High Percentage of Recent HIV Infection Among HIV-Positive Individuals Newly Diagnosed at Voluntary Counseling and Testing Sites in Poland

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Abstract

To gain insight into HIV transmission we estimated the proportion of those recently infected. We examined data from HIV-positive patients and a random 10% sample of HIV-negative patients tested at Voluntary Counseling and Testing sites in Poland in 2006. Archived samples from positive patients were tested by three assays to differentiate recent from long-standing infection. Using logistic regression, we examined the association of recent infection (at least one assay) with age, sex, HIV exposure category, and the interval between self-reported HIV exposure and previous HIV test. Of 13,511 tests, 154 (1.1%) were HIV positive, representing 19.7% ($n=783$) of new diagnoses in Poland in 2006. Demographic and behavioral data were linked for 95, of whom 45 (47%) were recently infected and 1,001 were HIV negative. New diagnoses were more likely to be injectors (17% vs. 2%), men who have sex with men (MSM) (37% vs. 12%), and less frequent condom users (7.8% vs. 14% always) compared to HIV negatives. The median number of partners during the past 12 months was one and two among positives and negatives, but was higher among MSM—four and three, respectively. Ever injectors were less likely to be recently infected (adjusted OR=0.15, 95%CI=0.03–0.73). Having two or more sexual partners in the past 12 months was an independent predictor of recent infection (4.01, 1.4–11.49). We found no evidence that age or sex predicted recent infection. These data reinforce health education campaigns for safe sex messages, especially among MSM. They also suggest, albeit based on a subset of new diagnoses, that interventions should not be limited to selected age/sex groups.

Introduction

HIV INFECTION REMAINS A major public health issue worldwide affecting an estimated 33 million people and contributing to 1.8 million deaths in 2009 alone.¹ One of the major difficulties in targeting prevention efforts is estimating HIV incidence, which is needed to understand the contribution of specific groups to propagating the HIV epidemic. This is especially challenging in countries in which infection rates are low, and setting up HIV-negative cohorts to monitor HIV incidence might not be a practical approach.

A number of alternate methods have been developed, including mathematical modeling, and approaches based on

Recent Infection Testing Algorithm (RITA) laboratory assays that aim to distinguish recent from long-standing HIV infection.^{2–5} Studies examining the validity of HIV incidence estimates derived from RITA in the framework of cross-sectional studies have reported that incidence estimates tend to be overestimated if additional factors are not taken into consideration, most notably the probability and frequency of testing, which is known to differ by HIV risk group.^{6–8} In the absence of such additional information, however, results from RITA studies are still helpful in estimating the proportion of recently infected in subpopulations, and combining it with information on trends in diagnosed cases to gain insight into ongoing HIV transmission.^{9,10}

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Poland has one of the lowest reported rates and estimated prevalence of HIV infection in Europe. Despite a documented early introduction of HIV infection to the injecting drug-using population, the estimated prevalence in the general population remains at <0.2%.¹ Until recently, the epidemic was driven by injection drug use (IDU), but since 2003 the proportion of individuals from other risk groups among new diagnoses has increased, and it is believed that the epidemic has been progressively spreading through sexual contacts, including among men who have sex with men (MSM).^{11–13} The annual number of newly diagnosed infections has increased, from 705 in 2005 to 939 in 2009 representing a 30% increase over the 4-year period.¹¹ At the same time, the proportion of men among new diagnoses has increased from 75% to over 80%, possibly pointing to the spread among MSM. In 2006, an increase in frequency of HIV-positive tests among MSM in the routine testing surveillance data from 4.4 per 100 tests in 2004 to 10.0 per 100 tests was noted.¹⁴ Since information on CD4 count and viral load at diagnosis is not collected, it is difficult to ascertain what proportion of these new diagnoses might, in fact, be due to new HIV infections, or may simply be explained by increased testing uptake.

In this study, we aimed to determine the fraction of recent infection among new diagnoses made in client-initiated testing sites, compare it across different demographic groups, and relate it to reported behavioral information.

Materials and Methods

Study population

We used the archived serum samples from individuals presenting for HIV testing in 2006 at any site within the network of Voluntary Counseling and Testing (VCT) run by the National AIDS Centre. There were 25 centers in the network in 2006 in major cities in Poland, located in different institutions, including medical facilities, public health authorities, and nongovernmental organizations. The consultants are trained to follow the same procedure by the National AIDS Center. VCT sites offer free of charge testing accompanied by pretest and posttest consultation with a trained advisor. The sites are accessible to everyone and do not specifically encourage a particular group to come forward for testing, as Poland has moved from a “risk group”-centered prevention model to a “risky behavior”-centered model.¹⁴ The network of VCT sites was created in 2001 as the tool to increase access to testing and remains the main testing option supported by the National Programme for Combating AIDS and Preventing HIV Infections. The annual number of clients increased six-fold from 2001 to 2007, and in 2006–2007 over 20% of all newly diagnosed HIV infections in Poland were detected in the VCT network.^{15,16} The system is complemented by general population campaigns encouraging people to test because of recent risky behavior and because of various life situations such as a new relationship or traveling abroad.

At presentation for testing, a consultant performs an individual risk assessment for each person requesting an HIV test, and completes a structured questionnaire. Individuals seeking testing are also asked to complete an additional questionnaire to include basic demographic information, which is then forwarded to the National AIDS Center for processing. A sample of blood is drawn and the questionnaire and sample are assigned the same unique identifying number.

Laboratory investigations

The samples reactive on the EIA screening assay were sent for confirmation with Western blot to a central laboratory. Archived serum samples that were confirmed to be HIV antibody positive on confirmatory assay were tested at the Health Protection Agency, London (in May 2007) to differentiate recent from chronic HIV infection. Three RITA assays were used on all samples:

- I. Avidity Index assay (modified Abbott AxSYM HIV1/2gO EIA), based on detection of low-avidity antibodies.¹⁷ Avidity Index values below 0.80 identified recent HIV infection.
- II. Detuned assay (less sensitive ELISA, Viranostika HIV-1 MicroElisa, BioMerieux, France) based on low titers of HIV antibodies.^{18,19} Specimens that were nonreactive on the less sensitive assay were considered to be obtained from recently HIV-infected persons.
- III. BED EIA HIV-1 Incidence Test (Calypte HIV-1 BED Incidence EIA, Calypte Biomedical Corporation, MD) based on a low ratio of HIV-1-specific IgG to total IgG in the sample.²⁰ Recent infection was recognized if the normalized optical density was below or equal to a 0.8 cut-off in a confirmatory test.

Statistical analysis

We compared differences in characteristics between individuals who tested HIV antibody positive and a 10% random sample (arbitrarily chosen at source) of those HIV antibody negative using Chi-square for categorical variables and Student's *t*-test or Wilcoxon test for continuous variables (age and numbers of sex partners in the previous 12 months). Using logistic regression analysis, we examined the possible association of being recently infected (vs. long-standing) with the following variables: age, sex, exposure category (IDU, MSM who were not IDU, heterosexual men and women who were not IDU–MSW), number of partners in the previous 12 months, interval between self-reported time of HIV exposure and testing (available categories ≤3 months, 3–12 months, and >12 months were combined into 12 and >12 months for easier interpretation), and whether they had a previous (negative) HIV test. We used a stepwise selection procedure retaining factors significant at the 0.1 level and factors confounding other effects. For continuous variables we considered linear and square root transformation selecting best model based on Akaike Information Criterion. Two-way interactions were examined. We assessed overall goodness of fit with the Hosmer–Lemeshow test. Analysis was performed in STATA 10.1.

We defined an individual as recently infected if they tested recent by any of the three assays. We performed sensitivity analysis defining recent infection as testing recent by all three assays.

Results

Of 13,511 HIV tests performed at VCT sites in Poland in 2006, 154 (1.1%) were confirmed to be HIV antibody positive of which 139 remaining sera were available for testing for recent infection by each of the three assays. Three were excluded because of implausible results (HIV negative on standard test), and we were able to link results to

demographic and behavioral data for 95 (68%) individuals. The demographic and behavioral data were also available for a random sample of HIV-negative individuals ($n=1001$).

The vast majority of individuals seeking a test were Polish (1 of 95 and 19 of 1,001 positives and negatives, respectively, were nationals of other countries). Newly diagnosed positive individuals were more likely to be male (75% vs. 59%), older (median age 30 vs. 25 years), homosexual/bisexual (37% vs. 12.5%), have used (19% vs. 4%) or injected drugs (17% vs. 2%), and used condoms less frequently (24% vs. 17% never and 8% vs. 14% always) than those testing negative. The median (IQR) number of sexual partners for HIV positives and neg-

atives was similar at 1 (1,5) and 2 (1,3), respectively. For homosexual/bisexual men, the number of sexual partners was somewhat higher at 4 (1,15) and 3 (2,6) for positive and negatives, respectively, and life-time use of condoms was higher (15% vs. 10% never and 6% vs. 24% always). Characteristics for both groups are given in Table 1.

The 154 individuals newly diagnosed as HIV positive at VCT sites represented 19.7% ($n=783$) of all new diagnoses in Poland in 2006. Characteristics of the 95 tested using RITA assays were broadly similar, in terms of age and sex, to all new diagnoses (Table 2). IDUs were, however, underrepresented in our sample, whereas MSM, and MSW were overrepresented.

TABLE 1. CHARACTERISTICS OF NEWLY DIAGNOSED HIV-POSITIVE AND HIV-NEGATIVE INDIVIDUALS (10% RANDOM SAMPLE) ATTENDING VOLUNTARY COUNSELING AND TESTING CLINICS IN POLAND IN 2006

	<i>New HIV diagnoses N=95</i>	<i>HIV negatives N=1001</i>	<i>p-value</i>
Sex			
Female	24 (25%)	409 (41%)	0.008
Male	71 (74%)	586 (59%)	
Not known	0	6	
Age (years)			
Median (IQR) [range]	30 (24,36) [19,59]	25 (22, 30) [14, 82]	<0.0001
Previous HIV test(s)			
Past 12 months	15 (17%)	126 (13%)	0.317
> 12 months	18 (20.5%)	164 (17%)	
Never	55 (62.5%)	682 (70%)	
Not known	7	29	
Use of illegal drugs			
Ever	17 (19%)	36 (4%)	<0.0001
Never	72 (81%)	958 (96%)	
Not known	6	6	
Injecting drug use			
Ever	16 (17%)	20 (2%)	<0.0001
Never	79 (83%)	930 (98%)	
Not known	0	51	
Sexual preference			
Homosexual/bisexual	34 (37%)	123 (12%)	<0.0001
Heterosexual	59 (63%)	863 (88%)	
Not known	2	15	
Number of sexual partners in past 12 months			
Median (IQR) [range]	1 (1, 5) [0, 100]	2 (1, 3) [0, 130]	0.9799
Number of sexual partners in past 12 months among MSM			
Median (IQR) [range]	4 (1,15) [1, 30]	3 (2,6) [0, 50]	0.7646
Lifetime use of condoms			
Never	22 (24%)	159 (17%)	0.035
Occasionally	38 (42%)	320 (34%)	
Often	23 (26%)	321 (34%)	
Always	7 (8%)	135 (14%)	
Not known	5	66	
Lifetime use of condoms among MSM			
Never	5 (15.1%)	10 (10.4%)	0.126
Occasionally	15 (45.5%)	31 (32.3%)	
Often	11 (33.3%)	32 (33.3%)	
Always	2 (6.1%)	23 (24.0%)	
Not known	0	6	
Self-reported time since HIV exposure			
≤ 12 months	71 (77%)	718 (78%)	0.434
> 12 months/no perceived exposure	22 (24%)	203 (22%)	
Not known	2	80	

MSM, men who have sex with men.

TABLE 2. NEW HIV DIAGNOSES AMONG VOLUNTARY COUNSELING AND TESTING CLIENTS INCLUDED IN RITA IN COMPARISON TO ALL NEW HIV DIAGNOSES (AGE ≥ 18) IN POLAND IN 2006

	Included in RITA sample, N = 95	New HIV diagnoses in Poland, N = 783
Sex		
Female	24 (25%)	164 (22%)
Male	71 (75%)	590 (78%)
Not known	0	29
Age (years)		
Median (IQR)	30 (24,36)	31 (26,38)
[range]	[19, 59]	[18, 67]
Age group		
< 30	47 (49%)	320 (43%)
30–39	32 (34%)	264 (35%)
≥ 40	16 (17%)	162 (22%)
Not known	0	37
Exposure category		
MSM	32 (34%)	50 (20%)
IDU	16 (17%)	126 (51%)
MSW	47 (49%)	73 (29%)
Not known	0	534
Residence region (voyevodship)		
Dolnośląskie	17 (19%)	106 (17%)
Kujawsko-pomorskie	6 (7%)	39 (6%)
Lubelskie	4 (4%)	18 (3%)
Lubuskie	1 (1%)	14 (2%)
Łódzkie	1 (1%)	46 (7%)
Małopolskie	0 (0%)	31 (5%)
Mazowieckie	8 (9%)	137 (22%)
Opolskie	0 (0%)	8 (1%)
Podkarpackie	1 (1%)	16 (3%)
Podlaskie	1 (1%)	8 (1%)
Pomorskie	11 (12%)	36 (6%)
Śląskie	29 (32%)	57 (9%)
Świętokrzyskie	0 (0%)	11 (2%)
Warmińsko-mazurskie	4 (4%)	38 (6%)
Wielkopolskie	2 (2%)	39 (6%)
Zachodniopomorskie	5 (6%)	24 (4%)
Unknown	5	155

IDU, injecting drug users; MSM, men who have sex with men; MSW, heterosexual men and women who were not IDU.

Regional differences between the two groups were also present.

Of the 95 newly diagnosed individuals with RITA assay results linked to demographic and behavioral data, 45 (47%, 95% CI 37–58%) tested recent by at least one assay and 21 (22%, 95% CI 14–31%) by all three assays. The percentage deemed to be recently infected varied according to assay used at 42 (44%), 28 (29%), and 25 (26%) using BED, detuned, and avidity index assays, respectively (Fig. 1). Table 3 displays the characteristics of clients with recent infection by any of the assays and by all the assays. The results were broadly similar when recent by any test was used in sensitivity analysis. Among repeat testers, 61% (20 of 33) were recent by any test compared to 40% (22 of 55) of those without a previous test. Among clients with self-perceived risk in the past 12 months 54% (38 of 71) were recent compared to 32% (7 of 22) of those whose perceived risk was 12 months previously or with no

FIG. 1. Venn diagram of the results of three assays to detect recent HIV infections. (A) Recent by detuned; (B) recent by BED EIA; (C) recent by avidity index (N = 95).

perceived risk. The proportion of recent infection was lower among clients reporting ever injecting drugs (19% vs. 53%) or use of illegal drugs (29% vs. 51%).

In logistic regression models, individuals who had ever injected were less likely to have been recently infected (adjusted OR, aOR = 0.15, 95% CI = 0.03–0.73). There was weak evidence to suggest that self-reported recent HIV exposure (past 12 months) and previous HIV testing were associated with recent infection. The strongest predictor of recent infection was the number of sexual partners in the past 12 months (≥ 2 vs. ≤ 1) (aOR = 4.01, 1.4 = 11.49) (Table 4). The univariable analysis shows that the effect of number of partners differed by exposure group with no significant association among IDU (0.58, 0.01–14.46), a moderate but not significant effect among MSW (2.43, 0.57–11.13), but a large and significant association among MSM (30.6, 2.7–1416.7).

Results were qualitatively similar when we undertook sensitivity analysis defining recent infection as testing recent by all three assays, although our ability to detect an effect was hampered by a lower number of events (data not shown).

Discussion

This is the first study to estimate the proportion of recent infections among newly diagnosed individuals in Poland. We found that a high proportion were recently infected, suggesting that the increasing trend in surveillance data is likely to be influenced by ongoing HIV transmission. These figures, akin to those reported by other investigators in countries with higher HIV prevalence,^{5,9,21–25} are surprising given that HIV test coverage in Poland is low, accounting for less than 10% of the adult population²⁶ and a growing number of late presenters.^{13,27}

TABLE 3. CHARACTERISTICS OF 45 RECENTLY INFECTED INDIVIDUALS OF 95 VOLUNTARY COUNSELING AND TESTING CLIENTS IN POLAND IN 2006

	Number recently infection (% recently infected)			
	Any RITA assay	p-value	All RITA assays	p-value
Sex				
Female	9 (38%)	0.263	5 (21%)	0.862
Male	36 (51%)		16 (23%)	
Age (years)				
<30	21 (45%)	0.613 (<i>p</i> -trend)	12 (26%)	0.957 (<i>p</i> -trend)
30–39	16 (50%)		1 (3%)	
≥40	8 (50%)		8 (50%)	
Previous HIV test(s)				
Yes	20 (56%)	0.146	11 (31%)	0.277
No	22 (40%)		9 (16%)	
Not known	3		1	
Use of illegal drugs				
Ever	5 (26%)	0.051	1 (5%)	0.048
Never	37 (51%)		19 (26%)	
Not known	3		1	
Injecting drug use				
Ever	3 (19%)	0.012	0 (0%)	0.019
Never	42 (53%)		21 (27%)	
Sexual preference				
Homosexual/bisexual	19 (56%)	0.307	9 (27%)	0.376
Heterosexual	24 (41%)		12 (19%)	
Not known	2		0	
Number of partners in past 12 months				
0–1	17 (34%)	0.004	7 (14%)	0.038
≥2	28 (64%)		14 (31%)	
Lifetime use of condoms				
Never/occasionally	26 (43%)	0.764	12 (20%)	0.473
Often/always	14 (47%)		8 (27%)	
Not known	5		1	
Self-reported time since HIV exposure				
≤12 months	38 (54%)	0.075	18 (25%)	0.251
>12 months/no perceived exposure	7 (29%)		3 (14%)	

The decision to be tested for HIV is not a random process, however, and those choosing to have an HIV test may do so because of perceived recent HIV exposure and/or symptoms, which may have inflated the proportion estimated to be recently infected among newly diagnosed VCT clients.²⁸ There is certainly a suggestion of this as, among those who reported an exposure in the past 12 months, the proportion that was recent was higher than among those with self-perceived exposure >12 months previously or with no perceived exposure (54% vs. 29%). The fairly high proportion of recent infection among the latter group, nonetheless, is of concern, as it possibly points to transmission in the settings perceived as not risky such as stable relationships or, on the other hand, low awareness of risks, underscoring the need for increased educational campaigns.

Unlike findings from studies in other countries^{17,22} we did not note a decreasing tendency of the proportion of recent infections with increasing age. This merits further attention as health education is often targeted mainly at the younger age groups.

We noted important differences between the exposure groups. Although clients who reported use of illegal drugs, including IDU, were far more likely to test HIV positive, the proportion of recent infections was much lower among them,

supporting surveillance data on the low relative contribution of this group to trends in current HIV diagnoses in Poland.⁹ It also suggests, however, a still high (undiagnosed) HIV prevalence among this group and ongoing transmission, be it sexual or parenteral.

Among homosexual/bisexual men, the number of sexual partners in the past 12 months was higher than that for all VCT clients as a whole. We also found that having two or more sexual partners in the past 12 months was highly associated with being recently infected, even after adjusting for other risk factors such as HIV testing history and self-reported time since HIV exposure. Previous findings have reported that a significant proportion of MSM declare having 10 or more sex partners in the previous 12 months with poor use of condoms for casual and regular partners.^{29,30} A similarly high level of risk was associated with the reemergence of an HIV epidemic in Western Europe and calls for greater efforts to strengthen health education messages, especially for men who have sex with men in Poland.³¹

In addition, even though the proportion of recent infection is high among heterosexual men and women, subgroup univariable analysis suggests that the effect of the number of partners on the probability of being recently infected is

TABLE 4. FACTORS ASSOCIATED WITH RECENT HIV INFECTION BY AT LEAST ONE OF THE FOLLOWING ASSAYS: BED, DETUNED, AVIDITY

	Univariable		Multivariable	
	OR (95% CI)	p-value	aOR (95% CI)	p-value
Exposure category				
IDU	0.2 (0.05–0.76)	0.0218	0.15 (0.03–0.73)	0.055
MSM	1.12 (0.5–2.53)		0.83 (0.27–2.54)	
MSW	1		1	
Previous HIV test				
Yes	1.85 (0.80–4.39)	0.147	2.06 (0.77–5.55)	0.152
No	1		1	
Self-reported time since HIV exposure				
<12 months	2.47 (0.9–6.78)	0.08	2.29 (0.59–8.91)	0.232
>12 months or no perceived risk	1		1	
Number of sex partners in past 12 months				
≥2	3.40 (1.45–7.93)	0.005	4.01 (1.4–11.49)	0.01
<2	1		1	

IDU, injecting drug users; MSM, men who have sex with men; MSW, heterosexual men and women who were not IDU.

smaller than among MSM. It suggests that the increasing trend of heterosexually acquired HIV infection in the surveillance data is not likely to be fully explained by increased testing uptake or testing because of symptoms. However, it is plausible that the number of partners is a less important driving factor of the HIV epidemic among heterosexuals than it is among MSM. This is consistent with the observation that in countries with concentrated epidemics, heterosexual spread is often fuelled by HIV transmission from the subpopulations most affected by HIV.¹

Self-perceived recent HIV exposure before testing is associated with an over two times higher chance of being a recent infection, although it was of borderline significance in univariable analysis and was not significant in multivariable analysis, possibly due to the small sample size. This provides some indication that self-perceived HIV exposure, together with behavioral indicators, may be helpful to identify those with recent HIV exposure.

Finally, the tested samples came from 2006; thus our findings could be validated against later surveillance data showing a consistent picture. This underscores the role of monitoring the proportion of recent infections in relation to recent behavior as a sensitive tool complementing routine HIV surveillance.

Our study is limited by a number of factors. First, we notice that among VCT clients, compared to the general population of Poland, the inhabitants of rural areas and persons with lower socioeconomic status are underrepresented.¹⁶ Next, the new diagnoses among the VCT clients may not be representative of all new diagnoses in Poland. Although the age and gender distributions are similar, several regions tend to be underrepresented among the new diagnoses in VCT. However, the samples included in our analysis cover the majority of the country and 12% of all new diagnoses and thus the results can be useful in an interpretation of the general trends observed in Poland. Different distributions of exposure category is difficult to interpret due to the large proportion of missing values in the surveillance data.

Moreover, the false recent rate (FRR) has not been studied in our population for any of the assays. Variable FRR of RITA tests could have introduced bias to our findings. It has been

shown that the FRR tends to increase late in HIV disease, in case of increasing immunosuppression and on antiretroviral therapy, especially for BED.^{6,32–34} Our study group did not include any persons on antiretroviral treatment or with clinical symptoms, making AIDS diagnosis less likely. Nonetheless, the information on the stage of HIV disease was not available and it could differ among subgroups studied. However, we used three different assays and using sensitivity analysis including as recent only those deemed to be so by all assays resulted in similar findings. Furthermore, the principles of the three assays differ and the factors affecting FRR, as well as the window period during which the infection would be classified as recent, may differ for each assay. Dual testing algorithms have been shown to reduce FRR, even without correction for late stages of disease.³⁵ The level of agreement among different test results was similar as reported in other studies, which also found good agreement between correlates of recent infection across different tests.^{35–38}

Finally, we were limited by a sample size that hampered our ability to detect important associations. That said, the HIV prevalence in Poland is low and the data presented here represent all new HIV diagnoses in VCT sites in the country over the study period.¹⁶

We have detected a high proportion of recent HIV infection among newly diagnosed individuals in VCT sites in Poland in 2006. While it indicates that a high proportion of newly infected individuals have sought an HIV test at such an early stage, our findings point to ongoing HIV transmission, which is unlikely to be driven by young men and women making their sexual debut. An ongoing monitoring of new infections among new diagnoses and an understanding of the factors associated with being newly infected are crucial to ensuring that HIV prevalence remains low in Poland.

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