Cohort study of predictors of unplanned hospital admissions among Regional People with HIV in NSW from 2012-2016; the impact of multimorbidity

Short Title	**Multimorbidity and admissions among People with HIV**
Name	**Natalie Edmiston**
	Staff Specialist Sexual Health
Address	**4 Shepherd Lane**
	Lismore NSW 2480
Telephone	**02 6620 2980**
Email	Natalie.edmiston@ncahs.health.nsw.gov.au

Research Support

Natalie Edmiston was a candidate in the NSW HETI Rural Research Capacity Building Program (RRCBP) 2015 Cohort. Funding was provided through NSW HETI for the candidate to work in a research capacity and be backfilled.

Acknowledgements

Kathy Petoumenos, Associate Professor, The Kirby Institute mentored the principal investigator, assisted in study design, supervised and provided advice on statistical analysis and reviewed and edited reports, manuscripts and presentations.

Jenny Heslop, HARP Manager, MNC Public Health was the organisational sponsor of the project.

David Smith, Medical Director, North Coast Sexual Health assisted in study design, collected data and reviewed and edited reports, manuscripts and presentations.

Kerith Duncanson and David Schmidt and the teaching staff of the RRCBP are acknowledged for providing feedback at all stages of the research process and for support of the principal researcher.

Participants of RRCBP 2015 Cohort and participants in the Writing for Publication Bootcamp 2016 are acknowledged for providing peer review.

Staff at Lismore Sexual Health Service are acknowledged for support of the research. Emanuel Vlahakis provided some patient data and reviewed a manuscript for publication. Amber Tarver and Marlene Herne provided administrative support. Andrew Buggie and Ariane Minc supported the research by participation in research discussions.

Erin Passmore is acknowledged for involvement in the 2012 research which provided baseline data for this research.

Abbreviations list

AHOD	Australian HIV Observational Database
AIDS	Acquired Immune Deficiency Syndrome
CIRS	Cumulative Illness Rating Scale
ED	Emergency Department
GP	General Practitioner
HAND	HIV associated Neurocognitive Deficit
HCV	Hepatitis C virus
HIV	Human Immunodeficiency Virus
II	Integrase Inhibitor
NRTI	Nucleoside Reverse Transcriptase Inhibitor
NNRTI	Non-nucleoside Reverse Transcriptase Inhibitor
PI	Protease Inhibitor
PWH	People with Human Immunodeficiency Virus
SHC	Sexual Health Clinic
UA	Unplanned admission
VACS	Veterans Aging Cohort Score

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Abstract

Objectives

People with HIV (PWH) have improved life expectancy in recent years but continue to experience significant multimorbidity and require unplanned care. We aimed to determine factors predictive of unplanned admission among a cohort of PWH in regional NSW.

Method

A prospective cohort study of PWH attending a regional HIV service was conducted. Baseline HIV specific results and multimorbidity markers including Cumulative Illness Rating Scale (CIRS) and Veterans Aging Cohort Score were assessed as predictors of time to first unplanned admission using cox regression analysis. Care coordination markers were compared between people experiencing unplanned admission and those not experiencing unplanned admission using x^2statistic for proportions and t-test for means. CIRS score was compared between baseline and follow-up. Multivariate regression analysis was used to determine factors associated with a change in CIRS score.

Results

A cohort of 181 PWH were followed for 5 years. During a total of 739 person years of follow-up, 39 (20.6%) patients reached the endpoint of unplanned admission. In multivariate analysis the baseline CIRS score was predictive of unplanned admission (p <0.001). Age, HIV specific markers and missed visits were not predictive of unplanned admission. Nine (6.47%) PWH died during the period of observation. All those that died had an unplanned admission prior to death.

For patients with an unplanned admission, discharge summaries were available in the notes for 22/39 (56.4 %). Of 180 PWH with a visit after baseline, 131 (72.8%) had a letter to a general practitioner in the observation period and 79 (43.7%) had 2 or more prescribers. Having 2 or more prescribers was more common in people with an unplanned admission than in those without an unplanned admission (64.1% vs 38.0%, p=0.004).

The mean (SD) follow-up CIRS score of 9.45 (±4.89) was not significantly different form the baseline CIRS score of 9.08 (±4.69; p=0.467). In multivariate analysis, baseline factors significantly associated with a change in the score were ever having a myocardial infarct (coeff -1.78, p=0.028) and ever having renal disease (coeff 1.70, p=0.006).

Conclusion

Unplanned admission among PWH is predicted by multimorbidity. Care for PWH should include coordinated management of other health conditions in order reduce their severity and potentially prevent unplanned admissions. In the cohort of PWH studied, multimorbidity did not significantly increase over 5 years of follow-up.

Keywords

HIV, comorbidity, patient admission, case management, cumulative illness rating scale

Executive Summary

Multimorbidity, generally considered to be the presence of two or more chronic health conditions in addition to HIV, has been shown to be common among people with HIV (PWH). Multimorbidity is associated with older age so as the median age of PWH in Australia increases, multimorbidity may be expected to increase. Multimorbidity is important as it increases the complexity of care and increases the risk of hospitalisation and mortality. In overseas studies multimorbidity has been shown to predict admissions among PWH. It has not been investigated as a predictor of admissions among Australian PWH.

This study is the first Australian study to investigate multimorbidity as measured by the Cumulative Illness Rating Scale (CIRS) as a predictor of unplanned admission among PWH. The study also explores changes in multimorbidity over time and care coordination for PWH.

Key Findings

Multimorbidity, as measured by the CIRS, was the only independent predictor of time to first unplanned admission among the cohort of PWH attending a regional HIV service in 2012. HIV specific measures and specific health conditions did not predict unplanned admission in multivariate analysis. It is evident that the cumulative effect of other health conditions is an important determinant of health care utilization among regional PWH.

The CIRS score remained stable over the five years of follow-up despite there being a strong association between age and CIRS score in this population. Similarly, the Veteran Aging Cohort Score did not significantly increase in this time despite age and markers known to increase with age such as serum creatinine being included in the calculation. It appears that multimorbidity among PWH may not be increasing at rates previously anticipated.

Ever having renal disease at baseline was associated with an increase in CIRS score in multivariate analysis, while ever having a myocardial infarction at baseline was associated with a decrease in CIRS score. Among the study cohort, fewer people had a current diagnosis of HIV associated neurocognitive deficit at follow-up compared to baseline. More people had a current diagnosis of vascular disease at follow-up compared to baseline, whereas most other conditions showed no significant change. Possibly vascular disease risk factor management is playing a role in limiting multimorbidity increases.

Discharge summaries were present in the patient record for slightly over half of the patients with an unplanned admission. Although a general practitioner (GP) was noted in the majority of patient records, correspondence to GPs was not consistent. Most PWH (72.2%) had a letter to the GP in the time of observation, but 62.2% had two or fewer letters in the time of the study. These levels of communication between hospital and specialist and between specialist and GP may be insufficient to prevent adverse drug interactions occurring. Slightly less than half of PWH had two or more prescribers and this was associated with having an unplanned admission. The number of prescribers but was not able to be assessed as a predictor because it was not collected at baseline, however the association indicates extra attention should be given to PWH who have more than one prescriber.

Recommendations

Recommendations for North Coast Public Sexual Health Clinics.

It is recommended that

1. HIV specialist teams obtain a CIRS score for PWH at entry to care and update this annually. The process of obtaining a CIRS score ensures the recording of all known chronic health conditions in an accessible format for future care. The CIRS score was the single most important predictor of unplanned admission.
2. Specialist HIV prescribers consider a multimorbidity approach to care for PWH with two or more prescribers or following first unplanned admissions.
3. Specialist HIV prescribers provide regular correspondence to patient's general practitioner (GP), particularly if the GP regularly prescribes for the PWH as having two or more prescribers was associated with unplanned admission.
4. Mechanisms are developed to ensure HIV prescribers are aware of admissions that occur for their patients in a timely manner and that discharge summaries are seen by the HIV prescriber. This will minimise the risk of adverse drug interactions and improve care coordination.
5. Research continue into factors associated with changes in multimorbidity as measured by CIRS. Multimorbidity remains a key concern for PWH and the aim of care for PWH is not merely suppression of HIV virus, but avoidance of long term health problems.
6. Specialists in North Coast Public Sexual Health Clinics assist local GPs to maintain current knowledge about HIV and its treatments, particularly in respect to drug-disease and drug-drug interactions. Shared care for HIV educational meetings for GPs are recommended as a possible format.

Further Recommendations

At a broader level it is recommended that

1. NSW Health maintain adequate funding to enable Sexual Health Clinics to provide co-ordinated care for PWH, particularly in regional areas where GPs able to prescribe antiretrovirals are not easily accessed.
2. The Royal Australian College of Physicians consider advocating for the importance of a multimorbidity approach to care with a focus on care coordination for all PWH attending HIV specialists who are not also their GP.
3. Education for health practitioners providing care for PWH include the concept of multimorbidity. Education providers such as Australian Society for HIV Medicine may wish to consider opportunities to provide education for GPs who are not the primary HIV prescriber.
4. Regional hospital physicians and emergency department doctors consider utilising CIRS score or similar to triage patients requiring a higher level of coordinated care.

Introduction

Almost universal availability of antiretrovirals and medical care for people with HIV (PWH) in Australia has led to dramatic improvements in health and life expectancy in recent years (1, 2). Despite these improvements, chronic health problems and utilization of hospital based care are ongoing issues for regional PWH. Hospitalisation in the Australian HIV Observational Database (AHOD) cohort was associated with age and prior diagnosis of Acquired Immune Deficiency Syndrome (AIDS) (3). In overseas cohorts of PWH, having multiple comorbid conditions increased the risk of hospital readmission (4) and emergency department (ED) use (5).

Chronic health conditions are common among PWH, including in Australia (6, 7). Among PWH, multimorbidity is defined as the presence of two or more chronic health conditions in addition to HIV, and is associated with age and having had AIDS or severe immunosuppression (8-10). As the median age of Australian PWH increases (11), particularly in regional areas of Australia (12), multimorbidity may become increasingly common. Predictions are that multimorbidity levels among PWH will rise dramatically in the coming years (13). There is some evidence that multimorbidity may be more common among PWH than among age matched members of the general population (6). A multimorbidity approach to care is advocated for people with multiple health problems and includes improving coordination of care across services (14).

Rationale

HIV is now a long term chronic health condition and PWH are growing older (15). In 1985, the proportion of PWH in Australia aged over 55 years was 2.7%. In 2010, it was 25.7% and by 2020 it is expected to be 44.3% (12). It is well documented that increasing age is associated with the acquisition of chronic health conditions (16). HIV is a chronic health condition of itself requiring lifelong medication and regular monitoring and medical review. HIV infection has been associated with increased risks of many chronic health conditions including vascular disease (17), renal disease (18), osteoporosis (19) and liver disease (20). Possible mechanisms include chronic inflammation (21), medication toxicity (22) and behavioural risks. It is apparent that chronic health conditions are common among PWH despite viral suppression.

As a result of HIV itself and the aging of the cohort of PWH, many PWH have multimorbidity, or the presence of two or more chronic health conditions. In HIV-specific literature multimorbidity is usually used to refer to the presence of two or more chronic health conditions in addition to HIV (9, 10, 23). Various measurements have been used to describe multimorbidity (24), including a Cumulative Illness Rating Scale (CIRS) (25), which includes all chronic health conditions and scores the severity of each health condition by impact on body systems. As PWH live longer the range of conditions affecting PWH will become increasingly broad so it is important to use a tool that encompasses all conditions.

The Veterans Aging Cohort Score (VACS) was developed as a mortality predicting score and includes CD4 lymphocyte cell count, HIV viral load, and general health measures of haemoglobin, liver and renal function (26). This score has been shown to accurately predict mortality in a range of North American and European cohorts (26, 27). In addition, VACS has been shown to predict hospitalisation (28). The usefulness of VACS is that it can be generated from routinely collected

pathology. In this cohort of PWH in regional NSW, a higher CIRS score was associated with older age and past AIDS and had a reasonable correlation with VACS (8). Others have found multimorbidity among PWH to be associated with age and having past AIDS or other markers of severe immune deficiency (9, 10). Furthermore, the development of a new comorbidity is predicted by older age and by lack of antiretroviral usage in PWH with a low CD4 count (29).

Multimorbidity is a concern for PWH and their health care providers because it increases the complexity of care (33). In non-HIV populations multimorbidity has been shown to increase the risk of hospitalisation (34, 35) and mortality (36). Despite viral suppression, PWH continue to have higher admission (37) and mortality rates (2) than the general population and multiple medical conditions have been associated with unplanned readmissions among PWH (4). The risks associated with multimorbidity may be partly mediated, through intermediary factors of polypharmacy (38), frailty (39, 40) and lack of care coordination.

Polypharmacy, which has been defined as being prescribed five or more regular medications, is closely associated with multimorbidity. PWH generally require one or more antiretroviral prescriptions plus prescriptions for other health conditions so daily medication burden can be substantial (30). Polypharmacy increases the risk of adverse drug interactions and hospitalisations and may contribute to an increased risk of mortality (31). Increased medication burden may also contribute to non-adherence to antiretrovirals (32).

Several doctors may be involved in providing health care to an individual with HIV (41). In regional NSW, few General Practitioners (GPs) maintain s100 prescriber status allowing prescription of antiretrovirals. Therefore, PWH require a HIV specialist and are encouraged to have a GP. People may also need to attend other specialists for comorbid conditions. As a result, regional PWH are particularly at risk of fragmentation of medical care. Fragmentation of care may increase the likelihood of hospital admissions, particularly unplanned admissions. Whilst all admissions can result in costs to the health system and have some risks, unplanned admissions, such as those that occur through ED, can be particularly problematic. For PWH, unplanned admissions may increase the risk of medication errors, particularly for PWH with renal disease or using a protease inhibitor(42). In hospital, medical practitioners not previously providing care to the PWH may be involved, further increasing the risk of fragmentation of care (4). Re-admissions, particularly if they occur at a different facility, can increase fragmentation of care (4).

Hospitalisation rates in the AHOD cohort are 50 – 300% higher than for age and sex matched peers(3). In NSW, hospitalisation rates for gay and bisexual men with HIV are double the rates of peers without HIV(37). In both the USA (43) and Canada (44) PWH are more likely to visit emergency departments (ED) and more likely to be admitted from ED than people without HIV.

Reasons for hospital admissions of PWH vary across the globe. Infectious conditions predominate in developing countries but a diverse range of system disease including respiratory, psychiatric, renal, liver and cardiovascular disease are the reasons for admission in developed countries (45). In USA populations, the most common serious health events in PWH on antiretrovirals are the same as for people without HIV; cardiovascular disease and malignancy (46).

In order to reduce unplanned admissions, the predictors of unplanned admissions need to be fully understood. Hospitalisation in the AHOD cohort was associated with age and prior AIDS (3). In overseas cohorts of PWH, having multiple comorbid conditions increased the risk of hospital readmission (4) and ED use (5). The VACS suggests chronic disease through the inclusion of non-HIV

specific disease markers and has been shown to predict hospitalisation (28). Specific conditions that have been implicated in increased ED use or hospitalisation among PWH include mental health and substance abuse disorders (47) and Hepatitis C Virus (HCV) (48, 49). Other factors implicated in potentially avoidable admissions among PWH include social isolation (50) and adverse drug reactions (51). Adverse drug reactions are common in PWH, particularly in those using protease inhibitors (38, 52). Missed visits for HIV care have been associated with a higher risk of hospital admission in a USA cohort (53). This complex range of factors associated with admission suggest the need for a coordinated approach to care.

Identification of PWH who have multimorbidity may facilitate a multimorbidity approach to care. Such an approach is recommended if a person has multiple treatment providers or frequently seeks unplanned care (14). The multimorbidity approach means being aware of all health conditions and medications to avoid adverse drug-drug or drug-disease interactions, reducing treatment burden and unplanned admissions and improving coordination of care across services (14). The current NSW HIV strategy (54) calls for a renewed focus on PWH having shared care with a GP and a specialist. In a review of shared care models for PWH, key findings were a lack of data for the benefit of shared care and that timely communication is essential for implementation of shared care (55). Multimorbidity management in the context of shared care is likely to require extensive efforts to ensure coordination. Communication between hospital and HIV specialist in the form of discharge summaries and between HIV specialist and GPs the form of letters are possible indicators to describe coordination of care.

In regional areas, access to medical care may be complicated by long travel times and less availability of public specialists' clinics. PWH in regional areas are older than the average age for Australian PWH (12) and are therefore more likely to have multimorbidity. A regional cohort is the ideal population to study multimorbidity and the results of research are likely to have important implications for health care of PWH in regional areas.

Research Aim

The primary objective of this study is to determine what factors predict unplanned hospital admissions among PWH accessing a regional HIV service. Our hypothesis is that multimorbidity, as measured by baseline CIRS score, predicts unplanned hospital admission. Multimorbidity has not previously been assessed as a predictor of admissions among Australian PWH.

The secondary objectives are to determine change in multimorbidity over time, as measured by the CIRS score and to determine factors predictive of change in CIRS scores. A further aim is to describe indicators of care coordination including communication between hospital, specialist and GPs and the number of prescribers for an individual PWH. Associations between these care coordination indictors and unplanned admissions will be explored.

The findings of the research will be of interest to PWH and their care providers, particularly those outside large urban centres. Service managers and policy managers may find the report useful to determine future priorities in care of PWH. The report also has relevance for GPs, physicians and health administrators as the concepts of multimorbidity and care coordination are relevant across all health disciplines.

Method

Study population

We conducted a prospective cohort study of PWH who had attended a regional sexual health clinic (SHC) between 1 July 2011 and 30 June 2012 and had at least one follow-up visit or admission after 30 June 2012. The clinic is located in a regional city and has an outreach clinic in a coastal town, providing HIV care to PWH residing up to 250km away. All PWH who were having HIV managed at the service were eligible for inclusion in the study. PWH who had HIV care elsewhere and attended as a single visit or who only attended for testing of sexually transmitted infections were excluded from the study.

During follow-up PWH attended for routine HIV care. At this service, routine care entailed a visit to one of three medical officers every three to six months, at which pathology tests were collected including CD4 lymphocyte cell count and HIV viral load. Weight was recorded and medications and other health conditions were reviewed. PWH were encouraged to have a GP for routine medical care. A hybrid medical record utilising paper and electronic medical record was in use at the time of the study. The electronic medical record consisted of a program for prescribing and letter writing and a second program for data collection; neither was linked to hospital medical records.

Study Procedure

We had previously conducted a cross-sectional analysis of this cohort which involved collection of baseline data and introduction of the CIRS score to clinic practice (8). The baseline data was collected for the last clinical visit in between 1 July 2011 and 30 June 2012. The baseline variables were age, gender, duration of HIV infection, history of AIDS diagnosis, nadir and current CD4 count, current HIV viral load, antiretroviral combination prescribed and total number of medications prescribed. Nadir CD4 count was divided into less than 200 cells/µL and 200 cells/µL or greater and current CD4 count was divided into four categories (table 1). Antiretroviral combinations were classified into combinations with two nucleoside reverse transcriptase inhibitors (NRTI) and either one non-nucleoside reverse transcriptase inhibitors (NNRTI), one boosted protease inhibitor (PI) or one integrase inhibitor (II). All other combinations were considered to be other combinations. The VACS was calculated from most recent laboratory results. The presence of a mental health diagnosis, vascular disease, diabetes, osteoporosis, renal disease, malignancy and HIV associated neurocognitive deficit was recorded. The definitions of these specific conditions are shown in Appendix 1. Missed visits were scheduled visits for which the patient did not attend in the preceding 12 months.

At baseline one of two medical officers completed a CIRS worksheet (Appendix 2) using the Fourteen-system Modified Version CIRS (25). The CIRS is based on fourteen body systems (e.g. respiratory, vascular, genitourinary) being rated on a five-point scale of severity of medical problems (0=no condition, 4=extremely serious condition), using published guidelines (25). Addition of all scores generated a CIRS score between 0 and 56. A score between 0 and 14 was recorded for the number of systems affected and for the number of systems rated three or more (i.e. very serious or extremely serious condition). The CIRS was usually completed after or during a clinic visit by the treating medical officer so did not rely solely on information previously written in the paper record. This method of augmenting chart review with a clinical visit has been shown to be the most likely to produce a comprehensive assessment of multimorbidity (24). The two medical officers collaborated to ensure consistency of scoring.

In the first six months of 2016, the CIRS worksheet was completed by the treating medical officer, after a PWH attended a clinic visit. Total CIRS score, number of systems affected and number of systems scoring three or more was recorded. The principal investigator provided training in completing the CIRS worksheet for two other treating medical officers and independently scored ten percent of records to avoid measurement bias. The principal investigator reviewed the paper records and completed the data collection tool (Appendix 3), following the first visit in 2016. For patients who did not have a visit in the first six months of 2016, including those that had moved or were deceased, the data collection tool and CIRS worksheet were completed based on the last visit.

The principal investigator reviewed each paper medical record for details of admissions for all PWH who had either an unplanned or a planned admission. The date and reason for the first unplanned and planned admissions to hospital was obtained from the discharge summary if a hard copy was filed in the paper record, or from the details written in the paper record if no discharge summary was present. The total number of planned and unplanned admissions were collected. Admissions were considered unplanned if they occurred via attendance at an ED. Discharge summaries were recorded as present in the notes if a hard copy was present in the paper medical record. Hospital records were not searched for details of admissions or for copies of discharge summaries. The reasons for admission were grouped into vascular, malignancy or other. The date of death and reason was obtained from medical records or notification forms.

Variables collected to describe care coordination were a GP being recorded in the notes, number of letters to a GP and number of prescribers. Viral load indicators of more than six months between measurements or any measurement greater than 500 copies/mL were used as additional indicators of coordinated care. For the time period 30 June 2012 to 30 June 2016, whether or not a GP was recorded in the notes and the number of letters written to the GP was recorded on the data collection tool (Appendix 3). Patients were considered to have more than one prescriber if the electronic medication record had medications listed with the prescriber indicated as “elsewhere” or if the paper record indicated a medication had been prescribed elsewhere. All viral load results for the period of observation were downloaded from the data collection program. This enabled determination of time periods of greater than six months between viral load measurements and episodes of viral load being greater than 500 copies/mL.

We recalculated the VACS using laboratory results from the last visit prior to 30 June 16. Current antiretroviral regimen at last visit and the presence of specified conditions in the two years prior to last visit were recorded. Baseline variables and variables recorded on the data collection tool (Appendix 3) were collated on a spreadsheet. Categorical data was numerically coded. All data was checked for missing data and inconsistencies, which were resolved by checking against the original patient records.

The research was submitted to Northern NSW Human Research Ethics Committee and determined to be a Quality Assurance activity, correspondence dated 16 December 2015.

Statistical Analysis

The primary outcome of interest was time to first unplanned admission. We conducted univariate and multivariate cox regression analyses to determine baseline variables predictive of time to first unplanned admission. The baseline variables considered were age, gender, duration of HIV diagnosis, history of AIDS diagnosis, nadir and current CD4 count, current HIV viral load, missed visits, antiretroviral combination prescribed, total number of medications prescribed, VACS, CIRS score, CIRS number of systems affected and CIRS number of systems rated three or greater. Patients were censored at time of first unplanned admission. Those patients without an unplanned admission were censored at first visit in 2016, or at last visit if no visits occurred in 2016 prior to 30 June 2016. Person years was calculated as the time from baseline to time of first unplanned

admission or censure. Factors in univariate analyses with p value < 0.1 were considered in multivariate analyses. The multivariate model was built using backward step-wise method. Included in the final model were all factors with p value < 0.05. We added specific chronic health conditions (Appendix 1) to the final model in two ways; firstly as ever having had the condition at baseline and secondly as having the condition within the two years prior to baseline.

For PWH with either a planned or unplanned admission, the proportion for whom a discharge summary was in the medical record was compared between first unplanned and first planned admission using x^2 statistic. We compared four care coordination variables for patients who had an unplanned admission to those that did not have an unplanned admission using x^2 statistic. The care coordination variables compared were number of letters to a GP, number of prescribers, gap in viral load monitoring of greater than six months or a viral load measured at greater than 500 copies/mL.

For changes from baseline to follow-up, we defined the follow-up time point as the first visit in 2016, or at last visit if no visits occurred in 2016 prior to 30 June 2016. Unpaired t-test was used to compare the mean follow-up CIRS score and mean follow-up VACS for patients who had an unplanned admission to those that did not have an unplanned admission. Changes in antiretroviral use from baseline to follow-up were described. Two sample test of proportions was used to calculate the statistical significance of the change in proportions form baseline to follow-up for integrase inhibitor use, protease inhibitor use and the prevalence of specific conditions.

We conducted univariate and multivariate regression analysis to determine baseline variables that predicted change in CIRS score. The change in CIRS score was calculated as the difference between CIRS score at follow-up and CIRS score at baseline. Variables considered were age, gender, duration of HIV diagnosis, history of AIDS diagnosis, nadir and current CD4 count, current HIV viral load, missed visits, antiretroviral combination prescribed and ever having a specific chronic health condition (Appendix 1). Factors in univariate analyses with p value < 0.1 were considered in multivariate analyses. The multivariate model was built using backward step-wise method. Included in the final model were all factors with p value < 0.05. Baseline CIRS score was added to the final model to assess the impact on the significant variables.

All statistical analysis was conducted on STATA Version 14 (56).

Results

Of 181 people in the study, 167 (92.3%) were men. The median age in 2012 was 51.9 years (IQR 46.2 – 57.7yrs, range 26-76.8yrs) and the median duration of HIV infection was 17.5 years (IQR 10.5 – 25.1 yrs, range .6-29.5yrs). Forty-seven (26.0%) PWH had previously been diagnosed with AIDS. Antiretrovirals prescribed to the study population in 2012 were two NRTIs plus a NNRTI in 32.0% (58/181), two NRTIs plus a PI in 25.4% (46/181), two NRTIs plus an II in 5.5% (10/181) and other combinations in 31.5% (57/181). The remaining 5.5% (10/181) were not taking antiretrovirals. Remaining baseline variables are shown in Table 1.

Table 1. Baseline Variables as Predictors of Time to First Unplanned Admission for People with HIV

		Univariate HR[#]	Univariate p value
Age *yrs, median (IQR)*	51.9 (46.2-57.7)	0.996	0.803
Gender			
Male *n(%)*	167 (92.3)	ref	
Female *n(%)*	14 (7.7)	0.978	0.971
Duration HIV *yrs, median (IQR)*	17.5 (0.6- 29.5)	0.995	0.800
Current ARV* regimen			
2 NRTIs[1] + NNRTI[2] *n(%)*	58 (32.0)	ref	
2 NRTIs[1] + PI[3] *n(%)*	46 (25.4)	1.433	0.410
2 NRTIs[1] + II[4] *n(%)*	10 (5.5)	0.555	0.574
Other *n(%)*	57 (31.5)	1.705	0.186
Nil *n(%)*	10 (5.5)	0.542	0.559
AIDS diagnosis			
Never *n(%)*	134 (74.0)	ref	
Ever *n(%)*	47 (26.0)	1.361	0.364
Nadir CD4 cell count			
200 cells/µL or more *n(%)*	84 (46.4)	ref	
Less than 200 cells/µL *n(%)*	95 (52.5)	0.898	0.740
Missing	2 (1.1)		
Current CD4 cell count			
<350 cells/µL *n(%)*	30 (16.6)	ref	
350- 499 cells/µL *n(%)*	30 (16.6)	0.780	0.631
500- 699 cells/µL *n(%)*	57 (31.5)	0.658	0.360
700 cells/µL or greater *n(%)*	64 (35.4)	0.592	0.252
Current viral load			
Less than 50 copies/mL *n(%)*	161 (89.0)	ref	
50 copies/mL or greater *n(%)*	20 (11.0)	1.632	0.270
Baseline missed visits			
Nil	147 (81.2)	ref	
1 or more	34 (18.8)	1.770	0.120

HR[#] = Hazard Ratio, ARV* = antiretrovirals; 1 = Nucleoside reverse transcriptase inhibitor; 2 = Non- nucleoside reverse transcriptase inhibitor; 3 = Protease inhibitor; 4 = Integrase inhibitor

In 2012, the mean (SD) CIRS score for the study population was 9.08 (±4.69) (range 1-27). The mean (SD) number of systems affected was 5.31 (±2.16)(range 1-13) and the mean (SD) number of systems with a score of 3 or greater was 0.72 (±1.02)(range 0-6). The mean (SD) VACS was 18.33 (±13.87)(range 0-84). The median number of medications was 5 (IQR 3-8, range 0 – 24). Twenty-eight (15.5%) were prescribed ten or more medications.

Unplanned Admission Outcomes

There was a total of 739 person years of follow-up to the end-point of first unplanned admission or censure. Thirty-nine people had a least one unplanned admission. While most people had only one unplanned admission (31/39, 79.5%), the maximum number of unplanned admissions was ten. The reasons for first unplanned admissions were vascular disease in nine (23.1%), malignancy in four (10.2%) and a variety of other conditions for the remainder. In contrast, 73 people had at least one planned admissions. The maximum number of planned admissions for an individual was five. There were nine deaths among the study population, of which four were due to malignancy. All those that died had an unplanned admission prior to death.

Predictors of Unplanned Admission

In univariate analysis, all multimorbidity markers at baseline were predictive of time to first unplanned admission. These markers were CIRS score, CIRS number of systems affected, CIRS number of systems rated three or more, VACS and number of medications (Table 2). Age, gender, ever having AIDS, and having missed visits were not predictive of time to first unplanned admission in univariate analysis. In addition, baseline antiretroviral regimen, nadir and baseline CD4 count and baseline viral load were not predictive of time to first unplanned admission (Table 1).

Table 2. Baseline Multimorbidity Markers as Predictors of Time to First Unplanned Admission

	Univariate HR	Univariate p value	Multivariate HR	Multivariate p value
No. of medications	1.078	0.034		
CIRS* score	1.165	<0.001	1.165	<0.001
CIRS* systems affected	1.317	<0.001		
CIRS* systems rated 3 or more	1.782	<0.001		
VACS**	1.033	0.002		

*CIRS = Cumulative Illness Rating Scale; **VACS = Veterans Aging Cohort Score

In multivariate analysis, only CIRS score was predictive of time to first unplanned admission. Specified conditions were added to the model to determine if they significantly predicted time to first unplanned admission. Regardless of whether specified conditions were considered as having been present in the two years prior to baseline or ever having, none of the conditions predicted unplanned admission once added to the model (not shown).

Care Coordination Variables and Associations with Unplanned Admissions

For the first unplanned admission, 22 of 39 (56.4%) PWH had a discharge summary present in the medical record. For the first planned admission, 45 of 73 (61.6%) PWH had a discharge summary present in the medical record. There was no statistical difference in the proportion of discharge summaries received between first planned and unplanned admissions (p=0.295).

Over the period of observation, there were nine deaths and 16 people transferred care or were lost to follow-up. In 2016, 156 (86.2%) people from the 2012 cohort remained in care at the service. Care coordination was compared for 180 individuals as data was missing for one individual. Over half of the population (98/180, 54.4%) had a gap of more than six months between viral loads. Thirty people (16. 7%) had a viral load measured at greater than 500 copies/mL on at least one occasion during the period of observation. Most (136/180, 75.6%) of the population had a GP recorded in the notes. However, 112 (62.2%) had two or fewer letters to the GP over the four years of the study; 50 (27.8%) had no letters to a GP during follow-up. Seventy-nine (43.7%) PWH had two or more prescribers.

Those who had an unplanned admission were more likely to have two or more prescribers than PWH who did not have an unplanned admission (p=0.004). There was no difference in the proportion of PWH who had one or more letters to a GP during the time of follow-up (p=0.336). Those with unplanned admissions were not more likely to have had a gap in viral load monitoring of greater than six months or a viral load measured at greater than 500 copies/mL in the time of follow-up (Table 3).

Table 3. Care coordination variables by Unplanned Admission status

	Overall n=180	No UA* n=142	UA* n= 38	p value
	N (%)	N (%)	N (%)	
1 or more letters to GP	131 (72.8)	101 (71.1)	30 (79.0)	0.336[1]
2 or more prescribers	79 (43.7)	54 (38.0)	25 (65.8)	0.004[1]
> 6 months between VL	98 (54.4)	73(51.4)	25(65.8)	0.114[1]
VL > 500 copies/mL	31 (17.2)	22 (15.5)	9 (23.7)	0.235[1]

*UA = Unplanned admission; [1] x^2 test

Follow-up Antiretroviral Use and Chronic Conditions

Follow-up variables were compared to baseline for 180 individuals. Antiretroviral regimens prescribed to the study population at most recent follow-up were 2NRTIs plus NNRTI for 36/180 (20.0%), 2NRTIS plus PI for 19/180 (10.6%), 2NRTIs plus II for 58/180 (32.2%) and other combinations for 65/180 (36.1%). Two of 180 PWH (1.1%) were not taking antiretrovirals (Fig. 1).

Regarding specific medications, over time there was a significant increase in II use from 37/180 (20.6%) in 2012 to 102/180 (56.7%) at most recent follow-up (p< 0.001), while PI use decreased non-significantly from 94/180 (52.2%) to 79/180 (43.9%) (p=0.114). The decrease in PI use was offset by an increase in use of the non-antiviral cyp3A4 enzyme inhibitor, cobicistat so overall there was no

change in the number of people using a cyp3A4 enzyme inhibitor (94/180 in 2012 vs 95/180 at follow-up, p=0.916).

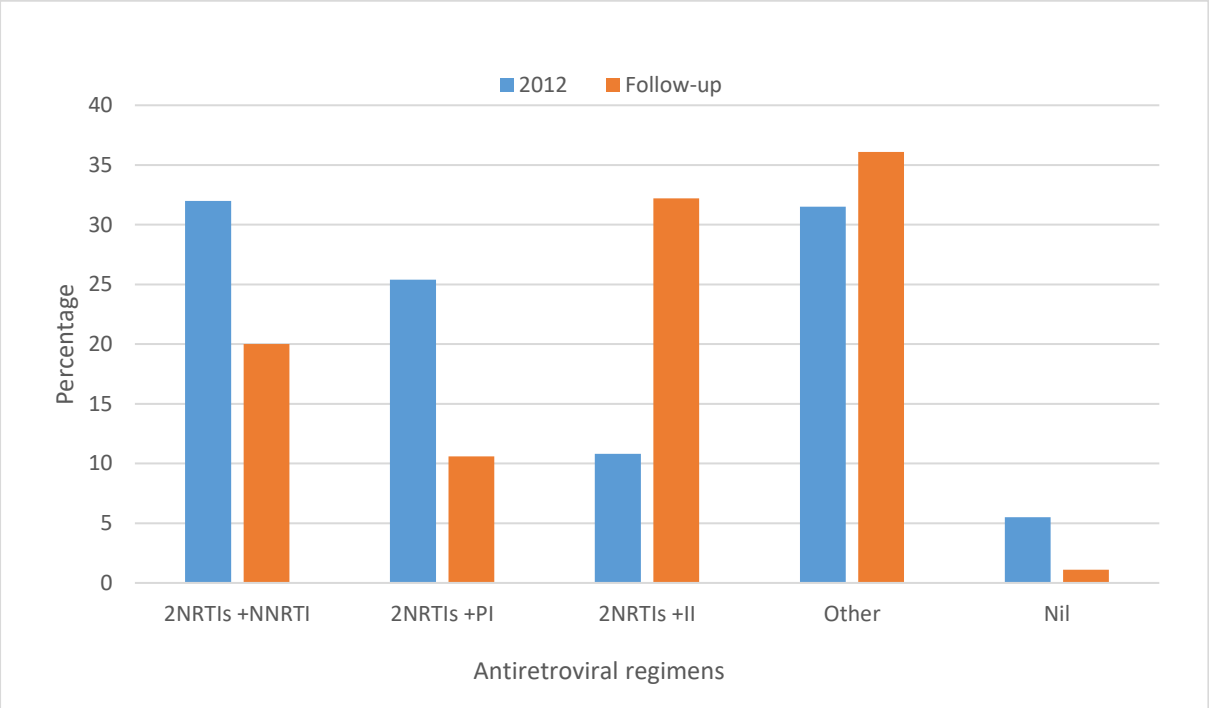

Fig 1. Percentage of people using antiretroviral regimens in 2012 (n=181) and at follow-up (n=180)

For the majority of specific health conditions, there was a minimal change in prevalence from 2012 to most recent follow-up. There was a significant increase in PWH with a diagnosis of vascular disease from 2012 (46.1%) to most recent follow-up (58.9%) (p=0.015) and a significant decrease in the diagnosis of HIV associated neurocognitive disorder (HAND), which was 5.6% in 2012 and 0.6% at most recent follow-up (p=0.006). There were non-significant increases in the prevalence of obesity (5.0% to 10.0%, p=0.070), malignancy (3.3% to 6.7%, p=0.147) and osteoporosis (6.7% to 10.6%, p=0.189). There was a non-significant decrease in the prevalence of HCV viral positivity from 7.8% to 5.6% (p=0.405).

Predictors of CIRS Change

Despite the population having aged over the duration of the study, the CIRS score and VACS at follow-up did not show a statistical increase from baseline. The mean (SD) follow-up CIRS score of 9.45 (±4.89) was not significantly different form the mean (SD) baseline CIRS score of 9.08 (±4.69) (p=0.467). The mean (SD) follow-up VACS of 20.39 (±15.48) was not statistically different from the mean (SD) baseline VACS of 18.33 (±13.87) (p=0.183). As anticipated, PWH who had an unplanned admission had a higher follow-up CIRS (p<0.001) and follow-up VACS (p=0.034) than those without an unplanned admission (Table 4).

Table 4. Follow-up CIRS score and VACS by Unplanned Admission status

	Overall n=180	No UA* n=142	UA* n= 38	p value
	Mean (SD)	Mean(SD)	Mean (SD)	
Follow-up CIRS score	9.45 (4.89)	8.41 (3.92)	13.34 (6.13)	<0.001[1]
Follow-up VACS	20.39 (15.48)	18.63 (12.51)	26.97 (22.52)	0.034[1]

*UA = Unplanned admission; [1] t-test

A multivariate model of factors associated with CIRS change was built using factors associated with CIRS change in univariate analysis with p value <0.1. These factors were ever having a mental health diagnosis (coeff 0.84, p=0.068), ever having a myocardial infarct (coeff -1.78, p=0.028) and ever having renal disease prior to 2012 (coeff 1.70, p=0.006). In multivariate analysis, both myocardial infarction (coeff -1.78, p=0.028) and renal disease (coeff 1.70, p=0.006) were significant at $p < 0.05$. When baseline CIRS score was including in the multivariate model, only ever having a myocardial infarct remained associated with a change in CIRS score (coeff -2.26, p=0.004).

Discussion

In this prospective cohort study, we have shown that among a cohort of PWH in regional NSW, baseline CIRS score predicts unplanned admission. Age, HIV specific markers and missed visits did not predict unplanned admission. Although VACS and number of medications were significant predictors of unplanned admission in univariate analysis, these did not predict unplanned admission in multivariate analysis. In this cohort, the two main reasons for unplanned admission among PWH were vascular disease and malignancy. In the cross-sectional analysis, there was no association between gaps in viral load monitoring greater than 6 months or viral load measurement greater than 500 copies/mL and unplanned admission. However, an association between having two or more prescribers and having an unplanned admission was found.

Discharge summaries were only present in the paper records for slightly more than half of individuals for whom an admission was documented. At least one letter was written to a GP by the HIV specialist for nearly three-quarters of the total cohort. Over the period of observation, CIRS score and VACS did not significantly change. A diagnosis of vascular disease was more frequent at follow-up whereas a diagnosis of HAND was less common at follow-up.

Hospitalisation in the AHOD cohort was associated with age and prior AIDS (3). Notably, age and prior AIDS were associated with baseline CIRS (8) in this cohort. The association between age and prior AIDs and hospital admission may be mediated through the development of multimorbidity. Comorbid conditions have been found to be one of the strongest predictors of hospital readmission (4) and emergency department use (5) among PWH in the US.

Although VACS predicted unplanned admission, this was not significant once CIRS score was included in the multivariate analysis. Other studies have found VACS to predict unplanned admission (28). CIRS score and VACS have been shown to be correlated in this study population (8). In this study, the predictive ability of CIRS score was not improved by including any of the specific conditions. In contrast, other studies have found mental health and substance abuse disorders are a significant role in ED visits (47) and that HCV may increase hospitalisation among PWH (48, 49). For PWH in this cohort, the cumulative effect of chronic health conditions predicts unplanned admissions and neither HIV nor any specific comorbidity contributed to unplanned admissions.

Previous modelling studies have predicted large increases in the number of PWH living with additional chronic health conditions (13). In a non-HIV population, the prevalence of multimorbidity doubled over approximately eight years of follow-up (57). In addition, within our cohort, CIRS score was associated with age so an increase in CIRS score would be expected as the population aged. Over a maximum of five years of follow-up there was no significant increase in CIRS score. Similarly, there was no increase in VACS despite the score including age and laboratory markers that are known to increase with age. It may be that a longer study is required to demonstrate changes in multimorbidity as PWH age. It is possible that a comprehensive approach to care as likely to occur when clinicians are documenting all chronic conditions, mitigated the increase in multimorbidity that was expected with time. Improvements in antiretrovirals as well as increased knowledge about the management of comorbidities in PWH may also contribute to avoiding increases in multimorbidity. The recent availability of direct acting agents for HCV treatment may have a role in reducing liver related multimorbidity in the future but is unlikely to have had a large impact at the time of this study.

The predictors of a change in multimorbidity as measured by CIRS score were having ever been diagnosed with renal disease, which increased CIRS score, and ever having had a myocardial infarct, which decreased CIRS score. When baseline CIRS score was taken into account, only ever having a myocardial infarction remained associated with CIRS score change. A potential explanation is that changes in lifestyle and medical care that are precipitated by a significant event such as a myocardial infarct are protective for longer term health. We are not aware of this relationship being previously reported and it may be specific to a cohort of PWH having frequent medical monitoring.

It is known that multimorbidity increases with age, but less is known about potentially modifiable factors that may contribute to increases in multimorbifity. Frailty has been identified as one factor in the development of incident multimorbidity among PWH (40). Medication burden may play a role as increased exposure to sedative and anticholinergic medications has been associated with an increase in progression to frail state in healthy community dwelling elderly men (58). In people without multimorbidity at baseline, lifestyle factors such as smoking, physical activity and weight predict incident multimorbidity (59) and dissatisfaction with current life and health may also be a risk (60). These factors warrant further exploration among PWH.

Particular health conditions that were found to have changed over time were a significant increase in vascular disease and a significant decrease in HAND. Vascular disease increases with age and this association has been demonstrated in HIV populations (61). Vascular disease among PWH has been shown to be associated with smoking status (62) and low CD4 to CD8 cell ratios (63). A diagnosis of HAND may be less likely in PWH with suppressed viral load and the increase in PWH who are on antiretrovirals may be the reason for the decrease in HAND. Another possible explanation is that neurocognitive changes previously considered to be HAND may be reclassified as vascular disease related changes as the prevalence of vascular disease increases.

As the current NSW HIV strategy (54) places emphasis on a renewed focus on shared care it is important to understand the type of care that PWH are receiving in regional areas. The findings of this study are that most but not all PWH had a GP recorded in their notes and had at least one letter to a GP in the time of observation which was a maximum of five years. These measurements do not take into account other communication that may occur between the specialist and GP such as telephone communication, email or copying of results. Understanding PWH's opinion as to whom is involved in their care may provide extra insights into the type of care PWH in regional areas receive and deserves further research.

Number of letters to GP and number of prescribers were only collected at follow-up, so they are not able to be included as predictors of unplanned admission. A significant association between unplanned admission and having two or more prescribers was found. It may be that having an unplanned admission resulted in the PWH attending a GP for prescriptions post discharge. Two or more prescribers may be a marker of higher multimorbidity explaining the association with unplanned admission. It is also possible that having two or more prescribers may contribute to unplanned admission through increased risk of adverse drug interactions.

Adverse drug reactions have been shown to be a factor in a significant number of urgent hospital admissions (51). It is well known that PWH are at high risk of drug interactions (38, 52). Doctors caring for PWH need to be aware who is prescribing for their patient and any changes in antiretrovirals need to be communicated to all other prescribers. Care coordination is important for PWH and this may be more so in regional NSW where access to antiretroviral prescribing GPs is limited. If admissions occur, it is important that all care providers are aware. Discharge summaries

are generally sent to one GP and will only be sent to the SHC if the patient indicates that their HIV specialist is their only doctor to admission staff. Use of either hospital or person based electronic medical records may increase the ability of specialists to be aware of unplanned admissions for PWH in their care. Access to this information needs to be balanced against any patients concern for confidentiality. Limited studies indicate PWH are comfortable with electronic sharing of personal medical records provided they are informed and have trust in the organisations involved (64, 65).

The importance of knowing all a patient's medical conditions and medications has been highlighted in a recent guideline on multimorbidity (14). The guideline's authors advocate a multimorbidity approach to care for anyone who receives care from multiple services, frequently seeks unplanned care or is prescribed ten or more medications. Our study has identified nearly half of the population as having two or more prescribers, 21% having at least one unplanned admission and 15% prescribed ten or more medications. Routine use of the CIRS offers a potential mechanism to facilitate a multimorbidity approach for these patients.

Completion of the CIRS results in all medical conditions being recorded in one place. The CIRS also identifies the severity of each of the conditions with higher severity being based on impact on the patient and level of medical intervention required to achieve management of the condition. Repeated measurements of CIRS can identify PWH with increasing CIRS scores and possibly increased medical care needs. Care coordination deserves consideration as a factor contributing to multimorbidity as this is modifiable. There is some evidence that care coordination for people with multimorbidity can improve prescribing behaviours and risk factor management (66) and these may be able to limit the progression of multimorbidity. Reducing multimorbidity may reduce unplanned admissions among PWH and therefore avoid costly care and the risk associated with unplanned care.

Strengths and Limitations

This study is primarily limited by its small sample size. The small size may mean that it is not sufficiently powered to demonstrate some of the associations found in other studies. The lack of an association between smoking and weight and CIRS change may be due to the small size of this study. A larger cohort study would likely have more power to demonstrate predictors of change in multimorbidity. However, this study is strengthened by prospective and detailed data collection. We undertook a comprehensive exploration of multimorbidity among PWH attending this service. The majority of PWH remained in care at the same service for the duration of period of observation meaning that endpoints were likely to be reasonably well measured. The results are limited to the 2012 cohort and do not include PWH newly attending the service, who may have different levels of multimorbidity.

Information regarding unplanned admissions was obtained from clinic based paper records, and there was not routine checking of hospital based electronic records for details of unplanned admissions as at the time of the study there was no linkage between hospital and clinic records. To access hospital records for research purposes would have been unethical in an observational study without patient consent. This method of ascertaining unplanned admissions is biased towards those that had a discharge summary in the paper record. All missing unplanned admissions were admissions for which a discharge summary was not received. It is likely that the actual proportion of unplanned admissions where a discharge summary was in the paper record is less than found in the study. Lack of outcomes for those not attending visits may also decrease our ability to show any association between missed visits and gaps in viral load measurements and unplanned admissions.

The study results are specific to this regional SHC and may not be generalizable to other populations. In Australia, regional SHCs tend to have older populations of PWH (67). Regional areas in Australia tend to have less availability of GPs able to be accessed without direct patient cost, which may increase utilization of emergency departments. Restriction of the definition of unplanned admission to those admitted overnight to a ward, is likely to reduce the impact of lack of GP access that may be specific to regional areas. It is unclear if regional PWH are more or less likely to have two prescribers than urban PWH. Less access to no direct cost GPs may reduce the prevalence of having two prescribers. However, there are less GPs able to prescribe antiretrovirals in rural areas, increasing the need for two prescribers for PWH in regional areas.

As CIRS score has been utilized at the SHC for some time, it is likely care at this service is informed by a multimorbidity approach. This may be a reason for the stabilization of multimorbidity in this cohort and means that the finding of no significant increase in multimorbidity over time may not be generalizable to other SHCs or other populations of PWH. The multimorbidity levels and rate of change for PWH who are newly diagnosed or newly attending this service are not explored in this study and are a potential area for future research.

The outcome of unplanned admission was prospective, reducing the risk of measurement bias in the scoring of CIRS at baseline. The follow-up CIRS score is at risk of measurement bias as scorers were aware of unplanned admissions at time of second scoring. Scorers were also aware of the baseline CIRS score. We expected that this would result in CIRS score increases as diagnoses were added over the time and the population aged. However, the mean CIRS score did not significantly increase for this population over time.

Conclusion and Recommendations

The research has demonstrated that among a cohort of PWH in regional NSW, baseline CIRS score predicts unplanned admission. At follow-up, having an unplanned admission was associated with having two or more prescribers. Discharge summaries were only present in the paper records for slightly more than half of individuals for whom an admission was documented. PWH receiving care at this service did not have significant increases in multimorbidity, and those with a past myocardial infarction were more likely to have a decrease in CIRS score at follow-up.

As CIRS score was the only significant predictor of unplanned admission, it is crucial that this is recorded in the medical records for PWH. The presence of gaps in communication between HIV specialists and hospital staff and between HIV specialists and GPs and the need to improve this communication has been highlighted. There is a need for further research on changes in multimorbidity and health service delivery factors that may prevent increases in multimorbidity.

The recommendations from this study are that within North Coast Public SHCs, CIRS score be obtained at entry to HIV care and updated annually. This will facilitate a multimorbidity approach to care which may be beneficial for PWH in regional NSW. Education and policy on care for PWH should include the concept of a multimorbidity approach to care. It is recommended that care coordination activities by the SHC be prioritised for PWH with GPs, particularly if the GP regularly prescribes for the PWH as having two or more prescribers was associated with unplanned admission. Mechanisms for enhancing care coordination include correspondence to GPs and education for GPs about shared care for HIV. Communication between hospital staff and HIV prescribers is recommended to be enhanced through system changes to ensure a higher proportion of discharge summaries are seen by the HIV prescriber.

Further research into factors associated with changes in multimorbidity as measured by CIRS is recommended. Multimorbidity remains a key concern for PWH and the aim of care for PWH is not merely suppression of HIV virus, but avoidance of long term health problems. In this service PWH did not have significant increases in multimorbidity despite expectations, possibly because of the care provided. In regional areas, SHCs should be supported to maintain a role in providing coordinated care for PWH.

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Appendix 1

Definitions for chronic health conditions

Condition	Definition
Hepatitis C	Current: Hepatitis C PCR positive
	Ever: Hepatitis C antibody positive
Hepatitis B	Ever: Hepatitis B core antibody positive
Mental health diagnosis	Being prescribed an antidepressant or antipsychotic or a diagnosis by a psychiatrist documented in clinical notes
Alcohol or other drug issue identified	Problematic alcohol or drug use (excludes cigarette smoking) identified by clinician or patient and documented in clinical notes
Vascular disease	Myocardial infarction, cerebrovascular accident, hypertension (Blood pressure >140/90 mmHg on >1 occasion or on treatment), hypercholesterolaemia (prescribed lipid-lowering agent or total cholesterol >5.5 mmol L^{-1}) or peripheral vascular disease
Diabetes	Fasting glucose >7.0 mmol L^{-1}, Random >11.1 mmol L^{-1}, positive glucose tolerance test or prescribed diabetes medication
Osteoporosis	T score < –2 0.5, fragility fracture or prescribed bisphosphonates for osteoporosis
Renal disease	Estimated glomerular filtration rate (eGFR) <60 mL min^{-1}, significant proteinuria (urine protein creatinine ratio 0.03 g/mmol or greater) or haematuria
Malignancy	Excluding non-melanoma skin cancers
HIV-associated neurocognitive disorder (HAND)	Neuropsychiatric assessment consistent with HAND, cerebrospinal fluid analysis or magnetic resonance imaging or spectroscopy results consistent with HAND
Obesity	Body mass index ≥30 kg/m^2

Appendix 2 CIRS Worksheet Client No :

Completed by: Date completed :

SYSTEM and SCORE	CONDITION and DATE	MANAGEMENT	ADMISSIONS/date Planned/unplanned
Cardiac			
Vascular			
Haematological			
Respiratory			
ENT and eye			
Upper GIT			
Lower GIT			
Hepatic/pancreatic			
Renal			
Genitourinary			
Musculoskeletal/skin			
Neurological			
Endocrine/metabolic			
Psychiatric			

Appendix 3 Data Collection Tool Client No. : Date completed:

Has the client had any of the following conditions since 1/7/12?	In the last 2 years	>2 yrs ago but since 1/7/12
Mental Health diagnosis (depression, bipolar, schizophrenia or any other dx by a psychiatrist requiring treatment)		
Vascular disease (MI,CVA, HT, Hypercholesteremia, Medical or surgical treatment for PVD or CVD)		
MI		
CVA		
Hypertension (BP >140/90 on > 1 occasion or on treatment)		
Diabetes (on treatment or fasting BSL >7.0mmol/L or random >11.1 mmol/L on >1 occasion)		
Osteoporosis		
Renal Disease (eGFR <60 or significant proteinuria or haematuria)		
Malignancy (excludes skin cancers)		
HAND diagnosis		
AIDS diagnosis		

Has any of the following occurred?	No	Yes	Date	Reason
Stopped smoking				n/a
HCV diagnosed				n/a
HCV cleared				n/a
Change of antiretrovirals				
How many other doctors advised?				
Planned Admissions				
Discharge summary in chart?				
Unplanned Admissions (via ED)				
Discharge summary in chart?				
Death				

Current ARV ?	2NRTIs +NNRTI	2NRTIs + PI	2 NRTIs + II	other	
Is the current GP indicated in the notes?				Yes	No
Is there a written care plan in the chart?				Yes	No
How many letters to GP since 1/7/12?					
How many different specialists has the person been referred to since 1/7/12?					
How many different specialists are actively involved in care of the person?					
How many different doctors prescribe for the person?					

CIRS score	No of systems	No of systems score ≥3

Hb g/dL	Platelets 10^9/L	eGFR mL/min	ALT µ/L	AST µ/L