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The effect of national HIV testing recommendations and local interventions on HIV testing practices in a Swiss university hospital: a retrospective analysis between 2012 and 2015

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Abstract

Objectives

Despite HIV testing recommendations published by the Federal Office of Public Health (FOPH) since 2007, many individuals living with HIV are diagnosed late in Switzerland. The aim of this study was to examine the effect of the 2013 FOPH HIV testing recommendations on HIV testing rates.

Setting

Ten clinical services at Lausanne University Hospital, Lausanne, Switzerland.

Participants

Patients attending between 1st January 2012 and 31st December 2015.

Design

Retrospective analysis using two existing hospital databases. HIV testing rates calculated as the percentage of tests performed (from the Immunology Service database) per number of patients seen (from the central hospital database).

Primary and secondary outcome measures

The primary outcome was testing rate change following the 2013 FOPH testing recommendations, comparing testing rates two years before and two years after their publication. Secondary outcomes were demographic factors of patients tested or not tested for HIV.

Results

147,884 patients were seen during the study period of whom 9,653 (6.5%) were tested for HIV, with 34 new HIV diagnoses. Mean testing rate increased from 5.6% to 7.8% after the recommendations (*P*=0.001). Testing rate increases were most marked in services involved in clinical trials on HIV testing, whose staff had attended training seminars on testing indications and practice. Testing rates were lower among older (aged >50 years), female and Swiss

patients compared to younger, male and/or non-Swiss patients, both globally (*P*=0.001) and in specific clinical services.

Conclusions

This simple two-database tool demonstrates clinical services in which HIV testing practice can be optimised. Improved testing rates in services involved in clinical trials on testing suggest that local engagement complements the effect of national recommendations. Whilst, overall, HIV testing rates increased significantly over time, testing rates were lower among patients with similar demographic profiles to individuals diagnosed late in Switzerland.

Strengths and limitations of this study

- A simple two-database tool was used to calculate HIV testing rates over a wide range of clinical services.
- The single-centre design enabled knowledge of clinical service structure and therefore the profile of patients being examined.
- Testing rates could be compared between clinical services as well as over time.
- Although the two-database tool is simple and robust, it does not provide a 'margin of improvement' for testing rates, as it examines only testing rates and not the parameters which could influence these.
- The patient denominator was taken as patients seen in each service rather than patients presenting specific indications for HIV testing, potentially lowering testing rate figures.

Introduction

HIV testing is key in diagnosing individuals living with HIV, thus enabling treatment and viral suppression; testing individuals early in infection reduces consequent morbidity, mortality and healthcare costs (1). HIV testing recommendations have been published in Switzerland by the Federal Office of Public Health (FOPH) since 2007 (2) and updated in 2010, 2013 and 2015 (3-5). The recommendations propose Physician-Initiated Counselling and Testing (PICT), which is targeted and opt-in, and requires testing to be offered to patients explicitly before being performed. The FOPH recommendations present the situations in which HIV testing is indicated, notably, symptoms and signs of acute HIV infection, AIDS-defining illness, HIV indicator diseases (IDs), and groups at high risk of HIV acquisition. The physician is responsible for recognising these situations in clinical practice. In contrast to PICT, the HIV testing recommendations of the United States (US) (6), France (7) and the United Kingdom (UK) (8) propose non-targeted and opt-out testing in health care settings in which local HIV seroprevalence is above a certain threshold (0.1% in the US and France; 0.2% in the UK). In this case, testing is performed regardless of clinical presentation or risk factors, unless the patient explicitly declines. Patient-, doctor- and system-related barriers exist to both targeted and non-targeted testing approaches (9-11) and may delay HIV diagnosis in positive individuals. In Switzerland, almost half of patients newly-diagnosed with HIV are identified late, with CD4 counts below 350 cells/mm^3 or an AIDS-defining condition (12), suggesting that testing practice is suboptimal.

In 2012, our group examined the effect of the 2010 FOPH HIV testing recommendations on the testing rates of selected clinical services at Lausanne University Hospital (LUH), Lausanne, and reported that there was no significant change in HIV testing practice associated with the recommendations' publication (13). Among the clinical services, the emergency department (ED) and the oncology service had particularly low testing rates at, respectively, 1% and 4% of all patients seen (13). Following the 2010 FOPH recommendations, which specifically

mentioned the ED as a service in which HIV testing should take place, we observed that 82% of ED doctors in French-speaking Switzerland were unaware of national HIV testing recommendations and that even those aware did not always propose testing when indicated (14). After providing training seminars on testing indications and the practical aspects of testing to address this lack of awareness, we observed other ED doctor-related barriers to proposing testing, notably, a preference to focus on the reason(s) for presenting over discussing HIV (11). In the oncology service, we observed that HIV testing of patients diagnosed with AIDS-defining cancers (ADCs) was not universal and was especially poor among patients with invasive cervical cancer (HIV testing rate 11%) (15). To investigate barriers to HIV testing in this service, we provided information seminars for doctors and nurses on HIV testing indications and testing practice and examined HIV testing rates among patients newly-diagnosed with *non*-ADCs. Among 239 patients enrolled in this study, the HIV testing rate increased from 4% (baseline) to 18% and patient acceptance of HIV testing offered was high (91%) (16).

In November 2013, the FOPH recommendations were updated, differing from the 2010 recommendations in three main ways (4). First, testing indications were graded such that HIV testing should be *expressly recommended* (for acute HIV infection and AIDS-defining conditions), *recommended* (for HIV *indicator diseases*, following the results of the HIV Indicator Diseases across Europe Study (17)) or *proposed* (where not diagnosing HIV could have severe consequences or for individuals at risk of HIV acquisition). Second, patients undergoing immunosuppressive therapy, including chemotherapy, were included as a group in whom HIV testing should be *proposed*. Third, it was stated explicitly that not performing an HIV test when indicated could have medico-legal consequences.

The aim of this study was to repeat the analysis of HIV testing practice in selected clinical services at our centre, this time examining the effect on testing rates of the 2013 FOPH HIV testing recommendations.

Methods

Ethics Statement

The study was approved by the ethics commission on human research of the canton of Vaud, Switzerland (protocol number 2016-00368). All patient data used were stripped of identifiers prior to analysis.

Study setting

The study was performed at Lausanne University Hospital (LUH), Lausanne, Switzerland, a 1500-bed teaching hospital where local HIV seroprevalence is 0.2-0.5% (18, 19). At this centre, doctors attend regular educational seminars as is standard in a teaching hospital but without necessarily a focus on HIV.

HIV testing

HIV testing performed in the Immunology Service at LUH uses a fourth generation screening assay to detect anti-HIV1/2 antibodies and p24 antigen (Cobas Elecsys HIV combi PT, Roche Diagnostics, Rotkreutz, Switzerland). Reactive samples undergo confirmation assays (p24 neutralisation assay and a line immunoassay for HIV-1/2 antibodies) before the release of a positive result as previously described (13). All HIV tests performed are entered in to the Immunology Service database, together with the requesting service, date of request, date of test and result.

Study participants

All patients aged ≥16 years old presenting to selected clinical services (described below) between 1st January 2012 and 31st December 2015 were eligible for inclusion.

Study design

The study was retrospective and single-centre. The primary outcome was the change in HIV testing rates between the two years before the FOPH 2013 HIV testing recommendations and the two years after, both globally and within each clinical service. The secondary outcome was

to determine which patient demographic factors were associated with HIV testing being performed.

Ten clinical services were selected for analysis: general internal medicine inpatients (IP), neurology IP, cardiology IP, intensive care units (ICU), emergency department (ED), psychiatry IP (excluding services for substance misuse where HIV testing is routine), oncology outpatients (OP), dermatology IP and OP, ear, nose and throat (ENT) surgery IP and OP, and non-ENT surgery IP (including vascular, cardiothoracic, gastrointestinal, maxillofacial surgery, urology and neurosurgery). The services were selected for ≥1 of the following reasons: 1) receiving patients with HIV testing indications (3, 4); 2) previous target of educational interventions (ED, oncology service (11, 14, 16, 20)); and 3) enabling comparison with testing rates prior to 2012 (13). Between 2012 and 2015, the oncology service underwent expansion, resulting in some units seeing a substantial increase in patient turnover. For the current study, we restricted analysis to units examined previously (13) or those taking part in clinical trials on HIV testing.

Using the central hospital database, the number of patients attending each service was obtained over four 12-month blocks, corresponding to each calendar year. Dates of all hospital visits and patient demographic parameters (age, sex, origin) were also obtained from this database The number of HIV tests performed during the same 12-month blocks was obtained from the Immunology Service database.

For each 12-month block, HIV testing rates were calculated as the percentage of tests performed per number of patients seen. For the testing rate calculations, the number of patients rather than the number of clinical episodes was taken as the denominator, to avoid underestimating testing rates in clinical services which may see the same patient several times, notably in the OP sector.

For the ED, to examine the effect of local clinical trials and associated educational interventions on HIV testing, testing rates were calculated monthly in addition to 12-monthly. For 12-monthly testing rates, the entire service was analysed whereas for the monthly testing rates, analysis

was restricted to the sections involved in the clinical trials. In the oncology service, testing rates were additionally compared between 2012 and 2013, in line with a clinical trial which ran from July to October 2013 (16). However, as the 2013 FOPH recommendations introduced 'proposing' testing to all patients undergoing immunosuppressive treatment, the specific effect of clinical trials after 2013 was not examined in this study. The results of these trials will be published elsewhere (manuscript in preparation).

Positive HIV tests

Occasionally, an HIV test (the fourth generation screening assay described above) is requested erroneously for patients of known positive HIV status instead of viral load. For all tests conducted and confirmed as positive, therefore, test dates were cross-referenced with electronic medical records to determine whether each positive test was a new or a known positive case.

Statistical analyses

Data are presented as means with standard deviation, medians with interquartile range and as percentages. Means were compared using Student's t-test and proportions compared using the Chi-squared test using two-way contingency tables. To examine the effect of the 2013 FOPH HIV testing recommendations, testing rates for each clinical service, and overall, were examined during the two years before and the two years after the publication of the recommendations (1st January 2012 to 31st December 2013 and 1st January 2014 to the 31st December 2015) and then compared. Although the updated FOPH recommendations were published in November 2013, the month of December 2013 was included in the 'before' analysis given that there is usually a lag period of at least one month between recommendations being published and being read and/or implemented (13). Oncology service testing rates were additionally compared between 1st January to 31st December 2012 and 1st January to 31st December 2013.

In our 2012 report on testing, we commented that patient origin may have an effect on testing, based on the observation that the medical OP service not examined in the present study had a particularly high percentage of patients from countries with high HIV prevalence (estimated to

be up to 65%, (13)). We therefore examined the effect of patient age, sex and origin on testing rates in each clinical service, and overall. Patient origin was categorised as Swiss, from neighbouring countries (France, Germany, Austria, Italy and Lichtenstein), from sub-Saharan Africa (SSA) and 'other', comprising countries not falling into the first three categories. When patient numbers were low in specific origin categories, analyses were performed by grouping patients in the latter three categories as 'non-Swiss'. Patients lacking data on origin were removed from analyses provided the proportion of patients removed was <10%; if the percentage was ≥10% in a specific service, analysis of origin data was not performed.

All analyses were performed using Microsoft Excel 2008 (Microsoft Corporation, Redmond, WA, USA).

Results

Study population

During the four-year study period, 147,884 patients were seen at the ten clinical services examined. Patient demographic profile did not change significantly during this time. In total, 9,653 patients underwent HIV testing (global HIV testing rate 6.5%). Supplementary Table 1 shows the demographic characteristics of patients tested and not tested.

The total number of patients attending the ten clinical services increased progressively over the four-year period from 34,861 to 36,460 patients but the difference in the number of patients attending before versus after the 2013 FOPH recommendations was not significant (*P*=0.14).

HIV tests and testing rates

The total number of tests performed increased over the four-year period, with a mean of 2,220±94.5 tests before and 2,803±171 tests after the 2013 FOPH recommendations (*P*=0.001). The global testing rates (for all clinical services together) also increased significantly between before and after the 2013 recommendations from 5.6% (2012-2013) to 7.8% (2014-2015) (*P*=0.002) (Table 1 and Figure 1). Testing rate increases were particularly marked in the ED

(from 4.2% to 5.6%, *P*=0.001, Table 1) and the oncology service (from 3.8%±0.8% to 23.6%±7.4%, *P*=0.0001, Figure 1).

Table 1. HIV testing rates and percentage of positive tests in clinical services in which new HIV diagnoses were made.

	Testing rate, mean % (SD)		*P*	2012-2013		2014-2015		2012-2013	2014-2015
Clinical service	2012-2013	2014-2015		Tests performed	Tests positive	Tests performed	Tests positive	% of tests positive	% of tests positive
Neurology	20.6 (1.5)	25.5 (1.4)	0.006	433	3	550	0	0.7	0
Internal medicine	10.8 (0.4)	13.8 (0.8)	0.001	662	6	820	1	0.9	0.1
Psychiatry	11.3 (0.04)	12.4 (0.8)	0.78	345	1	376	1	0.3	0.3
ICU	8.6 (0.3)	9.1 (0.5)	0.97	308	0	314	1	0	0.8
Dermatology	4.9 (0.1)	6.0 (0.3)	0.002	811	1	987	1	0.1	0.3
ED	4.2 (0.3)	5.6 (0.4)	0.001	987	7	1336	11	0.7	0.8
ENT	1.2 (0.2)	1.8 (0.3)	0.05	67	0	126	1	0	0
Total[1]	5.6 (0.2)	7.8 (0.4)	0.002	3938	18	4792	16	0.1	0.1

[1]As no new HIV diagnoses were made in the services of surgery, cardiology and oncology, the total numbers of tests performed before and after the 2013 recommendations differ from other total figures stated in the text.

Abbreviations: ICU, intensive care units, ED, emergency department; ENT, ear, nose and throat service; SD, standard deviation

Positive HIV tests

In total, 34 new HIV diagnoses were made (0.3% of tests performed). Among the 34 newly-diagnosed patients, median age was 42 years (IQR 34;48), 28 (82%) were men, 14 (41%) were Swiss and 20 were non-Swiss, including eight (24%) from SSA. Median CD4 count at diagnosis was 188 cells/mm^3 (IQR 32;363). There were 30 erroneous repeat HIV tests in patients of known positive status. However, re-testing enabled two patients who had been lost to follow-up to be re-integrated into care.

The rate of positive tests out of tests performed remained stable with time in each service, at between 0.1 and 0.9% (Table 1), with no change between before and after the 2013 FOPH recommendations (*P*=0.77). There were no positive tests among patients attending the services of cardiology, surgery and oncology, although testing rates in the cardiology and surgery services were at the lower end of all services studied (Figure 1).

Effect of patient demographic profile on testing

The breakdown of patients by age, sex and origin was examined using the two study databases. Globally, the proportion of patients attending the ten clinical services who were aged below 50 did not change over the four-year period, with a mean proportion of 31.8%±0.24%. Equally, the proportion of patients aged below 50 who were tested for HIV remained stable with a mean proportion of 51.3%±1.36%. However, in some services, the proportion of patients tested was higher among patients aged below 50 than among older patients (Table 2). Testing rates were also significantly higher among male than among female patients in several clinical services and overall (Table 2).

Table 2. HIV testing rates over the four-year study period by patient demographic profile.

	Age-related rates, mean % (SD)		*P*	Sex-related rates mean % (SD)		*P*	Origin-related rates mean % (SD)		*P*
	<50	>50		Male	Female		Swiss	Non-Swiss	
Neurology	55.3 (17.5)	13.5 (1.7)	<0.001	23.1 (2.4)	23 (2.7)	0.99	20.1 (1.3)	30.6 (2.6)	<0.001
Internal medicine	20.8 (1.7)	10.9 (1.5)	<0.001	14.1 (1.8)	10.9 (0.8)	<0.001	5.0 (0.4)	6.8 (0.4)	<0.001
Psychiatry	17.2 (0.8)	4.4 (0.8)	<.0001	12.8 (0.4)	10.7 (1.0)	0.17	15.5 (1.1)	14.6 (1.2)	0.94
ICU	15.2 (1.0)	7.2 (0.6)	<0.001	9.2 (0.5)	7.9 (0.4)	0.45	7.2 (0.3)	11.8 (1.1)	<0.001
Surgery	11.3 (1.5)	3.3 (0.4)	<0.001	6.8 (0.5)	8.0 (0.6)	0.48	2.6 (0.2)	4.6 (0.5)	<0.001
Dermatology	6.1 (0.6)	4.7 (0.5)	<0.001	7.1 (0.8)	4.0 (0.4)	<0.001	4.7 (0.4)	5.6 (0.3)	0.56
ED	12.1 (1.9)	2.1 (0.4)	>0.001	5.9 (0.6)	4.0 (0.7)	<0.001	4.8 (0.9)	7.0 (0.7)	<0.001
ENT	1.7 (0.7)	1.2 (0.2)	0.28	1.8 (0.5)	1.1 (0.2)	0.007	1.3 (0.2)	1.8 (0.3)	0.78
Cardiology	4.4 (1.3)	3.8 (0.3)	0.88	4.6 (0.2)	2.4 (0.3)	<0.001	1.9 (0.2)	3.3 (0.6)	0.0002
Oncology	7.5 (2.8)	3.5 (0.9)	<0.001	16.3 (8.1)	18.4 (10.4)	0.99	NA	NA	NA
Total	9.6 (0.8)	4.3 (0.4)	0.001	7.7 (0.8)	5.9 (0.7)	<0.001	3.1 (0.4)	5.1 (0.5)	<0.001

Abbreviations: ICU, intensive care units, ED, emergency department; ENT, ear, nose and throat service; SD, standard deviation; NA, not analysed (>10% of patients without origin data)

To examine patient origin, patients were pooled as Swiss and non-Swiss as the percentage of specific groups mentioned in the 2013 recommendations, notably patients from SSA, was low (Supplementary Table 1). In several services, and overall, testing rates were significantly higher among non-Swiss compared to Swiss patients (Table 2).

In the neurology service, testing practice changed with time. While there was a significant increase in testing rates between 2012 and 2015, the testing rates increased progressively among patients aged below 50 years while the testing rate among older patients remained stable (Supplementary Figure 1). While progressive increases in testing rates were observed over time in other clinical services, no such increase was observed among patients with a specific demographic profile.

Effect of local interventions

During local educational interventions in ED sections involved in clinical trials, monthly testing rates exceeded the mean rate for the ED as a whole (Figure 2). In the oncology service, testing rates increased significantly from 12% in 2012 to 16% in 2013 (P=0.0005), in addition to increasing between before and after the 2013 recommendations as described above.

Discussion

We have applied the same two-database tool with which we examined the effect of the 2010 FOPH recommendations to examine the effect of the 2013 FOPH recommendations at our centre. We observed a global increase in HIV testing following the 2013 recommendations, with significant increases in clinical services receiving educational interventions in the context of clinical trials on testing. As these services had among the lowest testing rates prior to 2012, our observed increase suggests that local engagement complements the effect of national testing recommendations.

As we observed in our previous study, testing rates in the neurology, internal medicine and psychiatry IP services were higher than those in other services (13). These three services see patients presenting with many of the conditions listed as testing indications in the 2013 recommendations. Further, the neurology and internal medicine IP services make up two of the three principal receiving services of patients admitted via the ED (OH, departmental data). Conversely, the cardiology service had relatively low testing rates. Whilst some patients attending

this service present with non-vascular cardiac pathology or with vascular pathology presenting non-acutely, the low testing rates are surprising given accumulating evidence of a pathophysiological link between HIV infection and endothelial damage (21, 22). However, while cardiovascular pathology (including myocardial infarction, cerebrovascular events and peripheral arterial disease) was mentioned as an indication for HIV testing in the 2010 FOPH recommendations (3), there is no mention of this indication in the 2013 update (4), and patients presenting with acute coronary syndromes to the LUH cardiology service are not tested routinely (OM, personal communication). The finding that testing rates were lower among dermatology patients than among surgery patients is also surprising. However, this may be explained by the high patient denominator in the dermatology service. All these observations highlight the importance of applying the two-database tool only when service structure (patient diagnosis profile, referral source, etc) is known, so that testing rates can be interpreted meaningfully.

In the ED, the testing rates were markedly higher than those reported previously (13, 14). In addition to the significant increase between before and after the recommendations, we observed a possible effect of local interventions in the form of training seminars and clinical trials. The positive effect of sustained attention on HIV testing practice has been described in a London university hospital ED setting (23). In their report, Rayment *et al* described a 30-month period of routine HIV testing provision in the ED with interventions including weekly meetings between ED and sexual health teams, training exercises, incentivisation, information technology solutions and the incorporation of nursing staff into the testing service (23). After around 24 months of these interventions, the testing rate, previously below 10%, increased to 20% and higher, demonstrating that local interventions positively affected testing rates in the ED but that constant commitment was required to achieve sustainability (23).

We observed that testing was significantly higher among non-Swiss than Swiss patients in some services. Testing rates differed with other demographic characteristics, being higher among male patients and those aged below 50 years. Due to the retrospective design of this study, we cannot identify why testing rates among Swiss, older and female patients were lower in some services but this observation is a concern. The latest data on late presentation among patients newly diagnosed

with HIV between 2009 and 2012 and enrolled in the Swiss HIV Cohort Study demonstrated that older age, female sex and SSA origin were risk factors for late presentation (12). Whilst the 2013 FOPH recommendations were associated with improving testing rates at our centre, perhaps future updates should mention the demographic profiles of individuals at risk of late presentation, to break the trend of under-testing patients not classically considered as high risk (1).

This study has limitations. As with any single-centre study, the results presented may not be applicable to other settings, particularly if service structure differs. Our interpretation of the different testing rates has been based on available supporting data, notably, patient demographic profile data and data from studies conducted previously within specific services. In some services, this meant restricting our analysis to specific units to ensure data quality. Although this two-database tool enables testing rates to be calculated and compared between clinical services, it does not provide a 'margin for improvement' in each setting. We have no data on the percentage of healthcare professionals aware of the FOPH HIV testing recommendations or the percentage of patients visiting each service who presented indications for testing. Since reporting low awareness of testing recommendations among ED doctors (14), LUH ED has maintained awareness at 100%, through educational interventions and recall aids such as pocket cards and posters. However, even when 100% of doctors are aware of the recommendations, the percentage able to identify patients with testing indications is lower. We recently observed a sensitivity of 30% among ED doctors for identifying testing indications in their patients (11).

In conclusion, we have described a simple two-database method of measuring testing rates which enables healthcare centres to identify clinical services in which testing rates can be optimised and to follow progress with time. HIV testing rates increased at our centre after the 2013 FOPH recommendations, particularly in services involved in clinical trials on testing. Against this increase, lower testing rates were observed among patients with demographic profiles similar to persons diagnosed late with HIV in Switzerland. We propose that the next FOPH HIV testing recommendations include a reminder that patients lacking the 'classical' demography for HIV acquisition who present with testing indications should be included in testing initiatives.

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Authors' contribution statement

Tosca Lazzarino contributed to study design, data collection and manuscript preparation. Sébastien Martenet contributed to data collection, data analysis and critical review. Rachel Mamin contributed to data collection, data analysis and critical review. Renaud A. Du Pasquier contributed to critical review. Solange Peters contributed to critical review. Matthieu Perreau contributed to critical review. Olivier Muller contributed to critical review. Olivier Hugli contributed to manuscript preparation and critical review. Matthias Cavassini contributed to study design, manuscript preparation and critical review. Katharine E.A. Darling contributed to study design, data collection, data analysis, manuscript preparation and critical review.

Data sharing statement

The database used for the analyses performed in the study is available on request

Competing interests statement

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Part of this work was presented as a poster at the 27th ECCMID meeting in Vienna, Austria, 22-25 April 2017.

Figure legends

Figure 1. Absolute number of HIV tests requested (Panel A) and HIV testing rate (Panel B) with time in the ten clinical services studied.

Asterisks indicate significant differences in rates (P<0.01) between before (2012-2013) and after (2014-2015) the publication of the Federal Office of Public Health HIV testing recommendations in November 2013.

Abbreviations: ICU, intensive care units; ED, emergency department; ENT, ear, nose and throat service.

Figure 2. Monthly HIV testing rates in the emergency department (ED) sections involved in clinical trials on HIV testing and the temporal relationship between HIV testing rates and clinical trials (black bar groups, 1 and 3), other training seminars (black bar group 2), and the publication of Federal Office of Public Health HIV testing recommendations (arrows, 2013 and 2015). The dotted line indicates the mean testing rate for all ED sections for the year 2012, the first year of this study.

[1]Clinical trial examining patients' understanding of and attitudes to HIV testing in the ED (20)

[2]Training seminars on testing following the publication of low awareness of HIV testing recommendations among ED doctors in French-speaking Switzerland (14)

[3]Clinical trial examining patient- and doctor-associated barriers to HIV testing in the ED and patient acceptance of rapid HIV testing (11)

Supplementary Figure 1. Number of patients aged < 50 and ≥ 50 years old who attended the neurology service over the four-year study period showing numbers of patients tested (black) and untested (grey) in each age category.

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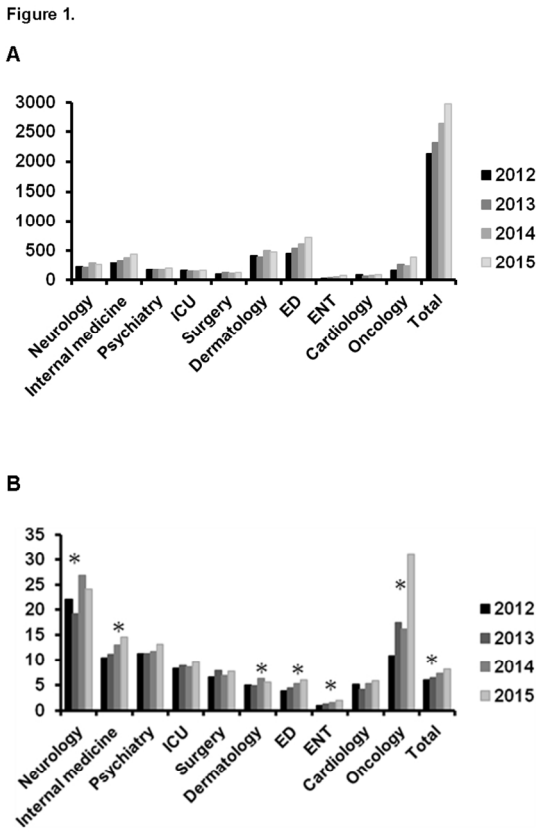

Figure 1. Absolute number of HIV tests requested (Panel A) and HIV testing rate (Panel B) with time in the ten clinical services studied.
Asterisks indicate significant differences in rates (P<0.01) between before (2012-2013) and after (2014-2015) the publication of the Federal Office of Public Health HIV testing recommendations in November 2013.
Abbreviations: ICU, intensive care units; ED, emergency department; ENT, ear, nose and throat service.

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Figure 2.

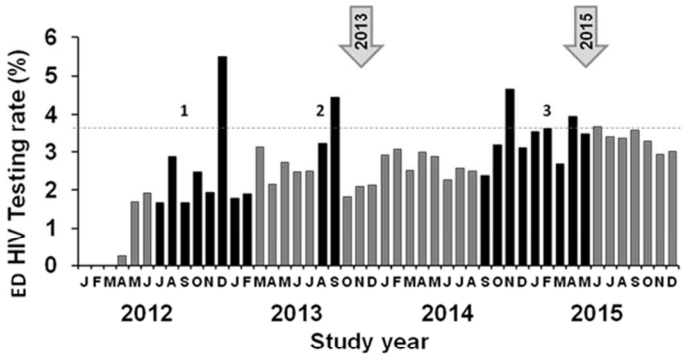


Figure 2. Monthly HIV testing rates in the emergency department (ED) sections involved in clinical trials on HIV testing and the temporal relationship between HIV testing rates and clinical trials (black bar groups, 1 and 3), other training seminars (black bar group 2), and the publication of Federal Office of Public Health HIV testing recommendations (arrows, 2013 and 2015). The dotted line indicates the mean testing rate for all ED sections for the year 2012, the first year of this study.

1Clinical trial examining patients' understanding of and attitudes to HIV testing in the ED (20)
2Training seminars on testing following the publication of low awareness of HIV testing recommendations among ED doctors in French-speaking Switzerland (14)
3Clinical trial examining patient- and doctor-associated barriers to HIV testing in the ED and patient acceptance of rapid HIV testing (11)

215x279mm (150 x 150 DPI)

Supplementary Table 1. Demographic characteristics of patients visiting the ten clinical services who were HIV tested or not HIV tested[1].

Clinical Service	M/F	Tested					Not tested				
		No. (%)	Swiss No. (%) Median Age [yrs] (range)	Neighbour countries No. (%) Median Age [yrs] (range)	SSA No. (%) Median Age [yrs] (range)	Other/ unknown No. (%) Median Age [yrs] (range)	No. (%)	Swiss No. (%) Median Age [yrs] (range)	Neighbour countries No. (%) Median Age [yrs] (range)	SSA No. (%) Median Age [yrs] (range)	Other/ unknown No. (%) Median Age [yrs] (range)
Neurology	M	595 (51)	411 (69) 65 (16-92)	72 (12) 60 (18-89)	11 (1.8) 45 (22-62)	101 (17) 51 (16-83)	1,491 (51)	1,084 (73) 72 (17-99)	182 (12) 72 (16-94)	13 (0.9) 55 (24-80)	212 (15) 59 (18-93)
	F	559 (49)	403 (72) 60 (16-95)	53 (9.5) 52 (16-87)	7 (1.2) 39 (16-55)	96 (17) 41 (16-87)	1,416 (49)	1,133 (80) 77 (16-102)	102 (7.5) 74 (19-95)	14 (1) 35 (28-56)	167 (11) 53 (16-95)
Internal medicine	M	1,439 (60)	960 (67) 67 (17-98)	158 (11) 71 (23-90)	43 (3) 49 (19-82)	278 (19) 58 (16-90)	3,766 (49)	2,776 (73.5) 76 (16-101)	470(12.5) 75 (27-97)	47(1.5) 46 (18-87)	473(12.5) 63 (16-100)
	F	940 (40)	688 (73) 68 (17-95)	81 (8.6) 71 (19-90)	32 (3.4) 38 (20-64)	139 (15) 55 (18-87)	3,859 (51)	3,104 (80) 82 (17-105)	333 (8.6) 80 (22-100)	37 (1) 50 (18-88)	385 (10) 63 (18-100)
Psychiatry	M	505 (58)	304 (60) 38 (17-93)	60 (12) 44 (20-87)	29 (5.7) 38 (19-45)	112 (22) 35 (18-76)	1,904 (50)	1,184 (62) 48 (16-99)	219 (11) 47 (18-96)	71 (3.7) 34 (18-65)	430 (23) 41 (16-92)
	F	362 (42)	238 (66) 42 (16-93)	29 (8) 44 (17-92)	11 (3) 27 (20-73)	84 (23) 39 (18-85)	1,902 (50)	1,379 (73) 56 (16-104)	158 (8.3) 47 (19-88)	61 (3.2) 36 (16-74)	304 (16) 39 (16-91)

ICU	M	927 (68)	618 (67) 61 (16-89)	111 (12) 61 (20-87)	21 (2.3) 47 (19-80)	177 (19) 53 (19-85)	3,593 (65)	2,562 (71) 68 (16-96)	447 (12) 65 (16-91)	27 (0.8) 42 (17-78)	557 (15) 55 (16-91)
	F	429 (32)	311 (73) 60 (16-90)	32 (7.5) 62 (28-85)	12 (2.8) 36 (26-55)	74 (17) 51 (22-89)	1,942 (35)	1,511 (78) 70 (16-96)	149 (7.7) 73 (18-94)	15 (0.8) 40 (18-73)	267 (14) 55 (17-94)
Surgery	M	584 (67)	400 (68.5) 63 (16-94)	62 (10.6) 65 (21-84)	16 (2.7) 38 (19-70)	106 (18.2) 53 (18-84)	2,866 (61)	2,098 (73.2) 68 (16-97)	327 (11.4) 69 (18-98)	31 (1.1) 41 (20-78)	410 (14.3) 58 (18-98)
	F	291 (33)	223 (77) 59 (17-90)	20 (6.9) 68 29-89)	8 (2.7) 56 (26-70)	40 (14) 44 (25-79)	1,839 (49)	1,436 (78) 70 (16-100)	144 (7.8) 69 (20-100)	17 (0.9) 44 (17-64)	242 (13) 50 (20-100)
Dermatology	M	1,631 (62)	1,029 (63) 59 (18-71)	184 (11) 48 (16-99)	72 (4.4) 34 (17-87)	346 (21) 43 (16-83)	9,317 (46)	5,820 (62.5) 60 (16-101)	1,233 (13.2) 49 (16-96)	307 (3.3) 34 (16-80)	1,957 (21) 45 (16-96)
	F	1,001 (38)	673 (67.2) 59 (17-88)	32 (3.2) 52 (16-96)	30 (3.0) 52 (19-85)	266(26.6) 43 (16-82)	11,083 (54)	7,095 (64) 54 (16-105)	1,172 (11) 45 (16-101)	265 (2.4) 33 (17-72)	2,551 (23) 39 (16-94)
ED	M	2,853 (60)	1,791 (62.8) 64 (16-98)	315 (11) 62 (18-90)	139 (4.9) 37 (17-83)	608 (21.3) 52 (16-90)	17,985 (52)	11,923 (66) 68 (16-105)	2,138 (12) 42 (16-99)	434 (2.4) 55 (16-87)	3,490 (19) 50 (16-111)
	F	1,864 (40)	1,291 (69.2) 63 (16-95)	164 (8.8) 66 (16-90)	59 (3.2) 37 (19-69)	350 (18.8) 46 (16-90)	16,672 (48)	12, 577 (75) 70 (16-106)	1,405 (8.4) 40 (16-102)	262 (1.6) 55 (16-88)	2,428 (16) 50 (16-100)
ENT	M	538 (78)	267 (49.6) 54 (17-93)	54 (10) 63 (27-85)	16 (2.8) 31 (19-57)	201 (37.6) 50 (17-78)	5,747 (52)	3,232 (56.2) 53 (16-95)	744 (12.9) 49 (16-101)	142 (2.5) 36 (16-74)	1,629 (28.4) 46 (16-92)
	F	260 (22)	175 (67.3) 56 (17-93)	20 (7.7) 52 (21-85)	12 (4.6) 23 (21-65)	53 (20.4) 42 (20-80)	5,003 (48)	3,379 (67.5) 56 (16-95)	460 (9.2) 50 (16-96)	81 (1.6) 38 (16-68)	1,083 (21.7) 46 (16-92)

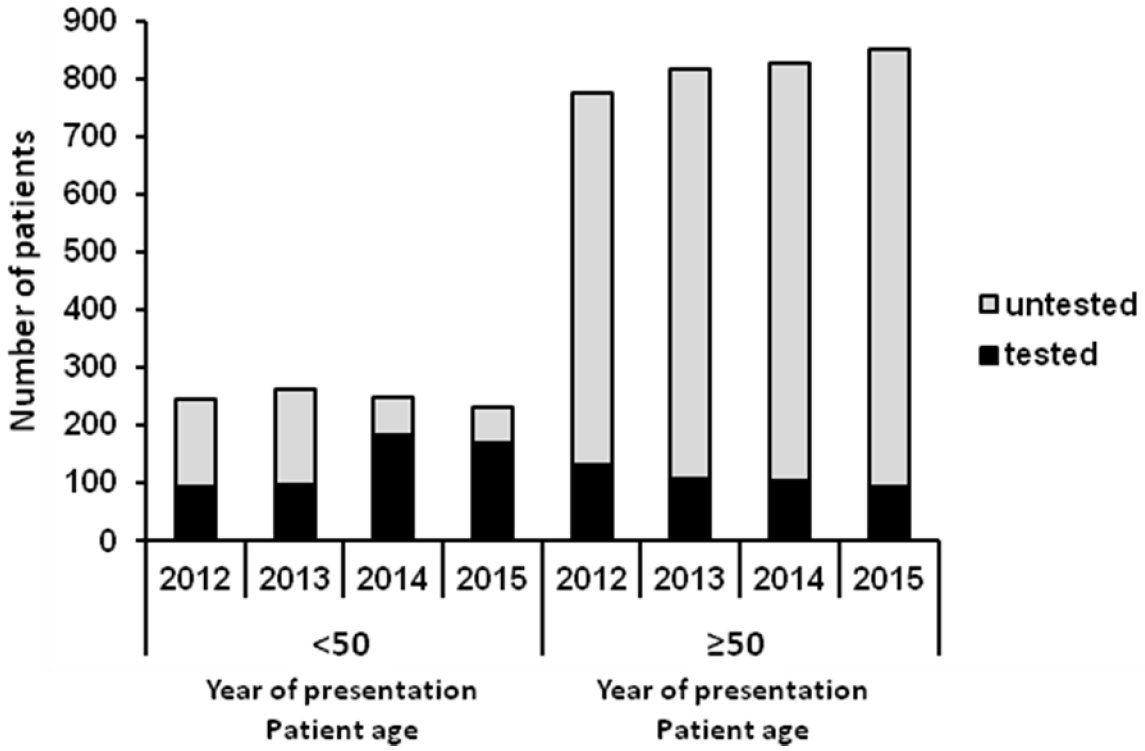
Cardiology	M	633 (74)	431 (68) 62 (20-95)	73 (12) 61 (22-83)	15 (2.4) 50 (24-73)	114 (18) 56 (16-83)	4,562 (67)	3,327 (73) 68 (16-98)	529 (12) 67 (17-99)	28 (0.6) 48 (23-76)	678 (16) 56 (16-97)
	F	224 (26)	167 (75) 60 (17-95)	20 (8.9) 70 (28-83)	5 (2.2) 37 (20-64)	32 (14) 57 (27-86)	2,279 (33)	1,787 (78) 73 (16-99)	207 (9.1) 75 (19-94)	15 (0.6) 49 (30-69)	270 (12) 55 (18-99)
Oncology	M	686 (63)	472 (71) 65 (23-90)	81 (12) 71 (23-90)	18 (2.7) 38 (19-72)	115 (18) 56 (17-85)	5,688 (48)	3,840 (67) 65 (16-99)	684 (12) 72 (16-100)	58 (1.0) 39 (18-76)	1,106 (20) 56 (16-94)
	F	401 (37)	313 (73) 60 (18-94)	26 (6.1) 68 (18-87)	6 (1.4) 46 (36-64)	56 (13) 51 (22-79)	6,246 (52)	4,409 (71) 60 (16-100)	563 (9) 68 (16-102)	86 (1.4) 46 (17-72)	1,188 (19) 51 (16-94)

[1] Figures presented are derived from the entire four-year study period. In this way, individual patients (not tested) have been counted once only, no matter how many times they may have presented and specific values may differ from elsewhere in the results section.

[2] Tested patients may have been tested more than once in different services, or undergone tests of confirmation. In this way, patient numbers may be greater than those cited elsewhere in the results section.

[3] Neighbour countries: France, Germany, Austria, Italy and Lichtenstein

Abbreviations: ICU, intensive care units, ED, emergency department; ENT, ear, nose and throat service



Academic Editor
BMJ Open
14th December 2017

Dear Editor,

RE:
The effect of national HIV testing recommendations and local interventions on HIV testing practices in a Swiss university hospital: a retrospective analysis between 2012 and 2015

We are submitting the manuscript of the above title to BMJ Open for consideration as a Research Article.

In 2012, we reported that the Swiss Federal Office of Public Health (FOPH) recommendations on HIV testing, published in 2010, had no effect on HIV testing practice at our 1,500-bed university hospital in Lausanne, Switzerland. The FOPH HIV testing recommendations were updated in November 2013. The aim of the current study was therefore to examine the effect of the 2013 update on HIV testing practice at our centre.

The study was a retrospective analysis performed between 1st January 2012 and 31st December 2015. It examined testing rates in ten clinical services selected because of 1) receiving patients with HIV testing indications, 2) being previous targets of educational interventions and/or 3) allowing comparison with testing rates prior to 2012.

We used a two-database tool to calculate testing rate as follows: the number of patients tested in a given service within a given time was divided by the number of patients attending that service during the same time period. The resulting figure was multiplied by 100 to give a percentage (HIV testing rate). HIV testing rates were then compared between before and after the publication of the 2013 FOPH testing recommendations.

A total of 147,884 patients were seen during the four-year study period of whom 9,653 (6.5%) were tested for HIV, with 34 new HIV diagnoses. The mean testing rate increased from 5.6% to 7.8%

after the recommendations (*P*=0.001). Testing rate increases were most marked in services involved in clinical trials on HIV testing (the emergency department and oncology service, *P*=0.001 in each case) whose staff had attended training seminars on testing indications and practice. Testing rates were lower among older (aged >50 years), female and Swiss patients compared to younger, male and/or non-Swiss patients, both globally (*P*=0.001) and in specific clinical services.

Our conclusion is that this simple two-database tool can be applied to identify clinical services in which HIV testing practice can be optimised. We observed improved testing rates in services involved in clinical trials on testing, suggesting that local engagement complements the effect of national testing recommendations. Finally, whilst overall, HIV testing rates increased significantly following the 2013 FOPH recommendations, testing rates were lower among patients with the same demographic profile as individuals diagnosed late in Switzerland.

We believe our study to be important as it provides a tool that can be applied to other settings so that HIV testing interventions can be targeted to the services which require them. By examining patient demographic profiles, it is also possible to tailor testing initiatives to specific populations and avoid a blanket approach which may miss key individuals. We are submitting to BMJ Open as we believe this paper to be of interest to a general medical readership; this two-database tool can be applied to any clinical service without the need for specific expertise in HIV medicine.

All authors are aware of this manuscript's submission to your journal.

We look forward to hearing from you.

Yours sincerely,

Dr Katharine Darling

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STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	#1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	#2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	#5
Objectives	3	State specific objectives, including any pre-specified hypotheses	#6
Methods			
Study design	4	Present key elements of study design early in the paper	#7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	#7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	#7-#8
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	#7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	#8-#9
Bias	9	Describe any efforts to address potential sources of bias	#8
Study size	10	Explain how the study size was arrived at	#7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	#9-#10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	#9-#10
		(*b*) Describe any methods used to examine subgroups and interactions	#9-#10
		(*c*) Explain how missing data were addressed	#9-#10
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	#10

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	#10
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Supp Table 1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	#10-#16
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	#10-#16
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	#10-#16
Discussion			
Key results	18	Summarise key results with reference to study objectives	#16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	#18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	#18
Generalisability	21	Discuss the generalisability (external validity) of the study results	#18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	#19, #5

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

The effect of national HIV testing recommendations and local interventions on HIV testing practices in a Swiss university hospital: a retrospective analysis between 2012 and 2015

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Secondary Subject Heading:	Diagnostics, Emergency medicine
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The effect of national HIV testing recommendations and local interventions on HIV testing practices in a Swiss university hospital: a retrospective analysis between 2012 and 2015

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Short title: Effect of testing recommendations on HIV testing rates

Key words: HIV testing recommendations, HIV testing, late HIV diagnosis, patient demography

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Abstract

Objectives

Despite HIV testing recommendations published by the Federal Office of Public Health (FOPH) since 2007, many individuals living with HIV are diagnosed late in Switzerland. The aim of this study was to examine the effect of the 2013 FOPH HIV testing recommendations on HIV testing rates.

Setting

Ten clinical services at Lausanne University Hospital, Lausanne, Switzerland.

Participants

Patients attending between 1st January 2012 and 31st December 2015.

Design

Retrospective analysis using two existing hospital databases. HIV testing rates calculated as the percentage of tests performed (from the Immunology Service database) per number of patients seen (from the central hospital database).

Primary and secondary outcome measures

The primary outcome was testing rate change following the 2013 FOPH testing recommendations, comparing testing rates two years before and two years after their publication. Secondary outcomes were demographic factors of patients tested or not tested for HIV.

Results

147,884 patients were seen during the study period of whom 9,653 (6.5%) were tested for HIV, with 34 new HIV diagnoses. Mean testing rate increased from 5.6% to 7.8% after the recommendations (*P*=0.001). Testing rate increases were most marked in services involved in clinical trials on HIV testing, whose staff had attended training seminars on testing indications and practice. Testing rates were lower among older (aged >50 years), female and Swiss

patients compared to younger, male and non-Swiss patients, both globally (*P*=0.001) and in specific clinical services.

Conclusions

This simple two-database tool demonstrates clinical services in which HIV testing practice can be optimised. Improved testing rates in services involved in clinical trials on testing suggest that local engagement complements the effect of national recommendations. Whilst, overall, HIV testing rates increased significantly over time, testing rates were lower among patients with similar demographic profiles to individuals diagnosed late in Switzerland.

Strengths and limitations of this study

- A simple two-database tool was used to calculate HIV testing rates over a wide range of clinical services.
- The single-centre design enabled knowledge of clinical service structure and therefore the profile of patients being examined.
- Testing rates could be compared within clinical services over time.
- Although the two-database tool is simple and robust, it does not provide a 'margin of improvement' for testing rates, as it examines only testing rates and not the parameters which could influence these.
- Due to the retrospective nature of this study, the denominator taken to calculate testing rates was the number of patients visiting each service, rather than the number of patients visiting the service who presented testing indications. Changes in testing rates within a service could therefore be due to changes in the number of patients meeting screening criteria rather than changes in testing practice *per se*.

Introduction

HIV testing is key in diagnosing individuals living with HIV and in enabling engagement in care, antiretroviral treatment and viral suppression. Testing individuals early in infection reduces consequent morbidity, mortality, healthcare costs and onward transmission (1). HIV testing recommendations have been published in Switzerland by the Federal Office of Public Health (FOPH) since 2007 (2), with updates in 2010, 2013 and 2015 (3-5). The recommendations propose Physician-Initiated Counselling and Testing (PICT), which is targeted and opt-in, and requires testing to be offered to patients explicitly before being performed. The FOPH recommendations present the situations in which HIV testing is indicated, notably, symptoms and signs of acute HIV infection, AIDS-defining illness, HIV indicator diseases, and groups at high risk of HIV acquisition. The physician is responsible for recognising these situations in clinical practice.

In contrast to PICT, the HIV testing recommendations of the United States (US) (6), France (7) and the United Kingdom (UK) (8) propose non-targeted and opt-out testing in health care settings in which local HIV seroprevalence is above a certain threshold (0.1% in the US and France; 0.2% in the UK). In this case, testing is performed regardless of clinical presentation or risk factors, unless the patient explicitly declines. Patient-, doctor- and system-related barriers exist to both targeted and non-targeted testing approaches (9-11) and may delay HIV diagnosis in positive individuals. In Switzerland, almost half of patients newly-diagnosed with HIV are identified late, with CD4 counts below 350 cells/mm^3 or an AIDS-defining condition (12), suggesting that testing practice is suboptimal.

In 2012, our group examined the effect of the 2010 FOPH HIV testing recommendations on the testing rates of selected clinical services at Lausanne University Hospital (LUH), Lausanne, and reported that there was no significant change in HIV testing practice associated with the recommendations' publication (13). Among the clinical services, the emergency department (ED) and the oncology service had particularly low testing rates at, respectively, 1% and 4% of

all patients seen (13). Following the 2010 FOPH recommendations, which specifically mentioned the ED as a service in which HIV testing should take place, we observed that 82% of ED doctors in French-speaking Switzerland were unaware of national HIV testing recommendations and that even those aware did not always propose testing when indicated (14). After providing training seminars on testing indications and the practical aspects of testing to address this lack of awareness, we observed other ED doctor-related barriers to proposing testing, notably, a preference to focus on the reason(s) for presenting over discussing HIV (11). In the oncology service, we observed that HIV testing of patients diagnosed with AIDS-defining cancers (ADCs) was not universal and was especially poor among patients with invasive cervical cancer (HIV testing rate 11%) (15). To investigate barriers to HIV testing in this service, we provided information seminars for doctors and nurses on HIV testing indications and testing practice, and examined HIV testing rates among patients newly-diagnosed with *non*-ADCs. Among 239 patients enrolled in this study, the HIV testing rate increased from 4% (baseline) to 18% and patient acceptance of HIV testing offered was high (91%) (16).

In November 2013, the FOPH HIV testing recommendations were updated, differing from the 2010 recommendations in three main ways (4). First, testing indications were graded such that HIV testing should be *expressly recommended* (for acute HIV infection and AIDS-defining conditions), *recommended* (for HIV *indicator diseases*, following the results of the HIV Indicator Diseases across Europe Study (17)) or *proposed* (where not diagnosing HIV could have severe consequences or for individuals at risk of HIV acquisition). Second, patients undergoing immunosuppressive therapy, including chemotherapy, were included as a group in whom HIV testing should be *proposed*. Third, it was stated explicitly that not performing an HIV test when indicated could have medico-legal consequences.

The aim of this study was to repeat the analysis of HIV testing practice in selected clinical services at our centre, this time examining the effect on testing rates of the 2013 FOPH HIV testing recommendations.

Methods

Patient and public involvement

Patients and public were not involved in the design of this study. The research question on HIV testing practice arose from the experience of some of our patients attending our HIV outpatient service of presenting late with HIV despite having visited different services at our hospital during the years preceding their HIV diagnosis.

Ethics Statement

The study was approved by the ethics commission on human research of the canton of Vaud, Switzerland (protocol number 2016-00368). All patient data used were stripped of identifiers prior to analysis.

HIV testing

HIV testing performed in the Immunology Service uses a fourth generation screening assay to detect anti-HIV1/2 antibodies and p24 antigen (Cobas Elecsys HIV combi PT, Roche Diagnostics, Rotkreutz, Switzerland). Reactive samples undergo confirmation assays (p24 neutralisation assay and a line immunoassay for HIV-1/2 antibodies) before the release of a positive result as previously described (13). All HIV tests performed are entered in to the Immunology Service database, together with the requesting service, date of request, date of test and result.

Study setting

The study was retrospective and single-centre, performed at LUH, Lausanne, Switzerland, a 1500-bed teaching hospital where local HIV seroprevalence is estimated to be between 0.2% (estimated from Swiss HIV Cohort Study data) and 0.5% (UNAIDS estimation) (18, 19). At this centre, doctors attend regular educational seminars as is standard in a teaching hospital but without necessarily a focus on HIV.

Ten clinical services were selected for analysis: general internal medicine inpatients (IP), neurology IP, cardiology IP, intensive care units (ICU), emergency department (ED), psychiatry IP (excluding services for substance misuse where HIV testing is routine), oncology outpatients (OP), dermatology IP and OP, ear, nose and throat (ENT) surgery IP and OP, and non-ENT surgery IP (including vascular, cardiothoracic, gastrointestinal, maxillofacial surgery, urology and neurosurgery). The services were selected for ≥1 of the following reasons: 1) receiving patients likely to preset with HIV testing indications by specialty (3, 4); 2) previous target of educational interventions (ED, oncology service (11, 14, 16, 20)); and 3) enabling comparison with testing rates prior to 2012 (13). Due to the retrospective nature of this study, it was not possible to identify patients presenting specific HIV testing indications. In order to make the number of patients presenting as close as possible to the number of patients presenting with testing indications, we restricted our analysis to patients presenting to selected subunits within each clinical service. For example, for the cardiology service, we included subunits receiving acute ischaemic heart disease admissions and excluded subunits related to congenital anomalies or cardiac transplant work-ups.

Between 2012 and 2015, the oncology service underwent expansion, resulting in some units seeing a substantial increase in patient turnover. For the current study, we restricted analysis to units examined previously (13) or those taking part in clinical trials on HIV testing.

Study design

All patients aged ≥16 years old presenting to the selected clinical services between 1st January 2012 and 31st December 2015 were eligible for inclusion. Using the central hospital database, the number of patients attending each service was obtained over four 12-month blocks, corresponding to each calendar year. Dates of all hospital visits and patient demographic parameters (age, sex, origin) were also obtained from this database The number of HIV tests performed during the same 12-month blocks was obtained from the Immunology Service database.

For each 12-month block, HIV testing rates were calculated as the percentage of tests performed per number of patients seen. For the testing rate calculations, the number of patients rather than the number of clinical episodes was taken as the denominator, to avoid underestimating testing rates in clinical services which may see the same patient several times, notably in the OP sector.

For the ED, to examine the effect of local clinical trials and associated educational interventions on HIV testing, testing rates were calculated monthly in addition to 12-monthly. For 12-monthly testing rates, the entire service was analysed whereas for the monthly testing rates, analysis was restricted to the sections involved in the clinical trials. In the oncology service, testing rates were additionally compared between 2012 and 2013, in line with a clinical trial which ran from July to October 2013 (16). However, as the 2013 FOPH recommendations introduced 'proposing' testing to all patients undergoing immunosuppressive treatment, the specific effect of clinical trials after 2013 was not examined in this study. The results of these trials will be published elsewhere (manuscript in preparation).

Positive HIV tests

Occasionally, an HIV test (the fourth generation screening assay described above) is requested erroneously for patients of known positive HIV status instead of viral load. For all tests conducted and confirmed as positive, therefore, test dates were cross-referenced with electronic medical records to determine whether each positive test was a new or a known positive case.

Statistical analyses

Data are presented as means with standard deviation, medians with interquartile range and as percentages. Means were compared using Student's t-test and proportions compared using the Chi-squared test using two-way contingency tables. To examine the effect of the 2013 FOPH HIV testing recommendations, testing rates for each clinical service, and overall, were examined during the two years before and the two years after the publication of the recommendations (1st January 2012 to 31st December 2013 and 1st January 2014 to the 31st December 2015) and

then compared. Although the updated FOPH recommendations were published in November 2013, the month of December 2013 was included in the 'before' analysis given that there is usually a lag period of at least one month between recommendations being published and being read and/or implemented (13). Oncology service testing rates were additionally compared between 1st January to 31st December 2012 and 1st January to 31st December 2013.

In our 2012 report on testing, we commented that patient origin may have an effect on testing, based on the observation that the medical OP service not examined in the present study had a particularly high percentage of patients from countries with high HIV prevalence (estimated to be up to 65%, (13)). We therefore examined the effect of patient age, sex and origin on testing rates in each clinical service, and overall. Patient origin was categorised as Swiss, from neighbouring countries (France, Germany, Austria, Italy and Lichtenstein), from sub-Saharan Africa (SSA) and 'other', comprising countries not falling into the first three categories. When patient numbers were low in specific origin categories, analyses were performed by grouping patients in the latter three categories as 'non-Swiss'. Patients lacking data on origin were removed from analyses provided the proportion of patients removed was <10%; if the percentage was ≥10% in a specific service, analysis of origin data was not performed.

All analyses were performed using Microsoft Excel 2008 (Microsoft Corporation, Redmond, WA, USA).

Results

Study population

During the four-year study period, 147,884 patients were seen at the ten clinical services examined. Patient demographic profile did not change significantly during this time. In total, 9,653 patients underwent HIV testing (global HIV testing rate 6.5%). Supplementary Table 1 shows the demographic characteristics of patients tested and not tested.

The total number of patients attending the ten clinical services increased progressively over the four-year period from 34,861 to 36,460 patients but the difference in the number of patients attending before versus after the 2013 FOPH recommendations was not significant (*P*=0.14).

HIV tests and testing rates

The total number of tests performed increased over the four-year period, with a mean of 2,220±94.5 tests before and 2,803±171 tests after the 2013 FOPH recommendations (*P*=0.001). The global testing rates (for all clinical services together) also increased significantly between before and after the 2013 recommendations from 5.6%±0.2% (2012-2013) to 7.8%±0.4% (2014-2015) (*P*=0.002) (Table 1 and Figure 1). Testing rate increases were particularly marked in the ED (from 4.2%±0.3% to 5.6%±0.4%, *P*=0.001, Table 1) and the oncology service (from 3.8%±0.8% to 23.6%±7.4%, *P*=0.0001, Figure 1).

Table 1. HIV testing rates and percentage of positive tests in clinical services in which new HIV diagnoses were made [1].

	Testing rate, mean % (SD)		*P*	2012-2013		2014-2015		2012-2013	2014-2015	*P* [2]
Clinical service	2012-2013	2014-2015		Tests performed	Tests positive	Tests performed	Tests positive	% of tests positive	% of tests positive	
Neurology	20.6 (1.5)	25.5 (1.4)	0.006	433	3	550	0	0.69	0	-
Internal medicine	10.8 (0.4)	13.8 (0.8)	0.001	662	6	820	1	0.91	0.12	-
Psychiatry	11.3 (0.04)	12.4 (0.8)	0.78	345	1	376	1	0.29	0.27	-
ICU	8.6 (0.3)	9.1 (0.5)	0.97	308	0	314	1	0	0.32	-
Dermatology	4.9 (0.1)	6.0 (0.3)	0.002	811	1	987	1	0.12	0.1	-
ED	4.2 (0.3)	5.6 (0.4)	0.001	987	7	1336	11	0.71	0.82	-
ENT	1.2 (0.2)	1.8 (0.3)	0.05	67	0	126	1	0	0.79	-
Total[1]	5.6 (0.2)	7.8 (0.4)	0.002	3938	18	4792	16	0.46	0.33	0.77

[1]As no new HIV diagnoses were made in the services of surgery, cardiology and oncology, the total numbers of tests performed before and after the 2013 recommendations differ from other total figures stated in the text.

[2] The difference in the percentage of positive tests between the two time periods, 2012-2013 and 2014-2015, was not calculated for individual clinical service as the numbers involved were so small. The *P* value shown is for the difference overall (all services combined).

Abbreviations: ICU, intensive care units, ED, emergency department; ENT, ear, nose and throat service; SD, standard deviation

Positive HIV tests

In total, 18 new HIV diagnoses (0.46% of tests performed) were made between 2012 and 2013 and 16 new diagnoses (0.33% of tests performed) were made between 2014 and 2015 (Table 1). The demographic characteristics did not differ significantly between the two time periods and so are presented here for all 34 newly-diagnosed patients: median age was 42 years (IQR 34;48), 28 (82%) were men, 14 (41%) were Swiss and 20 were non-Swiss, including eight (24%) from SSA. Median CD4 count at diagnosis was 188 cells/mm^3 (IQR 32;363).

There were 30 erroneous repeat HIV tests in patients of known positive status. However, re-testing enabled two patients who had been lost to follow-up to be re-integrated into care.

The rate of positive tests out of tests performed remained stable with time in each service, at between 0 and 0.9% (Table 1), with no change between before and after the 2013 FOPH recommendations (P=0.77). There were no positive tests among patients attending the services of cardiology, surgery and oncology, although testing rates in the cardiology and surgery services were at the lower end of all services studied (Figure 1).

Effect of patient demographic profile on testing

The breakdown of patients by age, sex and origin was examined using the two study databases. Globally, the proportion of patients attending the ten clinical services who were aged below 50 did not change over the four-year period, with a mean proportion of 31.8%±0.24%. Equally, the proportion of patients aged below 50 who were tested for HIV remained stable with a mean proportion of 51.3%±1.36%. However, in some services, the proportion of patients tested was higher among patients aged below 50 than among older patients (Table 2). Testing rates were also significantly higher among male than among female patients in several clinical services and overall (Table 2).

Table 2. HIV testing rates over the four-year study period by patient demographic profile.

	Age-related rates, mean % (SD)		*P*	Sex-related rates mean % (SD)		*P*	Origin-related rates mean % (SD)		*P*
	<50	>50		Male	Female		Swiss	Non-Swiss	
Neurology	55.3 (17.5)	13.5 (1.7)	<0.001	23.1 (2.4)	23 (2.7)	0.99	20.1 (1.3)	30.6 (2.6)	<0.001
Internal medicine	20.8 (1.7)	10.9 (1.5)	<0.001	14.1 (1.8)	10.9 (0.8)	<0.001	5.0 (0.4)	6.8 (0.4)	<0.001
Psychiatry	17.2 (0.8)	4.4 (0.8)	<.0001	12.8 (0.4)	10.7 (1.0)	0.17	15.5 (1.1)	14.6 (1.2)	0.94
ICU	15.2 (1.0)	7.2 (0.6)	<0.001	9.2 (0.5)	7.9 (0.4)	0.45	7.2 (0.3)	11.8 (1.1)	<0.001
Surgery	11.3 (1.5)	3.3 (0.4)	<0.001	6.8 (0.5)	8.0 (0.6)	0.48	2.6 (0.2)	4.6 (0.5)	<0.001
Dermatology	6.1 (0.6)	4.7 (0.5)	<0.001	7.1 (0.8)	4.0 (0.4)	<0.001	4.7 (0.4)	5.6 (0.3)	0.56
ED	12.1 (1.9)	2.1 (0.4)	>0.001	5.9 (0.6)	4.0 (0.7)	<0.001	4.8 (0.9)	7.0 (0.7)	<0.001
ENT	1.7 (0.7)	1.2 (0.2)	0.28	1.8 (0.5)	1.1 (0.2)	0.007	1.3 (0.2)	1.8 (0.3)	0.78
Cardiology	4.4 (1.3)	3.8 (0.3)	0.88	4.6 (0.2)	2.4 (0.3)	<0.001	1.9 (0.2)	3.3 (0.6)	0.0002
Oncology	7.5 (2.8)	3.5 (0.9)	<0.001	16.3 (8.1)	18.4 (10.4)	0.99	NA	NA	NA
Total	9.6 (0.8)	4.3 (0.4)	0.001	7.7 (0.8)	5.9 (0.7)	<0.001	3.1 (0.4)	5.1 (0.5)	<0.001

Abbreviations: ICU, intensive care units, ED, emergency department; ENT, ear, nose and throat service; SD, standard deviation; NA, not analysed (>10% of patients without origin data)

To examine patient origin, patients were pooled as Swiss and non-Swiss as the percentage of specific groups mentioned in the 2013 recommendations, notably patients from SSA, was low (Supplementary Table 1). In several services, and overall, testing rates were significantly higher among non-Swiss compared to Swiss patients (Table 2).

In the neurology service, testing practice changed with time. While there was a significant increase in testing rates between 2012 and 2015, the testing rates increased progressively among patients aged below 50 years while the testing rate among older patients remained stable (Supplementary Figure 1). While progressive increases in testing rates were observed over time in other clinical services, no such increase was observed among patients with a specific demographic profile.

Effect of local interventions

During local educational interventions in ED sections involved in clinical trials, monthly testing rates exceeded the mean rate for the ED as a whole (Figure 2). In the oncology service, testing rates increased significantly from 12% in 2012 to 16% in 2013 (P=0.0005), when training seminars on HIV testing were provided to medical and nursing staff, in addition to increasing between before and after the 2013 recommendations as described above.

Discussion

We have applied the same two-database tool with which we examined the effect of the 2010 FOPH recommendations (13) to examine the effect of the 2013 FOPH recommendations at our centre. We observed a global increase in HIV testing following the 2013 recommendations, with significant increases in clinical services receiving educational interventions in the context of clinical trials on testing. As these services had among the lowest testing rates prior to 2012, our observed increase suggests that local engagement complements the effect of national testing recommendations.

As we observed in our previous study, testing rates in the neurology, internal medicine and psychiatry IP services were higher than those in other services (13). These three services see patients presenting with many of the conditions listed as testing indications in the 2013 recommendations. Further, the neurology and internal medicine IP services make up two of the

three principal services which receive patients admitted via the ED (OH, departmental data). Conversely, the cardiology service had relatively low testing rates. Whilst some patients attending this service may have presented with non-vascular cardiac pathology or with vascular pathology presenting non-acutely, the low testing rates are surprising given accumulating evidence of a pathophysiological link between HIV infection and endothelial damage (21, 22). However, while myocardial infarction, together with cerebrovascular events and peripheral arterial disease, was mentioned as an indication for HIV testing in the 2010 FOPH recommendations (3), it was not mentioned in the 2013 update (4), and patients presenting with acute coronary syndromes to the LUH cardiology service are not tested routinely (OM, personal communication). Among cardiology patients who were tested over the four-year period, the rate of new HIV diagnoses was zero. The finding that testing rates were lower among dermatology patients than among surgery patients is also surprising. However, this may be explained by the high patient denominator in the dermatology service, and the possibility that patients seen did not present HIV testing indications. All these observations highlight the importance of applying the two-database tool only when service structure (patient diagnosis profile, referral source, etc) is known, so that testing rates can be interpreted meaningfully.

In the ED, the testing rates were markedly higher than those reported previously (13, 14). In addition to the significant increase between before and after the recommendations, we observed a possible effect of local interventions in the form of training seminars and clinical trials. The positive effect of local interventions on HIV testing practice has been described in a London university hospital ED setting, the authors adding that constant commitment was required to achieve sustainability (23).

We observed that testing was significantly higher among non-Swiss than Swiss patients in some services. Testing rates differed with other demographic characteristics, being higher among male patients and those aged below 50 years. Due to the retrospective design of this study, we cannot identify why testing rates among Swiss, older and female patients were lower in some services, and it is possible that these patients did not present HIV testing indications. It is noteworthy, however, from Swiss HIV Cohort Study data, that older age and female sex were observed as risk

factors for late presentation among patients newly diagnosed with HIV between 2009 and 2012 (12). Perhaps future updates of Swiss HIV testing recommendations should mention the demographic profiles of individuals at risk of late presentation, to avoid under-testing patients not classically considered as high risk (1).

This study has limitations. An important limitation was that the denominator used to calculate testing rates was taken as the number of patients presenting, with no means of identifying the number of patients who had HIV testing indications. We restricted our analysis to well-characterised subunits within each clinical service to optimise the percentage of patients presenting who had testing indications but this remains a limitation of our study. As with any single-centre study, the results presented may not be applicable to other settings, particularly if service structures differ. Although this two-database tool enables testing rates to be calculated and compared over time, it does not provide a 'margin for improvement' in each setting. We have no data on the percentage of healthcare professionals aware of the FOPH HIV testing recommendations, outside the ED setting, or the percentage of patients presenting testing indications who were not tested. In this way, whilst we observed improved testing rates with time, it is possible that this occurred through factors unrelated to the publication of the 2013 FOPH HIV testing recommendations.

In conclusion, we have described a simple two-database method of measuring testing rates which enables healthcare centres to identify clinical services in which testing rates can be optimised and to follow progress with time. HIV testing rates increased at our centre over time, particularly in services involved in clinical trials on testing. The lower testing rates we observed among Swiss, older and female patients merits examination, given that patients lacking the 'classical' demography for HIV acquisition should still be included in testing initiatives if they present with indications.

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Authors' contribution statement

Tosca Lazzarino contributed to study design, data collection and manuscript preparation. Sébastien Martenet contributed to data collection, data analysis and critical review. Rachel Mamin contributed to data collection, data analysis and critical review. Renaud A. Du Pasquier contributed to critical review. Solange Peters contributed to critical review. Matthieu Perreau contributed to critical review. Olivier Muller contributed to critical review. Olivier Hugli contributed to manuscript preparation and critical review. Matthias Cavassini contributed to study design, manuscript preparation and critical review. Katharine E.A. Darling contributed to study design, data collection, data analysis, manuscript preparation and critical review.

Data sharing statement

The database used for the analyses performed in the study is available on request

Competing interests statement

All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Part of this work was presented as a poster at the 27th ECCMID meeting in Vienna, Austria, 22-25 April 2017.

Figure legends

Figure 1. Absolute number of HIV tests requested (Panel A) and HIV testing rate (Panel B) with time in the ten clinical services studied.

Asterisks indicate significant differences in rates (P<0.01) between before (2012-2013) and after (2014-2015) the publication of the Federal Office of Public Health HIV testing recommendations in November 2013.

Abbreviations: ICU, intensive care units; ED, emergency department; ENT, ear, nose and throat service.

Figure 2. Monthly HIV testing rates in the emergency department (ED) sections involved in clinical trials on HIV testing and the temporal relationship between HIV testing rates and clinical trials (black bar groups, 1 and 3), other training seminars (black bar group 2), and the publication of Federal Office of Public Health HIV testing recommendations (arrows, 2013 and 2015). The dotted line indicates the mean testing rate for all ED sections for the year 2012, the first year of this study.

[1]Clinical trial examining patients' understanding of and attitudes to HIV testing in the ED (20)

[2]Training seminars on testing following the publication of low awareness of HIV testing recommendations among ED doctors in French-speaking Switzerland (14)

[3]Clinical trial examining patient- and doctor-associated barriers to HIV testing in the ED and patient acceptance of rapid HIV testing (11)

Supplementary Figure 1. Number of patients aged < 50 and ≥ 50 years old who attended the neurology service over the four-year study period showing numbers of patients tested (black) and untested (grey) in each age category.

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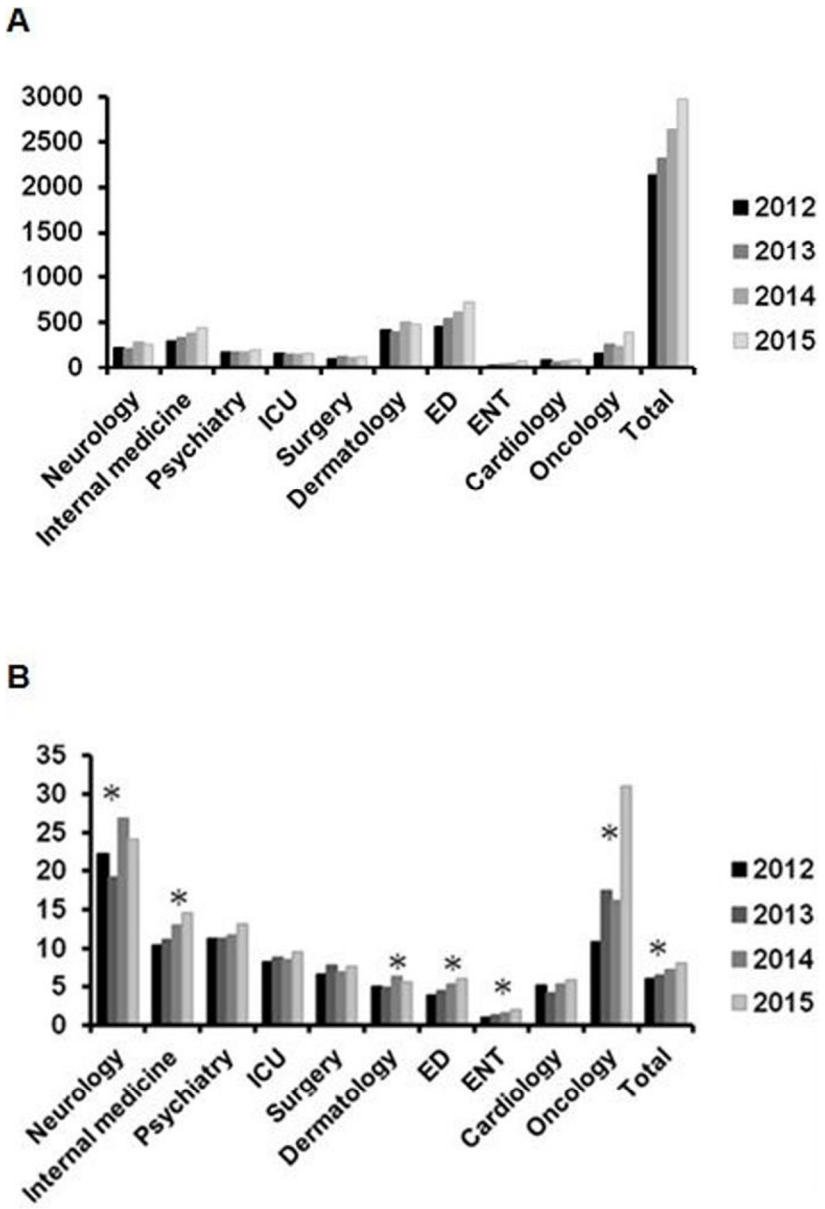

Figure 1. Absolute number of HIV tests requested (Panel A) and HIV testing rate (Panel B) with time in the ten clinical services studied.
Asterisks indicate significant differences in rates (P<0.01) between before (2012-2013) and after (2014-2015) the publication of the Federal Office of Public Health HIV testing recommendations in November 2013.
Abbreviations: ICU, intensive care units; ED, emergency department; ENT, ear, nose and throat service.

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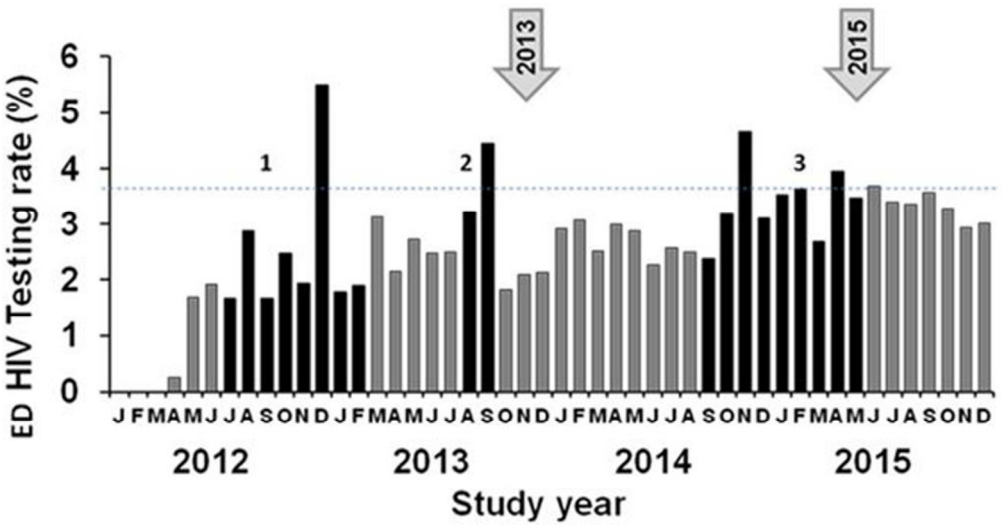

Figure 2. Monthly HIV testing rates in the emergency department (ED) sections involved in clinical trials on HIV testing and the temporal relationship between HIV testing rates and clinical trials (black bar groups, 1 and 3), other training seminars (black bar group 2), and the publication of Federal Office of Public Health HIV testing recommendations (arrows, 2013 and 2015). The dotted line indicates the mean testing rate for all ED sections for the year 2012, the first year of this study.

1Clinical trial examining patients' understanding of and attitudes to HIV testing in the ED (20)
2Training seminars on testing following the publication of low awareness of HIV testing recommendations among ED doctors in French-speaking Switzerland (14)
3Clinical trial examining patient- and doctor-associated barriers to HIV testing in the ED and patient acceptance of rapid HIV testing (11)

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Supplementary Table 1. Demographic characteristics of patients visiting the ten clinical services who were HIV tested or not HIV tested[1].

Clinical Service	M/F	Tested					Not tested				
		No. (%)	Swiss No. (%) Median Age [yrs] (range)	Neighbour countries No. (%) Median Age [yrs] (range)	SSA No. (%) Median Age [yrs] (range)	Other/ unknown No. (%) Median Age [yrs] (range)	No. (%)	Swiss No. (%) Median Age [yrs] (range)	Neighbour countries No. (%) Median Age [yrs] (range)	SSA No. (%) Median Age [yrs] (range)	Other/ unknown No. (%) Median Age [yrs] (range)
Neurology	M	595 (51)	411 (69) 65 (16-92)	72 (12) 60 (18-89)	11 (1.8) 45 (22-62)	101 (17) 51 (16-83)	1,491 (51)	1,084 (73) 72 (17-99)	182 (12) 72 (16-94)	13 (0.9) 55 (24-80)	212 (15) 59 (18-93)
	F	559 (49)	403 (72) 60 (16-95)	53 (9.5) 52 (16-87)	7 (1.2) 39 (16-55)	96 (17) 41 (16-87)	1,416 (49)	1,133 (80) 77 (16-102)	102 (7.5) 74 (19-95)	14 (1) 35 (28-56)	167 (11) 53 (16-95)
Internal medicine	M	1,439 (60)	960 (67) 67 (17-98)	158 (11) 71 (23-90)	43 (3) 49 (19-82)	278 (19) 58 (16-90)	3,766 (49)	2,776 (73.5) 76 (16-101)	470(12.5) 75 (27-97)	47(1.5) 46 (18-87)	473(12.5) 63 (16-100)
	F	940 (40)	688 (73) 68 (17-95)	81 (8.6) 71 (19-90)	32 (3.4) 38 (20-64)	139 (15) 55 (18-87)	3,859 (51)	3,104 (80) 82 (17-105)	333 (8.6) 80 (22-100)	37 (1) 50 (18-88)	385 (10) 63 (18-100)
Psychiatry	M	505 (58)	304 (60) 38 (17-93)	60 (12) 44 (20-87)	29 (5.7) 38 (19-45)	112 (22) 35 (18-76)	1,904 (50)	1,184 (62) 48 (16-99)	219 (11) 47 (18-96)	71 (3.7) 34 (18-65)	430 (23) 41 (16-92)
	F	362 (42)	238 (66) 42 (16-93)	29 (8) 44 (17-92)	11 (3) 27 (20-73)	84 (23) 39 (18-85)	1,902 (50)	1,379 (73) 56 (16-104)	158 (8.3) 47 (19-88)	61 (3.2) 36 (16-74)	304 (16) 39 (16-91)

ICU	M	927 (68)	618 (67) 61 (16-89)	111 (12) 61 (20-87)	21 (2.3) 47 (19-80)	177 (19) 53 (19-85)	3,593 (65)	2,562 (71) 68 (16-96)	447 (12.2) 65 (16-91)	27 (0.8) 42 (17-78)	557 (15) 55 (16-91)
	F	429 (32)	311 (73) 60 (16-90)	32 (7.5) 62 (28-85)	12 (2.8) 36 (26-55)	74 (17) 51 (22-89)	1,942 (35)	1,511 (78) 70 (16-96)	149 (7.7) 73 (18-94)	15 (0.8) 40 (18-73)	267 (14) 55 (17-94)
Surgery	M	584 (67)	400 (68.5) 63 (16-94)	62 (10.6) 65 (21-84)	16 (2.7) 38 (19-70)	106 (18.2) 53 (18-84)	2,866 (61)	2,098 (73.2) 68 (16-97)	327 (11.4) 69 (18-98)	31 (1.1) 41 (20-78)	410 (14.3) 58 (18-98)
	F	291 (33)	223 (77) 59 (17-90)	20 (6.9) 68 29-89)	8 (2.7) 56 (26-70)	40 (14) 44 (25-79)	1,839 (49)	1,436 (78) 70 (16-100)	144 (7.8) 69 (20-100)	17 (0.9) 44 (17-64)	242 (13) 50 (20-100)
Dermatology	M	1,631 (62)	1,029 (63) 59 (18-71)	184 (11) 48 (16-99)	72 (4.4) 34 (17-87)	346 (21) 43 (16-83)	9,317 (46)	5,820 (62.5) 60 (16-101)	1,233 (13.2) 49 (16-96)	307 (3.3) 34 (16-80)	1,957 (21) 45 (16-96)
	F	1,001 (38)	673 (67.2) 59 (17-88)	32 (3.2) 52 (16-96)	30 (3.0) 52 (19-85)	266(26.6) 43 (16-82)	11,083 (54)	7,095 (64) 54 (16-105)	1,172 (11) 45 (16-101)	265 (2.4) 33 (17-72)	2,551 (23) 39 (16-94)
ED	M	2,853 (60)	1,791 (62.8) 64 (16-98)	315 (11) 62 (18-90)	139 (4.9) 37 (17-83)	608 (21.3) 52 (16-90)	17,985 (52)	11,923 (66) 68 (16-105)	2,138 (12) 42 (16-99)	434 (2.4) 55 (16-87)	3,490 (19) 50 (16-111)
	F	1,864 (40)	1,291 (69.2) 63 (16-95)	164 (8.8) 66 (16-90)	59 (3.2) 37 (19-69)	350 (18.8) 46 (16-90)	16,672 (48)	12, 577 (75) 70 (16-106)	1,405 (8.4) 40 (16-102)	262 (1.6) 55 (16-88)	2,428 (16) 50 (16-100)
ENT	M	538 (78)	267 (49.6) 54 (17-93)	54 (10) 63 (27-85)	16 (2.8) 31 (19-57)	201 (37.6) 50 (17-78)	5,747 (52)	3,232 (56.2) 53 (16-95)	744 (12.9) 49 (16-101)	142 (2.5) 36 (16-74)	1,629 (28.4) 46 (16-92)
	F	260 (22)	175 (67.3) 56 (17-93)	20 (7.7) 52 (21-85)	12 (4.6) 23 (21-65)	53 (20.4) 42 (20-80)	5,003 (48)	3,379 (67.5) 56 (16-95)	460 (9.2) 50 (16-96)	81 (1.6) 38 (16-68)	1,083 (21.7) 46 (16-92)

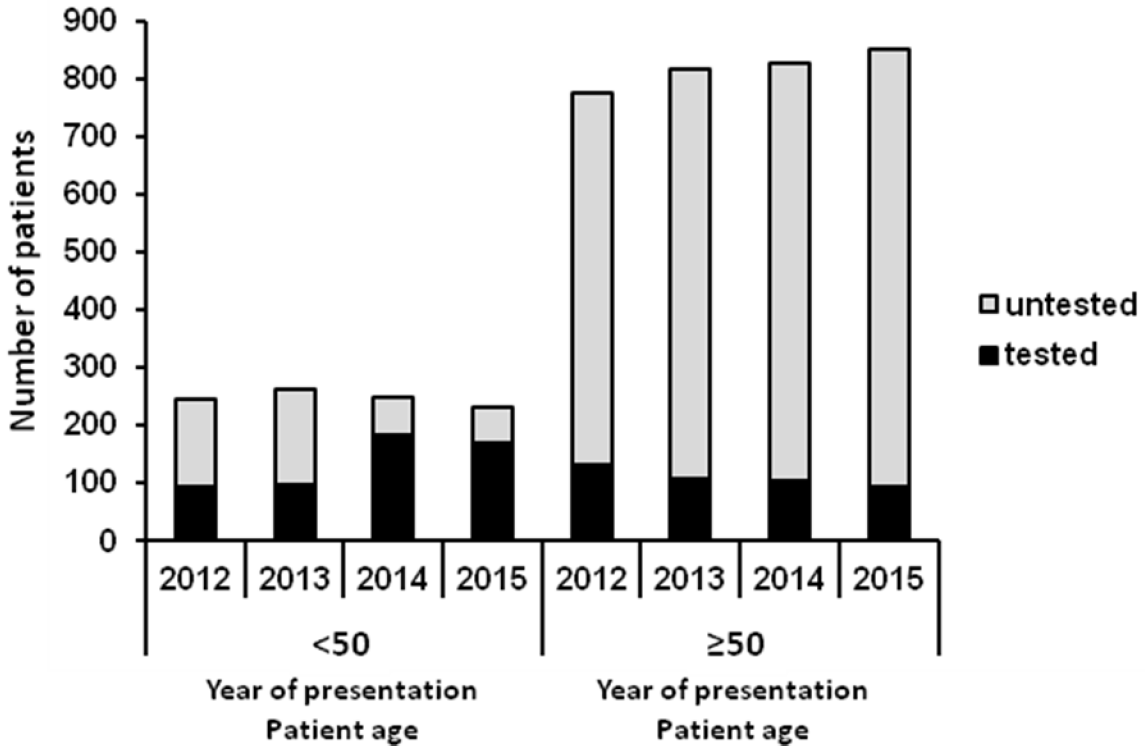
Cardiology	M	633 (74)	431 (68) 62 (20-95)	73 (12) 61 (22-83)	15 (2.4) 50 (24-73)	114 (18) 56 (16-83)	4,562 (67)	3,327 (73) 68 (16-98)	529 (12) 67 (17-99)	28 (0.6) 48 (23-76)	678 (16) 56 (16-97)
	F	224 (26)	167 (75) 60 (17-95)	20 (8.9) 70 (28-83)	5 (2.2) 37 (20-64)	32 (14) 57 (27-86)	2,279 (33)	1,787 (78) 73 (16-99)	207 (9.1) 75 (19-94)	15 (0.6) 49 (30-69)	270 (12) 55 (18-99)
Oncology	M	686 (63)	472 (71) 65 (23-90)	81 (12) 71 (23-90)	18 (2.7) 38 (19-72)	115 (18) 56 (17-85)	5,688 (48)	3,840 (67) 65 (16-99)	684 (12) 72 (16-100)	58 (1.0) 39 (18-76)	1,106 (20) 56 (16-94)
	F	401 (37)	313 (73) 60 (18-94)	26 (6.1) 68 (18-87)	6 (1.4) 46 (36-64)	56 (13) 51 (22-79)	6,246 (52)	4,409 (71) 60 (16-100)	563 (9) 68 (16-102)	86 (1.4) 46 (17-72)	1,188 (19) 51 (16-94)

[1] Figures presented are derived from the entire four-year study period. In this way, individual patients (not tested) have been counted once only, no matter how many times they may have presented and specific values may differ from elsewhere in the results section.

[2] Tested patients may have been tested more than once in different services, or undergone tests of confirmation. In this way, patient numbers may be greater than those cited elsewhere in the results section.

[3] Neighbour countries: France, Germany, Austria, Italy and Lichtenstein

Abbreviations: ICU, intensive care units, ED, emergency department; ENT, ear, nose and throat service



STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	#1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	#2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	#5
Objectives	3	State specific objectives, including any pre-specified hypotheses	#6
Methods			
Study design	4	Present key elements of study design early in the paper	#7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	#7
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	#7-#8
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	#7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	#8-#9
Bias	9	Describe any efforts to address potential sources of bias	#8
Study size	10	Explain how the study size was arrived at	#7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	#9-#10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	#9-#10
		(*b*) Describe any methods used to examine subgroups and interactions	#9-#10
		(*c*) Explain how missing data were addressed	#9-#10
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	#10

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	#10
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Supp Table 1
		(b) Indicate number of participants with missing data for each variable of interest	
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	#10-#16
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	#10-#16
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	#10-#16
Discussion			
Key results	18	Summarise key results with reference to study objectives	#16
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	#18
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	#18
Generalisability	21	Discuss the generalisability (external validity) of the study results	#18
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	#19, #5

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.