repetitions of the test. The results of this study will contribute to the formation of the national guidelines for the PMTCT programme. 90.3% (1000 out of 1108) of the interviewed women were tested during pregnancy, 38.2% of them once and 52.1% twice or more times (usually women living in a semi-urban area). However, 80% did the second test after 36 weeks of gestation (it is advisable before. Otherwise the effect of the PMTCT service offered is reduced). Among those tested, 94.7% had received schooling and had at least one level of secondary education, while in terms of employment, the most of them were housewives or unemployed. Among those not tested, it was found out that for the majority it was the second child's pregnancy, that they were farmers or had a seasonal job, lived in a remote rural area, had low income, had poor schooling and education. It can be said that the risk of contracting the virus during pregnancy, in Vietnam, is low (also due to the fact that Vietnamese women have stable sex life); this is why the use of repeating the HIV test has been questioned because of the costs for both the health system and the people, considering that most of the population lives in poverty; so that for women who were negative at the first test, proper counselling is provided during the rest of the pregnancy, without the need to repeat the test (Hanh, 2011).

5) *High acceptance of home-based HIV counseling and testing in an urban community setting in Uganda* (published in 2011 and realized between January and June 2009 on the population of Rubaga, part of the city of Kampala, Uganda). This study analyzed the level of acceptance of Home-Based HIV Counselling and

Testing (HBHCT) (i.e., HIV rapid test door to door), in a country, like Uganda, where coverage and access to tests remain low. HBHCT has proven to have a 69% acceptance level and therefore to increase HIV test absorption and to improve access. Indeed, 39% of participants had never been tested. In this study, it was found out that men were more likely to accept the test than women, but this probably may be due to the fact that the latter, especially in reproductive age, are more in touch with the healthcare system and have therefore more access, just think of the PMTCT programme, for example. These HBHCT strategies have great advantages of improving early identification of HIV-positive individuals, also increasing awareness of care treatment and limiting their sexual at-risk behaviour; but the success of such strategies could be hampered by the lack of qualified healthcare professionals and by high operating costs in view of limited resources (Sekandi, 2011).

6) *Risk factors for HIV and STI diagnosis in a community-based HIV/STI testing and counseling site for men having sex with men (MSM) in a large German city in 2011-2012* (published in 2015 and realized between 2011 and 2012). This article explains the risk factors of contracting HIV and other STI among MSM in Hamburg, leaning on Heine & Fiete, a local community part of CB-VCT. Here, HIV, HBV, HCV, syphilis, gonorrhoea and Chlamydia tests were conducted and offered in free and anonymous form; the choice on which tests to conduct on participants was based on pre-test counseling. Out of 1476 men tested, 1413 were tested for HIV, followed by syphilis (1380). 295 men were tested at least twice by Hein & Fiete in the last two years, 69% had a high school diploma or higher education degree, 87% were gay, 53% were single, and MSM had on average from 6 to 11 different sex partners over the past 12 months, unprotected anal sex (UAI) was reported by 61% of clients as the main reason for evidence. General data show how this CB-VCT site in Hamburg has reached MSM at high risk of contracting HIV and bacterial STI, and although a cost-effectiveness analysis has not been conducted, considering the high affluence and low overall costs, this test is used to reduce percentages of HIV and STI infections that are not diagnosed in a profitable way compared to traditional treatment settings. So far, there have not been cost problems since they were covered by public funds, but in the future, when the nucleic acid amplification test for Gonorrhoea and Chlamydia will be included, these costs will increase, and an option to contain them and minimize them could be the use of combined tests. However, this approach is only feasible in large cities where the respective gay communities are also significant; alternative approaches will also be needed to reach MSM living in rural areas, MSM that is less connected to gay communities and MSM who are less willing to self-identify as homosexuals (Marcus, 2015).

7) *The prevalence and correlates of receiving confirmatory HIV test results among newly diagnosed HIV-positive individuals at a community-based testing center* (published in 2012 and realized between March 2008 and February 2011 in New York City). This research studies the correlations between people who conduct HIV test and those who even make confirmation tests if they are positive. A study has shown that if every person over 15 years had a voluntary annual test in combination with immediate anti-retroviral therapy after diagnosis, the incidence and mortality of HIV would be reduced to less than 1 case per 1000 people from 2016 and the HIV prevalence would be reduced to less than 1% within 50 years. This research was done using both conventional test (ELISA) and rapid test. The HIV seropositive people opting for traditional HIV ELISA test are significantly more than those who opt for rapid test, as people who know they have contracted an infection prefer to go to the appropriate locations and practice ELISA. It emerged that 65% of people who were positive in the tests (both rapid and ELISA) then validated this result with a confirmation test, lower rate compared to those reported in other studies, ranging from 75 to 89%. It also emerged that the greatest probability to receive the confirmation test came from uninsured, homeless people and non-US citizens since these people will be able to access the assistance of organizations offering AIDS service and benefit from public advantages, like becoming beneficiaries of the New York State AIDS Drug Assistance Program. Here also the results are not consistent with other studies, indeed a piece of research on a sample of teenage girls at a clinic in Cleveland, Ohio, stated that those with private insurance were most likely to return for the confirmation test, while the homeless were those with a lesser likelihood. The explanations for these differences are: 1. the different composition and methodology of the sample; 2. the fact that the latter study was conducted between 1992 and 1995, i.e. before the introduction of antiretroviral drugs, so there were fewer "incentives" for the poorest people to return for the confirmation test. In addition, individuals tested off-site within a mobile unit are less likely to return for confirmatory tests, this time the result is consistent with previous studies. The main reason behind the latter one is that it depends on the

motivations: indeed, who goes to a GMHC center is mentally ready to conduct the test and to accept all possible consequences, but who goes to mobile units may have done so deciding on the moment and therefore is not ready for the possibility of a positive diagnosis. A possible solution to this problem may be to give those who conduct the test off-site the possibility to receive the results of the confirmatory tests in the same area where the test is being conducted. Finally, there are some promising developments that can help reduce the gap between test and treatment; indeed processes that give a positive HIV diagnosis, that do not require confirmation tests are being studied, but the link to treatment could start immediately instead of 1 week later (Feldman, 2012).

8) *Evaluation of Pharmacy-Based HIV Testing in a High-Risk New York City Community* (published in 2015 and realized between June 2010 and August 2011 in the neighbourhoods of East Harlem and Central Harlem in New York City). This study evaluated the delivery of HIV test based on pharmacy clients in neighbourhoods with high HIV infection rates. Research has shown that this strategy is feasible because it reaches at-risk populations by providing health counselling and vaccination services to all customers, consistently with US objectives. The cost-effectiveness link that these innovative strategies give, deserves greater attention because it facilitates access to treatments which would extend life, preserve health, prevent HIV transmission, and help reduce racial / ethnic disparities in health. The next step should be to include in research those factors that help overcome all those individual and structural barriers, such as information programmes directed to all pharmacy clients on HIV tests. The statistical results were: 332 participants, of which 99 were HIV positive and were excluded from this analysis, so the analytical sample is based on 233 clients of ESAP pharmacies. Most of the participants were males, born in the United States, unmarried, with an education going from high school up, about 20% were homeless. Among the at-risk behaviours: in the 30 days before the test, 55.3% reported that they did not use the condom and 10.3% had sex with people of the same sex; 88.4% dealt in their life with drug with 55.8% with non-injecting drugs. Most reported having been tested at least once in their life (most during the previous year) and having health insurance. It was also found out that great part of the people who went to the pharmacy, were sexually active and with multiple partners, that they had not recently been tested (<12 months) and had been taking drugs for the last 3 months; i.e. all those categories that can be catalogued as at higher risk of infection (Amesty, 2015).

9) *Early Identification of HIV: Empirical Support for Jail-Based Screening* (published in 2012 and realized between September 2008 and March 2011 in the cities of: Atlanta-GA, Chester-PA, Chicago-IL, Cleveland-OH, Columbia-SC, New Haven-CT, New York-NY, Philadelphia-PA, Providence-RI, Springfield-Massachusetts).

This article deals with the largest HIV prevention programme carried out in jails. Jails can be effective sites for diagnoses of new infections and to begin implementing routine care, as most of these people use drugs and abuse alcohol, behaviours that contribute to the transmission of the virus. One of the objectives of this study was to evaluate the connection with the HIV support community among those who then went out of jail. The results were: 210267 are the prisoners (not just the inmates) who were tested, and 1312 (0.62%) results were positive, 822 of the diagnoses were new (although this last screening is not uniform from site to site, indeed in some, the probability of new diagnoses was significantly higher). Among prisoners, 43% (329) were diagnosed within a correctional structure, of whom 62% (36) were male, 67% (39) black and 12% (7) Hispanic. Clients who accepted the test had an average jail stay of 75 days. Of the new diagnosed, as regards at-risk behaviours, 11% said they were using drugs in their lives, 19% had homosexual or bisexual orientation, 25% had sexual intercourse with other men in last 30 days. The results of this project suggest that HIV test conducted in jails is feasible and can lead to new infection diagnoses and these are essentially diagnosed at the initial stage of the disease. Unfortunately, the jails that adhere to such programmes are in the minority. Another advantage lies in the fact that projections within jails lead to a disease detection that would have been impossible to diagnose in other settings (De Voux, 2012).

10) *Biomarker-Based HIV Incidence in a Community Sample of Men Who Have Sex with Men in Paris, France* (published in 2012 and realized in 2009 in Paris).

This is the first community-based study to estimate the HIV incidence among MSM in France. Data are not positive. Indeed we have high levels of HIV transmission (3.8% of people per year) and a low rate of antiretroviral therapy absorption, as unfortunately happens for all high-income countries. The present study clearly shows that MSM frequenting gay places in Paris have a very high risk of contracting the disease (almost 18% have HIV and have high-risk behaviours). However, the acceptance rate was 58%, in line with

the percentage of gay places in the rest of Europe and Australia. The statistical results were: 1578 men invited to participate, 917 (58%) accepted and 886 (56%) completed the questionnaire and provided a blood sample. Of the 886 MSM participating, 157 (18%) were positive, of whom 31 (20%) were unaware of their infection; 94% reported having been tested earlier and of these, 63% within the previous year. In addition, antiretroviral drugs were reported in 9 out of the 12 samples (75%) positive to EIA-RI, among the men who reported being aware of their infection (Le Vu, 2012).

11) *Home-Based HIV Testing for Men Who Have Sex with Men in China: A Novel Community-Based Partnership to Complement Government Programs* (published in 2014 and realized in 2012 on MSM in Beijing). In China, the HIV test is available either through VCT clinics or through public hospitals. This article evaluated the feasibility of Home-Based HIV Self-Testing, because of the many barriers that still exist and are hard to overcome, such as the lack of time to visit clinics and the concern of discrimination from clinic staff (be it perceived or real). Results: 220 participants, 80% with homosexual orientation, 33 (15%) found positive with self-test and then linked to a local CDC (all of them were confirmed with Western blot); furthermore, 65% stated that they felt less stigmatized in conducting the test at a CBO and even more comfortable receiving certain services compared to traditional clinics; finally, only 49% had already been tested, although 87% of participants said they knew where to go to conduct the test. Self-test can offer a valid alternative to tests conducted in conventional places, having the benefit of reduced concerns about confidentiality, greater flexibility in execution, elimination of long waiting periods for screening results, as well as overcoming the barriers already cited. However, there are also concerns, such as: knowing exactly how to conduct exactly the test, difficulties in providing an adequate pre- and post-counseling service and knowing how to connect HIV-positive patients with care. HIV tests conducted with this approach can help increase coverage and consequently improve the quality of life of positive MSM. The next step is to expand this approach even in rural areas, well aware of the logistical problems in providing test kits in these places; indeed the participants in this study were internet users (the advertisement of this programme could only be found on the CCAVG website) relatively young and educated and therefore the results cannot be generalized to all MSM (Tao, 2014).

12) *Community-Based HIV-1 Early Diagnosis and Risk Behavior Analysis of Men Having Sex with Men in Hong Kong* (published in 2015 and realized between March 2010 and April 2011 between MSM of Hong Kong). In this study, it is shown how early HIV infection can be diagnosed by combining a DBS (dried blood spot) method with a rapid test, always in local community settings. This is because the rapid test is able to detect only the presence of the HIV specific antibody, while the traditional test gives more accurate results but has unaffordable costs for an NGO (Non-Governmental Organization) and therefore this setting was thought, that offered at the same time cost accessibility and higher sensitivity of the results (it can detect HIV-1 in the proviral DNA at a lower level). Results: 474 valid participants, only 24.5% claimed to have regular partners, 57.6% said they had up to 3 partners and 29.1% 4 up in the 3 months before the test; only 46.4% (220/474) regularly used condoms; 19 individuals were found HIV positive (4.01%), 13 of whom were found to be positive for both analyses, 3 only for rapid test but not for DBS (due to insufficient DNA and low proviral copies), 4 out of 19 positive claimed to have been found negative to tests conducted about 6 months earlier, suggesting they had been at risk and contracted the virus during this time period, other three individuals of the 19 were found to be positive only to DBS. Another alarming datum is the high rate of refusal (48%) and the objective for future studies is to improve this datum, given that Hong Kong is experiencing, for the second time in its history, a major HIV epidemic among MSM, with a large expansion even among heterosexuals (Liang, 2015).

This article does not consider cases where rapid testing is associated with hospital facilities (Bert et al., 2016); but only considers cases where the test is used for projects outside healthcare facilities and hospitals.

### **Test type**

Table 1 shows the test types used by every project, each of which is indicated by technical characteristics, i.e., test type, directions for use and response time, on which biological fluid it is possible to conduct them and, on this basis, sensitivity and specificity. Sensitivity is defined as the ability of the test to identify sick subjects while specificity is the ability of the test to identify healthy subjects as negative.

Almost all projects employed rapid tests with response time ranging from 10 to 20 minutes. The sensitivity of the analysed tests ranges from a minimum of 83.3 to a maximum of 99.9, considering that the sample can be analysed on blood, plasma, and oral fluid. With regard to the test specificity, there is a variation between

99.7 and 100 for groups at low risk. Most tests give the possibility to have a result by analysing whole blood or plasma, while only a few also give the possibility to conduct an analysis of the oral fluid.

**Table 1 Characteristics of employed tests**

| Reference article | Test type  | Directions for use and response time                   | Test on                         | practicable | Sensitivity  | Specificity  |
|-------------------|--|--|---------------------------------|-------------|--|--|
| 1                 | Rapid and conventional test. Rapid test: OraQuick Rapid HIV-1 Antibody Test or OraQuick Advance Rapid HIV-1/2 Antibody Test (OraSure Technologies, Bethlehem, Pennsylvania) on samples of whole blood or oral fluid  | Finds HIV 1 - 2 antibodies in response in 20 minutes   | Whole blood, oral fluid, plasma |             | Whole blood 99.6 (98.5-99.9), oral fluid 99.3 (98.4-99.7), plasma 99.6 (98.5-99.9) | Whole blood 100 (99.7-100), oral fluid 99.8 (99.6-99.9), plasma 99.9 (99.6-99.9) |
| 2                 | Rapid and conventional test. Rapid test: OraQuick Rapid HIV-1 Antibody Test or OraQuick Advance Rapid HIV-1/2 Antibody Test (OraSure Technologies, Bethlehem, Pennsylvania) on samples of whole blood or oral fluid. Those who had a positive test result were asked to conduct a confirmative test by Western Blot. | Finds HIV 1 - 2 antibodies with response in 20 minutes | Whole blood, oral fluid, plasma |             | Whole blood 99.6 (98.5-99.9), oral fluid 99.3 (98.4-99.7), plasma 99.6 (98.5-99.9) | Whole blood 100 (99.7-100), oral fluid 99.8 (99.6-99.9), plasma 99.9 (99.6-99.9) |
| 3                 | HIV rapid test: OraQuick Advance Rapid HIV-1/2 Antibody Tests (OraSure Technologies, Bethlehem, Pennsylvania) on samples of oral mucosa or sample of whole blood taken from the finger. Those who had a positive test result were asked to conduct a confirmative test by Western Blot.                              | Finds HIV 1 - 2 antibodies in response in 20 minutes   | Whole blood, oral fluid, plasma |             | Whole blood 99.6 (98.5-99.9), oral fluid 99.3 (98.4-99.7), plasma 99.6 (98.5-99.9) |  |
| 4                 | /  |  |                                 |             |  |  |

|   |  |   |   |  |   |
|---|--|---|---|--|---|
| 5 | <p>Rapid test door to door. The HIV-1/2 dosage (Abbott Laboratories, Illinois, United States of America) was used for the selection, for the confirmative test the HIV-1/2 STAT-PACK was used (ChemBio Diagnostic System Inc, New York, USA), as tie-breaker the Uni-Gold test was used (Trinity Biotech, Wicklow, Ireland). You are positive to the test if the Uni-gold gives a positive result.</p> | <p>Clearview HIV 1/2 STAT-PAK (antibodies HIV 1 - 2 results in 15 minutes), Uni-Gold Recombigen HIV-1/2 (antibodies HIV 1 - 2, resulting in 10 minutes)</p> | <p>Clearview HIV 1/2 STAT-PAK (test finger stick on capillary blood or whole venous blood), Uni-Gold Recombigen HIV-1/2 (whole blood, blood serum / plasma)</p> | <p>Clearview HIV 1/2 STAT-PAK test finger stick on capillary blood or whole venous blood 99.7 (98.9-100); Uni-Gold Recombigen HIV-1/2 whole blood, blood serum / plasma 100 (99.5-100.0)</p> | <p>Clearview HIV 1/2 STAT-PAK test finger stick on capillary blood or whole venous blood 99.9 (99.6-100.0), Uni-Gold Recombigen HIV-1/2 whole blood, blood serum / plasma 99.7 (99.0-100)</p> |
| 6 | <p>Abbott Architect HIV Ag/Ab Combo, reactive samples were confirmed by Mickrogen, recomLine HIV-1 &amp; HIV-2 IgG testing.</p>  | <p>Antibodies against HIV-1 and HIV-2 detects an HIV-1 antigen, results in 20 minutes</p>   | <p>finger stick on whole blood</p>  | <p>Finger stick on whole blood 99.9 (99.4-100)</p>   | <p>Finger stick on whole blood: subjects at low risk 100 (99.5-100), subjects at high risk 99.7 (98.9-100)</p>  |



|    |  |   |  |  |   |
|----|--|---|--|--|---|
| 7  | <p>Traditional HIV test (ELISA) and rapid test for rapid tests conducted at place the finger stick ones are used (Uni-Gold Recombigen; Trinity Biotech USA, Jamestown, NY), for tests conducted off-site or in the mobile unit HIV oral tests are used (OraQuick Rapid HIV-1 Antibody Test, OraSure Technologies, Bethlehem, PA). If these rapid tests are positive, the first ones are confirmed with enzymatic immunodosage (HIV-1/2 Antibody Plus EIA; Quest Diagnostics, San Jose, CA) or with Western blot (HIV-1 Western Blot; Unilab, Tarzana, CA), the second ones with confirmative oral tests (OraSure HIV-1 Western blot, OraSure Technologies, Bethlehem, PA).</p> | <p>Uni-Gold Recombigen HIV-1/2 (HIV 1 – 2 antibodies, resulting in 10 minutes), OraQuick ADVANCE Rapid HIV-1/2 Antibody Test (finds HIV 1 – 2 antibodies with response in 20 minutes)</p> | <p>Uni-Gold Recombigen HIV-1/2 (whole blood, blood serum / plasma), finds HIV 1 – 2 antibodies with response in 20 minutes, OraQuick ADVANCE Rapid HIV-1/2 Antibody Test (whole blood, oral fluid, plasma)</p> | <p>Uni-Gold Recombigen HIV-1/2 whole blood, blood serum / plasma 100 (99.5-100.0), OraQuick ADVANCE Rapid HIV-1/2 Antibody Test whole blood 99.6 (98.5-99.9), oral fluid 99.3 (98.4-99.7), plasma 99.6 (98.5-99.9)</p> | <p>Uni-Gold Recombigen HIV-1/2 whole blood, blood serum / plasma 99.7 (99.0-100), OraQuick ADVANCE Rapid HIV-1/2 Antibody Test whole blood 100 (99.7-100), oral fluid 99.8 (99.6-99.9), plasma 99.9 (99.6-99.9)</p> |
| 8  | <p>Rapid test. Salivary test OraQuick ADVANCE HIV-1/2 Antibody Test. If you are found positive, blood is collected through phlebotomy and sent to a laboratory for confirmation test through Western Blot, linking them to care.</p>   | <p>Finds HIV 1 – 2 antibodies with response in 20 minutes</p>   | <p>Whole blood, oral fluid, plasma</p>   | <p>Whole blood 99.6 (98.5-99.9), oral fluid 99.3 (98.4-99.7), plasma 99.6 (98.5-99.9)</p>  | <p>Whole blood 100 (99.7-100), oral fluid 99.8 (99.6-99.9), plasma 99.9 (99.6-99.9)</p>   |
| 9  | /  |   |  |  |   |
| 10 | <p>Genscreen ultra HIV Ag-Ab was used; Biorad and the blood sample was taken from the fingertip. Positive samples were confirmed by Western blot and then by EIA-RI.</p>   | <p>Finds HIV 1 – 2 antibodies in response in 20 minutes</p>   | <p>Finger stick on whole blood, plasma</p>   | <p>Whole blood or plasma 90 (96.7 – 83.3)</p>  | <p>Whole blood or plasma 99,5 (99,20 – 99,9)</p>  |
| 11 | <p>For Home-Based HIV Self-Testing project, the rapid test kit is used (Human Immuno-deficiency Virus HIV ½ Antibody Rapid Test, ABON Biopharm Co. Ltd, Hangzhou, China). Those who were positive were linked to a local CDC for a second screening test (Alere Determine HIV-1/2, Abbott Laboratories, Illinois, USA. In case of double positivity, confirmation test with Western blot (HIV Blot Version 2.2, MP Biomedicals Asia Pacific Pte. Ltd, Singapore).</p>  |   |  |  |   |

|    |  |  |                             |   |   |
|----|--|--|-----------------------------|---|---|
| 12 | Rapid test integrated with DBS (dried blood spot) to give more precision. Determine HIV 1/2 test was used (Abbott Laboratory, North Chicago, Illinois, USA). | Antibodies against HIV-1 and HIV-2 detects an HIV-1 antigen, results in 20 minutes | finger stick on whole blood | Finger stick on whole blood 99.9 (99.4-100) | Finger stick on whole blood: subjects at low risk 100 (99.5-100), subjects at high risk 99.7 (98.9-100) |
|----|--|--|-----------------------------|---|---|

source: own production

In Table 2 we can observe the market price where found, the presence of CE marking, the expiry date and the required degree Celsius for preservation. Suppliers, in the absence of CE marking, did not provide the price list. Prices vary considerably depending on the test type, minimum 8.90 € maximum 20 € each; the preservation period varies from 3 to 24 months, the minimum and maximum preservation range are also very variable. Many products did not obtain CE marking so at the moment they cannot be used in the European context.

**Table 2 Product characteristics of rapid tests**

| Test type  |      | EEC marking         | Expiry date (months)/preservation temperature °C |
|--|------|---------------------|--|
| OraQuick Advance Rapid HIV-1/2 Antibody Test (OraSure Technologies, Bethlehem, Pennsylvania) | 10 € | X                   | 30 months/ from 2° to 30°                        |
| HIV-1/2 (Abbott Laboratories, Illinois, United States of America)                            |      | There is no CE mark | 18 months/from 15° to 30°                        |
| HIV-1/2 STAT-PACK (Chembio Diagnostic System Inc, New York, USA)                             |      | There is no CE mark | 24 months/from 8° to 20°                         |
| Uni-Gold test (Trinity Biotech, Wicklow, Ireland)  |      | There is no CE mark | 12 months/from 2° to 27°                         |
| Abbott Architect HIV Ag/Ab Combo   | 9 €  | x                   | 3 months/from 2° to 8°                           |
| OraSure HIV-1 Western blot, OraSure Technologies, Bethlehem, PA                              |      | x                   | 24 months/from 1° to 30°                         |
| Genscreen ultra HIV Ag-Ab, Biorad  |      | There is no CE mark | 18 months/from 2° to 30°                         |
| HIV ½ Antibody Rapid Test, ABON Biopharm Co. Ltd, Hangzhou, China                            |      | There is no CE mark | 24 months/from 22 to 30°                         |
| Determine HIV 1/2 test (Abbott Laboratory, North Chicago, Illinois, USA)                     |      | There is no CE mark | 18 months/from 2° to 30°                         |
| HIV 1/2 GENIE FAST BIO-RAD   | 20 € | x                   | 18 months/from 2° to 30°                         |
| Alere Determine HIV-1/2, Abbott Laboratories, Illinois, USA                                  | 8,9  | x                   | 18 months/from 2° to 30°                         |

source: own production

**Conclusion**

The three parameters for the choice of the most effective test should be sensitivity, specificity, and price but, unfortunately, it is very often difficult to compare the characteristics of sensitivity and specificity of the different test types as they may have different performances according to the context in which they are used. Moreover, the accuracy of the results depends not only on the test characteristics but also on the capacity of the executor and on the quality and quantity of the sample taken (Ippolito, 2015). Test sensitivity indicators have considerable variations to be evaluated when choosing the test to be used; for the purposes of cost-effectiveness analysis, it is important in this case to evaluate whether in the diagnostic course an ELISA check-up test and CD4 count are provided for the therapy to be implemented, otherwise, where the social or infrastructure situation does not allow the access to a full diagnosis it is important to choose the rapid test with greater sensitivity indicator (Hanh, 2011; Sekandi, 2011). The typology of test analysed by literature is suitable for quick evaluation on the basis of the administration setting, on mobile stations or outside setting it is necessary to use rapid tests on oral fluid, while where the available setting is stable and equipped to ensure a low risk of infection with staff properly trained for testing activity, it is possible to conduct the test on whole blood or plasma. Specificity indicators do not show significant variations. The test cost must consider the variables of sensitivity, specificity and setting considered first. During the planning of diagnosis

courses, it is important to highlight test preservation periods, projects with long-term low turnout could lead to inefficiencies in the choice of short expiry products (3 months), but almost all the tests taken into consideration starting from literature have a medium long-term expiry 18-30 months. Except for a test typology (Abbott Architect HIV Ag / Ab Combo), all others have variable preservation temperatures that do not impact on the use of tests even in differentiated settings. As highlighted by literature, HIV rapid tests are cost-effective only in cases where the population at high risk for behaviour can be tested for behaviour and where the structuring of the test service is not guaranteed by proper infrastructure. HIV rapid tests have been identified as a valid diagnostic tool for the prevention of HIV and AIDS (National AIDS Commission, 2011, Ministry of Health, 2015). Piedmont Region is one of the first to identify the test as a tool to be taken into consideration according to the Regional Plan also in order to integrate the services already provided by the regional healthcare system (Seremi, 2016). HIV rapid tests answer to the need to identify any positivity in populations with a risk behaviour where there is no awareness of the serological state and there is no a culture of early diagnosis among the population. In Italy, most tests used in community based research projects cannot be used because of CE marking absence, limiting the possibility and choice. The article is based on projects identified in literature with significant results in terms of relapse; surely there will be better evidence in the future with projects based on fourth-generation HIV rapid testing and on self-diagnosis projects (Kelvin et al., 2016; Maksut et al., 2016)

## **DECLARATIONS**

### **Ethics approval and consent to participate**

Not applicable. This manuscript is a review of the literature.

### **Consent for publication**

Not applicable

### **Availability of data and material**

Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

### **Competing interests**

The authors declare that they have no competing interests.

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