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Research

Retention in care and mortality trends among patients receiving comprehensive care for HIV infection: a retrospective cohort study

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Abstract

Background: Studies examining the relation between comprehensive care and health outcomes associated with comorbidities unrelated to HIV infection have focused mainly on the health outcomes of HIV-infected people and comorbid substance use disorders. We aimed to assess the impact of retention in comprehensive HIV infection care on overall, AIDS-related and non–AIDS-related mortality.

Methods: Using a retrospective cohort design, we collected data for HIV-infected patients aged 19 years or more who first visited a comprehensive HIV infection clinic in Vancouver between Jan. 1, 2004, and Dec. 31, 2014. We defined retention in care as visit constancy (whether the patient attended the clinic at least once per given period) of 75% or greater. We used Poisson regression modelling to examine mortality trends. We performed Cox proportional hazards modelling to assess survival by retention during the first year of follow-up and identify factors associated with death.

Results: A total of 2101 patients were included in the study. Of the 2101, 1340 (63.8%) were retained in the first year of care, and 271 (12.9%) died during the study period. Among the 264 cases in which the cause of death was known, although the primary underlying cause of death (74 [28.0%]) was AIDS-related, half of all AIDS-related deaths (37/74 [50%]) occurred early in the study (2004–2007). In later years, most deaths (147/184 [79.9%]) were non–AIDS-related. Overall mortality was significantly reduced among patients with higher retention in care during the first year of follow-up (per 20% increase in visit constancy; adjusted hazard ratio [HR] 0.87, 95% confidence interval [CI] 0.79–0.96). Higher retention was also associated with reduced risk of AIDS-related death (adjusted HR 0.79, 95% CI 0.64–0.97).

Interpretation: Although there was an overall trend toward decreased AIDS-related mortality over time, retention in care markedly decreased the likelihood of death. Maintaining patient engagement in comprehensive ancillary care is a patient-centred way of decreasing mortality rates among HIV-infected people.

Thanks to modern antiretroviral therapy (ART), life expectancy for people with HIV infection has improved substantially in the last decade.[1] Comprehensive care models have been shown to improve health outcomes related to HIV infection, increasing adherence to HIV infection care and rates of viral load suppression.[2,3] Few studies have examined the relation between comprehensive care and health outcomes associated with comorbidities unrelated to HIV infection; these studies have focused mainly on the health outcomes of HIV-infected people and comorbid substance use disorders.[4–6]

At the end of 2014, there were about 75 500 people with HIV infection in Canada, with 16.0% (12 100) residing in British Columbia.[7] The John Ruedy Immunodeficiency Clinic at St. Paul's Hospital, Vancouver, was established in 2003 to address the needs of HIV-infected people without primary care or specialist access. At the end of December 2015, the clinic was caring for 1306 active patients (roughly 10% of those with HIV infection in BC). The clinic serves a diverse community of HIV-infected people and provides

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comprehensive and supportive HIV infection care. The primary objective of this study was to examine trends in all-cause and cause-specific mortality among patients enrolled in a comprehensive care HIV infection clinic. In particular, we wished to identify the impact of retention in care on overall, AIDS-related and non–AIDS-related mortality to better understand the relation between retention in comprehensive care HIV infection programs and improvement in overall health outcomes among people with HIV infection.

Methods

Study design and population

The John Ruedy Immunodeficiency Clinic is an interdisciplinary outpatient HIV clinic providing low-barrier access to comprehensive care. The clinic is staffed by an interdisciplinary team of family physicians, specialists, nurses, pharmacists, counsellors, social workers, peer navigators and nutritionists who provide numerous services to HIV-infected patients, including access to addiction services, an on-site pharmacy, rapid referral to HIV infection care and specialists treating infectious and noninfectious comorbidities, and rapid access to social work support and counselling. In BC, people infected with HIV have universal and free access to ART. Since 2011, ART initiation has been recommended to all those with HIV infection regardless of CD4 count.[8]

This retrospective cohort study included HIV-infected people aged 19 years or more enrolled in the clinic who first visited the clinic between Jan. 1, 2004, and Dec. 31, 2014. Inclusion in the study required at least 1 recorded visit to the clinic and at least 1 documented CD4 count and plasma viral load test during the study period. All patients were followed until the earliest of death, migration or study censor date (Dec. 31, 2015).

Data collection

We obtained data for the participants from the Drug Treatment Program, the clinic's internal database and BC Vital Statistics. The Drug Treatment Program, developed and managed by the BC Centre for Excellence in HIV/AIDS, collects demographic and HIV-related clinical, laboratory and treatment-related information for all people with HIV infection who have received ART in BC. Data collected by the program have been previously described.[9,10] Detailed clinical and demographic characteristics of enrolled patients were extracted from the clinic's internal database. For deceased patients, a trained research assistant used a standardized form to collect information on comorbidities, opportunistic infections, death and autopsy results (if available) from the hospital electronic health records. We obtained cause of death from BC's Vital Statistics Agency.

Primary outcomes

The primary outcome variables were overall and cause-specific mortality as determined from physician reviews based on the Coding Causes of Death in HIV (CoDe) protocol,[11] a widely used uniform classification system that has been previously evaluated.[12] Using CoDe, 2 of C.S., S.S. or M.P. independently reviewed each patient's deidentified information to ascertain cause of death. Two reviewers received a batch of 15 cases at a time; these were rotated so that each of the 3 reviewers was matched equally with the other 2 reviewers. To address any potential discrepancies, the reviewers attended an initial training session where a practice batch was given. In the event of disagreement, a third physician (R.B. or S.G.) served as a tiebreaker.

Underlying causes of death were classified into 3 categories: AIDS-related, non–AIDS-related and unknown/unclassifiable. They were then subdivided according to CoDe protocol categories, which include 18 specific code classes, 6 general classifications and 2 codes for unclassifiable causes.[12] The final list of subcategories used in this study included the following specific code classifications: AIDS-related (AIDS-related infection, AIDS malignancy and AIDS [ongoing active disease]), malignancy (other than AIDS- or hepatitis-related), substance use (active), chronic viral hepatitis (progression of/complication to), infection (other than AIDS-related), chronic obstructive pulmonary disease, myocardial infarction or other ischemic heart disease (general classifications: heart or vascular disease), psychiatric disease, and unclassifiable causes: other and unknown/unclassifiable causes. All causes of death apart from unknown/unclassifiable with a frequency less than 7 were grouped together as "other."

Covariates

We collected data for all patients on sex (male/female), age, risk factors for HIV infection (injection drug use, men who have sex with men [MSM], injection drug use and MSM, other [heterosexual risk of HIV infection alone or in combination with injection drug use or MSM, or accidental exposure], unknown), age at clinic enrolment, year of clinic enrolment, receipt of ART (ever during study period) (yes/no), baseline (most recent within 6 mo of first clinic visit) and most recent CD4 count, baseline and most recent HIV plasma viral load, retention in care during the first year of follow-up (yes/no) and ART adherence during the first year of follow-up (yes/no). For deceased patients, additional information was collected on chronic hepatitis B status (yes/no) and chronic hepatitis C status (yes/no), and the presence of AIDS-related illnesses in the year before death (yes/no).

We measured retention in care using visit constancy, or whether the patient attended the clinic at least once per given period.[13,14] We divided the number of intervals in which a patient had at least 1 primary or specialized care clinic visit by the total number of intervals during follow-up and reported the result as a percentage. We followed Adult Therapeutic Guidelines recommendations for laboratory and clinical monitoring for 2004–2015[15] and clinical expertise to determine visit constancy intervals. Twelve-month observation periods were broken down into four 3-month

intervals (2004–2008), three 4-month intervals (2009–2010) and two 6-month intervals (2011–2015). Patients with a visit constancy of 75% or greater were classified as retained in care. Consultation with clinic physicians suggested that this value best indicated retention in care, as many patients could not realistically attain 100% visit constancy. Visit constancy was also expressed in 20% intervals for consistency with the literature.[13]

We used pharmacy refill records (ART dispensation dates logged by the Drug Treatment Program) to assess ART adherence; this measure of adherence has been previously validated.[16] We divided the number of days for which ART was dispensed by the total number of days of follow-up during the first year to obtain the proportion of time for which the patient had ART coverage.[17] We defined optimal ART adherence as 95% or more; this cut-off has been consistently associated with virologic suppression[18,19] and decreased likelihood of resistance.[20]

Statistical analysis

We calculated all-cause and cause-specific mortality rates per 1000 person-years and used a Poisson regression model to examine trends for overall, AIDS-related and non–AIDS-related mortality.[21] We assessed agreement between physician reviews for cause of death using the κ statistic.[22] We compared characteristics of living and deceased patients, and between patients who died from AIDS-related and non–AIDS-related causes, using χ^2 statistics for categorical variables and the Wilcoxon rank sum test for continuous variables. We assessed survival using Cox proportional hazards models for overall, AIDS-related and non–AIDS-related mortality, stratified by retention during the first year of follow-up. We used unadjusted and adjusted Cox proportional hazards models[23] to identify factors independently associated with increased risk of death. We did not use ART adherence as a variable in the multivariate models, as it was found to be collinear with visit constancy. For the multivariate model, we used the Akaike information criterion for model selection.[24] We used the Supremum test to assess the proportionality assumption and nonsignificant p values. In a sensitivity analysis, we considered competing risks between AIDS-related and non–AIDS-related deaths, but model results were very similar (data not shown). All analyses were conducted with SAS software v9.4 (SAS Institute) with a level of significance set at 0.05.

Ethics approval

The study protocol received ethics approval from the University of British Columbia Providence Health Care Research Institute Research Ethics Board.

Results

There were 2123 people with HIV infection enrolled in the clinic with a first visit between Jan. 1, 2004, and Dec. 31, 2014; of these, 22 did not meet our inclusion criteria. Thus, 2101 patients were included in the study. They accounted for 11 954 person-years (median 5 yr [25th, 75th percentiles 2, 9]) of follow-up. Table 1 presents the patients' overall characteristics, stratified by death during the study period. Patients who remained alive were more likely than those who died to be MSM, to be younger at first visit, to have a higher CD4 count and lower plasma viral load at baseline and last visit, and to be retained in care and adherent to ART during the first year of follow-up ($p < 0.001$).

Mortality rate

Of the 2101 patients, 271 (12.9%) died during the study period. The overall crude mortality rate was 22.7 per 1000 person-years (95% confidence interval [CI] 20.0–25.5). Specific causes of death were classifiable for 264 cases (97.4%). After we removed the 7 cases with unknown/unclassifiable cause of death, interrater reliability for cause of death was 89% (95% CI 85%–93%), with a κ coefficient of 0.73 ($p < 0.001$).

Poisson regression analysis results for all classifiable causes of death are shown in Figure 1. There were no AIDS-related deaths recorded in 2004; the AIDS-related mortality rate decreased from 36.2 per 1000 person-years in 2005 to 2.6 per 1000 person-years in 2015 ($p < 0.001$). The non–AIDS-related mortality rate decreased from 37.4 per 1000 person-years in 2004 to 14.4 per 1000 person-years in 2015 ($p = 0.002$). Table 2 shows detailed classifications of underlying causes of death and crude mortality rates per 1000 person-years.

Characteristics associated with death and survival

Among the 264 patients for whom specific cause of death was classifiable, relative to patients who died from non–AIDS-related causes, those who died from AIDS-related causes were younger at first visit ($p = 0.005$) and at death ($p < 0.001$), had a lower CD4 count and higher plasma viral load at baseline and at death ($p < 0.001$), were less likely to be ART adherent in the first year of follow-up ($p = 0.007$) and had more AIDS-related illnesses in the year before death ($p < 0.001$) (Table 3).

The probability of death from all causes decreased from 15% to 7% as visit constancy increased ($p = 0.001$) (Figure 2); a decrease was observed for both AIDS-related (5% to 2%, $p = 0.03$) and non–AIDS-related (12% to 6%, $p = 0.07$) mortality. As 1 year of follow-up is required to assess visit constancy, all events occurring in the year that the patient enrolled in the clinic could not be included in this analysis. Consequently, the sample size was reduced to 190 deceased patients.

After we removed the 7 patients who died from unknown causes and 120 patients who were missing first-year visit constancy or baseline CD4 count/plasma viral load, 1974 patients were included in the Cox proportional hazards model assessing factors associated with increased risk of overall (Table 4) and AIDS-related and non–AIDS-related (Table 5) mortality. Higher visit constancy during

Table 1: Descriptive characteristics of patients enrolled in the John Ruedy Immunodeficiency Clinic, 2004–2015

Characteristic	No. (%) of patients*†		p value
	Alive at end of study period *n* = 1830	Died during study period *n* = 271	
Male sex	1596 (87.2)	228 (84.1)	0.2
Risk factor(s) for HIV infection			
Injection drug use only	123 (6.7)	63 (23.2)	
MSM only	705 (38.5)	51 (18.8)	
Injection drug use + MSM	161 (8.8)	34 (12.5)	
Other‡	696 (38.0)	101 (37.3)	
Unknown	145 (7.9)	22 (8.1)	< 0.001
Age at first clinic visit, yr, median (Q1–Q3)	41 (34–49)	46 (40–53)	< 0.001
Year of clinic enrolment			
2004–2005	421 (23.0)	124 (45.8)	
2006–2009	652 (35.6)	107 (39.5)	
2010–2014	757 (41.4)	40 (14.8)	< 0.001
Baseline CD4 count, cells × 10^6/L§			
< 50	81 (4.4)	48 (17.7)	
50–199	287 (15.7)	71 (26.2)	
200–349	397 (21.7)	59 (21.8)	
≥ 350	1055 (57.6)	93 (34.3)	< 0.001
Baseline plasma viral load, copies/mL§			
< 50	722 (39.4)	83 (30.6)	
50–99 999	835 (45.6)	127 (46.9)	
≥ 100 000	265 (14.5)	61 (22.5)	< 0.001
Hepatitis virus infection¶			
Chronic hepatitis B	103 (5.6)	10 (3.7)	0.3
Chronic hepatitis C	346 (18.9)	64 (23.6)	< 0.001
ART (ever during study period)	1671 (91.3)	243 (89.7)	0.4
Year of ART initiation			
Before 2000	371 (20.3)	108 (39.8)	
2000–2006	406 (22.2)	91 (33.6)	
2007–2015	974 (53.2)	57 (21.0)	
Unknown	79 (4.3)	15 (5.5)	< 0.001
Latest CD4 count, cells × 10^6/L**			
< 50	15 (0.9)	41 (16.0)	
50–199	104 (5.9)	75 (29.3)	
200–349	232 (13.3)	50 (19.5)	
≥ 350	1398 (79.9)	90 (35.2)	< 0.001
Latest plasma viral load, copies/mL**			
< 50	1495 (84.2)	143 (55.9)	
50–99 999	247 (13.9)	80 (31.2)	
≥ 100 000	33 (1.9)	33 (12.9)	< 0.001
Visit constancy (first yr), %			
< 75	554 (30.8)	92 (48.4)	
≥ 75	1242 (69.2)	98 (51.6)	< 0.001
ART adherence (≥ 95%; first yr)††	1085 (59.3)	81 (29.9)	< 0.001

Note: ART = antiretroviral therapy, MSM = men who have sex with men.
*Except where noted otherwise.
†Numbers do not total 2101 for some variables owing to incomplete data.
‡Includes risk of heterosexual transmission alone or in combination with MSM and/or injection drug use, as well as accidental exposure.
§Most recent within 6 months of first clinic visit.
¶Chronic hepatitis B: positive result of testing for hepatitis B surface antigen or hepatitis B virus DNA for 6 months or more; chronic hepatitis C: positive results of testing for hepatitis C virus antibody and RNA, or for hepatitis C virus genotypes 1a–4.
**Most recent before death or study censor date.
††Based on pharmacy refill frequency.

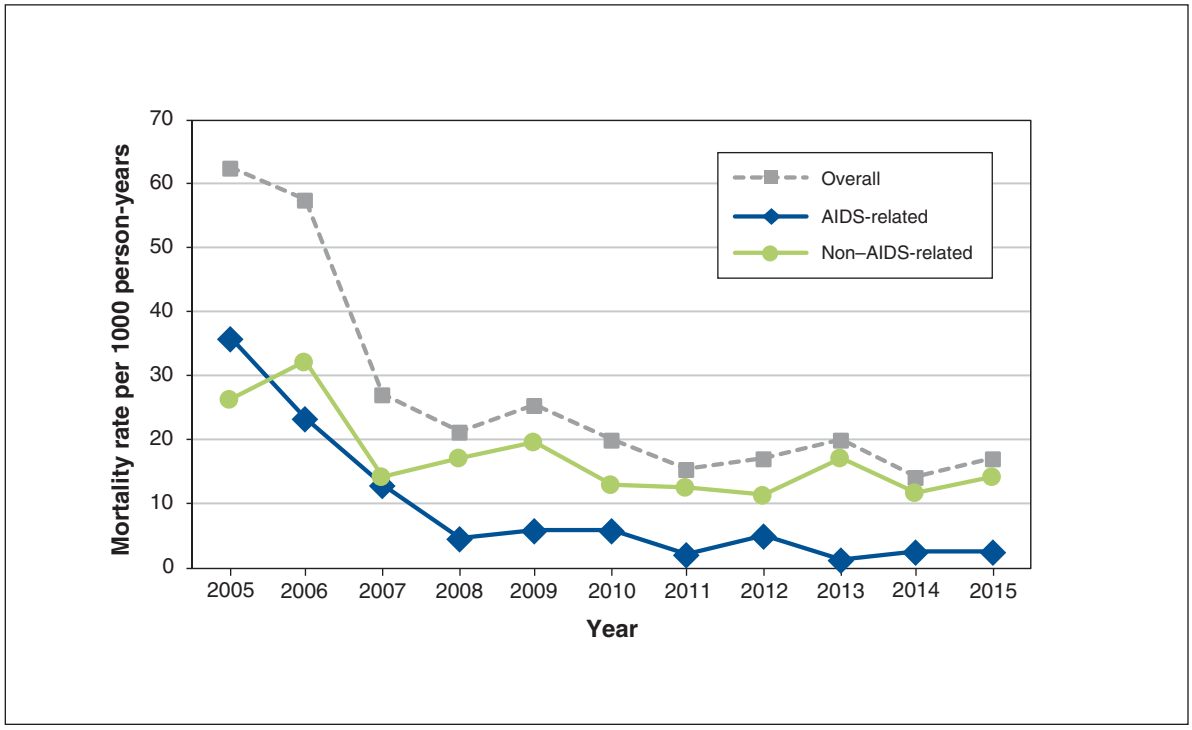

Figure 1: Crude rates for overall, AIDS-related and non–AIDS-related mortality per 1000 person-years over time from 2005 to 2015. The year 2004 has been omitted from analysis as there were no AIDS-related deaths in that year. Patients with unknown cause of death (n = 7) were excluded.

the first year of follow-up (per 20% increase; adjusted hazard ratio [HR] 0.87, 95% CI 0.79–0.96), being MSM (adjusted HR 0.50, 95% CI 0.29–0.87) and having a higher baseline CD4 count (adjusted HR 0.85, 95% CI 0.80–0.91) were associated with a lower risk of overall mortality, and higher visit constancy during the first year of follow-up was associated with a lower risk of AIDS-related death (per 20% increase; adjusted HR 0.79, 95% CI 0.64–0.97).

Interpretation

We describe retention in care and mortality trends among people with HIV infection who accessed a comprehensive care HIV clinic in an urban setting from 2004 to 2015. The overall probability of survival was significantly increased for patients with higher retention in care. Although the primary underlying cause of death was AIDS-related (28%), half of these deaths occurred in the earlier years of the study (2004–2007). Between 2008 and 2015, 54% of all deaths were non–AIDS-related, with non-AIDS malignant disease and substance use accounting for 33% of all deaths.

These finding are consistent with those of other studies conducted in similar settings[25,26] and with population-based studies conducted in BC.[27,28] The proportion of HIV-related deaths varied between studies, as the studies assessed different periods of time or people with different demographic characteristics. Trickey and colleagues[29] reported that, among people with HIV infection who survived for 10 years or more after starting ART, death was more likely to result from non–AIDS-related nonliver cancer than from AIDS-related causes (25% v. 16%). In our study, non–AIDS-related nonliver cancers and substance use were the most commonly reported non–AIDS-related causes of death and the most commonly reported causes of death after 2007. Together, these findings suggest that, among HIV-infected people receiving long-term ART, non–AIDS-related nonliver cancers are a major cause of mortality. The decline in AIDS-related mortality and AIDS diagnoses over the study period in the current study corresponds to local efforts in the expansion and early uptake of ART,[8,30,31] and the increase in deaths due to non-AIDS malignant disease is consistent with previous studies.[27,28,32,33]

Non–AIDS-related comorbidities including substance use and psychiatric conditions may reduce retention in care among people with HIV infection.[34] In addition, providing support services for people with HIV infection improves ART adherence.[35] Our findings suggest that access to a comprehensive care clinic that provides interdisciplinary services for HIV-infected people can lead to a substantially higher probability of overall survival (and a reduction in AIDS-related mortality). Our results align with those of Sherer and colleagues[36] showing that complementing HIV-infection–related services with services not related to HIV infection is associated with better retention and better outcomes in this population.

Table 2: Underlying cause of death and crude mortality rates per 1000 person-years for the clinic cohort, 2004–2015 (11 954 total person-years)

Cause of death	No. (%) of patients *n* = 2101	Crude mortality rate per 1000 person-years (95% CI)
AIDS-related*	74 (3.5)	6.2 (4.9–7.8)
AIDS infection	31 (1.5)	2.6 (1.8–3.7)
AIDS malignant disorder	28 (1.3)	2.3 (1.6–3.4)
AIDS (ongoing active disease)	15 (0.7)	1.3 (0.7–2.1)
Non–AIDS-related	190 (9.0)	15.9 (13.7–18.3)
Malignant disease (other than AIDS- or hepatitis-related)	44 (2.1)	3.7 (2.7–4.9)
Substance use (active)	44 (2.1)	3.7 (2.7–4.9)
Chronic viral hepatitis (progression of/complication to)	16 (0.8)	1.3 (0.8–2.2)
Infection (other than AIDS-related)	11 (0.5)	0.9 (0.5–1.6)
Chronic obstructive pulmonary disease	10 (0.5)	0.9 (0.4–1.5)
Heart or vascular disease	9 (0.4)	0.8 (0.3–1.4)
Psychiatric disease	8 (0.4)	0.7 (0.3–1.3)
Myocardial infarction or other ischemic heart disease	7 (0.3)	0.6 (0.2–1.2)
Other†	41 (2.0)	3.4 (2.5–4.7)
Unknown/unclassifiable	7 (0.3)	0.6 (0.2–1.2)

Note: CI = confidence interval.
*There were no AIDS-related deaths in 2004.
†Includes deaths related to accident or other violent death, central nervous system, diabetes mellitus, digestive system disease, endocrine system, hematological system, liver failure, pancreatitis, renal failure, respiratory disease, stroke and suicide.

Limitations

This study has several limitations. First, it was an observational study, and causation cannot be inferred. Second, the retrospective nature of the study led to incomplete data capture and constraint on the variables available for analysis. Several variables (e.g., chronic hepatitis B [*n* = 10 among deceased patients]) were excluded from the survival analysis owing to low counts or collinearity with other variables (e.g., hepatitis C virus infection and injection drug use, and year of clinic enrolment and visit constancy exhibited collinearity in our study population[37]). Also, a single research assistant was responsible for clinical data collection. To minimize the possibility of measurement error, data extraction for medical conditions was standardized based on given operational definitions. Any discharge records or autopsy reports included were transcribed directly from the medical records without individual interpretation from the research assistant. In addition, the research assistant received training in data extraction and had various practice sessions to ensure that the data collected for the reviews were as accurately transcribed as possible. Third, it should be noted that the Cox proportional hazards model for AIDS-related and non–AIDS-related mortality excluded deceased patients whose cause of death was unknown and those with less than 1 year of follow-up in the clinic, which reduced the sample size from 271 to 190. The 81 patients (29.9%) excluded likely were not attending the clinic or were presenting late for care. Fourth, the relation between retention in care and death is affected by the increments (continuous) or threshold (dichotomized) used to delineate visit constancy. The threshold of 75% that we used was significantly associated with decreased overall, AIDS-related and non–AIDS-related mortality in multivariate modelling (data not shown). This value, however, has not been validated or used in the literature to indicate retention in care. To keep with existing literature, we expressed visit constancy as a continuous variable, in 20% increments; narrowing the increments further would have resulted in a slight weakening of the inverse relation between visit constancy and death, whereas wider increments would have yielded a stronger relation. We observed that the greatest reduction in all types of mortality occurred when patients attended at least 50% of clinic visits in their first year of follow-up (Figure 2). Further exploration to determine the threshold that best indicates retention in care is needed, particularly in relation to marginalized and stigmatized populations, who experience high barriers to clinic attendance.[38] Fifth, the CoDe protocol has been previously evaluated, with most categories showing high initial agreement[12]; however, several categories that we used in the present study, including non–AIDS-related infection, chronic obstructive lung disease, psychiatric disease, and heart or vascular disease, yielded 43%–56% agreement. The low agreement in these categories may have been due to small samples (e.g., 2 cases of chronic obstructive lung disease, with disagreement on 1 case). Our determinations of cause of death are bolstered by the high interrater reliability (89%) between physicians. Finally, although the study highlights trends in mortality among people with HIV infection and the impact of retention in comprehensive HIV infection care, caution should be used in generalizing the findings to other vulnerable populations. However, similar results may be observed in other clinics where ART can be accessed free of charge and comprehensive, interdisciplinary care for marginalized and vulnerable people with HIV infection is provided.

Conclusion

Higher retention in care was associated with a lower risk of death in our study. On the other hand, non–AIDS-related causes accounted for a higher number of deaths during the later years of the study. Subsequent studies should examine how various elements of comprehensive care models benefit people infected with HIV, how these models can be implemented on a larger scale and how they compare with models of nonintegrated HIV infection care.

Table 3: Descriptive characteristics of deceased patients, 2004–2015

Characteristic	Underlying cause of death; no. (%) of patients*†		p value
	AIDS-related n = 74	Non–AIDS-related n = 190	
Male sex	63 (85.1)	159 (83.7)	0.8
Risk factor(s) for HIV infection			
Injection drug use only	23 (31.1)	38 (20.0)	
MSM only	11 (15.9)	38 (20.0)	
Injection drug use + MSM	10 (13.5)	23 (12.1)	
Other	23 (31.1)	77 (44.5)	
Unknown	7 (9.5)	14 (7.4)	0.2
Age at first clinic visit, yr, median (Q1–Q3)	42 (38–50)	46 (41–54)	0.005
Year of clinic enrolment			
2004–2005	40 (54.0)	79 (41.6)	
2006–2009	21 (28.4)	85 (44.7)	
2010–2014	13 (17.6)	26 (13.7)	0.05
Baseline CD4 count, cells × 10^6/L‡			
< 50	33 (44.6)	15 (7.9)	
50–199	21 (28.4)	50 (26.3)	
200–349	7 (9.5)	49 (25.8)	
≥ 350	13 (17.6)	76 (40.0)	< 0.001
Baseline plasma viral load, copies/mL‡			
< 50	11 (14.9)	71 (37.4)	
50–99 999	37 (50.0)	84 (44.2)	
≥ 100 000	26 (35.1)	35 (18.4)	< 0.001
ART (ever during study period)	64 (86.5)	175 (92.1)	0.2
Latest CD4 count, cells × 10^6/L§			
< 50	36 (52.2)	5 (2.7)	
50–199	19 (27.5)	57 (30.6)	
200–349	6 (8.7)	44 (23.7)	
≥ 350	8 (11.6)	80 (43.0)	< 0.001
Latest plasma viral load, copies/mL§			
< 50	22 (32.4)	117 (62.9)	
50–99 999	27 (39.7)	55 (29.6)	
≥ 100 000	19 (27.9)	14 (7.5)	< 0.001
Calendar period at time of death			
2004–2005	15 (20.3)	15 (7.9)	
2006–2007	22 (29.7)	28 (14.7)	
2008–2009	10 (13.5)	35 (18.4)	
2010–2011	10 (13.5)	31 (16.3)	
2012–2013	9 (12.2)	41 (21.6)	
2014–2015	8 (10.8)	40 (21.0)	0.001
Age at death, yr, median (Q1–Q3)	45 (39–52)	51 (44–59)	< 0.001
Hepatitis virus infection			
Chronic hepatitis B	1 (1.4)	9 (4.7)	0.5
Chronic hepatitis C	12 (16.2)	49 (25.8)	0.4
AIDS-related illness (yr before death)	52 (70.3)	42 (22.1)	< 0.001
Visit constancy (first yr), %			
< 75	27 (45.8)	83 (47.4)	
≥ 75	32 (54.2)	92 (52.6)	0.4
ART adherence (≥ 95%; first yr)	10 (13.5)	69 (36.3)	0.007

Note: ART = antiretroviral therapy, MSM = men who have sex with men.
*Except where noted otherwise.
†Numbers do not total 264 for some variables owing to incomplete data.
‡Most recent within 6 months of first clinic visit.
§Most recent before death.

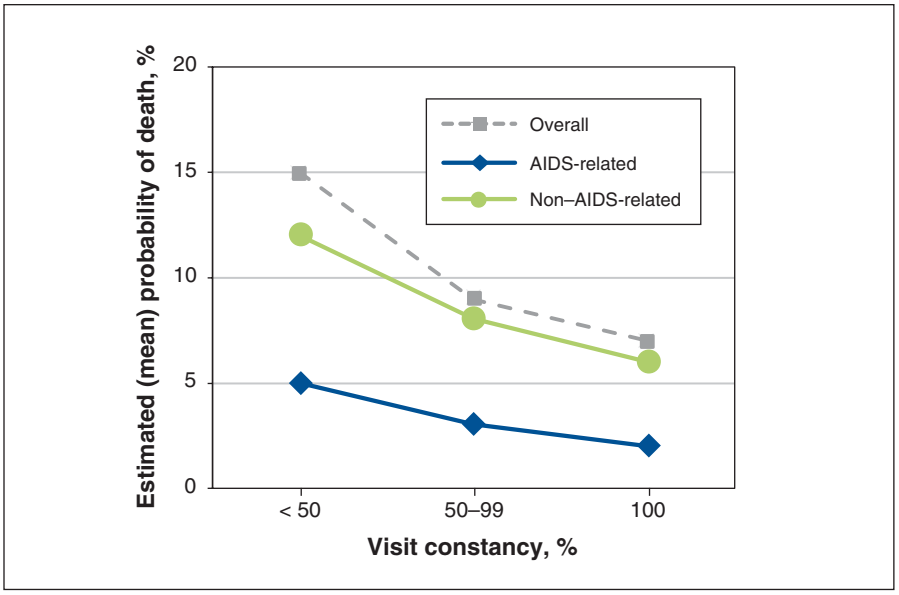

Figure 2: Probability of overall, AIDS-related, and non–AIDS-related mortality by level of visit constancy during the first year of follow-up (190 deceased patients) (Cox proportional hazards model). Patients who did not have data for first-year visit constancy or baseline CD4 count/plasma viral load were excluded from the model (*n* = 120).

Table 4: Cox proportional hazards model for overall deaths among clinic patients, 2004–2015* (*n* = 1974, of whom 190 died and had documented cause of death)

Variable	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Sex		
Female	1.00 (–)	NS†
Male	0.85 (0.61–1.18)	
Age at first clinic visit (per 10-yr increment)	1.55 (1.40–1.73)	1.75 (1.53–2.00)
Risk factor(s) for HIV infection		
Injection drug use + MSM	1.00 (–)	1.00 (–)
Injection drug use only	2.12 (1.39–3.24)	2.75 (1.61–4.68)
MSM only	0.35 (0.23–0.55)	0.50 (0.29–0.87)
Other	0.61 (0.41–0.90)	0.68 (0.42–1.11)
Unknown	1.00 (0.58–1.73)	0.81 (0.34–1.11)
Baseline CD4 count (per increment of 100 cells/μL)‡	0.80 (0.75–0.85)	0.85 (0.80–0.91)
Baseline plasma viral load (log10 copies/mL)‡	1.12 (1.02–1.21)	NS†
Visit constancy (first yr), % (as a continuous variable, per 20% increase)	0.85 (0.77–0.94)	0.87 (0.79–0.96)
ART (ever during study period)		
No	1.00 (–)	NS†
Yes	0.79 (0.52–1.19)	

Note: ART = antiretroviral therapy, CI = confidence interval, HR = hazard ratio, MSM = men who have sex with men, NS = not selected.
*Model excludes patients whose cause of death was unknown, those who did not have 1 year of data to assess visit constancy and those whose baseline CD4 count/plasma viral load were missing.
†Variable not included in adjusted HR.
‡Most recent within 6 months of first clinic visit.

Table 5: Cox proportional hazards model for AIDS-related and non–AIDS-related deaths among clinic patients, 2004–2015* (*n* = 1974)

Variable	AIDS-related		Non–AIDS-related	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Sex				
Female	1.00 (–)	NS†	1.00 (–)	NS†
Male	0.90 (0.47–1.71)		0.83 (0.57–1.22)	
Age at first clinic visit (per 10-yr increment)	1.23 (1.01–1.52)	1.55 (1.22–2.22)	1.70 (1.50–1.93)	1.78 (1.53–2.07)
Risk factors for acquiring HIV				
Injection drug use + MSM	1.00 (–)	1.00 (–)	1.00 (–)	1.00 (–)
Injection drug use only	2.63 (1.25–5.52)	2.78 (1.05–7.37)	1.90 (1.13–3.19)	2.73 (1.45–5.16)
MSM only	0.27 (0.11–0.63)	0.30 (0.09–1.00)	0.39 (0.23–0.66)	0.58 (0.31–1.09)
Other	0.50 (0.24–1.04)	0.51 (0.20–1.30)	0.65 (0.41–1.04)	0.76 (0.42–1.36)
Unknown	1.02 (0.39–2.67)	0.50 (0.06–4.24)	0.99 (0.51–1.93)	0.94 (0.36–2.45)
Baseline CD4 count (per increment of 100 cells/μL)‡	0.50 (0.42–0.59)	0.66 (0.55–0.79)	0.89 (0.84–0.95)	0.90 (0.84–0.97)
Baseline plasma viral load, log10 copies/mL‡	1.47 (1.23–1.75)	NS†	1.01 (0.91–1.12)	NS†
Visit constancy (first yr), % (as a continuous variable, per 20% increase)	0.75 (0.61–0.93)	0.79 (0.64–0.97)	0.88 (0.78–0.98)	0.90 (0.80–1.01)
ART (ever during study period)				
No	1.00 (–)	NS†	1.00 (–)	NS†
Yes	0.54 (0.28–1.08)		0.95 (0.56–1.61)	

Note: ART = antiretroviral therapy, CI = confidence interval, HR = hazard ratio, MSM = men who have sex with men, NS = not selected.
*Model excludes patients whose cause of death was unknown and those who did not have 1 year of data to assess visit constancy.
†Variable not included in adjusted HR.
‡Most recent within 6 months of first clinic visit.

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