

Temporal Trends in Age at HIV Diagnosis in Cohorts in the United States, the Caribbean, and Central and South America

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Abstract In the United States (USA), the age of those newly diagnosed with HIV is changing, particularly among men who have sex with men (MSM). A retrospective analysis included HIV-infected adults from seven sites in the Caribbean, Central and South America network (CCASAnet) and the Vanderbilt Comprehensive Care Clinic (VCCC-Nashville, Tennessee, USA). We estimated the proportion of patients <25 years at HIV diagnosis by calendar year among the general population and MSM. 19,466 (CCASAnet) and 3,746 (VCCC) patients were included. The proportion <25 years at diagnosis in VCCC increased over time for both the general population and MSM ($p < 0.001$). Only in the Chilean site for the general population and the Brazilian site for MSM were similar trends seen. Subjects <25 years of age at diagnosis were less likely to be immunocompromised at enrollment at both the VCCC and CCASAnet. Recent trends in the USA of

greater numbers of newly diagnosed young patients were not consistently observed in Latin America and the Caribbean. Prevention efforts tailored to young adults should be increased.

Resumen En EUA, recientemente se han reportado cambios en la edad al diagnóstico de VIH, particularmente en hombres que tienen sexo con hombres (HSH). Este estudio es un análisis retrospectivo de la cohorte CCASAnet, constituida por adultos viviendo con VIH de 7 sitios en Latinoamérica y el Caribe, y un sitio en EUA (Clínica VCCC, Nashville, Tennessee). Estimamos la proporción de <25 años de edad al diagnóstico de VIH por año calendario en la población general y HSH. Incluimos 19 466 sujetos de CCASAnet y 3 746 de VCCC. La proporción de <25 años, en población general y en HSH se incrementó en el tiempo en VCCC ($p < 0.001$). Una tendencia similar se observó en la población general chilena y en los HSH brasileños. En toda la cohorte los <25 años, significativamente estaban menos inmunocomprometidos a su ingreso a la atención médica. Nuestros resultados sugieren enfocar

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los esfuerzos de prevención de VIH de acuerdo a las características de la epidemia de cada sitio.

Keywords HIV · AIDS · Latin America · The Caribbean · Age · HIV diagnosis

Introduction

Much progress has been made in the treatment of human immunodeficiency virus (HIV) infection over the past thirty years of the epidemic, resulting in marked improvement in life expectancy. In many estimates, people with recently acquired HIV infection can have a life expectancy which is nearly the same as that of uninfected individuals [1]. Recent data show an annual HIV diagnosis rate in the United States that has decreased by 33.2 % from 2002 to 2011, and a nearly 50 % decrease in annual HIV diagnosis in women [2]. Globally, there were 2.3 million new infections in 2012, representing a decline of 33 % from new infections in 2001 [3].

However, some characteristics of those who are newly diagnosed in the United States are changing. Age at diagnosis is shifting towards younger individuals. Overall, estimated HIV incidence among those aged 13–24 increased from 21.2 per 100,000 in 2007 to 23.7 per 100,000 in 2010 [4]. Recent data demonstrated that HIV diagnosis rate was decreasing from 2002 to 2011 in all age groups except for ages 13–27. In this group, the HIV diagnosis rate went from 12.5 per 100,000 in 2002 to 17.3 per 100,000 in 2011, representing a 38.4 % increase [2]. This change is also evident within the men-who-have sex with men (MSM) population in the United States, particularly among young MSM. The number of HIV diagnoses increased 132.5 % from 2002 to 2011 among those with male-to-male sexual contact as probable route of transmission [2]. Although among Hispanic/Latino males HIV incidence remained essentially unchanged from 2008 to 2010, 79 % of new HIV infections among this group were attributable to MSM transmission [4].

Though trends in age at HIV diagnosis in the United States show that an increasing proportion of new diagnoses occur in younger individuals, it is not known if a similar change is happening in other parts of the world. Latin America is home to 1.4 million HIV-infected individuals [5], and in countries such as Argentina, Brazil, Chile, Honduras, Mexico and Peru, estimated HIV prevalence rates are lower than 1 % in the general adult population [6]. The regional epidemic is concentrated in specific subgroups such as MSM, sex workers, prison inmates and injection drug users (IDU) [7–11]. For example, MSM in Latin America are over 30 times more likely to be HIV-positive compared to reproductive-aged men in the general population [12]. In

contrast, the Caribbean is the most heavily affected region by HIV outside of sub-Saharan Africa. Women account for approximately half of all HIV infections in the Caribbean [13]. Countries in Latin America and the Caribbean each have unique patterns in the characteristics of their HIV epidemic, and little has been published regarding the trends in terms of age at HIV diagnosis overall or within MSM subgroups. Understanding differences (such as presenting CD4 count, clinical AIDS, and enrollment in care) between younger and older individuals at diagnosis may be critical to expanding prevention efforts and understanding shifts within the epidemic.

In this study, we describe trends related to age at HIV diagnosis in a large cohort of HIV-infected individuals in Central and South America and the Caribbean, and compare this group with a single-site cohort in the southeastern United States. We compare characteristics among those diagnosed at younger (<25) versus older ages. As a secondary objective, we study trends of age at diagnosis among those who reported male-to-male sex as their probable route of HIV transmission.

Methods

Participants and Setting

The Caribbean, Central and South America network for HIV epidemiology (CCASAnet) cohort (www.ccasanet.org) has been described elsewhere [14]. The collaboration was established in 2006 as region 2 of the International Epidemiologic Databases to Evaluate AIDS (IeDEA; www.iedea.org) with the purpose of collecting retrospective clinical HIV data to describe the unique characteristics of the epidemic in Latin America and Caribbean. The Vanderbilt Comprehensive Care Clinic (VCCC) in Nashville, Tennessee, U.S.A. and seven CCASAnet sites contributed patient data to this study: Centro Medico Huesped, Buenos Aires, Argentina (CMH-Argentina); Instituto de Pesquisa Clinica Evandro Chagas, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil (FC-Brazil); Fundación Arriarán, Santiago, Chile (FA-Chile); Le Groupe Haïtien d'Etude du Sarcome de Kaposi et des Infections Opportunistes, Port-au-Prince, Haiti (GHESKIO-Haiti); Instituto Hondureño de Seguridad Social and Hospital Escuela, Tegucigalpa, Honduras (IHSS/HE-Honduras); El Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico (INCMNSZ-Mexico); and El Instituto de Medicina Tropical Alexander von Humboldt, Lima, Perú (IMTAvH-Perú). Institutional review board approval was obtained locally for each participating site, the VCCC, and the CCASAnet Data Coordinating Center at Vanderbilt University, Nashville, Tennessee, U.S.A.

HIV-infected individuals at least 18 years of age at enrollment into care with a known year of HIV diagnosis were included. Patients enrolled prior to 1995 or for whom date of birth, date of enrollment, or year of HIV diagnosis were missing were excluded. Enrollment was defined as the first time the patient was seen for care at one of the participating sites.

Outcomes

The primary outcome of interest was age at HIV diagnosis over time. Patients whose exact date of HIV diagnosis was unknown but could be approximated to the year were included in the primary analysis. Characteristics at clinic enrollment were analyzed including age, sex, CD4⁺ count (closest measurement to enrollment within 180 days before or after), probable route of transmission (heterosexual, MSM, other, or unknown), and clinical AIDS at enrollment (defined as WHO stage IV or CDC stage C, no more than 30 days after enrollment).

Statistical Analysis

Trends in age at HIV diagnosis (<25 vs. ≥25 years) were assessed according to year of diagnosis in the VCCC cohort and the seven participating CCASAnet sites. This age cut point was determined based on the US Centers for Disease Control surveillance data methods, which use similar age groups [4]. The proportion of patients <25 years of age at diagnosis was modeled separately for each site using logistic regression; calendar year of HIV diagnosis was included in each model using natural splines with knots placed at the 33rd and 66th quantiles for year of diagnosis. Likelihood ratio tests examined temporal trends and tested whether these trends were non-linear. This analysis was repeated including only those patients with MSM as the self-reported probable route of transmission. In secondary analyses, the same model was used to estimate the proportion of patients <25 years of age at enrollment at each site, among all patients and separately among those self-reported as MSM. Clinical and demographic characteristics were compared between cohorts using Kruskal–Wallis and χ^2 tests according to the variable type. Statistical analyses were performed using R version 2.14.0 (www.r-project.org). Analysis scripts are available at <http://biostat.mc.vanderbilt.edu/ArchivedAnalyses>.

Results

Selection of Patients for Analysis

A total of 23,212 patients were included: 19,466 from CCASAnet sites ($n = 1,954$ from CMH-Argentina;

$n = 4,017$ from FC-Brazil; $n = 1,444$ from FA-Chile; $n = 6,982$ from GHESKIO-Haiti; $n = 999$ from IHSS/HE-Honduras; $n = 897$ from INCMNSZ-Mexico; and $n = 3,173$ from IMTAvH-Peru) and 3,746 from VCCC. A total of 619 patients (2.6 %) were excluded because date of HIV diagnosis was unknown.

Characteristics at Enrollment

Characteristics at enrollment for patients included in the analysis are shown in Table 1. Among CCASAnet and VCCC participants, 61.5 and 75.5 % were male, respectively. The highest proportion of females was from the Haitian cohort, representing 53 % of all females in the CCASAnet cohort. The median age at enrollment was 36 and 38 years for CCASAnet and VCCC, respectively. Probable route of transmission was unknown in 46.3 % of the CCASAnet cohort, mainly due to the GHESKIO-Haiti cohort in which it is not routinely recorded; probable route was also unknown for 58 and 33 % of patients from CMH-Argentina and IHSS/HE-Honduras, respectively. The probable route of transmission was unknown for 21 % of patients in VCCC. In the CCASAnet cohort, 23.1 % were reported to have MSM risk versus 41.0 % in VCCC ($p < 0.001$). Patients with an AIDS-defining event at enrollment were more prevalent in CCASAnet sites compared to VCCC (34.2 vs. 13.0 %, $p < 0.001$), and median CD4⁺ count at enrollment to care was 194 versus 324 cells/mm³ ($p < 0.001$), respectively. Median time between diagnosis of HIV infection and enrollment to care was longer for VCCC (1.0 years) than for CCASAnet (0.3 years) ($p < 0.001$).

Patient Characteristics Stratified by Cohort, Age at HIV Diagnosis and Probable Route of Transmission

Patient characteristics at enrollment to care according to age at HIV diagnosis are shown in Table 2. Compared to patients 25 years or older at HIV diagnosis, younger patients were more likely to be female in both cohorts (45 vs. 37 % in CCASAnet and 28 vs. 24 % in VCCC; $p < 0.001$ and $p = 0.010$, respectively). Subjects less than 25 years of age at diagnosis were less likely to have clinical AIDS at enrollment than those ≥25 years of age (28 vs. 35 % in CCASAnet and 8 vs. 14 % in VCCC; $p < 0.001$ in both cases). Patients less than 25 years of age at diagnosis had higher median CD4⁺ count at enrollment to care compared with those ≥25 years of age (255 vs. 186 cells/mm³ in CCASAnet and 389 vs. 306 cells/mm³ in VCCC; $p < 0.001$ for both). Median time between diagnosis and enrollment to care was significantly longer for those <25 years compared with those ≥25 years of age in both CCASAnet (0.9 vs. 0.3 years, $p < 0.001$) and VCCC (2.5 vs. 0.8 years, $p < 0.001$).

Table 1 Demographic and clinical characteristics of patients at clinic enrollment

Characteristic	CMH- Argentina (<i>n</i> = 1,954)	FC- Brazil (<i>n</i> = 4,017)	FA- Chile (<i>n</i> = 1,444)	GHESKIO- Haiti (<i>n</i> = 6,982)	IHSS/HE- Honduras (<i>n</i> = 999)	INCMNSZ- Mexico (<i>n</i> = 897)	IMTA ^v H- Peru (<i>n</i> = 3,173)	CCASAnet (<i>n</i> = 19,466)	VCCC (<i>n</i> = 3,746)	Combined (<i>n</i> = 23,212)
Sex, <i>n</i> (%)										
Female	549 (28.1 %)	1,323 (32.9 %)	178 (12.3 %)	3,951 (56.6 %)	462 (46.2 %)	104 (11.6 %)	926 (29.2 %)	7,493 (38.5 %)	916 (24.5 %)	8,409 (36.2 %)
Male	1,405 (71.9 %)	2,694 (67.1 %)	1,266 (87.7 %)	3,031 (43.4 %)	537 (53.8 %)	793 (88.4 %)	2,247 (70.8 %)	11,973 (61.5 %)	2,830 (75.5 %)	14,803 (63.8 %)
Age at enrollment, median	37 (31, 44)	35 (29, 42)	35 (29, 41)	38 (32, 46)	36 (30, 43)	33 (28, 41)	34 (28, 42)	36 (30, 44)	38 (31, 45)	36.4 (30, 44)
Years between diagnosis and enrollment, median	1.9 (0.2, 5.6)	0.2 (0, 1.2)	0.5 (0.2, 1.8)	0.3 (0.1, 1.8)	0.1 (0, 1.4)	0.3 (0.1, 0.7)	0.3 (0, 2.5)	0.3 (0.1, 2.1)	1 (0.2, 6.6)	0.4 (0.1, 2.6)
Route of infection, <i>n</i> (%)										
Heterosexual	469 (24.0 %)	1,824 (45.4 %)	379 (26.2 %)	0 (0.0 %)	606 (60.7 %)	262 (29.2 %)	2,048 (64.5 %)	5,588 (28.7 %)	1,014 (27.1 %)	6,602 (28.4 %)
MSM	265 (13.6 %)	1,425 (35.5 %)	1,036 (71.7 %)	0 (0.0 %)	62 (6.2 %)	596 (66.4 %)	1,113 (35.1 %)	4,497 (23.1 %)	1,537 (41.0 %)	6,034 (26.0 %)
Other	89 (4.6 %)	227 (5.7 %)	22 (1.5 %)	0 (0.0 %)	6 (0.6 %)	14 (1.6 %)	6 (0.2 %)	364 (1.9 %)	414 (11.1 %)	778 (3.4 %)
Unknown	1,131 (57.9 %)	541 (13.5 %)	7 (0.5 %)	6,982 (100.0 %)	325 (32.5 %)	25 (2.8 %)	6 (0.2 %)	9,017 (46.3 %)	781 (20.8 %)	9,798 (42.2 %)
Clinical stage at enrollment, <i>n</i> (%)										
AIDS	187 (9.6 %)	2,205 (54.9 %)	713 (49.4 %)	1,610 (23.1 %)	286 (28.6 %)	466 (52.0 %)	1,187 (37.4 %)	6,654 (34.2 %)	488 (13.0 %)	7,142 (30.8 %)
Not AIDS	1,605 (82.1 %)	1,812 (45.1 %)	726 (50.3 %)	5,370 (76.9 %)	444 (44.4 %)	427 (47.6 %)	1,930 (60.8 %)	12,314 (63.3 %)	3,258 (87.0 %)	15,572 (67.1 %)
Unknown	162 (8.3 %)	0 (0.0 %)	5 (0.3 %)	2 (<0.1 %)	269 (26.9 %)	4 (0.4 %)	56 (1.8 %)	498 (2.6 %)	0 (0.0 %)	498 (2.1 %)
Median CD4 at enrollment, cells/mm ³	317 (169, 505)	290 (111, 504)	228 (84, 412)	164 (68, 260)	125 (60, 225)	160 (55, 323)	205 (74, 365)	194 (79, 337)	324 (149, 520)	212 (85, 370)
Missing CD4 at enrollment, <i>n</i> (%)	628 (32.1 %)	889 (22.1 %)	85 (5.9 %)	255 (3.7 %)	172 (17.2 %)	24 (2.7 %)	16 (0.5 %)	2,069 (10.6 %)	74 (2.0 %)	2,143 (9.2 %)

CMH Centro Medico Huesped, Buenos Aires, Argentina

FC Instituto de Pesquisa Clinica Evandro Chagas, Fundação Oswaldo Cruz, Rio de Janeiro, Brazil

FA Fundación Arriarán, Santiago, Chile

GHESKIO Le Groupe Haitien d'Etude du Sarcome de Kaposi et des Infections Opportunistes, Port-au-Prince, Haiti

IHSS/HE Instituto Hondureño de Seguridad Social and Hospital Escuela, Tegucigalpa, Honduras

INCMNSZ, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

IMTA^vH Instituto de Medicina Tropical Alexander von Humboldt, Lima, Perú

CCASAnet Caribbean, Central and South America Network

VCCC Vanderbilt Comprehensive Care Clinic, Nashville, TN, USA

MSM men who have sex with men

Table 2 Patient Characteristics at Enrollment According to Cohort, Age at HIV diagnosis, and MSM Population

Characteristic	Entire population		MSM population					
	CCASAnet		VCCC		CCASAnet MSM		VCCC MSM	
	<25 years (n = 2,902)	≥25 years (n = 16,564)	<25 years (n = 727)	≥25 years (n = 3,019)	<25 years (n = 873)	≥25 years (n = 3,624)	<25 years (n = 324)	≥25 years (n = 1,213)
Sex, n (%)								
Female	1,315 (45.3 %)	6,178 (37.3 %)	205 (28.2 %)	711 (23.6 %)				
Male	1,587 (54.7 %)	10,386 (62.7 %)	522 (71.8 %)	2,308 (76.4 %)				
Age at enrollment, median	24 (22, 26)	38 (32, 45)	25 (23, 31)	40 (34, 46)	24 (22, 26)	36 (31, 42)	25 (23, 31)	39 (34, 44)
Age at diagnosis, median	22 (20, 24)	36 (31, 43)	22 (20, 24)	36 (31, 42)	22 (21, 24)	34 (29, 40)	22 (21, 24)	35 (30, 40)
Years between diagnosis and enrollment, median	0.9 (0.1, 4.4)	0.3 (0.1, 1.8)	2.5 (0.2, 9.6)	0.8 (0.2, 5.8)	0.5 (0.1, 3.1)	0.3 (0.1, 1.7)	1.2 (0.2, 9.0)	0.9 (0.2, 6.0)
Probable route of infection, n (%)								
Heterosexual	928 (32.0 %)	4,660 (28.1 %)	188 (25.9 %)	826 (27.4 %)				
MSM	873 (30.1 %)	3,624 (21.9 %)	324 (44.6 %)	1,213 (40.2 %)				
Other	86 (3.0 %)	278 (1.7 %)	64 (8.8 %)	350 (11.6 %)				
Unknown	1,015 (35.0 %)	8,002 (48.3 %)	151 (20.8 %)	630 (20.9 %)				
Clinical stage at enrollment, n (%)								
AIDS	818 (28.2 %)	5,836 (35.2 %)	57 (7.8 %)	431 (14.3 %)	290 (33.2 %)	1,726 (47.6 %)	19 (5.9 %)	166 (13.7 %)
Not AIDS	2,007 (69.2 %)	10,307 (62.2 %)	670 (92.2 %)	2,588 (85.7 %)	567 (64.9 %)	1,829 (50.5 %)	305 (94.1 %)	1,047 (86.3 %)
Unknown	77 (2.7 %)	421 (2.5 %)	0 (0.0 %)	0 (0.0 %)	16 (1.8 %)	69 (1.9 %)	0 (0.0 %)	0 (0.0 %)
CD4 at enrollment	255 (124, 422)	186 (73, 324)	389 (239, 539)	306 (132, 513)	302 (148, 475)	235 (87, 420)	384 (242, 528)	329 (1,524, 529)
Missing CD4 at enrollment, n (%)	305 (10.5 %)	1,764 (10.6 %)	16 (2.2 %)	58 (1.9 %)	89 (10.2 %)	439 (12.1 %)	4 (1.2 %)	19 (1.6 %)

MSM men who have sex with men, CCASAnet Caribbean, Central and South America Network, VCCC Vanderbilt Comprehensive Care Clinic, Nashville, TN, USA

When analyses were limited to the self-reported MSM population, results were similar (Table 2).

Trends by Calendar Year

Figure 1 shows trends in the proportion of patients diagnosed with HIV under the age of 25 years for each of the CCASAnet sites and VCCC. The estimated percentage of patients <25 years at diagnosis changed over time ($p < 0.001$) and non-linearly ($p < 0.001$) at VCCC, ranging from below 20 % from 1998 to 2005 followed by an increase thereafter. In contrast, among CCASAnet sites, only in FA-Chile was a similar trend seen. For most sites (CMH-Argentina, GHESKIO-Haiti, IHSS/HE-Honduras, INCMNSZ-Mexico and IMTAVH-Peru), the percentage of patients <25 decreased over time. In contrast, in FC-Brazil there was not a statistically significant trend in patient age at diagnosis over calendar year ($p = 0.21$).

In the secondary analysis, Fig. 2 shows trends in the proportion of self-reported MSM who were diagnosed under the age of 25 years by study site. At the VCCC, the proportion of MSM who were under 25 years at diagnosis increased in recent years, even more dramatically than in the general population. Among MSM in CCASAnet sites, only in FC-Brazil and INCMNSZ-Mexico was there a statistically significant trend over time ($p < 0.05$): the proportion of MSM <25 years at HIV diagnosis increased over time in FC-Brazil, whereas this proportion decreased in INCMNSZ-Mexico.

Similar analyses were performed to investigate trends in age at enrollment to care. Trends in the proportion <25 years at enrollment were similar to trends in the proportion <25 at diagnosis at the VCCC, both among the general patient population and MSM (see Electronic supplementary material). Trends were not as consistent across CCASAnet sites: in the general patient population the proportion <25 years at enrollment increased in recent years in FA-Chile and GHESKIO-Haiti, whereas it remained nearly the same in other CCASAnet sites. In contrast, among MSM, the proportion <25 at enrollment increased in FC-Brazil, FA-Chile, and IMTAVH-Peru.

Discussion

Despite advances in HIV prevention, access to effective antiretroviral therapy, increases in life expectancy, and reductions in vertical transmission, the HIV epidemic continues globally and many challenges remain. Improved awareness of the unique trends occurring within and between countries and regions may be key to understanding local HIV epidemics. The present study is the first to examine age at HIV diagnosis in Latin America and the

Caribbean during the HAART era. We compared trends in age at HIV diagnosis from a single-site HIV clinic in the southeastern United States to seven sites in Latin America and the Caribbean. Similar to U.S. national statistics [2, 4] the VCCC had a greater proportion of newly diagnosed individuals who were <25 years of age in recent years. Interestingly, similar trends were not consistently observed in the Latin American and Caribbean cohorts.

The relatively stable demographic trends in Latin America and the Caribbean observed in our study could be explained by many factors. It may be that relatively fewer individuals <25 years of age within the region are being infected when compared with the United States. It is possible that shifts in age at diagnosis in the HIV epidemic in Latin America will occur in the near future, and that this is an important time to intervene and intensify surveillance efforts in young adults. In contrast, it may be that greater proportions of younger individuals in this region are infected, but are not aware of their status—perhaps because they are not being tested at similar rates as those ≥ 25 years of age. Alternatively, those <25 years may be getting infected and even diagnosed, but not entering into care. Unfortunately, we were only able to assess demographic trends in HIV diagnosis among patients who had entered care.

Reasons for this shift in the United States towards younger age at HIV diagnosis, particularly among MSM, have been examined. In a recent analysis of data from 20 U.S. cities participating in the 2005, 2008, and 2011 National HIV Behavioral Surveillance System (NHBS), unprotected anal intercourse once in the past 12 months increased from 48 % in 2005 to 57 % in 2011 among MSM studied and MSM represented the majority of new HIV infections in all but two states [15]. In a recent survey of 200 predominantly black MSM aged 16–24, belief that an undetectable viral load reduced infectiousness was associated with unprotected receptive anal intercourse with HIV-positive partners [16]. These studies suggest that risk compensation (i.e., increasing risky behaviors based on a perceived lower risk) combined with lack of awareness of a partner's HIV status, and less access to (or engagement with) health care providers could contribute to the increase in HIV incidence for young MSM. This group represents a crucial demographic target towards which improved HIV prevention efforts should be tailored.

In contrast, our secondary analyses investigating trends in age at diagnosis among MSM did not show a clear pattern in Latin America. At our site in Brazil, we noted a rise in the diagnosis of MSM less than 25 years of age in recent years, whereas our Mexican site had a decrease and other sites presented little evidence of temporal trend. In Latin America, information published about the local situation in terms of MSM and new HIV diagnoses is scarce.

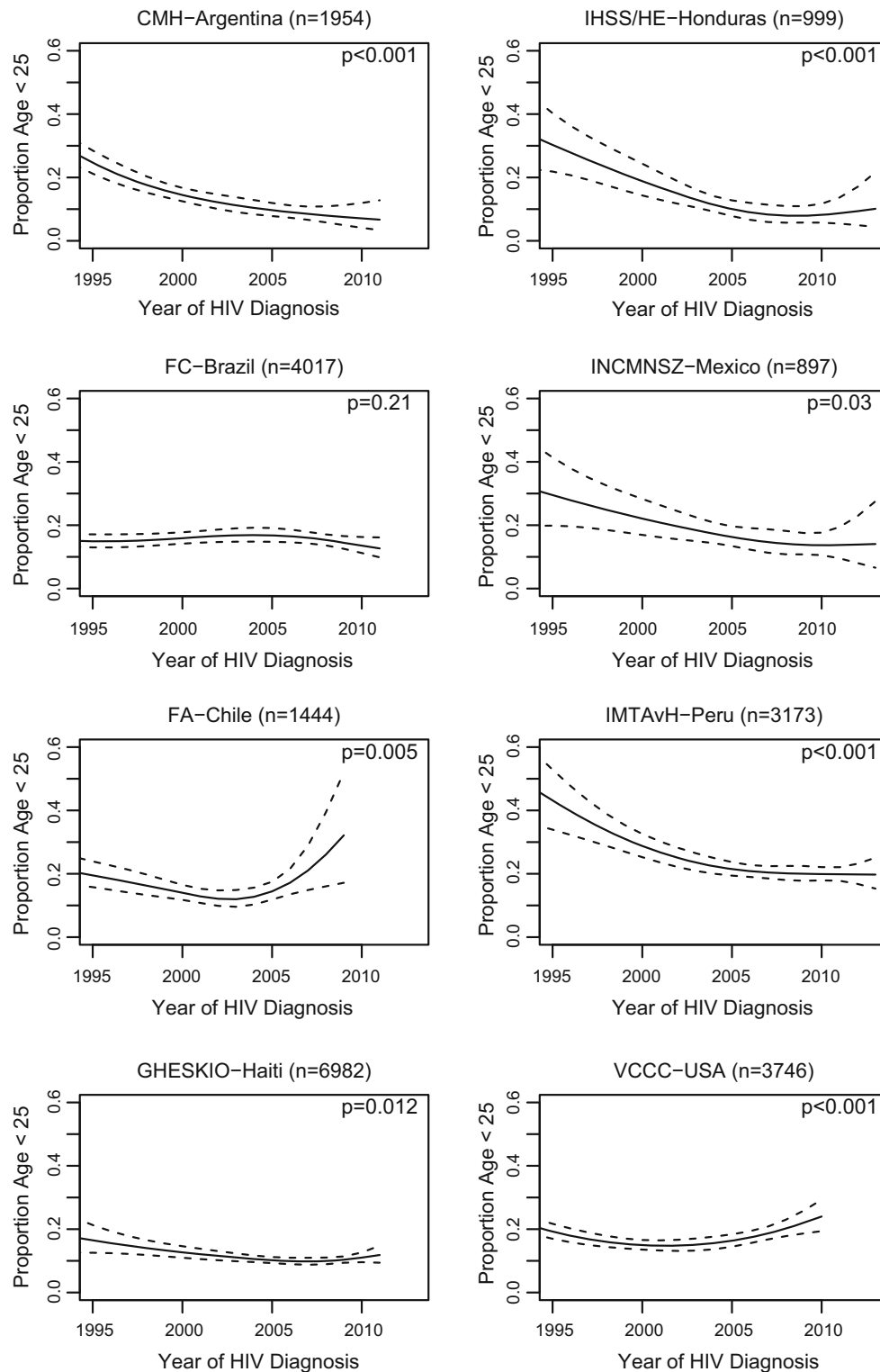


Fig. 1 Trends in the proportion of patients <25 years of age at HIV diagnosis according to site

Brazil previously reported an increase of 22 % of HIV diagnosis in MSM in the last decade [17], Argentina reported an increase of 33.9–44.4 % from 2001 to 2012 [18], while in Chile the proportion of MSM diagnosed with

HIV remained relatively unchanged from 1988 to 2012 [19]. National campaigns are often directed towards traditionally characterized risk populations such as MSM, which would presumably lead to more testing [20, 21],

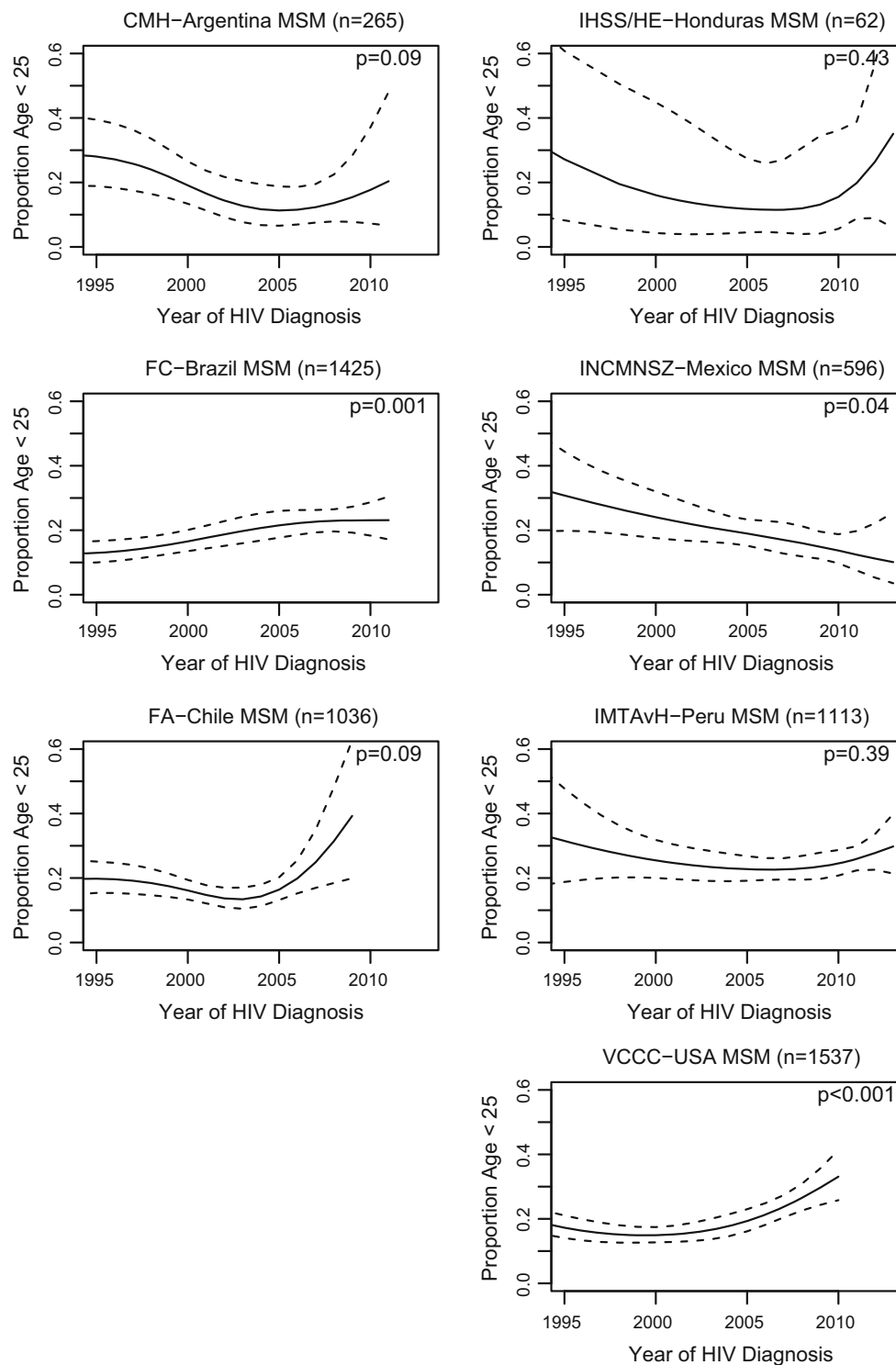


Fig. 2 Trends in the proportion of patients <25 years of age at HIV diagnosis among men who have sex with men (MSM) according to site

although the impact these campaigns might have on age at diagnosis among MSM is unclear. The differences between the proportion of patients who report being MSM across different sites within CCASAnet are also noteworthy, and may reflect important differences between countries, clinic

settings, and cultures, in regards to HIV stigma, access to HIV testing and treatment, and education levels. Alternatively, it may be that due to the self-report of sexual orientation (and perhaps varying willingness to do this depending on the country of origin and associated stigma

[22, 23]) our data on MSM should be interpreted with caution. Importantly, a substantial number of study subjects, including all patients at our site in Haiti, had an unknown route of transmission. In the beginning of the HIV epidemic within Haiti, 50–60 % of men diagnosed with HIV endorsed homosexual or bisexual activity. Over time in the early to mid-1980s, the epidemic in Haiti shifted to predominantly heterosexual transmission [24]. However, more recent data showed the majority of Haitian MSM reported bisexual activity, and 30 % reported male-to-male intercourse as their perceived risk factor for HIV acquisition. This ongoing interplay between homosexual/bisexual/heterosexual subgroups may serve to drive the spread of HIV by creating connections between epidemics [22].

Another notable finding of our study is that those who were <25 years at HIV diagnosis were less likely to have AIDS by clinical stage at enrollment compared with those who were ≥25 years of age. This was true both for the CCASAnet sites and the VCCC in the U.S., among the entire population and among MSM. Those <25 years of age at diagnosis also tended to have higher CD4 counts at enrollment. There are several possible reasons for these findings. Older age is known to be associated with late testing [25–27]. HIV infection typically has a clinical latency phase of many years' duration before the development of symptoms, which often prompt testing and HIV diagnosis. Thus, these results may be consistent with the hypothesis that infection is occurring at higher rates among the young but that diagnoses are lagging. Time from HIV diagnosis until enrollment tended to be longer among those <25 years at diagnosis, in both cohorts, which may also reflect that those <25 are generally experiencing fewer symptoms and feel less need to engage in care. Also, stigma related to HIV has been associated with later entry to care and lower CD4 counts at diagnosis [28, 29]. Younger MSM were more likely to score high on internalized stigma scales in one study when compared with those >30 year of age [30]. Hence, this population may be more likely to fail to disclose their sexual orientation, possibly contributing to a shift towards more advanced disease stages among those not declared as MSM.

In both cohorts of our study those less than 25 years of age were more likely to be female. To some extent this may reflect diagnosis related to pregnancy, although this is only speculative, as no such data were available. This finding is not consistent with other publications that have reported heterosexual transmission as a risk factor for late presentation to care [31].

There are additional limitations to our study, inherent within any retrospective cohort design. Date of HIV diagnosis was missing for >3 % of patients at our sites in Chile, Haiti, Mexico, and the United States. CCASAnet is comprised of seven sites within Latin America and the

Caribbean, and these sites may not accurately reflect the demographic trends of each country or of the region as a whole. As mentioned earlier, our study only included patients who entered care—not all who were diagnosed with HIV—and measurement of probable route of transmission was inconsistent across sites. With these limitations noted, our study is the first to our knowledge to describe recent trends in ages at HIV diagnosis in Latin America and the Caribbean, and therefore provides an important look into the course of the epidemic in this region.

In conclusion, the epidemiology of HIV is complex, diverse, and dynamic. As the epidemic progresses worldwide, it continues to shift and change amongst those affected by HIV, and understanding these often subtle changes may be key to halting the epidemic's progression. As described elsewhere in the U.S., the proportion of patients less than 25 years at HIV diagnosis has increased at the VCCC in recent years for both the general population and for MSM. In contrast, similar increasing trends were not observed in Latin America and the Caribbean, except at the site in Chile in the general population and at the site in Brazil among MSM. The reasons for the dissimilar trends in age at HIV diagnosis are unclear and warrant further investigation. Interestingly, younger subjects at HIV diagnosis in both cohorts were less likely to have AIDS and lower CD4 count at entry to care. With increasing survival of HIV-infected individuals through growing access to antiretroviral treatment, there remains an urgent need for accurate tools to identify risk factors for infection among changing groups. An improved understanding of trends in the U.S., Latin America, and the Caribbean may support targeted testing, particularly among younger people and potentially younger MSM. This would allow clinicians, scientists, community activists, and educators to stay in step with local drivers of the epidemic and to direct policies in prevention efforts towards vulnerable groups at risk for acquiring HIV.

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