

A prospective evaluation of the feasibility and utility of additional tools to obtain information from recently diagnosed HIV infected patients

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Summary

Question under study: Can additional information be obtained from recently HIV diagnosed individuals?

Methods: A 1-year prospective Swiss study, including all newly diagnosed HIV-infected patients. Information on circumstances of HIV infection was collected through physician- and patient questionnaires and patient interviews. Information on timing of infection was linked with an HIV-antibody avidity assay.

Results: Of 710 newly HIV diagnosed patients, 543 (76%) physician questionnaires (PhyQ) and 145 (20%) patient questionnaires (PaQ) were returned. PhyQ required fewer reminders (57% vs 28% spontaneous return). Patients whose doctors had returned the PhyQ were comparable to total population group. In contrast, a strong bias towards well educated recently infected Swiss men having sex with men (MSM) was seen in patients returning PaQ or agreeing to an interview. 83% of patients claimed that they knew

the infection source and 85% infection place. Unprotected sexual contact was the most frequently cited infection source (92%; n = 404). Men mainly claimed occasional (43%) and women steady (61%) partners as the most likely source of HIV-infection. Serum for timing of infection was available in 98% of patients. Recent infections (RI) were highest in MSM (51%) and intravenous drug users (IDU, 54%). Compared to women, heterosexual men were more than twice as likely to be diagnosed with a RI.

Conclusion: Relevant additional information on circumstances of HIV infection in newly diagnosed patients can easily be collected from treating physicians. Collecting information from patients is not a feasible option, with the exception of qualitative interviews in a selected group of patients.

Key words: HIV infection; feasibility; return rate; circumstances; recent infections; partner type

Introduction

For 20 years, the Swiss Federal Office of Public Health (SFOPH) has collected epidemiological data on all newly diagnosed HIV infections in Switzerland [1, 2]. These data are retrieved through a primary physician questionnaire, including questions on risk behaviour, stages and clinical signs of HIV infection. However, detailed information on circumstances, place, and timing of HIV infection is missing. Personal observations from clinical cases suggest that it should be possible to obtain additional data relevant for prevention efforts both from treating physicians and their patients.

Knowledge on how and where HIV is currently being transmitted, and who has recently

been infected will provide important information on current and future HIV transmission modes. Thus, preventive efforts can be targeted or adapted to address specific risk groups. The Swiss Aids Transmission (CHAT) study was set up to evaluate the feasibility and usefulness of collecting additional detailed information from newly diagnosed HIV patients, including an estimate on timing of infection.

Various serological testing algorithms for recent HIV seroconversion (STARHS) have been developed in order to distinguish between recent and older infections in HIV-infected individuals. These tests make use of the fact that both the concentration and affinity of HIV antibodies in

early infection are lower than at later stages [3, 4]. One such test is the HIV-1 BED incidence enzyme immunoassay (EIA) (named after the

branched peptide sequences for HIV subtypes B, E, D used in the assay) [5].

Methods

Study design: data were collected prospectively between July 05 and June 06. All patients >16 years of age with a newly diagnosed HIV infection were included in the study. The study was approved by the local ethical committee.

Patient data were collected through the regular SFOPH physician questionnaire (CF), an additional CHAT physician questionnaire, a CHAT patient questionnaire, a patient interview and a blood sample. For subsequent data merger, coordination and patient anonymity, all patients were given an individualised study-ID.

I. The SFOPH physician questionnaire (CF): upon confirmation of an HIV infection, physicians are asked to complete a complementary form (CF) distributed by the SFOPH.

II. The CHAT physician questionnaire (PhyQ): physicians were asked to complete an additional CHAT questionnaire. The PhyQ aimed at collecting additional information on place (geographical location) circumstances (partner type) of infection, as well as signs and symptoms of primary HIV infection (PHI).

III. The CHAT patient questionnaire (PaQ): patients were asked to fill in a separate questionnaire, which was available in all three national languages (German, French, Italian) and English. As a result, only patients fluent in one of these 4-languages were able to complete this questionnaire. As all patients remained anonymous, treating physicians were responsible for forwarding questionnaires to patients. The PaQ aimed at collecting additional information on timing, circumstances (partner type, condom use), sexual practices and signs and symptoms of primary HIV infection (PHI). The PaQ was available in a long (14 pages) and a short version (6 pages). Both questionnaire versions were distributed (at random) to patients (questionnaires details under www.infekt.ch).

IV. A qualitative interview with consenting patients: on PaQ, patients had the option to sign up for a personal in-

terview. Qualitative interviews were performed and evaluated by the „Fachhochschule Nordwestschweiz in Olten, Hochschule für Soziale Arbeit, Institut für Integration und Partizipation“. Results are presented elsewhere (only in German)

(http://www.bag.admin.ch/hiv_aids/00829/03471/index.html?lang=de).

V. Estimation of timing of HIV infection – the HIV-1 BED Incidence assay: to supplement clinical information on the timing of HIV infection, the HIV-1 BED incidence assay (Calypte Biomedical Corporation, Lake Oswego, Oregon, USA) was performed. The BED assay has been used in several epidemiological studies [6–8]. Further details on the use of the BED HIV-1 assay to estimate incidence are available [9].

Patient blood samples were coded and tested batchwise at the Swiss National Centre for Retroviruses (SNCR). Timing of infection was divided into recent infections (<6 month upon HIV-diagnosis) and older infections (>6 month prior to diagnosis). Results of this sub analysis have been published elsewhere [10].

Feasibility testing

Feasibility measurement was based on questionnaire return rate and response rate to individual questions in the questionnaire (completeness). A reminder system was put in place, with a maximum of 2 reminders, for both PhyQ and PaQ (in written). In both cases, physicians were provided with a cross out option indicating reason(s) for missing or not returned questionnaires. Feasibility of laboratory testing regarding timing of infection was based on the availability of additional blood samples.

Definition of Swiss nationality

For this study, foreigners with a permanent Swiss residence >10 years were considered as “Swiss nationals”. A similar exposure, to the Swiss HIV prevention campaign was assumed.

Results

Feasibility

During the study period, a total of 710 newly diagnosed HIV infections were reported. Of those, 543 PhyQ were completed and returned to the CHAT study centre, 67 were returned empty and 100 PhyQ were never returned. Reasons for the 167 empty or missing PhyQ included physician refusal (65%), patient refusal (7%), or physicians' inability to complete the questionnaire (28%, eg, patient disappearance, living abroad, not able, or deceased). Figure 1 shows a flow chart of CHAT questionnaire return rate.

Return rate of PhyQ was clearly higher (76%, 543/710) than the PaQ (27%, 145/543). However, the low return rate of PaQ includes 117 patients

who could not be reached for reasons of language. In addition, considerably more effort was needed to collect PaQ compared to PhyQ. In total 64% (271/426) of PaQ had to be reminded at least once, compared to 35% (246/710) PhyQ (figure 2).

After language screening, 426 (78%, 426/543) PaQ could be sent to treating physicians who forwarded them to the respective patient. Physicians were later contacted regarding PaQ distribution. 361 (66%, 361/543) physicians confirmed having forwarded the PaQ to patients (loss = 65 PaQ). Reasons for not forwarding PaQ to patients were: patient unknown (n=36), patient living abroad (n = 15), patient not able or deceased (n = 14). A higher proportion of German speaking patients

Figure 1
Flow chart of CHAT questionnaire return rate.

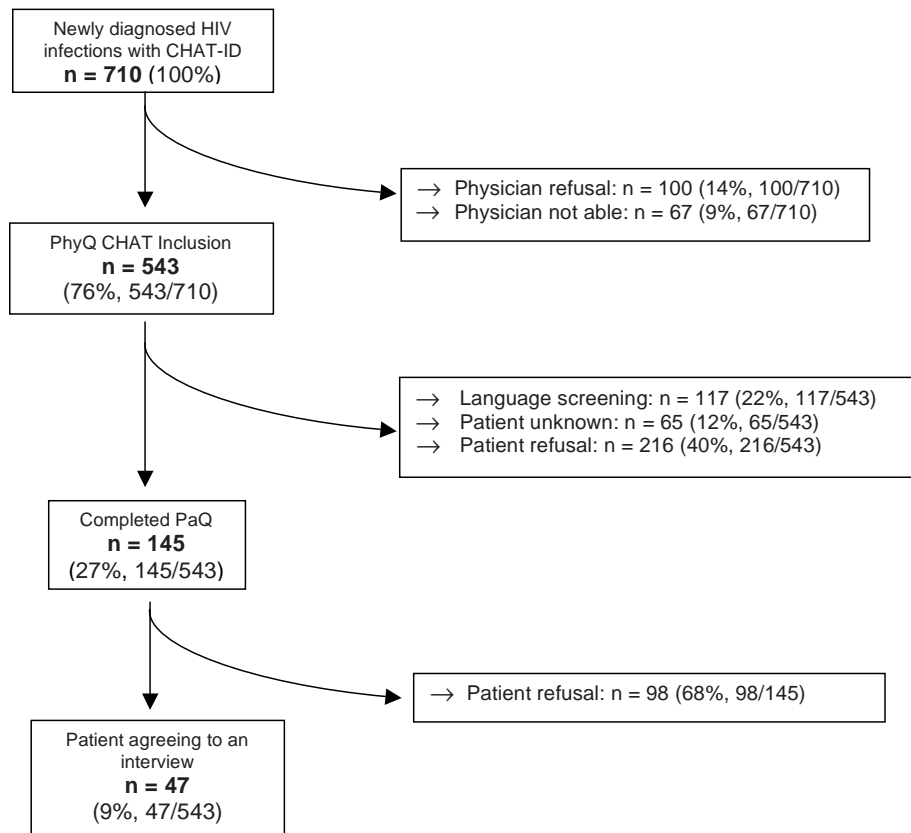
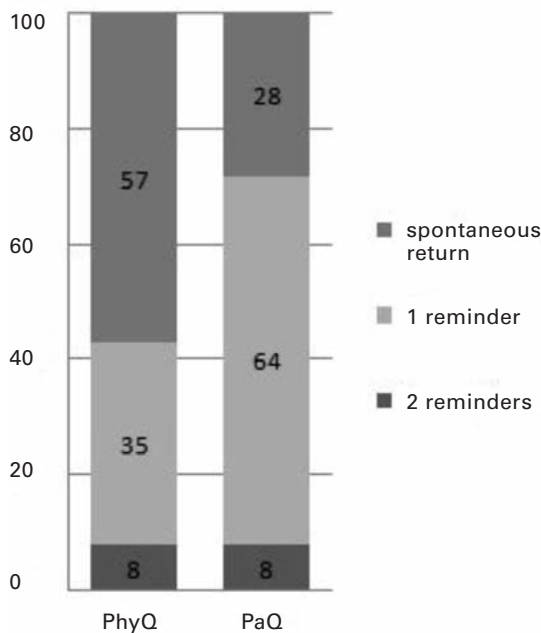


Figure 2
Demonstrated additional effort needed for the return of PhyQ and PaQ.



Of the 710 physician questionnaire (PhyQ) sent out, 610 were returned (n = 543 completed, n = 67 empty). Of the 426 patient questionnaires (PaQ) sent out, 145 were returned to the CHAT study centre. Spontaneous return represented those questionnaires returned without any preceding reminders.

(46%, 97/212 received a German PaQ) completed the PaQ as opposed to French (36%, 35/98 received a French PaQ), Italian (32%, 6/19 received an Italian PaQ), or English (22%, 7/32 received an English PaQ). Questionnaire length had no effect on return rate, with a 35% (29/82 received PaQ) return rate for the short and 38% (32/85 received PaQ) return rate for the longer version of the questionnaire. A total of 47 patients (9%, 47/543) patients agreed to an interview (11% of 426 total questionnaires sent out).

Of the 543 PhyQ, 11 (2%) patients had no BED test result. Reasons for missing BED results were not enough serum (n = 3), samples never reaching the NCR laboratory (n = 6), anonymous testing (n = 2).

CHAT population characteristics

Table 1 shows the demographics of newly diagnosed HIV patients during the study period. The total patient population (n = 710) did not differ from the patient population included in the CHAT survey (n = 543). Gender distribution, age, transmission mode, nationality and timing of HIV infection were comparable between the two groups. In contrast, a clear selective trend was seen in patients completing the PaQ (n = 145) or agreeing to a personal interview (n = 47). Male

sex, higher level of education, homosexual transmission and Swiss nationality were over represented in these two groups. In addition, patients with a recent infection were more likely to fill in the PaQ and agree to an interview (table 2).

The majority of newly diagnosed HIV infections occurred in Swiss men, through homosexual transmission. On average, women were younger than men at the time of diagnosis. The majority of foreigners were of African origin, with a larger

Table 1

Demographics of all newly diagnosed HIV patients during the study period, with a comparison between patients with a completed physician questionnaire (PhyQ), patient questionnaire (PaQ), or agreeing to a personal interview.

	All patients n = 710	PhyQ n = 543	PaQ n = 145	Interview n = 47
Gender n; (% of total)				
– men	489 (66%)	372 (69%)	128 (88%)	43 (91%)
– hetero men	133 (28%)	110 (30%)	18 (12%)	3 (6%)
– women	240 (34%)	169 (31%)	17 (12%)	4 (9%)
– unknown	2 (<1%)	2 (<1%)	–	–
Age; mean (SD) years				
– Total	38 (11)	38 (11)	40 (10)	39 (10)
– men	39 (11)	39 (11)	41 (11)	39 (10)
– women	36 (11)	35 (10)	37 (10)	31 (3)
Education n; (% of total)				
– can read/write	–	35 (6%)	4 (3%)	1 (2%)
– primary school.	–	135 (22%)	19 (13%)	6 (13%)
– t/hs/uni ¹	–	318 (52%)	117 (81%)	39 (83%)
– unknown	–	122 (20%)	5 (3%)	1 (2%)
Transmission source known: n, (% of total)				
– Yes	–	437 (83%)	122 (84%)	42 (89%)
– No	–	91 (17%)	23 (16%)	5 (11%)
– No answer	–	15 (3%)	–	–
Transmission mode n; (% of total)				
– heterosexual	317 (45%)	256 (47%)	34 (24%)	7 (15%)
– MSM	253 (36%)	218 (40%)	98 (71%)	37 (79%)
– IDU	57 (8%)	39 (7%)	5 (4%)	2 (4%)
– other/unknown	83(12%)	30(6%)	8 (6%)	1 (2%)
Nationality² n; (% of total)				
– Swiss	362 (51%)	320 (59%)	115 (79%)	40 (85%)
– hetero	126 (18%)	108 (20%)	24 (17%)	11 (11%)
– MSM3	178 (25%)	168 (31%)	82 (57%)	33 (70%)
– IDU4	40 (6%)	35 (5%)	4 (3%)	2 (2%)
– other/unknown	18 (2%)	15 (3%)	5 (3%)	–
– Non-Swiss	302 (43%)	223 (41%)	30 (21%)	7 (15%)
– Europe	–	54 (9%)	17 (12%)	5 (11%)
– Africa	–	118 (20%)	9 (6%)	1 (2%)
– other	–	42 (14%)	4 (3%)	–
– unknown	–	9 (2%)	–	1 (2%)
– Unknown	46 (6%)	–	–	–

¹ Swiss nationality = all Swiss nationals and patients with permanent residence in Switzerland > 10 years;

² t/hs/uni = traineeship / high school diploma / university degree; 3 MSM = men who have sex with men; 4 IDU = intravenous drug users

percentage of foreigners in the female population compared to men (79% vs. 50%, respectively)

Additional information on timing, source and place of HIV infection

Eighty percent of patients (437/543) said they knew or had some idea as to how they became infected with HIV. MSM were most knowledgeable, with only 21 men (10%, of total MSM) claiming not to know their infection source compared to 18% and 26% among heterosexual men and women, respectively. Among patients claiming to know the infection source, 85% (373/437) indicated unprotected sexual contact (SC) as the only possible infection source. Patients indicating SC as a source of

HIV infection had the option of giving further specifications as to the most likely “partner type” involved during HIV transmission. A very high percentage of patients (93%) were able to provide this additional information. Among MSM and heterosexual men, occasional partners were the most frequently mentioned source of infection, followed by steady, anonymous, and unknown partners. In women, the steady partner was by far the most frequently mentioned risk partner, followed by occasional, anonymous, and unknown partners (table 3).

All patients answered the question on place of HIV infection, with 84% (454/543) claiming to know where they got infected. Switzerland was the

Table 2

Recent infections (RI), nationality and gender in newly diagnosed HIV patients, with a comparison between patients with a completed physician questionnaires (PhyQ), patient questionnaire (PaQ), or agreeing to a personal interview.* BED results (timing of infection) were not available in all patients. Total sample size is smaller than for demographics (table 1)

	All patients n = 597*	PhyQ n = 532*	PaQ n = 145	Interview n = 47
RI and source of infection				
Total	223 (37%)	196 (37%)	70 (48%)	22 (47%)
- MSM (% of total MSM)	-121 (52%)	-111 (51%)	-53 (54%)	-
- Hetero (% of total hetero)	-61 (22%)	-57 (22%)	-13 (38%)	-
- IDU (% of total IDU)	-27 (57%)	-21 (54%)	-2 (40%)	-
- other / unknown (% of total o/u)	-14 (32%)	-7 (25%)	-2 (25%)	-
RI and nationality**				
Total CH with BED results	332	314	-	-
- Swiss with RI (% of total CH with BED)	-162 (49%)	-152 (48%)	-	-
Total foreigners with BED results	253	218	-	-
- Foreigners with RI (% of total foreigners with BED)	-56 (22%)	-44 (20%)	-	-
RI and gender n (% of total hetero with BED)				
- hetero men	-38 (32%)	-36 (33%)	-7 (39%)	-
- hetero women	-23 (12%)	-21 (15%)	-6 (38%)	-

* BED results (timing of infection) were not available in all patients. Total sample size is smaller than for demographics (table 1)

** Swiss nationality = all Swiss nationals and patients with permanent residence in Switzerland >10 years

Table 3

Unprotected sexual contact as a source of HIV infection and distribution of partner type(s) (steady, occasional, anonymous, unknown/no response) as indicated by patients on the PhyQ.

Partner type	Infection route: unprotected sexual contact # patients (%)		
	MSM	Hetero. men	Women
Steady	45 (24%)	26 (30%)	62 (61%)
Occasional	86 (45%)	36 (41%)	29 (29%)
Anonymous	37 (20%)	18 (21%)	2 (2%)
Unknown/ no response	22 (12%)	7 (8%)	7 (7%)
Total patients (n)	190	87	100

most frequently cited place (57%; 259/454), with a minority claiming HIV infection outside Switzerland. Swiss nationals in particular, indicated Switzerland as the most likely place of infection (72% of Swiss nationals). Of Swiss nationals infected abroad, 70% (n = 55) indicated having been on a tourist or business trip as compared to permanent residence 30% (n = 24). In Switzerland, most patients indicated a city (89%) as opposed to agglomeration (5%) or more rural (6%) areas as the most likely place of infection. The most frequently cited cantons of HIV acquisition were the canton of Zurich (79 reported cases), followed by Geneva (n = 37) and Vaud (n = 24).

Information on recentness of HIV infection (BED assay) was available in 532 patients (with a

PhyQ). Results on recency are shown in table 2. RI were particularly frequent in MSM (51%, 111/218), and IDU (54%, 21/39), with lower levels in the heterosexual population (22%, 57/256). In heterosexuals, men were more than twice as likely to be diagnosed with a recent infection compared to women (35%, 38/110 vs. 14%, 23/169). In addition, Swiss nationals were more than twice as likely to be diagnosed with a recent infection compared to foreigners. Most foreigners who reported having been infected outside Switzerland were diagnosed with an old infection (92%, n = 103). In contrast, Swiss nationals infected outside Switzerland during a holiday or business trip, showed a high percentage of recent infections (65%, n = 55).

Discussion

The CHAT study is the first study to collect information directly from newly HIV diagnosed patients. An unexpectedly high proportion of patients answered the additional questions included in the PhyQ and PaQ, confirming the feasibility of collecting increased detailed information from newly diagnosed HIV infected patients. This study shows that patients were not only surprisingly aware of

how and where they might have been infected with HIV, but were also able to provide further detailed information regarding the most likely partner type involved during HIV transmission. Nonetheless the source of information highly determined return rate with a better return rate for the PhyQ including considerably fewer reminders. Surprisingly, for the PaQ other factors besides total questionnaire

length determined return rate in this population group. Regional aspects and language seemed to have a greater impact, with German speaking patients having the highest return rate compared to French, Italian or English speaking patients.

Despite a loss of 23% (n = 167), population characteristics of patients with a completed PhyQ were comparable to the total patient population newly diagnosed with HIV. In contrast, returned PaQ showed a strong bias towards well educated Swiss homosexuals, making this source of information considerably less representative. A handicap of the PaQ was the necessity to screen for language, discriminating against patients unable to speak one of the Swiss national languages or English.

For future systematic epidemiological monitoring, the HIV-1 BED incidence assay was evaluated as a potential tool for monitoring recent infections in Switzerland. In this study, an additional blood test was available for almost all patients, supporting the feasibility of such a monitoring system. MSM and IDU had an increased probability of being diagnosed with a RI. This result is most probably driven by the fact that practitioners are increasingly sensitised to HIV screening in these groups. In contrast, migrants mostly of African origin were more frequently diagnosed with an old infection, consistent with an HIV acquisition prior to arriving in Switzerland. In heterosexuals, women were considerably less likely to be diagnosed with a recent infection. A higher percentage of foreigners in the female population might partly explain for this difference. In addition, a short holiday or business trip might increase HIV risk behaviour. These patients might very well have been aware of an increase in HIV risk behaviour during their journey, initiating an HIV screening test after returning to Switzerland.

As expected, cities such as Zurich, Geneva and Lausanne were designated as high-risk areas, with more rural areas being less important.

In conclusion, information regarding timing, source and place of HIV infection in newly diagnosed individuals can easily be obtained from reporting physicians. Based on findings from this study, the physician CF distributed by the SFOPH has been adapted to include this additional information. Ability to monitor potential changes in HIV transmission trends could thus be improved. As a result, prevention messages can more easily be adapted or tailored to current or future risk behaviour, specifically focusing on aspects such as gender, nationality, specific risk situations and geographical areas.

Timing of HIV infection can be used as a novel standard or quality control for the ability of the health care system to detect patients in the earliest and most infectious stages of HIV-infection [11]. This would not only optimise patient care but would also insure the spread of presently important HIV prevention messages at an early stage of infection, when transmission risk is at its highest.

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References

- Gebhardt M. Recent trends in new diagnoses of HIV infections in Switzerland: probable increase in MSM despite an overall decrease. *Euro Surveill.* 2005;10(12):E051208.
- Gebhardt M. Rates of new HIV diagnoses in Switzerland remain high but no longer rising. *Euro Surveill.* 2005;10(2):E050217.
- Janssen RS, Satten GA, Stramer SL, Rawal BD, O'Brien TR, Weiblen BJ, et al. New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes. *JAMA.* 1998;280(1):42-8.
- Parekh BS, McDougal JS. Application of laboratory methods for estimation of HIV-1 incidence. *Indian J Med Res.* 2005;121(4):510-8.
- Parekh BS, Kennedy MS, Dobbs T, Pau CP, Byers R, Green T, et al. Quantitative detection of increasing HIV type 1 antibodies after seroconversion: a simple assay for detecting recent HIV infection and estimating incidence. *AIDS Res Hum Retroviruses.* 2002;18(4):295-307.
- Hu DJ, Vanichseni S, Mock PA, Young NL, Dobbs T, Byers RH Jr, et al. HIV type 1 incidence estimates by detection of recent infection from a cross-sectional sampling of injection drug users in Bangkok: use of the IgG capture BED enzyme immunoassay. *AIDS Res Hum Retroviruses.* 2003;19(9):727-30.
- Fang CT, Field SP, Busch MP, Heyns AP. Human immunodeficiency virus-1 and hepatitis C virus RNA among South African blood donors: estimation of residual transfusion risk and yield of nucleic acid testing. *Vox Sang.* 2003;85(1):9-19.
- Gouws E, Williams BG, Sheppard HW, Enge B, Karim SA. High incidence of HIV-1 in South Africa using a standardized algorithm for recent HIV seroconversion. *J Acquir Immune Defic Syndr.* 2002;29(5):531-5.
- Gupta SB, Gill ON, Graham C, Grant AD, Rogers PA, Murphy G. What a test for recent infection might reveal about HIV incidence in England and Wales. *AIDS.* 2000;14(16):2597-601.
- Schupbach J, Gebhardt MD, Tomasik Z, Niederhauser C, Yerly S, Burgisser P, et al. Assessment of recent HIV-1 infection by a line immunoassay for HIV-1/2 confirmation. *PLoS Med.* 2007;4(12):e343.
- Pilcher CD, Tien HC, Eron JJ Jr, Vernazza PL, Leu SY, Stewart PW, et al. Brief but efficient: acute HIV infection and the sexual transmission of HIV. *J Infect Dis.* 2004;189(10):1785-92.

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