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Changing Epidemiologic Profile and the Outcome of HIV and AIDS among Patients in a Referral Hospital in the Philippines: A 33-year Longitudinal Cohort

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Abstract

Background: From a relatively slow-rising epidemic, HIV has accelerated its pace in the Philippines since 2007. This study analyzed the epidemiology, clinical profile, and factors affecting the disease outcome of Filipinos infected with HIV seen at the Research Institute for Tropical Medicine (RITM).

Methods: Patients aged >18 years with confirmed HIV infection and entered to care at RITM from 1989 to July 2015 were included in the analysis. Clinical and laboratory profiles were reviewed. The factors associated with AIDS-defining conditions or HIV-associated mortality (as a combined outcome) and HIV-associated mortality alone were evaluated using competing risk regression.

Results: Of 4,942 patients included in the study, majority were men who have sex with men, local workers, with a median age of 35 years (IQR 29.90-41.78) and CRF01_AE as the common HIV subtype. Incidence rate of AIDS-defining condition or HIV-associated mortality (as a combined outcome) was 8.47 per 100 patient-years (95% confidence interval [CI] 7.88-9.120) and the incidence rate of HIV-associated mortality was 3.35 per 100 patient-years (95% CI: 3.01-3.74). Educational attainment, migrant work, heterosexual exposure, tuberculosis and other opportunistic infections, low CD4 cell count, anemia and patients not on antiretroviral therapy were significantly associated with the risks of having the study outcomes.

Conclusion: The epidemiologies of patients with HIV have changed over time but the efficacy of ART remained. Late presentation in clinical care is significant predictor of poor outcome hence the need to scale up HIV testing for early HIV diagnosis. A holistic approach to care is important.

Keywords

HIV; AIDS; Antiretroviral therapy; CD4 cell

Introduction

It was in 1984 when the first case of HIV was reported in the Philippines. Previously HIV was relatively slow rising epidemic. By 2007, however, the HIV epidemic has rapidly accelerated it space. It took ten years for the number of new HIV cases to double from 154 cases in 1996 to 309 cases in 2006 and merely two years for the 342 new HIV cases in 2007 to increase almost a hundred fold to 629 new HIV cases in 2009. There was also a marked a shift in the demographic of patients who were acquiring the infection. The combined number of those infected through homosexual and bisexual contact has continually exceeded the number of cases that were infected through heterosexual contact. Whereas overseas Filipino workers (OFW), who presumably acquire the infection outside the country, used to comprise majority of newly diagnosed cases, recent report showed they merely comprised 11% of new cases [1].

Antiretroviral therapy (ART) became universally accessible in the country by 2006. From over a hundred patients on treatment, it increased to 12,533 by end of 2015 [2] and to 24,754 patients by end of 2017 [3].

In 1989, through a grant from the Japan Foundation for AIDS Prevention (JFAP), the Research Institute for Tropical Medicine (RITM) started a cohort study on the natural history of HIV among Filipinos. This cohort study eventually evolved into a research-based clinical services and setting the standard of care for HIV in the country. The cohort, continued to be a rich source of demographic, clinical and laboratory data that help inform national guidelines and policies for HIV and AIDS treatment and control.

Methods

Study population and outcome definition

Since 1989, medical records of patients with HIV seen at RITM utilized clinical research forms (CRFs). Electronic copies of these CRFs were made for each clinic visits. Anonymized and de-identified data were extracted and analyzed from the electronic files.

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All patients 18 years old and above with confirmed HIV infection who entered into care at RITM from 1989 to July 2015 and with at least one prospective follow up were included in the analysis. The two outcome variables were occurrence of AIDS-defining condition or HIV-related mortality (as a combined outcome) -patients were considered to have this outcome if he/she developed AIDS-defining conditions or died due to HIV-associated illness. If the patient developed both of these events eventually across the duration of the study, the earliest event, which took place, was taken as the final outcome.

HIV-related mortality- defined as death related to HIV. Censored observations were considered as those individuals that did not experience or develop the outcome of interest after entry into care up until July 2015. Loss to follow-up (LTFU) was defined as no clinic visit within 24 months prior to the last RITM database closed date (July 2015), not including transferred cases. Death not associated with HIV was accounted as competing risk.

Definition of variable of interest

Baseline CD4 count, viral load (VL) and hemoglobin level were defined as the closest measurements within the defined window period of 6 months prior to entry into care and 1 month after entry into care. Patients were considered hepatitis B co-infected if they had any record of a positive hepatitis B surface antigen test in the database. Prior AIDS-defining condition at baseline were defined as having a Center for Disease Control and Prevention (CDC) category C illness at any time prior and 1 month after entry into care [4].

Statistical analysis

To explore the factors associated with the two outcome of interest: 1) AIDS-defining illness and/or HIV-associated mortality and 2) HIV-associated mortality, we used competing risk regression analysis. Covariates included age, sex, education, occupation, mode of HIV exposure, number of sexual partners, HBV status, prior CDC category C illnesses, prior opportunistic infections, baseline hemoglobin level, CD4 count and viral load and antiretroviral therapy.

Predictors to be included in the multivariate model were selected based on a significance level of ≤ 0.10 in the univariate analysis. Predictors were retained in the multivariate model if one or more categories exhibited a *p*-value ≤ 0.05. Patient with missing data were included in the analyses but hazard ratios for missing categories are not reported.

All data management and analysis were performed using Stata software version 13.1 (Stata Corp., College Station, TX, USA).

Ethical consideration

All data were treated in a strictly confidential manner according to the ethical principles of the Helsinki Declaration of 1964 revised by the World Medical Organization in Fortaleza, 2013 [5], and Philippine data privacy law [6]. Patient information was anonymized and de-identified prior to analysis. The study protocol was approved by the ethical review board of RITM.

Results

Demographic characteristics

Of the 5,474 patients with demographic data enrolled at RITM, 4,942 (90.2%) met the inclusion criteria for a total of 8,460 follow up years. Although majority of the patients were male, the difference became more apparent starting 2007 where male comprised 97% compared to 68.85% prior to 2007. Patients were younger upon entry into care starting 2007 compared to previous years median age 35.29 Inter quartile range (IQR 29.90-41.78) *versus* 28.19 (IQR 25.12-32.32) (*p*=<0.0001). There were significantly fewer overseas workers, more patients with higher educational attainment and reporting either homosexual or bisexual behaviors starting 2007compared to previous years. Although majority of patients who entered onto care prior to 2007 had no available CD4 test data, most patients in both eras had very low baseline CD4 cell count (Table 1).

Characteristics	Prior to 2007 (n=443)		2007 onwards (n=4,449)		*p*-value
	No	%	No	%	
Sex					
Male	305	68.85	4,393	97.64	
Female	138	31.15	101	2.24	<0.001
Missing	0	0	5	0.11	
Age at entry into care (in years)					
18-30	131	29.57	3,106	69.04	
31-40	188	42.44	1,106	24.58	<0.001
41 and above	124	27.99	287	6.38	
Median Age (IQR)	35.29	(29.90-41.78)	28.19	(25.12-32.32)	<0.0001
Education					
Never attended school/Some High School	56	12.64	67	1.49	
High School Graduate/ Vocational Course/some college	170	38.37	1,191	26.47	<0.001
College Graduate of or higher	177	39.95	2,998	66.64	
Missing	40	9.03	243	5.4	
Occupation					
Overseas Worker	150	33.86	121	2.69	
Local Worker	169	38.15	3,105	69.02	<0.001
Unemployed	69	15.58	774	17.2	
Missing	55	12.42	499	11.09	
Reported Mode of infection					
Bisexual	49	11.06	1,321	29.36	
Homosexual contact	91	20.54	2,423	53.86	
Heterosexual contact	269	60.72	270	6	<0.001
Others	13	2.93	46	1.02	
Unknown	21	4.74	439	9.76	
Number of sexual partners					
Single	15	3.39	441	9.8	
More than one	16	3.61	3,532	78.51	<0.001
Unknown	412	93	526	11.69	
Baseline CD4 count (cells/ uL)					
<200 (% tested)	78	17.61	1,697	43.14	
200-350 (% tested)	32	7.22	1,107	28.14	
>350 (% tested)	59	13.32	1,129	28.7	<0.001
Not tested	274	61.85	566	12.58	

Table 1: Demographic characteristics

Clinical profile

Majority of patients had no opportunistic infection upon entry into care. The most common presenting illnesses were tuberculosis (9.2%) and *Pneumocystis jirovecii* pneumonia (2.4%). Among those with hepatitis B screening, only about 7% were reactive to HBs antigen test. The median CD4 cell count was 273 cells/mm^3 (IQR 71-375) and median hemoglobin level was 14.1 g/dl (IQR 12.9-15.3) among those on ART, 68.5% were on non-nucleoside reverse transcriptase (NNRTI)-based regimen. Only 2.7% of patients had viral load testing before ART initiation (Table 2).

HIV Subtype

Among patients with HIV subtype information, 71.33% was CRF01_AE and 23.43% were subtype B. Subtype B was the predominant subtype prior to 2008 and the frequency of CRF01_AE started to increase in the succeeding years (Table 2 and Figure 1).

Baseline characteristics	No	%
Opportunistic Infections prior to entry into care		
No OICs	4,211	85.21
TB	457	9.25
PCP	118	2.39
Others	156	3.16
HBV status (n=2,778 tested)		
No (% tested)	3,262	66.01
Yes (% tested	258	5.22
Not tested	1,422	28.77
Baseline CD4 cell count (cells/ml)		
<200 (% tested)	1,775	35.92
200-350 (% tested)	1,139	23.05
>350 (% tested)	1,188	24.04
Not tested	840	17
Median (IQR)	237	(71-375)
Viral load (copies/ml)		
≤ 10,000 (% tested)	22	16.54
>10,000 (%tested)	111	83.45
Not tested	4,809	97.31
Median (IQR)	142,818	(29,554-519,282)
Baseline Hemoglobin Level (g/dl)		
<9 (% tested)	151	3.06
10-11 (% tested)	494	10
>11 (% tested)	3,474	70.3
Not tested	823	16.65
Median (IQR)	14	(12.9-15.3)
ART Regimen Status		
NNRTI-based therapy	3,386	68.51
Others	436	8.82
Not on ART treatment	1,120	22.66
HIV Subtype		
B (% tested)	67	23.43
CRF01_AE (% tested)	204	71.33
Others	15	5.24
Not tested	4,656	94.21

Table 2: Baseline clinical and laboratory profile (n=4,942)

Clinical outcome

Among the 4,942, 717 (14.5%) patients developed new AIDS-defining condition or HIV associated mortality (as a combined outcome), giving an incidence rate of 8.47 per 100 patient years (95% confidence interval [CI] 7.88-9.12). The rate of lost to follow-up (LTFU) was 2.7 (95% CI: 2.39-3.11) per 100 patient-years.

Meanwhile, HIV-associated mortality occurred in 326 patients (6.6%) at an incidence rate of 3.35 per 100 patient years (95% CI: 3.01-3.74).

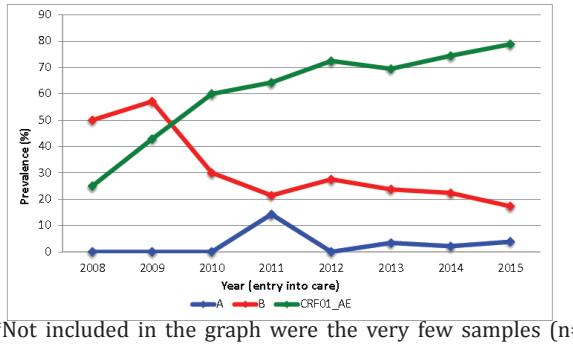
Low level of education, overseas worker, heterosexual exposure, TB and other OIs, low CD4 cell count, low hemoglobin level and not being on ART were all significantly associated with both combined outcomes and HIV-associated mortality (Tables 3 & 4).

The cumulative probability of progressing to AIDS or death and mortality were significantly increased among heterosexual males and overseas workers (Supplemental Figures 1 & 2).

Discussion

We reported the outcome of the biggest and longest running cohort of patients with HIV in the Philippines. Although ART became universally available in the country since 2006, this is the first study that provided evidence based on largest database of patients with regard to the efficacy of ART in reducing HIV related morbidity and mortality (1.188 per 100 patient year, CI .96-1.47 *vs.* 15.1 per 100 patient year, CI 13.19-17.27). Similar to other cohort studies from various regions in the world, our study showed not only the benefit of ART [7-10] but it also demonstrated that advanced HIV disease, as evidenced by low CD4 count, presence of AIDS defining illness and low hemoglobin count could adversely affect outcome [11-16].

We were also able to document the shift in the demographic of the HIV epidemic in the country overtime. In the past decade we observed that the transmission was predominantly local and driven by men who have sex with men (MSM). Although HIV was initially identified among gay men in the early 80's, a global re-emergence of MSM driven HIV was observed beginning early part of year 2000 [17,18].



**Not included in the graph were the very few samples (n=6) tested before 2007.

**Other subtypes not included in the graph were subtypes CRF02_AG (seen 1/1 patient with HIV subtype result in 2002 and 1/2 patients with HIV subtype results in 2006), subtype G (seen in 1/4 patients with HIV subtype results in 2008), subtype C (seen 1/10 patients with HIV subtype results in 2010 and 1/59 patients with HIV subtype results in 2013), B + CRF01_AE (seen in 1/94 patients with HIV subtype results in 2014) and CRF52_01B (seen 1/59 patients with HIV subtype results in 2013).

Figure 1: Distribution of different HIV subtypes among patients with HIV subtype results in the recent years, RITM Observational Database

Co-variables	No. of patients	Follow-up years	No. of AIDS or deaths	Rat per 100 patient-years	95% CI		Univariate				Multivariate			
							HR	95% CI		*p*-value	HR	95% CI		*p*-value
Total	4,942	8460.5	717	8.47	7.88	9.12								
Sex														
Male	4,698	7708.05	615	7.98	7.37	8.63	1				1			
Female	239	749.83	101	13.47	11.08	16.37	2.28	1.83	2.82	<0.001	0.9	0.68	1.19	0.446
Missing	5	2.62	1	38.13	5.37	27.66								
Age at entry into care (in years)														
18-30	3,237	4930.12	364	7.38	6.66	8.18	1				1			
31-40	1,294	2509.24	243	9.68	8.54	10.98	1.52	1.29	1.79	<0.001	1.14	0.97	1.35	0.118
41 and above	411	1021.14	110	10.77	8.94	12.99	1.91	1.53	2.38	<0.001	1.02	0.8	1.3	0.86
Education														
College Graduate of or higher	3,175	5487.9	373	6.8	6.14	7.52	1				1			
Never attended school/Some High School	123	298.68	48	16.07	12.11	21.33	2.71	2	3.68	<0.001	1.36	0.96	1.93	0.08
High School Graduate or Vocational Course or some college	1,361	2278.3	244	10.71	9.45	12.14	1.58	1.35	1.85	<0.001	1.24	1.05	1.46	0.012
Missing	283	395.62	52	13.14	10.02	17.25								
Occupation														
Local Worker	3,274	5216.61	381	7.3	6.61	8.08	1				1			
Overseas Worker	271	843.43	113	13.4	11.14	16.11	2.52	2.05	3.1	<0.001	1.5	1.21	1.87	<0.001
Unemployed	843	1439.82	131	9.1	7.67	10.8	1.25	1.03	1.53	0.027	1.07	0.87	1.32	0.497
Missing	554	960.64	92	9.58	7.81	11.75								
Reported Mode of infection														
Heterosexual contact	539	1595.07	208	13.04	11.38	14.94	1				1			
Bisexual	1,370	2067.17	143	6.92	5.87	8.15	0.37	0.3	0.45	<0.001	0.62	0.49	0.79	<0.001
Homosexual contact	2,514	4049.93	301	7.43	6.64	8.32	0.41	0.34	0.49	<0.001	0.7	0.57	0.86	0.001
Others	59	108.17	14	12.94	7.67	21.85	0.75	0.46	1.24	0.262	0.82	0.49	1.36	0.434
Unknown	460	640.16	51	7.97	6.05	10.48								
Number of sexual partners														
Single	456	1122.19	58	5.17	4	6.69	1				1			
More than one	3,548	4903.54	331	6.75	6.06	7.52	1.01	0.76	1.33	0.963	1.17	0.86	1.56	0.338
Unknown	938	2434.77	328	13.47	12.09	15.01								
AIDS Defining illnesses prior to entry into care														
No OICs	4,211	6919.32	521	7.53	6.91	8.2	1				1			
TB	457	928.67	118	12.71	10.61	15.22	2	1.62	2.48	<0.001	1.52	1.2	1.93	0.001
PCP	118	251.75	27	10.73	7.36	15.64	1.72	1.14	2.6	0.001	1.34	0.86	2.09	0.199
Others	156	360.76	51	14.14	10.74	18.6	2.29	1.68	3.1	<0.001	1.44	1.03	1.99	0.031
Total	4,942	8460.5	717	8.47	7.88	9.12								
HVB status														
No (% tested)	3,262	5779.4	347	6	5.4	6.67	1				1			
Yes (% tested)	258	519.66	29	5.58	3.88	8.03	0.96	0.65	1.41	0.83	1.02	0.69	1.52	0.917
Not tested	1,422	2161.44	341	15.78	14.19	17.54								
Baseline CD4 count (cells/uL)														
>350 (% tested)	1,188	2135.12	96	4.5	3.68	5.49	1				1			
<200 (% tested)	1,775	2516.02	288	11.45	10.2	12.85	2.5	1.99	3.13	<0.001	2.41	1.42	2.9	<0.001
200-350 (% tested)	1,139	1862.66	79	4.24	3.4	5.29	0.96	0.71	1.28	0.768	2	1.44	2.41	<0.001
Not tested	840	1946.7	254	13.05	11.54	14.76								
Viral load (copies/ml)														
≤ 10000 (% tested)	22	70.63	2	2.83	0.71	11.32	1				1			
>10,000 (%tested)	111	388.05	18	4.64	2.92	7.36	1.65	0.36	7.51	0.515	1.68	0.34	8.29	0.523
Not tested	4,809	8001.82	697	8.71	8.09	9.38								
Baseline Hemoglobin Level (g/dl)														
>11 (% tested)	3,474	5847.01	311	5.32	4.76	5.94	1				1			
<9 (% tested)	151	213.3	45	21.1	15.75	28.26	4	2.89	5.52	<0.001	2.03	1.42	2.9	<0.001
>10-11 (% tested)	494	761.3	116	15.24	12.7	18.28	2.97	2.38	3.7	<0.001	1.87	1.44	2.41	<0.001
Not tested	823	1638.9	245	14.95	13.19	16.94								
Initial ART Regimen														
Triple NNRTI-based therapy	3,386	6221.05	389	6.25	5.66	6.91	1				1			
Others	436	886.21	72	8.12	6.45	10.24	1.34	1.05	1.72	0.02	1.25	0.96	1.64	0.103
Not on ART treatment	1,120	1353.23	256	18.92	16.74	21.38	2.33	1.99	2.72	<0.001	2.27	1.92	2.68	<0.001

*Patients with missing data were included but hazard ratio (HRs) for missing categories not reported.

Table 3: Risk factors associated with AIDS defining illnesses or HIV associated mortality (n=4924)

Co-variables	No. of patients	Follow-up years	HIV related mortality	Rat per 100 patient-years	95% CI		Univariate				Multivariate			
							HR	95% CI		*p*-value	HR	95% CI		*p*-value
Total	4,942	9720.9	326	3.35	3.01	3.74								
Sex														
Male	4,698	8757.77	248	2.83	2.5	3.21	1				1			
Female	239	960.2	78	8.12	6.51	10.14	3.99	3.05	5.25	<0.001	0.79	0.55	1.13	0.192
Age at entry into care (in years)														
18-30	3,237	5467.5	135	2.47	2.09	2.92	1				1			
31-40	1,294	3043.22	120	3.94	3.3	4.72	1.89	1.48	2.42	<0.001	1.21	0.94	1.56	0.147
41 and above	411	1210.17	71	5.87	4.65	7.4	3.08	2.28	4.16	<0.001	1.16	0.82	1.64	0.407
Education														
College Graduate of or higher	3,175	6222.14	127	2.04	1.72	2.43	1				1			
Never attended school/Some High School	123	386.52	39	10.09	7.37	13.81	6.03	4.14	8.78	<0.001	1.6	1	2.58	0.05
High School Graduate or Vocational Course or some college	1,361	2674	128	4.79	4.03	5.69	2.4	1.88	3.07	<0.001	1.51	1.16	1.95	0.002
Missing	283	438.23	32	7.3	5.16	10.33								
Occupation														
Local Worker	3,274	5883.91	144	2.45	2.08	2.88	1				1			
Overseas Worker	271	1086.41	85	7.82	6.33	9.68	4.62	3.5	6.1	<0.001	1.65	1.24	2.21	0.001
Unemployed	843	1658.79	60	3.62	2.81	4.66	1.48	1.09	1.99	0.001	1.2	0.87	1.65	0.268
Missing	554	1091.79	37	3.39	2.46	4.68								
Reported Mode of infection														
Heterosexual contact	539	2060.7	152	7.38	6.29	8.65	1				1			
Bisexual	1,370	2290.3	44	1.92	1.43	2.58	0.17	0.12	0.24	<0.001	0.43	0.3	0.62	<0.001
Homosexual contact	2,514	4577.4	96	2.1	1.72	2.56	0.19	0.15	0.25	<0.001	0.49	0.37	0.66	<0.001
Others	59	111	12	10.81	6.14	19.04	0.96	0.55	1.67	0.874	1.04	0.53	2.02	0.915
Unknown	460	681.6	22	3.23	2.13	4.9								
Number of sexual partners														
Single	456	1272.79	12	0.94	0.54	1.66	1				1			
More than one	3,548	5342.23	77	1.44	1.15	1.8	1.15	0.63	2.12	0.65	1.5	0.78	2.85	0.222
Unknown	938	3105.87	237	7.63	6.72	8.67								
AIDS Defining illnesses prior to entry into care														
No OICs	4,211	7769.84	237	3.05	2.69	3.46	1				1			
TB	457	1182.54	45	3.81	2.84	5.1	1.48	1.06	2.05	0.021	1.56	1.05	2.33	0.028
PCP	118	351.24	9	2.56	1.33	4.92	1.06	0.55	2.04	0.865	1.4	0.63	3.09	0.41
Others	156	417.28	35	8.39	6.02	11.68	3.25	2.25	4.71	<0.001	2.4	1.64	3.53	<0.001
Total	4,942	9720.9	326	3.35	3.01	3.74								
HVB status														
No (% tested)	3,262	6686.31	65	0.97	0.76	1.24	1				1			
Yes (% tested)	258	557.12	6	1.08	0.48	2.4	1.09	0.47	2.52	0.848	1.31	0.55	3.14	0.541
Not tested	1,422	2477.46	255	10.29	9.1	11.64								
Baseline CD4 count (cells/uL)														
>350 (% tested)	1,188	2373.8	33	1.39	0.99	1.96	1				1			
<200 (% tested)	1,775	2883.26	112	3.88	3.23	4.67	2.79	1.91	4.08	<0.001	4.87	3.28	7.23	<0.001
200-350 (% tested)	1,139	2060.41	17	0.83	0.51	1.33	0.61	0.34	1.08	0.089	1.69	0.91	3.12	0.096
Not tested	840	2403.43	164	6.82	5.86	7.95								
Viral load (copies/ml)														
≤ 10000 (% tested)	22	72.67	1	1.38	0.19	9.77	1				1			
>10,000 (%tested)	111	436.77	4	0.92	0.34	2.44	0.69	0.07	6.43	0.745	0.84	0.08	8.71	0.885
Not tested	4,809	9211.45	321	3.48	3.12	3.89								
Baseline Hemoglobin Level (g/dl)														
>11 (% tested)	3,474	286.01	26	9.09	9.09	13.35	1				1			
<9 (% tested)	151	912.93	39	4.27	4.27	5.85	8.01	5.1	12.58	<0.001	3.11	1.86	5.19	<0.001
>10-11 (% tested)	494	6525.37	82	1.26	1.26	1.56	3.6	2.45	5.28	<0.001	1.95	1.26	3.02	0.003
Not tested	823	1996.59	179	8.97	8.97	10.38								
Initial ART Regimen														
Triple NNRTI-based therapy	3,386	7090.72	84	1.18	1.18	1.47	1				1			
Others	436	1225.8	30	2.45	2.45	3.5	2.26	1.51	3.4	<0.001	2.01	1.29	3.14	0.002
Not on ART treatment	1,120	1404.38	212	15.1	15.1	17.27	9.41	7.31	12.13	<0.001	9.74	7.32	12.95	<0.001

*Patients with missing data were included but hazard ration (HRs) for missing categories not reported

Table 4: Risk factors associated with HIV-related mortality (n=4924)

Although the requirement for HIV testing for OFW remains, the number of new infections in this population continues to decline. This is the result of the regular pre-departure seminars provided by hiring companies, government agencies and non-government organizations. The increasing frequency of CRF01_AE, the predominant subtype in Southeast Asia, is consistent with local HIV transmission [19,20]. A phylogenetic study is underway to determine possible timeline ofCRF01_01 introduction in the country and relationship to circulating strain in the region.

We reported better outcome among homosexual males patients. This was similar to the findings of Zhou et al. in 2005 [16] and Garriga et al. in 2015 [13] although the study of Coelho et al. in 2016 [10] did not show similar result. Most OFWs were heterosexual male seafarers. Access to ART and other medical services would be more difficult while in foreign country or on board a vessel for overseas workers in general. Some men who self-reported as heterosexuals maybe closeted gay men and fear of discrimination could have adversely affected their health seeking behavior and adherence to medication. Homosexual males who have no issues regarding gender identity may be more comfortable in seeking information and assessing care and have better social support system.

There has been concern regarding response to ART among patients with CRF01_AE, the predominant subtype in Southeast Asia since efficacy trials were conducted in predominantly subtype B western countries. Our study and other cohorts in the region have demonstrated efficacy of ART comparable to the western countries [16].

Although our data came from the biggest real world clinical cohort in the Philippines, being a retrospective and purely observational study, there were many missing variables. Almost one third of patients had no viral hepatitis B screening. HIV viral load testing prior to ART is not part of local treatment guideline; hence, this information was not available in 97% of patients.

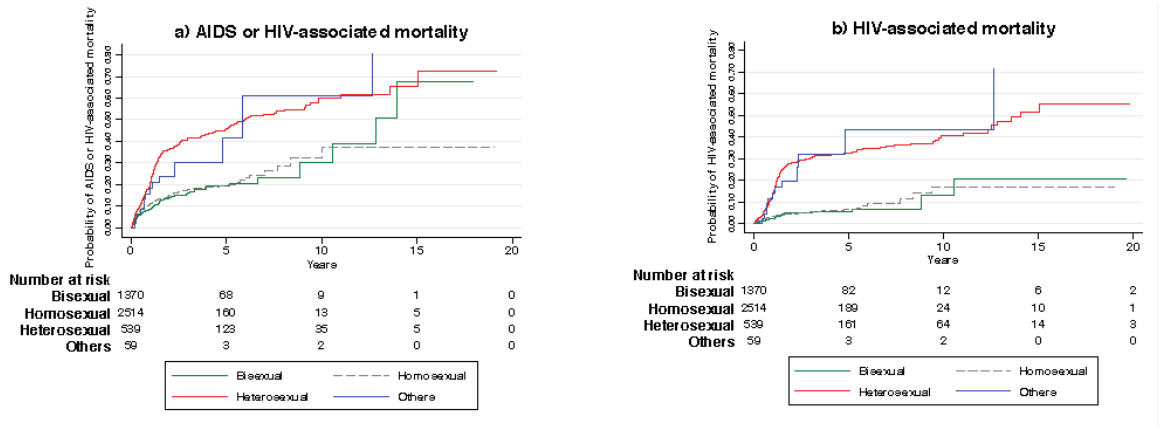
We showed that CRF01_AE has become the predominant subtype in the recent years. With few patients with HIV subtype data and majority of patients were MSM, we could not generalize this trend for the whole country nor to other key affected population.

Conclusion

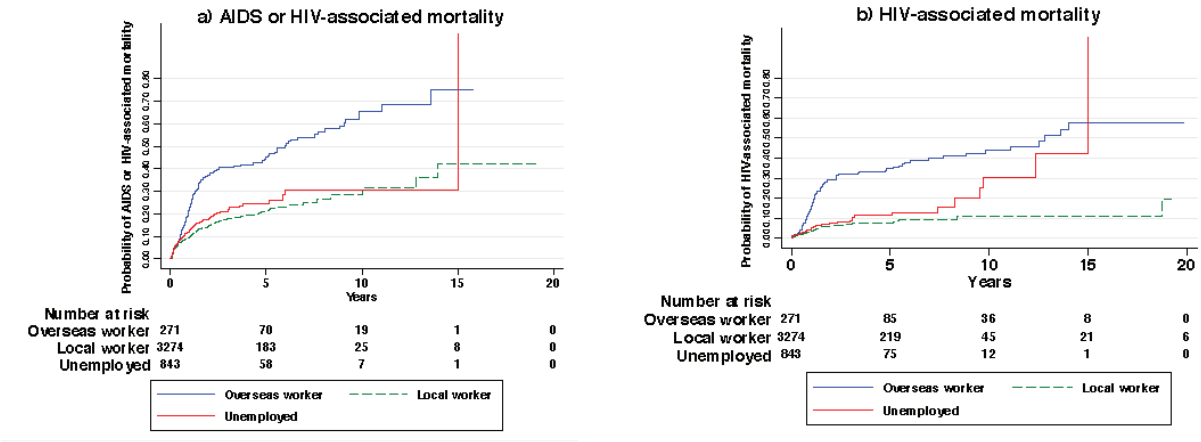
In summary we have shown how the demographic and molecular epidemiology of HIV changed over time. We also demonstrated the efficacy of ART for our patients. Late presentation in clinical care is a very significant predictor of poor outcome hence the need to scale up HIV testing for early HIV diagnosis. A holistic approach to care that would address the social and psycho emotional needs of patients is important. A care plan including identifying clinic, support group or mechanism to access ART for overseas worker must be in place as well as support for men who have issues regarding sexuality and disclosure.

References

1. Department of Health-Epidemiology Bureau. HVI/AIDS and ART Registry of the Philippines. Department of Health. 2018, Philippines.
2. Department of Health-Epidemiology Bureau. HVI/AIDS and ART Registry of the Philippines. Department of Health. 2015, Philippines.
3. Department of Health-Epidemiology Bureau. HVI/AIDS and ART Registry of the Philippines. Department of Health. 2017, Philippines.
4. CDC. 1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults. Morbidity and Mortality Weekly Report. United States Centers for Disease Control and Prevention 1993;1941.
5. World Medical Association. World Medical Association Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects. JAMA 2013 Nov;310(20):2191-2194.
6. The LAWPHiL Project. Republic Act No. 10173. An act protecting individual personal information in information and communications systems in the government and the private sector, creating for this purpose a national privacy commission, and for other purposes. ARELLANO LAW FOVNDATION.
7. Al-Mozaini MA, Mansour MK, Al-Hokail AA, Mohmed MA, Daham MA, et. al. HIV-Care Outcome in Saudi Arabia; a Longitudinal Cohort. J AIDS Clin Res. 2014 Nov;5(11).
8. Farahani M, Vable A, Lebelonyane R, Seipone K, Anderson M, et al. Outcomes of the Botswana national HIV/AIDS treatment programme from 2002 to 2010: a longitudinal analysis. Lancet Glob Health. 2014 Jan;2(1):e44-e50.
9. Hung CC, Chen MY, Hsieh SM, Sheng WH, Chang SC. Clinical spectrum, morbidity, and mortality of acquired immunodeficiency syndrome in Taiwan: a 5-year prospective study. J Acquir Immune Defic Syndr. 2000 Aug;24(4):378-385.
10. Coelho L, Grinsztejn B, Castilho JL, De Boni R, Quintana MS, et al. Mortality in HIV-infected women, heterosexual men, and men who have sex with men in Rio de Janeiro, Brazil: an observational cohort study. Lancet HIV. 2016 Oct;3(10):e490-e498.
11. Coelho LE, Cardoso SW, Amancio RT, Moreira RI, Ribeiro SR, et al. Predictors of opportunistic illnesses incidence in post combination antiretroviral therapy era in an urban cohort from Rio de Janeiro, Brazil. BMC Infect Dis. 2016 Mar;16:134.
12. Duong T, Jourdain G, Ngo-Giang-Huong N, Le Coeur S, Kantipong P, et al. Laboratory and Clinical Predictors of Disease Progression following Initiation of Combination Therapy in HIV- Infected Adults in Thailand. PLoS One. 2012;7(8):e43375.
13. Garriga C, de Olalla PG, Miró JM, Ocaña I, Knobel H, et al. Mortality, Causes of Death and Associated Factors Relate to a Large HIV Population- Based Cohort. PLoS One. 2015 Dec;10(12):e0145701.
14. Melaku Z, Lamb MR, Wang C, Lulseged S, Gadisa T, et al. Characteristics and outcomes of adult Ethiopian patients enrolled in HIV care and treatment: a multi-clinic observational study. BMC Public Health. 2015 May;15:462.
15. Mugisha V, Teasdale CA, Wang C, Lahuerta M, Nuwagaba-Biribonwoha H, et al. Determinants of Mortality and Loss to Follow Up among Adults Enrolled in HIV Care Services in Rwanda. PLoS One. 2014 Jan;9(1):e85774.
16. Zhou J, Kumarasamy N, Ditangco R, Kamarulzaman A, Lee CK, et al. The TREAT Asia HIV Observational Database: baseline and retrospective data. J Acquir Immune Defic Syndr. 2005 Feb;38(2):174–179.
17. Beyrer C. Global prevention of HIV infection for neglected populations: men who have sex with men. Clin Infect Dis. 2010 May;50.
18. Sullivan PS, Hamouda O, Delpech V, Geduld JE, Prejean J, et al. Reemergence of the HIV epidemic among men who have sex with men in North America, Western Europe, and Australia, 1996-2005. Ann Epidemiol. 2009 Jun;19(6):423-431.
19. Angelis K, Albert J, Mamais I, Magiorkinis G, Hatzakis A, et al. Global Dispersal Pattern of HIV Type 1 Subtype CRF01_AE: A Genetic Trace of Human Mobility Related to Heterosexual Sexual Activities Centralized in Southeast Asia. J Infect Dis. 2015 Jun;211(11):1735-1744.
20. Tee KK, Kantor R, Sungkanuparph S, Takebe Y, Li P, et al. Transmission Networks of HIV-1 Among Men Who Have Sex With Men in East and Southeast Asia. J Acquir Immune Defic Syndr. 2015 Sep;70(1):e28-e30.



Supplementary Figure 1: Cumulative probabilities of a) AIDS-defining conditions or HIV-associated mortality by reported mode of infection and b) HIV-associated mortality by reported mode of infection



Supplementary Figure 2: Cumulative probabilities of a) AIDS-defining conditions or HIV-associated mortality by occupation and b) HIV-associated mortality by occupation