Late HIV Testing in a Cohort of HIV-Infected Patients in Puerto Rico

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Objective: Late HIV testing (LT), defined as receiving an AIDS diagnosis within a year of one's first positive HIV test, is associated with higher HIV transmission, lower HAART effectiveness, and worse outcomes. Latinos represent 36% of LT in the US, yet research concerning LT among HIV cases in Puerto Rico is scarce.

Methods: Multivariable logistic regression analysis was used to identify factors associated with LT, and a Cochran–Armitage test was used to determine LT trends in an HIV-infected cohort followed at a clinic in Puerto Rico specialized in the management and treatment of HIV.

Results: From 2000 to 2011, 47% of eligible patients were late testers, with lower median CD4 counts (54 vs. 420 cells/mm3) and higher median HIV viral load counts (253,680 vs. 23,700 copies/mL) than non-LT patients. LT prevalence decreased significantly, from 47% in 2000 to 37% in 2011. In a mutually adjusted logistic regression model, males, older age at enrollment and past history of IDU significantly increased LT odds, whereas having a history of amphetamine use decreased LT odds. When the data were stratified by mode of transmission, it became apparent that only the category men who have sex with men (MSM) saw a significant reduction in the proportion of LT, falling from 67% in 2000 to 33% in 2011.

Conclusion: These results suggest a gap in early HIV detection in Puerto Rico, a gap that decreased only among MSM. An evaluation of the manner in which current HIV-testing guidelines are implemented on the island is needed. [*P R Health Sci J 2015;34:148-154*]

Key words: Late HIV diagnosis, Puerto Rico HIV, AIDS diagnosis, Late HIV testing, HIV trends

In 2009, an estimated 32% of persons diagnosed with HIV in the United States (US) were diagnosed with AIDS within 1 year of their initial HIV diagnosis (1), a phenomenon referred to as late testing (LT). LT patients tend to delay initiating HIV treatment and are prone to requiring more complicated treatments, worse overall prognoses (2), the diminished recovery of CD4 T-lymphocytes (3), and higher mortality, even after the receipt of antiretroviral therapy (4). A patient who is unaware that he or she is infected with HIV runs the risk of unknowingly transmitting the virus; in addition, the medical costs associated with that individual's treatment are likely to increase substantially (5).

Although US Latinos represent 20% of all new HIV infections, they account for 36% of late testers (1). The heterogeneity of the "Latino" classification complicates addressing this disparity given that it comprises people from over 20 countries (6), with differing risk factors, behaviors, and rates of infections. For example, 25% of all Puerto Ricans diagnosed with HIV received the infection via past or current injection drug use (IDU), a transmission method that is significantly associated with LT; this compares to the only 6% of Mexicans who acquired the infection in a like manner (1). Additionally, the prevalence of undiagnosed HIV infections in Puerto Rico (PR), estimated at 36%, is twice that of said prevalence in the US (7). Puerto Ricans are the second largest Hispanic/Latino group in the US (8). There are an estimated 4.9 million Puerto Ricans living on the mainland and 3.7 million living on the island, all of whom are free to migrate to and from the US (8). Therefore, LT among HIV-infected persons on the island may be relevant to the epidemiology of HIV among Puerto Ricans on the mainland.

However, data concerning LT among HIV-infected persons in PR are scarce. A review of the scientific literature identified no publications that examined the epidemiology of LT among HIV-

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infected individuals living in PR. Determining the prevalence of and factors associated with LT should inform efforts to decrease this important public health problem by providing data to design programs targeting those identified at greatest risk for LT. The main objective of this study was to determine factors associated with and describe trends of LT in a cohort of HIV-infected individuals who entered HIV care in PR from 2000 through 2011.

Materials and Methods

Data were obtained from baseline questionnaires completed by participants of the Retroviral Research Center (RRC) longitudinal cohort study of confirmed HIV-infected patients followed for care at the Ramón Ruiz Arnau University Hospital (inpatient and ambulatory clinics) in Bayamón, PR. Invited participants were HIV-infected adults 18 years of age or older followed for HIV care at the RRC and its clinics. After consent was obtained, a baseline questionnaire was administered, and baseline laboratory tests were performed. The baseline questionnaire included 12 months of retrospective medical history supplemented with hospital and medical record abstraction (9). Participants were then interviewed at 6-month intervals thereafter and compensated $10 towards their transportation expenses. The institutional review board of the Universidad Central del Caribe approved the study. More details regarding inclusion criteria for the general cohort study, patient consent, and IRB approval have been published elsewhere (9, 10).

The RRC is the only center that has followed (since 1992) an open cohort of HIV/AIDS patients presenting for care in the Bayamón area (11), and this cohort is the only large HIV cohort on the island. RRC collects information on patient factors via a registry organized into various categories, including socio-demographics; risk-related practices; psychosocial, clinical, and immunological modules; and standard surveillance information (e.g., mode of transmission and CD4 and viral load counts). The Bayamón area is 1 of 8 health care regions in PR (12) and contains 16% of the island population and the second highest HIV/AIDS prevalence (13).

We defined LT (per the CDC definition) as receiving an AIDS diagnosis within 1 year of having one's first reported positive HIV test (14). Given that some of the factors associated with LT might also be associated with delayed entry into HIV care, the study sample was further restricted to include only those late testers, with timely entry defined as joining the study cohort within 1 year of one's first reported positive HIV test. This restriction was done to minimize potential confounding by care delays and to decrease opportunities for LT misclassification (15). The 1-year time span to define timely entry is within the range of other published studies (16). In the cohort study, AIDS was defined per the 1993 CDC AIDS definition (17), which includes immunological (CD4 count<200 cells/mm3) and/or clinical (the presence of an AIDS-defining condition) diagnoses. HIV and AIDS diagnoses dates were abstracted from medical records. Every cohort participant who had an available date of entry into the study and a first reported HIV test date was included in our analysis.

Demographics, illicit drug use, lifestyle, and clinical characteristics extracted from the modular questionnaires were described by gender and LT status. Mode of transmission included heterosexual, men who have sex with men (MSM), and injection drug use (IDU). Lifestyle covariates and drug use were collected as "ever use" (yes/no), with the exception of a variable asking patients reporting a history of IDU if they had injected such drugs at any time in the year before the study enrollment. Using this information, the following trichotomous variables were created: "non-IDU," "recent IDU" (if the participant had injected drugs in the year prior to study entry), and "remote IDU" (if the participant reported IDU but claimed additionally that such use had not taken place in the year prior to study enrollment).

Pearson's chi-square test was used to compare differences in the distribution of categorical variables by LT. Student's t-test was used to compare means for normally distributed continuous variables by LT status, and the Wilcoxon rank-sum test was used to test the difference between medians for non-normally distributed continuous variables by LT status. Statistically significant associations (2-sided alpha of <0.05) for LT in the bivariate analysis were entered simultaneously into a multivariable logistic regression model. Effect modification by gender and IDU level (recent versus remote) was examined based on observed differences in risk factors for LT among males and IDU in bivariate analysis. Crude odds ratios (OR) or adjusted odds ratios (AOR) and 95% confidence intervals (CI) are reported. Cumulative AIDS prevalence was calculated as the proportion of total AIDS diagnoses among the sample of HIV-infected patients. Changes in LT trends over time were measured with the Cochran-Armitage test and stratified by gender and mode-of-transmission categories. Statistical analysis was conducted using SAS 9.2 (Cary, NC).

Results

RRC cohort patients

From 2000 to 2011, a total of 1582 patients entered the cohort. The median age was 40 years (range 18 to 79 years). Most patients were men (66%, including 29% MSM), nearly one third did not complete the 10th grade of education (31%), and over one third (35%) of all the study participants had been imprisoned at least once. The most common modes of transmission were heterosexual (50%) and IDU (33%, including the MSM/IDU category). Most of the study participants (99%) reported illicit drug use. Cocaine was reported as the most commonly used drug (53%); 26% of the users who reported having taken cocaine further clarified that it had been crack cocaine. Over a third (35%) of the study participants had

injected drugs at some point in their lifetime; most of these last (60%) were recent injectors. The proportion reporting IDU was higher among men (42%) than women (20%) (Table 1).

Overall, 45% (n = 719) of the cohort were diagnosed with AIDS at enrollment. Seventy-eight percent had immunologic AIDS (n = 562), 18% (n = 127) had both clinical and immunologic AIDS, and approximately 2% (n = 17) had clinical AIDS, alone (Figure 1). The median number of days from first reported positive HIV test to entry into the study was 353 (interquartile range [IQR] = 64 – 2615 days). The median CD4 count and HIV viral loads were 253 cells/mm3 (IQR = 80 - 470 cells/mm3), and 38,200 copies/mL (IQR = 2,950 - 204,000 copies/mL), respectively. Thirty-five percent (n = 546) of the study participants had an HIV viral load greater than 100,000 copies/mL. The median CD4 and viral load counts did not differ significantly by gender (p = 0.07 and p = 0.19, respectively).

Analytic sample

Among those who entered the study within 1 year of their first reported positive HIV test (n = 795) (timely entry), the median number of days from the HIV test to entry into the cohort, was 64 (IQR = 43 - 96). The median CD4 count and HIV viral load were 216 cells/mm3 (IQR = 57 - 433 cells/mm3) and 73,670 copies/mL (IQR = 12,200 - 346,750 copies/mL), respectively. These participants were less likely to be male, smokers, or drug users and were less likely to report a history of incarceration. The proportion of patients who reported IDU as their mode of transmission was 19% (compared to 33% of the entire study population that so reported) (Table 1).

Nearly half (47%, n = 377) of those with timely entry already had a recorded AIDS diagnosis and were classified as LT. Ninety percent (n = 339) of late testers had an AIDS diagnosis within the first 3 months after their first reported positive HIV test, including 49% (n = 184) who were concurrently diagnosed with HIV and AIDS at entry (Figure 2). Most AIDS diagnoses were immunological (77%, n = 289) (Figure 1). The median CD4 and viral load counts among the LT group were 54 cells/mm3 (IQR = 21 - 116 cells/mm3) and 253,680 copies/mL (IQR = 73,670 - 684,000 copies/mL), respectively, compared to 420 cells/mm3 (IQR = 295 - 596 cells/mm3) and 23,700 copies/mL (IQR = 4190 - 82120 copies/mL), respectively,

Table 1. Characteristics of HIV-infected patients whose entry into care in the RRC cohort from 2000 to 2011 was timely.

	Overall N = 1582	Timely entry* (n = 795) (%)	Entry not timely (n = 787)	p-Value	OR (95% CI)
Gender (n = 1582)				0.03	0.80 (0.65 to 0.98)
Male	1051 (66%)	508 (64)	543 (69)		
Female	531 (34%)	287 (36)	244 (31)		
Age in years (n = 1582)				0.06	
<30	224 (14)	124 (16)	100 (13)		REF
30–44	845 (53)	402 (50)	443 (56)		0.60 (0.44 to 0.82)
≥45	513 (32)	269 (34)	244 (31)		0.74 (0.53 to 1.03)
Education (n = 1569)				0.28	
≤9th grade	485 (31)	236 (30)	249 (32)		0.84 (0.65 to 1.09)
10-12th grade	612 (39)	299 (38)	313 (40)		0.86 (0.67 to 1.10)
>12th grade	472 (30)	251 (32)	221 (28)		REF
Lifestyle profile (lifetime)					
Smokes (n = 1576)	1134 (72)	522 (66)	612 (78)	<0.01	0.54 (0.43 to 0.68)
Uses alcohol (n = 1575)	811 (51)	417 (53)	394 (50)	0.33	1.1 (0.91 to 1.34)
Has been in prison (n = 1570)	547 (35)	178 (23)	369 (47)	<0.01	0.33 (0.26 to 0.41)
CDC mode of transmission categories (n = 1495)				<0.01	
IDU	447 (30)	139 (18)	308 (42)		0.28 (0.22 to 0.36)
IDU/MSM	38 (2.5)	6 (1)	32 (4)		0.12 (0.05 to 0.29)
MSM	262(17.5)	151 (20)	111 (15)		0.87 (0.65 to 1.15)
Hetero	748 (50)	458 (61)	290 (39)		REF
Drug use prevalence (ever)					
Cocaine and crack (n = 1578)	833 (53)	323 (41)	510 (65)	<0.01	0.37 (0.30 to 0.45)
Cannabinoid (n = 1575)	729 (46)	305 (38)	424 (54)	<0.01	0.53 (0.43 to 0.64)
Heroin (n = 1577)	590 (37)	200 (25)	390 (50)	<0.01	0.34 (0.28 to 0.42)
Speedball (n = 1572)	517 (33)	166 (21)	351 (45)	<0.01	0.33 (0.26 to 0.41)
Amphetamine (n = 1570)	369 (24)	130 (16)	239 (31)	<0.01	0.45 (0.35 to 0.57)
Ecstasy (n = 1120)	42 (4)	18 (3)	24 (4)	0.32	0.73 (0.39 to 1.36)
IDU (n = 1575)				<0.01	
Remote IDU	200 (13)	56 (7)	144 (18)		0.24 (0.17 to 0.34)
Recent IDU	344 (22)	113 (14)	231 (30)		0.30 (0.23 to 0.39)
Non-IDU	1031 (65)	623 (79)	408 (52)		REF

*Timely entry = entered cohort within 1 year of first reported HIV test

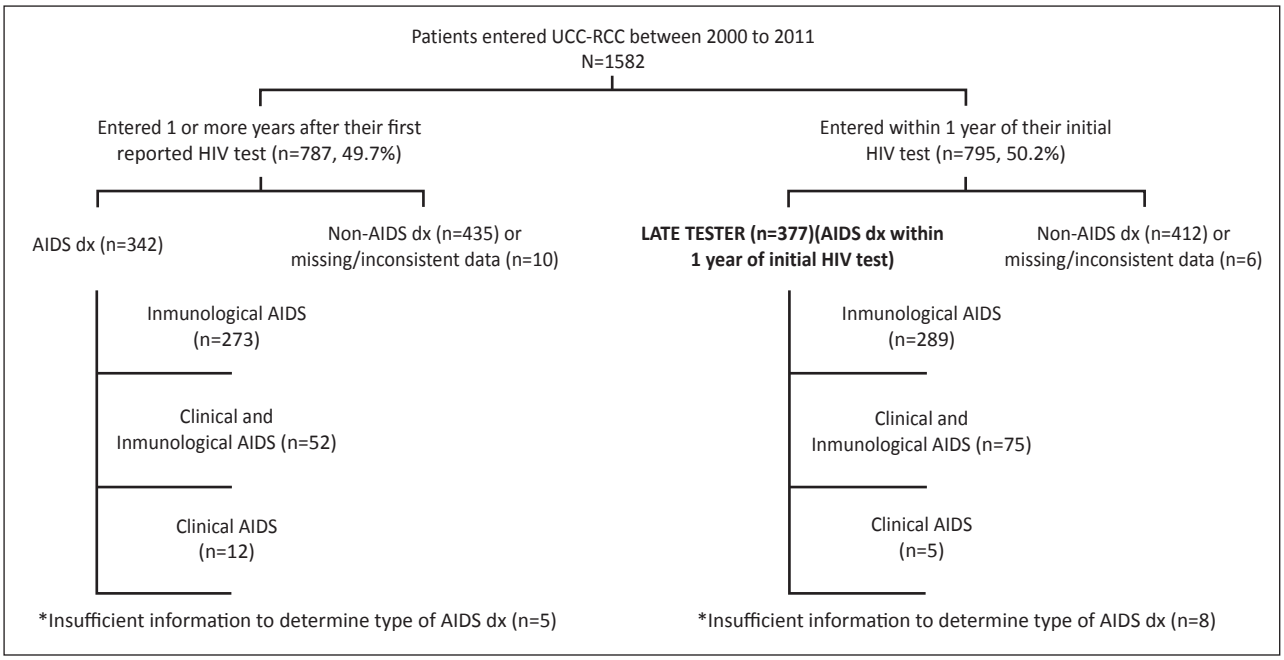

Figure 1. Flow diagram showing the distribution of AIDS diagnoses for patients who entered the cohort within one year of their first reported HIV tests versus that of those entering after one year of their first reported HIV test. *Patients had no or missing data with respect to viral load, CD4 counts, or both; patients had specific dates of first AIDS diagnoses.

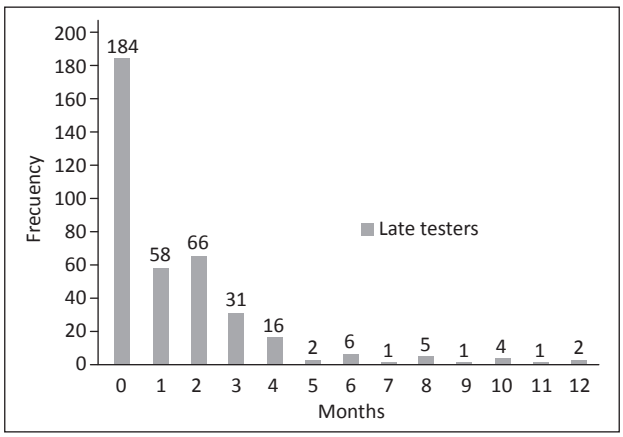

Figure 2. Distribution of time to AIDS diagnosis (in months) among 377 late testers (LT).

for non-late testers. Among late testers, the CD4 count was similar for males and females. However, the median viral load was significantly lower in males (209,630; IQR = 67,400 - 594,000) compared to females (404,875 copies/mL; IQR = 97,100 - 750,000) (p = 0.02).

Factors associated with late testing

Factors independently associated with increased odds of LT included being male, being in the older age category, compared to the younger age categories, and reporting IDU (Table 2). Having a history of imprisonment and a history of amphetamine use decreased the odds of LT. Factors remaining significantly associated with LT in the multivariable logistic model were being male (AOR = 1.59; 95% CI = 1.15 to 2.17), being of a relatively older age (30-44 years: AOR = 1.68; 95% CI = 1.09 to 2.62; ≥45 years: AOR = 3.31; 95% CI = 2.08 to 5.27), remote IDU (AOR = 2.42; 95% CI = 1.24 to 4.69), and having a history of amphetamine use (AOR = 0.52; CI = 0.31 to 0.87).

Trends in late testing over time

Yearly LT prevalence ranged from a high of 58% to a low of 32%. Overall, LT prevalence showed a significantly decreasing yearly trend during the study period (from 47% in 2000 to 36% in 2011, p = 0.04, n = 795; Figure 3a). Among males, only those reporting MSM as their mode of transmission showed a statistically significant decrease in prevalence of LT from 67% in 2000 to 33% in 2011 (p<0.01, n = 151; Figures 3a and b). Also among males, non-statistically significant increasing yearly trend of LT prevalence was observed for heterosexual transmission (46% to 54%; p = 0.72, n = 255; Figure 3c).

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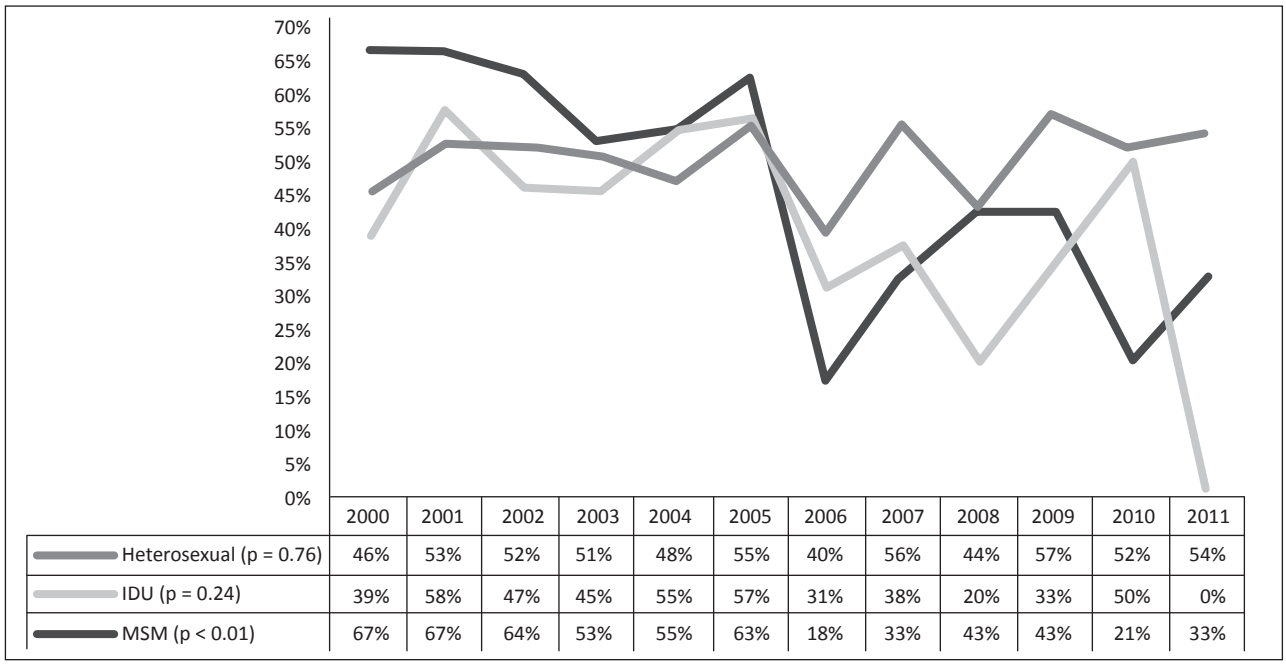
Table 2. Characteristics of HIV patients entering "timely" care (as defined in the Analytical Sample section) at the UCC-RCC from 2000 to 2011, by LT status:

	Timely entry* n = 795 (%)	Late (AIDS dx) n = 377 (%)	Not Late (no AIDS dx) n = 418 (%)	p-Value	OR (95% CI)
Gender (n = 795)				0.04	
Male	508 (64)	255 (68)	253 (61)		1.36 (1.02 to 1.82)
Female	287 (36)	122 (32)	165 (39)		REF
Age (n = 795)				<0.01	
<30	124 (16)	40 (11)	84 (20)		REF
30–44	402 (50)	174 (46)	228 (54)		1.7 (1.1 to 2.6)
≥45	269 (34)	163 (43)	106 (25)		3.4 (2.1 to 5.3)
Education (n = 786)				0.16	
≤9th grade	236 (30)	124 (33)	112 (27)		1.4 (0.98 to 1.99)
10–12th grade	299 (38)	136 (37)	163 (39)		1.1 (0.75 to 1.46)
>12th grade	251 (32)	112 (30)	139 (34)		REF
Lifestyle profile (ever)					
Smokes (n = 792)	522 (66)	244 (65)	278 (67)	0.64	0.93 (0.69 to 1.25)
Uses alcohol use (n = 791)	417 (53)	208 (55)	209 (50)	0.14	1.23 (0.93 to 1.63)
Stay in prison (n = 788)	178 (23)	71 (19)	107 (26)	0.02	0.68 (0.48 to 0.95)
CDC mode of transmission categories (n = 795)				0.43	
IDU	139 (18)	61 (17)	78 (20)		0.80 (0.54 to 1.17)
IDU/MSM	6 (1)	2 (0.6)	4 (1)		0.51 (0.09 to 2.81)
MSM	151 (20)	67 (19)	84 (21)		0.81 (0.56 to 1.18)
Hetero	458 (61)	228 (64)	230 (58)		REF
Drug prevalence					
Cocaine and crack (n = 794)	323 (41)	147 (39)	176 (42)	0.36	0.88 (0.66 to 1.16)
Cannabinoid (n = 794)	305 (38)	133 (35)	172 (41)	0.08	0.78 (0.58 to 1.04)
Heroin (n = 793)	200 (25)	86 (23)	114 (27)	0.15	0.79 (0.57 to 1.1)
Speedball (n = 789)	166 (21)	68 (18)	98 (24)	0.06	0.72 (0.51 to 1.02)
Amphetamine (n = 790)	130 (16)	44 (12)	86 (21)	<0.01	0.51 (0.34 to 0.75)
Ecstasy (n = 565)	18 (3)	5 (2)	13 (4)	0.10	0.42 (0.15 to 1.21)
IDU (n = 792)				<0.01	
Remote IDU	56 (7)	34 (9)	22 (5)		1.62 (0.93 to 2.84)
Recent IDU	113 (14)	38 (10)	75 (18)		0.53 (0.34 to 0.81)
Non-IDU	623 (79)	304 (81)	319 (77)		REF

*Timely entry = entered cohort within 1 year of first reported HIV test

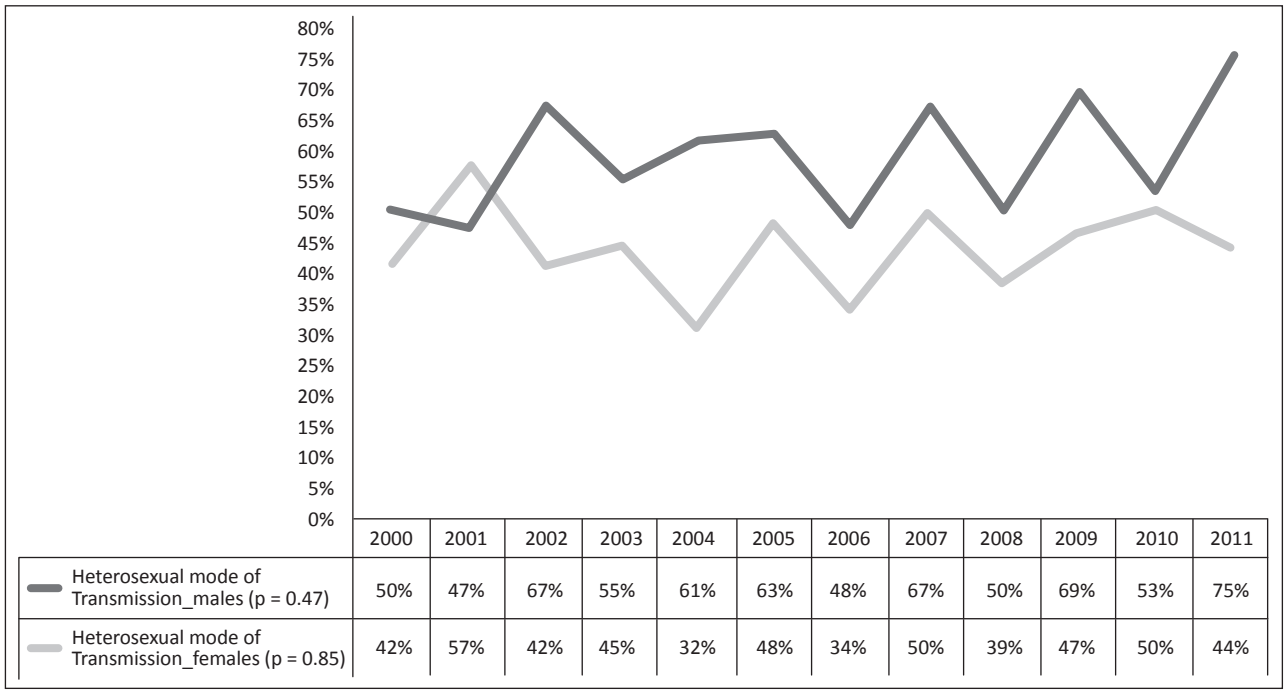
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Overall trend (p = 0.04)	47%	54%	53%	51%	51%	58%	32%	45%	43%	50%	40%	36%
Males (p = 0.04)	49%	52%	64%	52%	60%	64%	33%	45%	42%	54%	37%	42%
Females (p = 0.56)	43%	56%	38%	48%	30%	50%	30%	44%	43%	44%	57%	31%

Figure 3a. Yearly trends of LT overall and by gender



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Heterosexual (p = 0.76)	46%	53%	52%	51%	48%	55%	40%	56%	44%	57%	52%	54%
IDU (p = 0.24)	39%	58%	47%	45%	55%	57%	31%	38%	20%	33%	50%	0%
MSM (p < 0.01)	67%	67%	64%	53%	55%	63%	18%	33%	43%	43%	21%	33%

Figure 3b. Yearly trends of LT by mode of transmission



	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Heterosexual mode of Transmission_males (p = 0.47)	50%	47%	67%	55%	61%	63%	48%	67%	50%	69%	53%	75%
Heterosexual mode of Transmission_females (p = 0.85)	42%	57%	42%	45%	32%	48%	34%	50%	39%	47%	50%	44%

Figure 3c. Yearly trends of LT for heterosexual mode of transmission by gender

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