

Early diagnosis and retention in care of HIV-infected patients through rapid salivary testing: a test-and-treat fast track pilot study

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SUMMARY

Aim of this study was to evaluate the efficacy and the retention-in-care of individuals diagnosed during six years of salivary HIV testing (EASY-test project). Among those linked-to-care at the Infectious Diseases Department of San Raffaele Hospital (Milan, Italy), the proportion of patients engaged, retained in care and virologically suppressed after the antiretroviral treatment was 96%, 100% and 95.2%, respectively. Results from our study suggest that salivary HIV testing may help bring to light cases of HIV infection otherwise undiagnosed, and thus favour a more rapid and wider reduction of the HIV infection burden at the population level.

KEY WORDS: HIV, HIV salivary testing, Retention in care, HIV virological suppression, HAART.

Received July 16, 2015

Accepted September 11, 2015

HIV investigators are currently discussing a 'test-and-treat' strategy, validating the treatment as prevention (TasP) approach to reduce transmission of HIV infection at the population level and reach the goal of an "AIDS-free generation" (Nachega *et al.*, 2014). The rationale for this strategy relies on data showing that patients with suppressed HIV viral load are less infectious and hence less likely to transmit HIV infection through risk behaviors (Quinn *et al.*, 2000; Tovanabutra *et al.*, 2002; Gardner *et al.*, 2011). The aim of this strategy should thus be to increase the number of people who become aware of their HIV infection through expanded testing efforts, assist these people in entering medical care, and initiate antiretroviral thera-

py (ART) at earlier stages of disease (Gardner *et al.*, 2014).

These goals are far from being reached even in high-income countries: easier access to the HIV test must be considered the starting point of the program, but many HIV-infected persons in the United States are not engaged in regular care or receiving ART (Marks *et al.*, 2010; Molitor *et al.*, 2005; Pollini *et al.*, 2011). The Centers for Disease Control and Prevention (CDC) estimated that among persons with HIV who were aware of their infection, 45% were retained in care and 31% had a suppressed viral load (VL) (Hall *et al.*, 2013).

In Italy the picture may be different: in a cohort of patients followed by Infectious Diseases Department of Modena between January 1996 and December 2011, 962 subjects had an HIV diagnosis during the study period: 891 (92.6%) were linked to care, 570 were on ART and 516 (90.5%) of them had undetectable HIV-RNA levels (Lazzaretti *et al.*, 2012).

However, the estimated hidden proportion of

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undiagnosed HIV infection in Italy is about 30% (Centro Nazionale di Epidemiologia, Sorveglianza e Promozione della Salute. Available at: <http://www.epicentro.iss.it>).

Test access, isolation and stigma remain significant barriers to HIV diagnosis and to initiating HIV care in many cases, with important differences according to geographical area and risk factors for HIV infection; it is thought that direct linkage to HIV care at the time of diagnosis is critical to promoting timely care initiation (Torian *et al.*, 2008; Pollini *et al.*, 2011).

The Infectious Diseases Department of San Raffaele Hospital, Milan adopted the strategy of the point of care testing model, developing a Prevention Program called "EASY test Project", by offering a new rapid HIV and HCV test on oral fluid (Parisi *et al.*, 2103; Parisi *et al.*, 2014). Aim of this study was to evaluate the efficacy and retention in care rate of individuals diagnosed as "HIV infection/disease carriers" during the six years of the EASY test project, based on an operative plan characterized by a direct linkage between point of care and clinical Department. Subjects were initially tested for HIV by a rapid salivary assay; when the salivary test was reactive, diagnosis was confirmed by a standard blood assay.

The "EASY test Project" is a cross-sectional study of community, developed under the patronage of the Infectious Diseases Department of San Raffaele Hospital, in collaboration with Milan Council, Department of Prevention-Reference Centre for HIV and STDs (Local Public Health Unit in Milan) and supported by ANLAIDS-Lombardia association (National Association for the Fight against AIDS).

After signing the informed consent form, the subjects who underwent the test were counseled and supported by a psychologist or infectious disease specialist. Tests were performed as previously described (Parisi *et al.*, 2103; Parisi *et al.*, 2014).

All patients tested on saliva and resulting provisionally HIV-Ab-positive were offered a free blood test at the laboratory of San Raffaele Hospital: IV generation ELISA (Abbott® - Wiesbaden, Germany) confirmed by Western blot analysis (GeneLabs Diagnostics® - Bangkok, Thailand), as required by national guidelines (Legge 135/90); a first infectivologist visit for

diagnosed cases was guaranteed within two/three working days.

Patients with confirmed HIV infection who decided to be followed at the Infectious Diseases Department of our hospital were defined as linked to care and included in the present analysis. Among patients linked to care, the number of those actually followed in our clinic (retained in care), the number of those who started therapy (engaged in care) and those who have an undetectable VL (HIV-RNA <50 copies/mL after at least six months of treatment i.e.; virologically suppressed) was assessed. Specifically, we defined retained-in-care patients who attended at least two visits after the diagnosis and engaged-in-care those who started ART within one year from the diagnosis ("Continuum of care").

The denominator used to calculate the proportion of patients engaged and retained in care was the number of patients linked to care. The denominator used to calculate the proportion of patients virologically suppressed was the number of patients linked in care minus the number of those who had started antiretroviral therapy less than 6 months previously. Our method assumed all out-of-care patients as not virologically suppressed.

The source of clinical data for patients linked, engaged and retained in care, was the electronic clinical chart currently in use at the Infectious Diseases Department, which is updated at each ambulatory visit. HIV-RNA was quantified by the PCR molecular system (Real Time HIV-1 RNA PCR, Abbott® - Wiesbaden, Germany).

From 2008 to 1st February 2015, 11,549 subjects were tested with a rapid test on a saliva sample during the EASY test prevention program; 79 out of 11,549 (0.7%) resulted provisionally HIV-Ab positive; in all of them HIV infection was confirmed by standard blood test (100% linked to care patients).

Twenty-seven out of 79 (34%) patients with an HIV diagnosis confirmed by blood testing attended the first visit at our clinic. Of these 27, 24 (89%) were male [20 (83%) males who have sex with males, MSM], their median age was 32 (IQR 27.5-38.5) years and 20 (74%) were born in Italy.

Two out of the 27 (7%) patients linked to care dropped out after the first visit because they decided to be followed in clinics closer to the

their residence area: thus, 25 patients linked to care were retained in care (25/25, 100%). One of those retained in care refused antiretroviral therapy: at 21st August 2015, 24/25 (96%) patients started antiretroviral therapy (engaged in care).

Virological suppression could not be defined for 3/24 (12.5%): one has been on antiretroviral treatment for less than 6 months and two did not attend at regular visits. Thus, 21 out 24 (87.5%) patients at 21st August 2015 were eligible for calculation of the proportion of those virologically suppressed, because they had been engaged in care for more than 6 months and with HIV-RNA <50 copies/mL. Of those, 1/21 (4,8%) have a detectable viral load, while 20/21 (95,2%) are virologically suppressed (Figure 1). The proportions of patients engaged (96%), retained in care (100%) and virologically suppressed (95.2%) are all high, thus confirming that the described approach to HIV diagnosis and linkage to care is not only feasible, but also effective in uncovering undiagnosed HIV infection and favouring HIV virological suppression also at a population level. Importantly, the Veterans Health Administration in the United States considered the implementation of salivary HIV testing in primary care a cost effective

approach to identify patients with HIV (Knapp and Chan, 2015).

The main limit of our study is the small sample size. Furthermore, although this analysis is based on data from a six-year prevention programme, the results can be applied to the general population of a great city of Northern Italy, but may be not representative of all national and international settings.

Data from a Netherland cohort suggest that combining wider and easier HIV testing approach with earlier initiation of antiretroviral therapy might help reduce HIV spread at the general population level (Den Hengel *et al.*, 2015). The results of our study may contribute to address this unmet need in confirming that salivary HIV testing followed by standard blood testing for provisionally positive cases may contribute to bring to light cases of HIV infection otherwise undiagnosed, thus favouring rapid linkage to care. As most of the cases linked to care were also promptly engaged in care, and as engagement in care was followed by virological suppression in most cases, the studied approach might well contribute to prevent the spread of HIV. In a scenario of persisting high risk behaviours, this HIV testing approach, in a “street lab” connected with a clinical center for

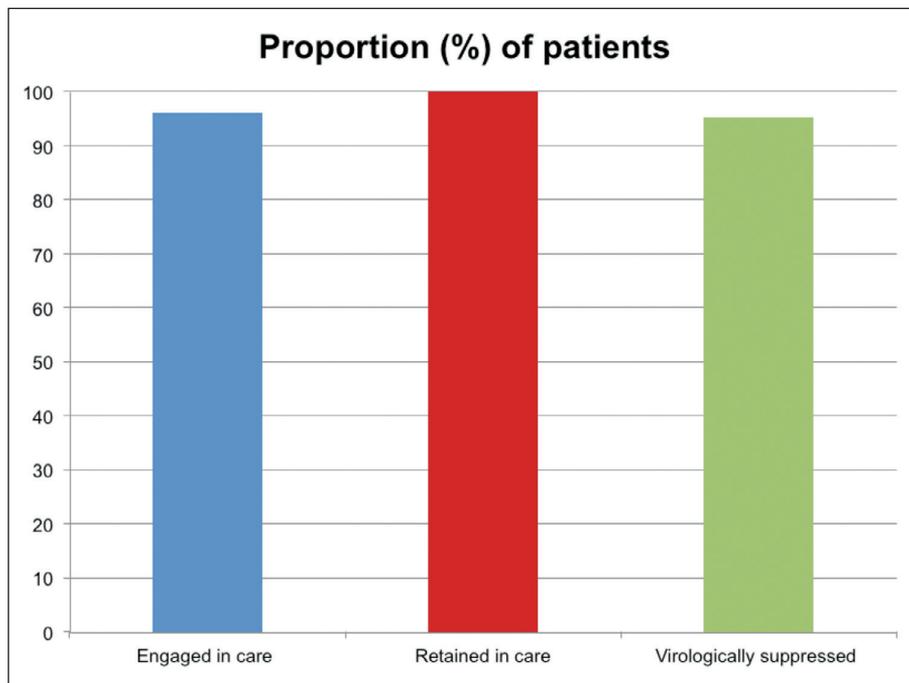


FIGURE 1 - Continuum of care after HIV diagnosis with point-of-care salivary testing: proportion of patients retained, engaged in care and virologically suppressed.

HIV treatment, may be particularly useful in geographical areas or in social settings where standard testing procedures are difficult to implement.

We acknowledge the contribution of the health workers of Points of Care and Medicine of Laboratory - San Raffaele Institute in Milan, and Prevention Department, Reference Centre for HIV and STDs - Local Public Health Unit of Milan, for the FREEDAY Easy test.

The authors thank Prof. Mauro Moroni, Donatella Mainieri and all the volunteers of ANLAIDS Lombardia Association.

This work was supported by unrestricted educational grants from Abbvie, Campoverde di Aprilia (LT), Italy; Biopharma, Pomezia (Rome), Italy; Bristol-Myers Squibb, Rome, Italy; Boehringer Ingelheim, Milan, Italy; Gilead, Milan, Italy; Janssen-Cilag, Cologno Monzese (Mi), Italy; OROFINO Pharma group, Rome, Italy; MSD, Rome, Italy; Takeda, Rome, Italy.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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