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Hospitalizations in a cohort of HIV patients in Australia, 1999–2007

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Abstract

Objectives—To describe hospitalization rates, risk factors and associated diagnoses in people with HIV in Australia between 1999 and 2007.

Design—Retrospective cohort study of people with HIV ($n = 842$) using data linkage between the Australian HIV Observational Database and administrative hospital morbidity data collections.

Methods—Incidence rate ratios with 95% confidence intervals were estimated using Poisson regression models to assess risk factors for hospitalization. Predictors of length of stay were assessed using generalized mixed models. The association between hospitalization and mortality was assessed using Cox regression.

Results—In 4519 person-years of observation, there were 2667 hospital admissions; incidence rate of 59 per 100 person-years. Hospitalization rates were 50–300% higher in this cohort than comparable age and sex strata in the general population. Older age (incidence rate ratio 1.46, 95% confidence interval 1.28–1.65 per 10-year increase) and prior AIDS (incidence rate ratio 1.71, 95% confidence interval 1.24–2.35) were significantly associated with hospitalization. Other predictors of hospitalization included lower CD4 cell counts, higher HIV RNA, longer duration of HIV infection and experience with more drug classes. Lower CD4 cell counts, older age and hepatitis C virus antibody positivity were independently associated with longer hospital stay. Non-AIDS diseases were the principle reason for admission in the majority of cases. Mortality was associated with more frequent hospitalization during the study period.

Conclusion—Hospitalization rates are higher in people with HIV than the general population in Australia and are associated with markers of advanced HIV disease despite the widespread use of combination antiretroviral therapy.

Keywords

AIDS; antiretroviral therapy; HIV; hospitalization; incidence

Introduction

Combination antiretroviral therapy (cART) has led to substantial declines in mortality and AIDS-related morbidity in HIV-infected individuals with access to these drugs [1–3]. Data on health service utilization in North America and Europe reflect this trend, with decreasing hospitalization rates since cART became available [4–12]. After the first few years of cART availability, however, some studies [6,9] found that hospital admissions started to increase again, particularly for non-AIDS conditions.

In an era of improved survival, many people with HIV infection will live to experience the impact of prolonged exposure to ART [13–15], ageing and, often, coinfection with viral hepatitis. To effectively plan and provide for the evolving healthcare needs of people living with HIV infection, healthcare utilization and current and emerging comorbidities of importance need to be monitored in this population. In Australia, state health department hospital admission data collections are a useful source of information on morbidity and healthcare utilization in the population. In this study, we used linked data from hospital admission data collections in two Australian states and the Australian HIV Observational Database (AHOD) cohort to describe rates of, and reasons for, hospitalization in patients with HIV infection in Australia during the period 1999–2007. We also investigated risk factors for hospitalization and longer inpatient length of stay, and whether patients with a history of hospitalization have an increased risk of mortality.

Methods

Study population

AHOD is an observational, clinical cohort study of patients with HIV infection in Australia, which has been described elsewhere in detail [16]. Briefly, data are collected from 27 clinical sites in six of the eight states/territories of Australia, including hospitals, sexual health clinics and general medical practices that offer specialist HIV care. For this analysis, the study population was restricted to patients recruited to AHOD by 31 March 2007, who were recruited in the states of New South Wales (NSW) and Western Australia (where established data linkage infrastructure existed at the time this study commenced), provided written informed consent to data linkage and had at least one prospective follow-up visit after the baseline date.

Data collection

Prospective data collection in AHOD commenced in mid-1999, with retrospective data provided where available. Data for AHOD are transferred electronically to the National Centre in HIV Epidemiology and Clinical Research, Sydney, Australia, every March and September from participating sites. Core variables include: date of birth, sex, name code (i.e. first two letters of first and last names), date of first positive HIV test, date of most recent clinic visit, HIV exposure category, hepatitis B virus (HBV) and hepatitis C virus (HCV) status, CD4 cell counts, HIV viral load, ART histories, AIDS-defining illness history and date and cause of death. All data are subject to standardized quality control procedures.

Hospital admissions within the AHOD cohort were ascertained via data linkage with the NSW Admitted Patient Data Collection and the Western Australia Hospital Morbidity Data Collection. These data collections cover all inpatient separations (discharges, transfers and deaths), including information about the patient's diagnosis and procedures undertaken, from all public and private hospitals in NSW and Western Australia, respectively. Each record represents an episode of care, which ends when a patient is discharged from hospital, dies or

is transferred to another type of care. Date and cause of death data were obtained from death registers in both states.

In Australia, it is standard practice for HIV to be coded as a diagnosis for known cases of HIV infection, regardless of the reason for hospital admission. Therefore, HIV as a diagnosis code was used to identify suitable matches in this study. As the population in NSW is large, all linked hospital morbidity and death records for patients with HIV as a diagnosis code were selected from the NSW data linkage system prior to linkage with the AHOD cohort. The goal was to reduce the number of false-positive matches that may have arisen from using name codes instead of full names. In Western Australia, a HIV diagnosis code was confirmed for all matches after data linkage. Deterministic data linkage with the AHOD cohort was performed using matches on all, or part of, the following variables: name code, sex, date of birth and date of death (if deceased). Linked data were extracted and forwarded to the researchers in January–February 2009. For each episode of care, the date of admission and discharge, reason for separation, diagnosis [according to the International Classification of Diseases, 10th ed., Australian Modification (ICD10-AM)] and procedure codes, Major Diagnostic Category (aggregated ICD10-AM codes) and Australian Refined Diagnosis Related Group were included. Pregnancy- or childbirth-related episodes of care were excluded.

Ethical approval was obtained from all relevant institutional review boards. This study was conducted in accordance with the Helsinki Declaration of 1975, as revised in 1983.

Definitions and outcome

The primary outcome variable was hospital admission. We defined a hospital admission as one or more episodes of care ending with a hospital discharge or death. Inpatient length of stay was calculated as the number of days from the date of admission in the first episode of care to the date of separation in the final episode of care for each hospital admission. The minimum inpatient length of stay was 1 day, and included same day admission and discharge. In this analysis, the Major Diagnostic Category variable was used to describe the principal reason for admission in an aggregated manner, with the exception of admissions that had opportunistic infections and AIDS-related cancers coded as the principal diagnosis. These were extracted and summarized as separate groups.

For the purpose of this analysis, viral load measures less than 400 copies/ml were replaced with the value 399 copies/ml and defined as undetectable because more sensitive assays were not uniformly available throughout the study period. Coinfection with HBV or HCV was defined as the detection of HBV surface antigen or HCV antibody, respectively. Patients who never tested positive for HBV surface antigen or HCV antibody were considered negative for the duration of the study. The date of each patient's first positive HIV test was used to estimate the duration of HIV infection as a time-dependent variable in this analysis. Patients were considered lost to follow-up if they were not dead and had no clinic visit recorded in AHOD in the 12 months prior to 31 March 2007.

Statistical analysis

Person-years were accrued from the date of enrolment in AHOD, except for patients recruited in NSW prior to 1 July 2000. For these patients, person-years were accrued from 1 July 2000, from which time the NSW Admitted Patient Data Collection recorded patient names. Person-years were terminated at the first of the following dates: date of death, the date 6 months after the last AHOD visit or 31 March 2007. In the analysis of risk factors for hospital admission, patients contributed person-years at risk only for periods when they were not hospitalized.

To investigate independent risk factors for hospital admission, incidence rate ratios (IRRs) were estimated with 95% confidence intervals (CIs) using random-effects Poisson regression methods to take into account within-person variation for repeated measures. The test for heterogeneity using the random-effects variance parameter estimate was significant ($P < 0.01$), indicating the suitability of the random-effects model. The following fixed covariates were tested: sex, HIV exposure, prior AIDS at baseline and HCV and HBV coinfection status. Age, time since first positive HIV test, CD4 cell count, log HIV RNA, AIDS-defining illness after baseline, calendar year and treatment exposure (including number of antiretroviral regimens and number of drug classes ever) were tested as time-dependent covariates in the models. Covariates were entered into the multivariate model if they had a P value of less than 0.10 in the univariate analysis and the model was adjusted for state. The final multivariate model was determined using a forward step-wise approach and only included covariates with a two-sided statistical significance ($P < 0.05$). The log-likelihood ratio statistic was used to assess contribution to the model. Missing data were excluded in tests for trend for ordinal categorical covariates or tests for homogeneity for nominal categorical covariates. All covariates with a P value of less than 0.10 in the univariate analysis that were not significant in the multivariate model are presented, adjusted for the final multivariate model.

We calculated crude hospital admission rates per 100 person-years, with 95% CI, for major diagnostic groups in three time periods (i.e. 1999–2001, 2002–2004 and 2005–2007). We explored whether hospitalization during the study period was an independent risk factor for mortality using Cox proportional hazards methods. Finally, we assessed predictors of inpatient length of stay using a generalized mixed model with a Poisson likelihood function [17,18].

Analyses were performed using Stata (version 10; StataCorp LP, College Station, Texas, USA) and R (version 2.5; R Foundation for Statistical Computing, Vienna, Austria).

Results

A total of 950 patients were recruited to AHOD in NSW ($n = 657$) and Western Australia ($n = 293$) and had complete data submitted by 31 March 2007. Of these, 842 patients consented to data linkage and had at least one follow-up visit after the baseline date for this study. During the study period, the follow-up rate in AHOD was 80%, and 58% of patients were admitted to hospital at least once (Table 1). The majority of patients were men (94%) and reported homosexual contact as a probable HIV exposure (82%). At baseline, the median age of the cohort was 41 years [interquartile range (IQR) 35–48] and the median time since the first positive HIV test was 7 years (IQR 4–12). One-fifth of patients had been diagnosed with an AIDS-defining illness prior to baseline, and 88% had prior ART experience. Patients who were admitted to hospital at least once during follow-up had a longer estimated duration of HIV infection, were slightly older and had a lower CD4 cell count and higher HIV RNA levels at baseline (Table 1). They were also more likely to have had a prior AIDS diagnosis, more ART regimens and been exposed to three drug classes.

Hospitalization rates and risk factors

In total, 2667 hospital admissions were identified during the study period. Patients were at risk of hospitalization for 4519 of the total 4547 person-years of observation accrued during the study. The crude hospitalization rate was 59 per 100 person-years (95% CI 57–61). In comparable 10-year age strata, hospital admission rates were 1.5–3 times higher in men between 25 and 64 years of age in AHOD compared with the general Australian population [19].

Independent risk factors for hospitalization included prior AIDS at baseline (IRR 1.71, 95% CI 1.24–2.35), older age (IRR 1.46 per 10-year increase, 95% CI 1.28–1.65), higher HIV RNA

(IRR 1.16 per 1 log increase, 95% CI 1.11–1.21) and calendar year (Table 2). Longer estimated durations of HIV infection (5–7, 7–12 and ≥ 12 years compared with 0–4 years) were also associated with an increased risk of hospitalization (IRR 2.48, 2.48 and 2.45; 95% CI 2.00–3.07, 1.92–3.20 and 1.82–3.31, respectively). Exposure to four drug classes (compared with ≤ 1) was also significantly associated with hospitalization (IRR 2.66, 95% CI 1.53–4.62), as was exposure to two drug classes, although to a lesser extent (IRR 1.36, 95% CI 1.05–1.76). Higher CD4 cell counts were significantly associated with a decreased risk of hospitalization (IRR 0.91 per 100 cell increase, 95% CI 0.89–0.93).

Reasons for hospitalization

Of the major diagnostic groups, gastrointestinal diseases had the highest crude hospitalization rates in all calendar year periods, except for 2005–2007, when the rate of kidney and urinary tract diseases was the highest (Table 3). A large proportion of the kidney and urinary tract-related admissions between 2002 and 2007 were for two patients who had dialysis recorded as the principal diagnosis code (189 of the 242 admissions). The crude hospital admission rate for neurological diseases increased during the study period, from 3.11 per 100 person-years (95% CI 2.24–4.31) in 1999–2001 to 5.91 per 100 person-years (95% CI 4.75–7.36) in 2005–2007. In contrast, hospital admission rates for mental health decreased from 4.31 per 100 person-years (95% CI 3.27–5.69) in 1999–2001 to 1.00 (95% CI 0.64–1.54) and 0.96 (95% CI 0.56–1.65) per 100 person-years in 2002–2004 and 2005–2007, respectively. More than half of mental health admissions had depression recorded as the principal diagnosis. Hospitalization rates for other major diagnostic groups remained relatively stable during the study period. Hospitalization rates for nonopportunistic infections/parasitic diseases, AIDS and non-AIDS-defining cancers were among the five most frequent major diagnostic groups in 1999–2001 and remained common reasons for admission during the study period.

Association between hospitalization and mortality

A total of 64 deaths occurred during the study period; the crude mortality rate was 1.4 per 100 person-years (95% CI 1.1–1.8) (Table 4). After adjusting for other significant risk factors, patients with at least four hospital admissions had an increased risk of mortality (hazard ratio 4.37, 95% CI 2.45–7.78) compared with those who were admitted to hospital one to three times during the study period. Conversely, patients with no hospital admissions had a 91% reduced risk of mortality (hazard ratio 0.09, 95% CI 0.03–0.27) compared with those admitted one to three times during the study period. Older age, lower CD4 cell counts and higher HIV RNA levels were also independently associated with mortality.

Inpatient length of stay

The inpatient length of stay in our study ranged from 1 to 191 days, with a mean of 4.6 days (standard deviation 10.0) and a median of 1 day (IQR, 1–4). Lower CD4 cell counts, higher HIV RNA, older age and HCV positivity were independently associated with a longer inpatient stay in this study (Table 5).

Discussion

Our data indicate that older age, longer duration of HIV infection, treatment experience with four drug classes and indicators of advanced immune deficiency are independently associated with hospitalization in patients with HIV infection in Australia during the cART era. Of the major diagnostic groups, hospitalization rates for gastrointestinal diseases were highest for most of the study period. Longer inpatient length of stay was associated with older age, HCV coinfection and indicators of advanced immune deficiency. Hospitalization during follow-up was an independent risk factor for mortality. In comparable age and sex strata, hospitalization

rates were around 50–300% higher in patients with HIV infection in our study than in the general Australian population.

Our finding that immunodeficiency was associated with hospitalization, inpatient length of stay and mortality in patients with HIV infection in Australia during the cART era is consistent with previous studies of health service utilization [4–6,11,12,20–22] and mortality in HIV-infected populations [23,24]. Although antiretroviral drug-related toxicity may also have led to increased morbidity [15,25] and, therefore, hospitalizations in our cohort, our data suggest that immunodeficiency and virological failure were more important risk factors.

The majority of hospital admissions in the AHOD cohort between 1999 and 2007 were for non-AIDS conditions, in accord with previous studies [4,7,9]. Hospitalization rates for gastrointestinal diseases were higher than other major diagnostic groups in this study, except for 2005–2007. Although rates of gastrointestinal diseases were common in the US HIV Outpatients Study (1994–2005), renal-related admissions were lower than those in our study [4]. The higher rates of kidney and urinary tract-related admissions in the later period in AHOD can, for the most part, be explained by the frequent admission of two patients for dialysis between 2002 and 2007.

Despite the decline in incident AIDS-related cancers in Australia since the availability of cART [26], hospitalization rates for AIDS-defining cancers remained common between 1999 and 2007. For many of these hospitalizations, chemotherapy was recorded as the principal reason for admission. Hospitalization rates for non-AIDS cancers were similar to AIDS cancers in our study, consistent with the US HIV Outpatients Study in 2000–2005 [4].

There is evidence from previous studies [5,27,28] that liver-related hospitalizations have increased in HIV-infected individuals with HCV coinfection, a history of injection-drug user (IDU) or both since cART became available. HCV coinfection has also been identified as an independent risk factor for hospitalization [11,27]. Although HCV was not an independent risk factor for hospitalization in our study, it was associated with longer length of stay. The relatively low prevalence of HCV coinfection, IDU or both in AHOD compared with the John Hopkins University cohort in the US and the EuroSIDA cohort, may, in part, explain the different findings.

Our study has several strengths. First, AHOD is a multisite cohort with a relatively large sample size and follow-up rate of 80%. Second, data linkage enabled efficient collection of data on statewide hospital admissions in our cohort.

This study also had limitations. Ascertainment of hospital admissions were most likely affected by the use of name codes rather than full names as a matching variable in the data linkage; although previous studies linking Australian HIV/AIDS registries to death [29] and cancer [30] registries reported 82–99% sensitivity and 92–100% specificity. To reduce the likelihood of multiple matches in the populous state of NSW, we first restricted the linked hospital morbidity and death records to individuals with HIV recorded as a diagnosis. However, we cannot exclude that, in some instances, HIV was not coded as a diagnosis in the hospital data despite a patient being HIV positive. This misclassification would have resulted in under-ascertainment of hospitalizations in NSW and may, in part, explain the lower hospitalization rates in NSW compared with Western Australia. Service delivery may also have affected the different hospitalization rates between the two states; HIV services are more centralized in the smaller state of Western Australia where all AHOD patients are recruited via the tertiary hospital compared with NSW, where patients are recruited via general medical practices, sexual health centres and tertiary referral hospitals. To account for any differences between the states in our analysis, we adjusted for state in the multivariate models.

Another limitation of this study is the lower follow-up rate among patients who were not hospitalized during the study period. We assume that, similar to other clinical cohorts [31], those who remained under follow-up represent a sicker group of patients who utilize health services more frequently. In this case, our study may have overestimated the true hospitalization rates in people with HIV infection in Australia. Furthermore, AHOD is a highly treated study population and not necessarily representative of all patients with HIV infection in Australia. It is also essentially a closed cohort and, therefore, not ideal for studying changes over time. For this reason, the unexpected, increased IRRs for hospitalization in 2005 and 2006–2007 and the association with longer inpatient length of stay in 2006–2007 should be interpreted with caution.

To conclude, men receiving care for HIV infection in Australia are currently hospitalized at higher rates than men of similar age in the general population. Older, sicker individuals, as indicated by markers of advanced immunodeficiency, frequency of hospitalization or both, are at greater risk of hospitalization and death. Finally, many hospitalizations were for non-AIDS diseases, highlighting the importance of treating non-AIDS diseases and related risk factors in addition to those traditionally associated with HIV disease.

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K.F, J.A. and M.G.L. conceived and designed the study and K.F. drafted the analysis plan. K.F. coordinated the study, managed the data and drafted the manuscript. K.F. and H.W. conducted the statistical analyses. K.F., H.W., M.G.L. and B.D. interpreted the results. All authors commented on the analysis plan and drafts of the manuscript and approved the final manuscript draft for journal submission.

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Table 1
Baseline demographic and clinical characteristics of the 842 patients with HIV infection from New South Wales and Western Australia in the Australian HIV Observational Database cohort by hospitalization status, 1999–2007

	All patients	Patients who were hospitalized at least once during follow-up	Patients who were not hospitalized during follow-up	<i>P</i> ^a
Total patients, <i>n</i> (%)	842	488	354	
Total person-years	4519	2782	1737	
Female sex, <i>n</i> (%)	47 (6)	35 (7)	12 (3)	0.018
Age (years), median (IQR)	41 (35–48)	41 (36–49)	40 (35–46)	0.011
State, <i>n</i> (%)				<0.001
New South Wales	559 (66)	260 (53)	299 (84)	
Western Australia	283 (34)	228 (47)	55 (16)	
Clinic type, <i>n</i> (%)				<0.001
Tertiary hospital	401 (48)	284 (58)	117 (33)	
Sexual health centre	150 (18)	76 (16)	74 (21)	
General medical practice	291 (35)	128 (26)	163 (46)	
Hepatitis B virus coinfection, <i>n</i> (%)				0.594
Negative/never tested	803 (95)	467 (96)	336 (95)	
Positive	39 (5)	21 (4)	18 (5)	
Hepatitis C virus coinfection, <i>n</i> (%)				0.089
Negative/never tested	745 (88)	424 (87)	321 (91)	
Positive	97 (12)	64 (13)	33 (9)	
HIV exposure, <i>n</i> (%)				0.006
Homosexual contact ^b	690 (82)	385 (79)	305 (86)	
Other	132 (16)	93 (19)	39 (11)	
Missing	20 (2)	10 (2)	10 (3)	
Years since first positive HIV test, <i>n</i> (%)				0.042
0–4	229 (27)	114 (23)	115 (32)	
5–7	167 (20)	101 (21)	66 (19)	
7–12	241 (29)	150 (31)	91 (26)	
≥12	194 (23)	118 (24)	76 (21)	
Missing	11 (1)	5 (1)	6 (2)	
Median (IQR)	7 (4–12)	7 (3–11)	8 (4–12)	0.021
Prior AIDS, <i>n</i> (%)	174 (21)	123 (25)	51 (14)	<0.001
CD4 cell count (cells/μl), median (IQR)	480 (309–675)	432 (260–624)	528 (377–730)	<0.001
HIV viral load (log copies/ml), median (IQR) ^c	2.60 (2.60–3.84)	2.60 (2.60–4.04)	2.60 (2.60–3.52)	0.042
Prior ART, <i>n</i> (%)	738 (88)	435 (89)	303 (86)	0.123
Number of ART regimens ever, <i>n</i> (%)				<0.001
≤1	275 (33)	137 (28)	138 (39)	
2–3	222 (26)	121 (25)	101 (29)	
4–6	176 (21)	105 (22)	71 (20)	

	All patients	Patients who were hospitalized at least once during follow-up	Patients who were not hospitalized during follow-up	<i>p</i> ^a
≥7	169 (20)	125 (26)	44 (12)	
Number of drug classes ever, <i>n</i> (%)				0.004
≤1	158 (19)	78 (16)	80 (23)	
2	393 (47)	221 (45)	172 (49)	
3	291 (35)	189 (39)	102 (29)	
4 ^d	—	—	—	
NRTI ever, <i>n</i> (%)	731 (87)	432 (89)	299 (84)	0.086
NNRTI ever, <i>n</i> (%)	430 (51)	263 (54)	167 (47)	0.054
Protease inhibitor ever, <i>n</i> (%)	552 (66)	339 (69)	213 (60)	0.005
Fusion inhibitor ever, <i>n</i> (%) ^d	—	—	—	—
Cumulative NRTI exposure (years), median (IQR)	3.0 (1.0–4.9)	3.2 (1.0–5.4)	2.6 (0.7–4.3)	0.002
Cumulative NNRTI exposure (years), median (IQR)	0.0 (0.0–1.5)	0.1 (0.0–1.3)	0.0 (0.0–1.5)	0.463
Cumulative protease inhibitor exposure (years), median (IQR)	1.3 (0.0–2.9)	1.6 (0.0–2.9)	0.8 (0.0–2.9)	0.025
Complete follow-up in AHOD cohort (%)	80	84	75	0.002
Median number of AHOD visits during study period (IQR)	28 (16–37)	33 (24–42)	21 (9–30)	<0.001

AHOD, Australian HIV Observational Database; ART, antiretroviral therapy; IQR, interquartile range; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-NRTI.

^a *P* value for Pearson χ^2 test for categorical variables or Wilcoxon rank-sum test for continuous variables.

^b Injecting drug use also reported for some participants in this group.

^c All HIV viral load measures below 400 copies/ml were changed to 399 copies/ml (i.e. 2.60 log copies/ml) for the purpose of this analysis.

^d Patients were not on fusion inhibitors at baseline.

Table 2
Predictors of hospitalization among 842 patients with HIV infection from New South Wales and Western Australia in the Australian HIV Observational Database cohort, 1999–2007

	Person-years	n	Incidence rate per 100 person-years (95% CI)	Univariate IRR (95% CI)	p	Multivariate ^d adjusted IRR (95% CI)	p	p ^b
Total	4519	2667	59 (57–61)	–	–	–	–	–
Age (per 10-year increase) ^c	4519	2667	–	1.86 (1.65–2.09)	<0.001	1.46 (1.28–1.65)	<0.001	<0.001
Sex								
Female	265	114	43 (36–52)	1.00		–	–	–
Male	4254	2553	60 (58–62)	1.37 (0.78–2.42)		–	–	–
Hepatitis B virus coinfection								
Negative/never tested	4299	2596	60 (58–63)	1.00		1.00		
Positive	220	71	32 (26–41)	0.57 (0.30–1.09)	0.091	0.77 (0.40–1.49)		
Hepatitis C virus coinfection								
Negative/never tested	3973	2374	60 (57–62)	1.00		–	–	–
Positive	546	293	54 (48–60)	0.78 (0.53–1.16)	0.221	–	–	–
HIV exposure								
Homosexual contact ^d	3683	2250	61 (59–64)	1.00		–	–	–
Other	744	371	50 (45–55)	0.78 (0.55–1.11)	0.170	–	–	–
Missing	92	46	50 (37–67)	0.66 (0.28–1.52)	0.324	–	–	–
Time since first positive HIV test (years) ^c								
0–4	411	136	33 (28–39)	1.00		1.00		<0.001
5–7	748	458	61 (56–67)	2.86 (2.31–3.53)	<0.001	2.48 (2.00–3.07)	<0.001	<0.001
7–12	1447	865	60 (56–64)	3.31 (2.62–4.18)	<0.001	2.48 (1.92–3.20)	<0.001	<0.001
≥12	1873	1147	61 (58–65)	4.07 (3.15–5.27)	<0.001	2.45 (1.82–3.31)	<0.001	<0.001
Missing	39	61	154 (120–199)	–	–	–	–	–
Prior AIDS								
No	3544	1757	50 (47–52)	1.00		1.00		
Yes	975	910	93 (87–100)	2.23 (1.65–3.01)	<0.001	1.71 (1.24–2.35)	0.001	0.001
CD4 cell count (per 100 cells increase, cells/ μ l) ^c	4519	2667	–	0.89 (0.87–0.92)	<0.001	0.91 (0.89–0.93)	<0.001	<0.001
HIV viral load (per 1 log increase, copies/ml) ^c	4519	2667	–	1.09 (1.05–1.14)	<0.001	1.16 (1.11–1.21)	<0.001	<0.001

	Person-years	n	Incidence rate per 100 person-years (95% CI)	Univariate IRR (95% CI)	p	Multivariate ^a adjusted IRR (95% CI)	p	p ^b
Number of drug classes ever ^c								
≤1	552	239	43 (38–49)	1.00		1.00		<0.001
2	1769	932	53 (49–56)	1.70 (1.33–2.18)	<0.001	1.36 (1.05–1.76)	0.022	
3	2173	1415	65 (62–69)	2.04 (1.56–2.68)	<0.001	1.16 (0.85–1.57)	0.345	
4	26	81	317 (255–394)	6.75 (4.03–11.33)	<0.001	2.66 (1.53–4.62)	0.001	
AIDS event after baseline ^c								
No	4378	2517	57 (55–60)	1.00		1.00		
Yes	141	150	106 (90–125)	1.63 (1.21–2.19)	0.001	1.11 (0.81–1.51)		
Calendar year ^c								
1999–2000 ^e	461	280	61 (54–68)	1.00		1.00		<0.001
2001	698	389	56 (50–62)	1.06 (0.90–1.24)	0.491	1.06 (0.90–1.24)	0.504	
2002	682	381	56 (51–62)	1.12 (0.95–1.31)	0.184	1.07 (0.91–1.27)	0.403	
2003	669	369	55 (50–61)	1.13 (0.96–1.33)	0.130	0.97 (0.81–1.16)	0.746	
2004	656	329	50 (45–56)	1.13 (0.95–1.33)	0.165	0.94 (0.78–1.13)	0.510	
2005	630	422	67 (61–74)	1.63 (1.39–1.91)	<0.001	1.27 (1.05–1.54)	0.014	
2006–2007 ^f	724	497	69 (63–75)	1.92 (1.63–2.24)	<0.001	1.55 (1.27–1.89)	<0.001	

CI, confidence interval; IRR, incidence rate ratio.

^aModel adjusted for state.

^bP value for test for homogeneity for nominal, categorical covariates, test for trend for ordinal, categorical covariates.

^cTime-dependent covariate.

^dInjecting drug use also reported for some participants in this group.

^eIncludes data from 1 July 1999 to 31 December 2000.

^fIncludes data from 1 January 2006 to 31 March 2007.

Table 3
Hospitalization rates for major diagnostic groups among 842 patients with HIV infection from New South Wales and Western Australia in the Australian HIV Observational Database cohort, 1999–2007

	1999–2001			2002–2004			2005–2007		
	1159 person-years			2006 person-years			1354 person-years		
	<i>n</i>	Rate per 100 person-years		<i>n</i>	Rate per 100 person-years		<i>n</i>	Rate per 100 person-years	
All causes	669	57.73 (53.52–62.28)		1079	53.77 (50.66–57.08)		919	67.89 (63.64–72.43)	
Major diagnostic groups									
Opportunistic infections	33	2.85 (2.02–4.01)		58	2.89 (2.23–3.74)		34	2.51 (1.79–3.52)	
Cancers, AIDS defining ^a	52	4.49 (3.42–5.89)		98	4.88 (4.01–5.95)		46	3.40 (2.55–4.54)	
Cancers, non-AIDS defining ^b	59	5.09 (3.94–6.57)		52	2.59 (1.97–3.40)		54	3.99 (3.06–5.21)	
Cardiovascular and other circulatory diseases	37	3.19 (2.31–4.41)		65	3.24 (2.54–4.13)		47	3.47 (2.61–4.62)	
Drug use and drug-induced organic mental disorders ^c	7	0.60 (0.29–1.27)		6	0.30 (0.13–0.67)		8	0.59 (0.30–1.18)	
Ear, nose, mouth and throat diseases	16	1.38 (0.85–2.25)		32	1.59 (1.13–2.26)		24	1.77 (1.19–2.65)	
Endocrine and metabolic diseases	9	0.78 (0.40–1.49)		15	0.75 (0.45–1.24)		15	1.11 (0.67–1.84)	
Eye diseases	10	0.86 (0.46–1.60)		11	0.55 (0.30–0.99)		15	1.11 (0.67–1.84)	
Gastrointestinal diseases	86	7.42 (6.01–9.17)		126	6.28 (5.27–7.48)		127	9.38 (7.88–11.16)	
Haematological diseases	25	2.16 (1.46–3.19)		26	1.30 (0.88–1.90)		12	0.89 (0.50–1.56)	
Hepatobiliary system and pancreas diseases	29	2.50 (1.74–3.60)		98	4.88 (4.01–5.95)		31	2.29 (1.61–3.26)	
Injuries, poisoning and toxic effects of drugs	20	1.73 (1.11–2.68)		26	1.30 (0.88–1.90)		18	1.33 (0.84–2.11)	
Kidney and urinary tract diseases ^d	22	1.90 (1.25–2.88)		74	3.69 (2.94–4.63)		168	12.41 (10.67–14.44)	
Mental health diseases	50	4.31 (3.27–5.69)		20	1.00 (0.64–1.54)		13	0.96 (0.56–1.65)	
Musculoskeletal system and connective tissue diseases	32	2.76 (1.95–3.90)		70	3.49 (2.76–4.41)		64	4.73 (3.70–6.04)	
Neurological diseases	36	3.11 (2.24–4.31)		73	3.64 (2.89–4.58)		80	5.91 (4.75–7.36)	
Nonopportunistic infections/parasitic diseases	67	5.78 (4.55–7.35)		89	4.44 (3.60–5.46)		57	4.21 (3.25–5.46)	
Reproductive system diseases	9	0.78 (0.40–1.49)		24	1.20 (0.80–1.78)		18	1.33 (0.84–2.11)	
Respiratory system diseases	20	1.73 (1.11–2.68)		38	1.89 (1.38–2.60)		25	1.85 (1.25–2.73)	
Skin, subcutaneous tissue and breast diseases	24	2.07 (1.39–3.09)		32	1.59 (1.13–2.26)		24	1.77 (1.19–2.65)	
Other	26	2.24 (1.53–3.30)		46	2.29 (1.72–3.06)		39	2.88 (2.11–3.94)	

^aIncludes 146 hospital admissions (16 patients) wherein chemotherapy was recorded as the principal diagnosis.

^bIncludes 14 hospital admissions (two patients) wherein chemotherapy was recorded as the principal diagnosis.

^cIncludes alcohol and other drugs.

^dIncludes 189 hospital admissions (two patients) with dialysis recorded as the principal diagnosis (43 in 2002–2004; 146 in 2005–2007).

Table 4
Hospitalization as a predictor of mortality among 842 patients with HIV infection from New South Wales and Western Australia in the Australian HIV Observational Database cohort, 1999–2007

	Person-years	No. of deaths	Mortality rate per 100 person-years (95% CI)	Univariate hazard ratio (95% CI)	p	Multivariate ^d adjusted hazard ratio (95% CI)	p	p ^b
Total	4547	64	1.4 (1.1–1.8)	–	–	–	–	–
Hospital admissions ^{c,d}								
None	2600	4	0.2 (0.1–0.4)	0.06 (0.02–0.18)	<0.001	0.09 (0.03–0.27)	<0.001	
1–3	1474	23	1.6 (1.0–2.4)	1.00		1.00		
≥4	473	37	7.8 (5.7–10.8)	6.67 (3.80–11.70)	<0.001	4.37 (2.45–7.78)	<0.001	
Age (years) ^d								
<45	2403	26	1.1 (0.7–1.6)	1.00		1.00		
≥45	2144	38	1.8 (1.3–2.4)	1.59 (0.96–2.65)	0.073	1.88 (1.11–3.19)	0.019	
Sex								
Female	267	3	1.1 (0.4–3.5)	1.00		–	–	–
Male	4280	61	1.4 (1.1–1.8)	1.37 (0.42–4.44)	0.603	–	–	–
Hepatitis B virus coinfection								
Negative/never tested	4326	61	1.4 (1.1–1.8)	1.00		–	–	–
Positive	221	3	1.4 (0.4–4.2)	0.98 (0.31–3.14)	0.976	–	–	–
Hepatitis C virus coinfection								
Negative/never tested	3997	55	1.4 (1.1–1.8)	1.00		–	–	–
Positive	550	9	1.6 (0.9–3.2)	1.19 (0.59–2.41)	0.623	–	–	–
HIV exposure								
Homosexual contact ^e	3706	49	1.3 (1.0–1.8)	1.00		–	–	–
Other	748	14	1.9 (1.1–3.2)	1.37 (0.73–2.58)	0.325	–	–	–
Missing	93	1	1.1 (0.2–7.7)	0.88 (0.12–6.43)	0.900	–	–	–
Time since first positive HIV test (years) ^d								
0–4	413	3	0.7 (0.2–2.3)	1.00		–	–	–
5–7	752	5	0.7 (0.3–1.6)	0.97 (0.23–4.12)	0.964	–	–	–
7–12	1457	27	1.9 (1.3–2.7)	2.76 (0.81–9.42)	0.105	–	–	–
≥12	1886	29	1.5 (1.1–2.2)	2.29 (0.66–7.95)	0.191	–	–	–

	Person-years	No. of deaths	Mortality rate per 100 person-years (95% CI)	Univariate hazard ratio (95% CI)	<i>p</i>	Multivariate ^d adjusted hazard ratio (95% CI)	<i>p</i>	<i>P^b</i>
Missing	40	0	—	—	—	—	—	—
Prior AIDS								
No	3562	43	1.2 (0.9–1.6)	1.00		1.00		
Yes	985	21	2.1 (1.4–3.3)	1.77 (1.05–2.98)	0.033	0.87 (0.50–1.51)	0.614	
CD4 cell count (cells/ μ l) ^d								
>200	4125	30	0.7 (0.5–1.0)	1.00		1.00		<0.001
101–200	240	11	4.6 (2.5–8.3)	6.49 (3.24–12.98)	<0.001	3.67 (1.78–7.57)	<0.001	
≤100	164	20	12.2 (7.9–18.9)	18.33 (10.31–32.58)	<0.001	6.48 (3.35–12.52)	<0.001	
Missing	18	3	17.1 (5.5–52.9)	—	—	—	—	—
HIV viral load (per 1 log increase, copies/ml) ^d								
≤400	2633	24	0.9 (0.6–1.4)	1.00		1.00		0.012
401–10 000	1052	8	0.8 (0.4–1.5)	1.15 (0.50–2.63)	0.748	1.05 (0.45–2.42)	0.911	
≥10 001	842	29	3.5 (2.4–5.0)	4.92 (2.79–8.68)	<0.001	2.01 (1.04–3.87)	0.038	
Missing	20	3	14.8 (4.8–45.8)	—	—	—	—	—
Number of drug classes ever ^d								
≤1	555	8	1.4 (0.7–2.9)	1.00		—	—	—
2	1777	22	1.2 (0.8–1.9)	0.84 (0.37–1.89)	0.678	—	—	—
3	2189	34	1.6 (1.1–2.2)	1.03 (0.47–2.26)	0.935	—	—	—
4	26	0	—	—	—	—	—	—
AIDS event after baseline ^d								
No	4402	54	1.2 (0.9–1.6)	1.00		1.00		
Yes	145	10	6.9 (3.7–12.9)	6.13 (2.98–12.62)	<0.001	1.12 (0.52–2.39)	0.771	
Calendar year ^d								
1999–2000 ^f	465	8	1.7 (0.9–3.4)	1.00		—	—	—
2001	702	10	1.4 (0.8–2.6)	0.56 (0.10–3.17)	0.511	—	—	—
2002	686	6	0.9 (0.4–1.9)	0.22 (0.03–1.89)	0.169	—	—	—
2003	673	7	1.0 (0.5–2.2)	0.60 (0.07–5.33)	0.650	—	—	—
2004	659	13	2.0 (1.2–3.4)	0.43 (0.04–4.40)	0.480	—	—	—
2005	633	8	1.3 (0.6–2.5)	0.41 (0.04–4.35)	0.458	—	—	—

	Person-years	No. of deaths	Mortality rate per 100 person-years (95% CI)	Univariate hazard ratio (95% CI)	Multivariate ^d adjusted hazard ratio (95% CI)	<i>p</i>	<i>p^b</i>
2006–2007 ^g	729	12	1.7 (0.9–2.9)	0.44 (0.04–4.88)	–	0.503	–

CI, confidence interval.

^aModel stratified by state.

^b*P* value for test for homogeneity for nominal, categorical covariates, test for trend for ordinal, categorical covariates.

^cDuring period of follow-up.

^dTime-dependent covariate.

^eInjecting drug use also reported for some participants in this group.

^fIncludes data from 1 July 1999 to 31 December 2000.

^gIncludes data from 1 January 2006 to 31 March 2007.

Table 5
Predictors of inpatient length of stay among 842 patients with HIV infection from New South Wales and Western Australia in the Australian HIV Observational Database cohort, 1999–2007

	Univariate β (SE)	<i>P</i>	Multivariate β (SE)	<i>P</i>
Total				
Age (per 5-year increase) ^a	0.05 (0.02)	0.028	0.08 (0.02)	<0.001
Sex (female)	−0.10 (0.21)	0.629	–	
Hepatitis B virus coinfection	−0.03 (0.27)	0.900	–	
Hepatitis C virus coinfection	0.24 (0.14)	0.085	0.32 (0.14)	0.023
HIV exposure (Homosexual contact) ^b	−0.02 (0.13)	0.878		
Time since first positive HIV test (years) ^a				
0–4	Reference			
5–7	0.21 (0.12)	0.070	–	
8–11	0.13 (0.10)	0.205	–	
≥12	0.14 (0.10)	0.136	–	
Prior AIDS	0.17 (0.11)	0.108	–	
CD4 cell count (per 100 cells increase, cells/ μ l) ^a	−0.10 (0.02)	<0.001	−0.08 (0.02)	<0.001
HIV viral load (per 1 log ₁₀ increase, copies/ml) ^a	0.15 (0.02)	<0.001	0.13 (0.02)	<0.001
Number of drug classes ever ^a				
≤1	Reference			
2	0.03 (0.15)	0.835	–	
3	0.10 (0.15)	0.494	–	
4	−0.24 (0.33)	0.464	–	
AIDS event after baseline ^a	0.17 (0.11)	0.108		
Calendar year ^a				
1999–2000 ^c	Reference		Reference	
2001	−0.09 (0.13)	0.499	−0.02 (0.13)	0.891
2002	−0.07 (0.14)	0.594	−0.03 (0.13)	0.849
2003	0.19 (0.13)	0.133	0.20 (0.13)	0.114
2004	−0.04 (0.14)	0.783	−0.01 (0.14)	0.938
2005	−0.07 (0.14)	0.605	−0.006 (0.14)	0.966
2006–2007 ^d	0.16 (0.12)	0.195	0.25 (0.12)	0.044

[†] Model adjusted for state.

^a Time-dependent covariate.

^b Injecting drug use also reported for some participants in this group.

^c Includes data from 1 July 1999 to 31 December 2000.

^d Includes data from 1 January 2006 to 31 March 2007.