Antiretroviral Therapy (ART) Use, Human Immunodeficiency Virus (HIV)-1 RNA Suppression, and Medical Causes of Hospitalization Among HIV-Infected Intravenous Drug Users in the Late ART Era

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Background. Antiretroviral therapy (ART) has reduced the rates and changed the causes of hospital admission. However, human immunodeficiency virus-positive intravenous drug users (HIV-IDU) continue to have increased hospitalizations and discharge diagnosis are less defined in the late ART era. Our aim was to examine ART use, HIV-1 RNA suppression, and hospital discharge diagnoses among HIV-IDU admitted to an urban hospital.

Methods. A retrospective analysis was made of HIV-IDU admitted for medical causes for the first time (2006–2010). Surgical, obstetric, or mental (except HIV-associated neurocognitive disorder) diagnoses were excluded. Clinical characteristics, number of admissions, and primary discharge diagnoses were determined for each patient.

Results. Three hundred and seventy-five admissions were recorded among 197 hospitalized HIV-IDU. Lifetime prevalence of ART use was 83.2% (164 of 197) and the rate of HIV-1 RNA <50 copies/mL was 38.1% (75 of 197). Primary discharge diagnosis groups were as follows: bacterial infections (59.2%), chronic end-organ damage (16.8%), complications derived from injected drug use (16.8%), malignancies (9.1%), and opportunistic infections (6.6%). Chronic end-organ damage was diagnosed more frequently in patients with HIV-1 RNA <50 copies/mL (36% vs 4.9%; $P < .000$), and complications derived from injected drug use (23.8% vs 5.3%; $P < .0008$) and acquired immune deficiency syndrome (AIDS) opportunistic infections (19.8% vs 1.3% $P < .019$) were usually diagnosed in patients with HIV-1 RNA detectable viral load.

Conclusions. Human immunodeficiency virus-positive intravenous drug users are admitted to hospitals mainly for non-AIDS-related illnesses; however, sustained HIV-1 RNA viral load suppression is poor and determines hospital discharge diagnoses. Providers need to be aware of the management of HIV-related comorbidities and reinforce strategies to improve ART retention in this population.

Keywords. antiretroviral therapy; HIV-infected drug users; hospitalization.

With the widespread use of antiretroviral therapy (ART), hospitalization rates, length of stay, and morbidity and mortality have dramatically declined among patients infected with human immunodeficiency virus (HIV) [1–10]. The causes of hospitalization and death in regions where ART is available have shifted from predominantly acquired immune deficiency syndrome (AIDS)-defining opportunistic infections to non-AIDS-related comorbidities [1, 2, 4–7, 9, 10].

Despite a recent reduction in the number of HIV infections attributed to injected drug use in developed countries, drug users still represent a large proportion of individuals living with HIV infection in the era of ART [11] and continue to have disproportionately high hospitalization rates compared with other HIV categories [1, 3, 7, 8, 12]. Late HIV diagnosis, low CD4 counts, and not receiving ART drugs and comorbidities are strong predictors of hospitalization among HIV-positive intravenous drug users (HIV-IDU) [2, 3, 5, 8–10, 12].

However, for HIV-IDU, the causes of hospitalization in the late ART era are less well defined, and whether the use of ART has been able to change the causes of hospital admission in the same way as in the non-drug user HIV population remains unclear.

It should be noted that hospitalizations have become a major outcome measure and constitute a considerable component of excess healthcare costs in this special population [3, 13, 14]. Thus, analyzing the clinical characteristics of admitted patients is a useful strategy to assess the effectiveness of health programs and provide areas of interest to improve healthcare to HIV-IDU.

Therefore, the aim of this study was to examine ART use, HIV-1 RNA suppression, and hospital discharge diagnoses among HIV-IDU admitted to an urban hospital in the late ART era.

MATERIAL AND METHODS

A retrospective analysis was undertaken in HIV-IDU admitted for the first time to the Infectious Diseases Unit of The Hospital del Mar from January 2006 to December 2010. The Hospital del Mar is a large tertiary teaching hospital, located in the old part of the city of Barcelona (Spain). The catchment area consists mainly of old buildings, the unemployment rate is high, and there is an overrepresentation of immigrants, people with legal problems, drug trafficking, and commercial sex. The Infectious Diseases unit has 20 beds.

Human immunodeficiency virus-positive IDU aged 18 years or older residing in the hospital area of influence and who had injected an illegal drug in the previous 6 months were included in the study. Human immunodeficiency virus-positive IDU admitted to other hospital services for surgical, obstetric, or mental causes (except HIV-associated neurocognitive disorder) were excluded.

Specialized HIV care, including ART, treatment of substance use disorders, and hospitalization are guaranteed free of cost through Spanish Health System for HIV-IDU.

Demographics and clinical characteristics (CD4 cell count, presence or absence of an AIDS diagnosis, usage of ART, date of hospital admission, discharge diagnosis, and outcomes) were obtained directly from the HIV-infected patient database of the Medical Documentation Service of the Hospital for each patient infected with HIV.

Antiretroviral therapy was defined as a combination of at least 3 drugs from 2 or more classes of antiretroviral agents. On admission, patients were classified as either ART-naive, current ART users, or dropouts (patients who had been on ART but had discontinued the medication more than 1 month before admission).

The International Classification of Diseases (ICD-9 and ICD-10) was used to determine hospital discharge diagnosis. For more than 1 diagnosis, the primary diagnosis leading to hospitalization was used. To characterize causes associated with hospitalizations over the 5-year period, the diagnoses were grouped for analysis as follows: AIDS opportunistic infections, malignancies, chronic end-organ damage (vascular, liver, kidney, lung), nonopportunistic infections, and complications derived from injected drug use (overdose, soft tissue infections, and bacteriemia).

Descriptive statistics were expressed as mean, standard deviation, median and range for quantitative variables, and absolute frequencies and percentages for qualitative variables. The χ^2 or nonparametric tests were applied. Values from $P < .05$ were considered statistically significant. Statistical analysis was made with SPSS version 15.0 (SPSS, Chicago, IL).

RESULTS

Over the 5-year period, 197 HIV-IDU were hospitalized and 78 (39.6%) patients were readmitted, yielding a total of 375 admissions; this figure represents 14.9% (375 of 2518) of the total admissions to the Infectious Disease Unit.

The clinical characteristics of HIV-IDU admitted to the unit are shown in Table 1.

Substance use disorders were treated in 80% of HIV-IDU at an outpatient center. Lifetime prevalence of ART use was 83.2% (164 of 197) and prevalence of ART use at admission was 50% (99 of 197). Antiretroviral therapy at admission was currently used in 61.3% (97 of 158) of patients receiving treatment of substance use disorders versus 5.1% (2 of 39) who were not ($P < .000$). Reasons for not using ART at admission were dropouts from ART in 66.3% (65 of 98) and naive to ART in 33.7% (33 of 98).

Complete viral suppression was observed in 38.1% (75 of 197) of patients. These patients had a higher median CD4 cell count (442 vs 209 cells/μL; $P < .01$) and CD4 cell count > 350 cells/μL (62 of 75 [82.6%] vs 12 of 122 [9.8%]; $P < .000$) than patients who had HIV-1 RNA detectable viral load.

Hospital discharge diagnoses are shown in Table 2. Bacterial infections were the leading cause of hospitalization, mainly bacterial pneumonia, followed by chronic end-organ damage and complications of injected drug use. Acquired immune deficiency syndrome-defining illnesses were diagnosed in 27 of 197 (13.6%) HIV-IDU (6.6% AIDS opportunistic infections, 5.5% recurrent pneumonia, and 1.5% AIDS malignancies).

Causes of inpatient hospitalization according to HIV-1 RNA suppression are shown in Table 3. Patients with HIV-1 RNA

Table 1. Clinical Characteristics of HIV-Infected Drug Users Admitted to Hospital

Patients no.	197
Number of patients readmitted (%)	78 (39.6%)
Number of hospitalizations per person (median, range)	1.3 (1–6)
Age (mean + SD)	40.6 ± 7
Male no. (%)	134 (68%)
Origin no. (%)	
Spanish	173 (87.8%)
Non-Spanish	24 (12.2%)
Main drug dependency no. (%)	Heroin 168 (85.7%)
	Cocaine 29 (14.7%)
Treatment of substance use disorder no. (%)	158 (80.2%)
CDC stage no. (%)	
A	47 (23.9%)
B	73 (37.1%)
C	77 (39%)
Hepatitis C coinfection no. (%)	193 (98%)
CD4 count (cells/μL) (median, range)	327.98 (8–1086)
CD4 count <200 (cells/μL) no. (%)	58 (29.4%)
CD4 count 200–350 (cells/μL) no. (%)	65 (33.0%)
CD4 count >350 (cells/μL) no. (%)	74 (37.6%)
ART use at admission no. (%)	
Current use	99 (50.2%)
Dropouts	65 (33.0%)
Naive	33 (16.8%)
HIV-1 RNA <50 copies/mL no. (%)	75 (38.1%)

Abbreviations: ART, highly active antiretroviral therapy; CDC, Centers for Disease Control and Prevention; HIV, human immunodeficiency virus; SD, standard deviation.

<50 copies/mL were admitted for chronic end-organ damage, particularly for complications of hepatitis C (20.0% vs 2.5%; $P < .000$). In contrast, patients who had a detectable viral load HIV-1 RNA viral load were admitted for complications derived from injected drug use and opportunistic infections.

Hospital readmissions were observed in 39.6% (78 of 197) of patients. Risk factors for readmission were as follows: HIV-1 RNA >50 copies/mL (odds ratio [OR], 4.8; 95% confidence interval [CI], 2.4–9.4; $P > .0001$), CD4 cell count >350 cells (OR, 3.6; 95%CI, 1.9–6.8; $P > .0001$), and women (OR, 2.1; 95% CI, 1.1–4.0; $P > .03$). Causes of readmissions were as follows: bacterial infections, 95 of 178 (53.3%); injected drug use-related complications, 49 of 178 (27.5%); chronic end-organ damage, 26 of 178 (14.6%); and AIDS opportunistic infections, 8 of 178 (4.5%). No patient died in the study period.

DISCUSSION

The results of this study show that HIV-IDU admitted to hospital were not in an advanced stage of HIV infection, and the most common causes of hospitalization were related to non-AIDS illnesses. Nevertheless, HIV-infected intravenous drug users were often readmitted.

A leading factor in reducing the hospital admission rate for both HIV-related and non-HIV-related illnesses is the use of ART [2, 4, 5, 8, 9, 12]. In this respect, the present study shows that half of the HIV-IDU were not receiving ART at hospital admission (33% dropouts and 16.8% naive). Although substance abuse treatment leads to greater initiation of ART among HIV-IDU and higher subsequent antiretroviral adherence [15–19], only 61.3% (97 of 158) of patients receiving drug addiction treatment were on ART at admission. In Spain, all patients controlled at drug addiction centers are referred for HIV specialty care, indicating that a subgroup of HIV-IDU enrolled in substance use disorder treatment who are referred for specialized HIV care do not initiate, or discontinue, the appropriate HIV care. Interruptions of HIV treatment during follow-up and losses to follow-up at HIV treatment centers are well documented clinical events among HIV patients who continue to inject drugs [20, 21].

The rate of successful ART was low at admission in the present study but similar to cohort studies that included active injected drug use [19, 22–24]. This observation implies that adherence interventions should be applied for active drug injectors at the time of ART initiation. In this regard, clinical guidelines and policy recommendations support integrating substance use disorder treatment into HIV medical care [25–26] to facilitate the use of directly observed therapy that sustains treatment adherence and leads to clinically significant improvements in health outcomes [27–34].

Other factors associated with a reduction in hospitalizations rates in HIV patients are a higher nadir and proximal CD4 counts >350 cells/μL [2, 4–9]. This study revealed that two thirds of patients had CD4 counts <350 cells/μL. Historically, HIV-IDU started ART with significantly lower CD4^{+} T cell counts, had more advanced HIV disease, and worse immune recovery compared with other HIV groups [35]. These data emphasize the need for including in specific health programs to achieve immune recovery and successful therapy in HIV-IDU.

The majority of hospitalizations observed were not related to HIV in this study, and it highlights the importance of providers being aware of the management of HIV-related comorbidities and of patients being included in preventive health programs to reduce the probability of hospitalization.

Bacterial pneumonia and other bacterial infections were the most common causes of admission, as described in other HIV-transmission categories [36]. Pneumococcal vaccination is a reasonable prevention strategy for patients infected with HIV at all stages of immunodeficiency, and efforts should be directed towards improving vaccination levels among HIV-IDU [36].

Liver disease was the main cause of chronic end-organ damage observed in this study, particularly among patients on ART.

Table 2. Hospital Discharge Diagnoses Among HIV-Infected Intravenous Drug Users, and Etiologies of Hospitalization Among HIV-Intravenous Drug Users

Groups of Causes	Diagnoses	No. (%)	Etiologies	No.
Bacterial infections	Pneumonia	70 (35.5%)	*Streptococcus pneumoniae*	47
			Haemophilus influenzae	6
			Nonfiliated	17
	Enteric infections	15 (7.7%)	*Salmonella* sp	7
			Escherichia coli	5
			Campylobacter jejuni	3
	Urinary tract infections	8 (4.0%)	*E coli*	6
	Meningitis	4 (2.0%)	*S pneumoniae*	3
			Neisseria meningitidis	1
Chronic end-organ damage	Hepatitis C	21 (10.7%)	Decompensated cirrhosis	21
	Cardiovascular disease	9 (4.6%)	Chronic heart failure	9
	Kidney disease	3 (1.5%)	Acute nephritis	3
Complications of IDU	Soft tissue infections/bacteriemia	21 (10.7%)	Cellulitis	17
			Endocarditis	3
			Osteomyelitis	1
	Overdose	12 (6.1%)	Overdose	12
Malignancies	Non-AIDS malignancies	15 (7.5%)	Lung	9
			Colorectal	3
			Breast	2
			Hodgkin's lymphoma	1
	AIDS-malignancies	3 (1.5%)	Non-Hodgkin's lymphoma	3
AIDS opportunistic infections	AIDS opportunistic infections	13 (6.6%)	*Pulmonary tuberculosis*	6
			Pneumocystis	4
			jirovecii Cerebral toxoplasmosis	2
			Esophageal candidiasis	1
ART secondary effects	ART secondary effects	3 (1.5%)	Anemia zidovudine	2
			Acute renal failure tenofovir	1

Abbreviations: AIDS, acquired immune deficiency syndrome; ART, antiretroviral therapy; HIV, human immunodeficiency virus; IDU, intravenous drug use.

However, treatment of hepatitis C virus (HCV) is restricted in drug users owing to their continued use of injected drugs. An alternative is the provision of assessment and treatment via opioid substitution treatment clinics, which has proven to be an effective means of engaging populations with a high HCV prevalence [37, 38].

Furthermore, unlike non-intravenous drug user HIV patients, skin and soft tissue infections are also common, injection-related complications that lead intravenous drug user to hospitalization. By providing environments in which these patients can receive supervised injection, overdose management, and education, supervised injecting facilities can reduce

Table 3. Groups of Causes of Inpatient Hospitalization Among HIV-Infected Drug Users

Groups of Causes	Total Group No. (%)	HIV-1 RNA 50 < Copies/mL No. (%)	HIV-1 RNA 50 > Copies/mL No. (%)	P
Bacterial infections	97 (59.2%)	31 (41.3%)	66 (54.1%)	.081
Chronic end-organ damage	33 (16.8%)	27 (36.0%)	6 (4.9%)	.0000
Complications derivates of IDU	33 (16.%)	4 (5.3%)	29 (23.8%)	.0008
Malignancies	18 (9.1%)	12 (12.0 %)	6 (7.4%)	.277
AIDS opportunistic infections	13 (6.6%)	2 (1.3%)	12 (9.8%)	.019
HAART secondary effects	3 (1.5%)	3 (4.0%)	0 (0.0%)	.026

Abbreviations: AIDS, acquired immune deficiency syndrome; ART, antiretroviral therapy; HAART, highly active ART; HIV, human immunodeficiency virus; IDU, intravenous drug use.

hospitalization rates for complications of intravenous drug use and support the importance of implementing needle and syringe programs for drug users [39].

Apart from the limitation of being a cross-sectional study, including the lack of a non-intravenous drug user HIV-positive control group, the study was conducted at a single center, and thus the sample might not be representative of the whole population since the impact of external factors may have significantly affected the admission patterns and demographics of this study population. However, the hospital where the study was conducted is located in one of the areas of the city with a high prevalence of intravenous drug use and immigration, and these findings may be consistent with those of other centers. Furthermore, the study was conducted over an extended period of time.

In summary, HIV-IDU are admitted mainly for non-AIDS-related illnesses in the late ART era; however, current ART use is low and the discontinuation of ART is frequent. To reduce the probability of hospitalization, providers need to be aware of the management of HIV-related comorbidities, especially hepatitis C coinfection, and include patients in preventive health programs. Integrated and multidisciplinary care of the patients infected with HIV-1 should be implemented to achieve successful HIV-1-RNA suppression among HIV-IDU.

Note

References

1. Gebo KA, Fleishman JA, Moore RD. Hospitalizations for metabolic conditions, opportunistic infections, and injection drug use among HIV patients: trends between 1996 and 2000 in 12 states. J Acquir Immune Defic Syndr 2005; 40:609–16.
2. Mocroft A, Monforte Ad, Kirk O, et al. Changes in hospital admissions across Europe: 1995–2003. Results from the EuroSIDA study. HIV Med 2004; 5:437–47.
3. Fleishman JA, Gebo KA, Reilly ED, et al. Hospital and outpatient health services utilization among HIV-infected adults in care 2000–2002. Med Care 2005; 43:40–52.
4. Betz ME, Gebo KA, Barber E, et al. Patterns of diagnoses in hospital admissions in a multistate cohort of HIV-positive adults in 2001. Med Care 2005; 43:3–14.
5. Krentz HB, Dean S, Gill MJ. Longitudinal assessment (1995–2003) of hospitalizations of HIV-infected patients within a geographical population in Canada. Krentz HIV Med 2006; 7:457–66.
6. Moore RD, Gebo KA, Lucas GM, Keruly JC. Rate of comorbidities not related to HIV infection or AIDS among HIV-infected patients, by CD4 cell count and HAART use status. Clin Infect Dis 2008; 47:1102–4.
7. Buchacz K, Baker RK, Moorman AC, et al. Rates of hospitalizations and associated diagnoses in a large multisite cohort of HIV patients in the United States, 1994–2005. AIDS 2008; 22:1345–54.
8. Yehia BR, Fleishman JA, Hicks PL, et al. Inpatient health services utilization among HIV-infected adult patients in care 2002–2007. J Acquir Immune Defic Syndr 2010; 53:397–404.
9. Crum-Cianflone NF, Grandits G, Echols S, et al. Trends and causes of hospitalizations among HIV-infected persons during the late HAART era: what is the impact of CD4 counts and HAART use? J Acquir Immune Defic Syndr 2010; 54:248–57.
10. Kerr JC, Stephens TG, Gibson JJ, Duffus WA. Risk factors associated with inpatient hospital utilization in HIV-positive individuals and relationship to HIV care engagement. J Acquir Immune Defic Syndr 2012; 60:173–82.
11. Centers for Disease Control and Prevention (CDC). HIV infection and HIV-associated behaviors among injecting drug users—20 cities, United States, 2009. MMWR Morb Mortal Wkly Rep 2012; 61:133–8.
12. Floris-Moore M, Lo Y, Klein RS, et al. Gender and hospitalization patterns among HIV-infected drug users before and after the availability of highly active antiretroviral therapy. J Acquir Immune Defic Syndr 2003; 34:331–7.
13. Palepu A, Tyndall MW, Leon H, et al. Hospital utilization and costs in a cohort of injection drug users. CMAJ 2001; 165:415–20.
14. Barash ET, Hanson DL, Buskin SE, Teshale E. HIV-infected injection drug users: health care utilization and morbidity. J Health Care Poor Underserved 2007; 18:675–86.
15. Palepu A, Horton NJ, Tibbetts N, et al. Uptake and adherence to highly active antiretroviral therapy among HIV-infected people with alcohol and other substance use problems: the impact of substance abuse treatment. Addiction 2004; 99:361–8.
16. Wood E, Hogg RS, Kerr T, et al. Impact of accessing methadone on the time to initiating HIV treatment among antiretroviral-naive HIV-infected injection drug users. AIDS 2005; 19:837–9.
17. Roux P, Carrieri MP, Villes V, et al. The impact of methadone or buprenorphine treatment and ongoing injection on highly active antiretroviral therapy (HAART) adherence: evidence from the MANIF2000 cohort study. Addiction 2008; 103:1828–36.
18. Roux P, Carrieri MP, Cohen J, et al. Retention in opioid substitution treatment: a major predictor of long-term virological success for HIV-infected injection drug users receiving antiretroviral treatment. Clin Infect Dis 2009; 49:1433–40.
19. Weber R, Huber M, Rickenbach M, et al. Uptake of and virological response to antiretroviral therapy among HIV-infected former and current injecting drug users and persons in an opiate substitution treatment programme: the Swiss HIV Cohort Study. HIV Med 2009; 10:407–16.
20. Kavasery R, Galai N, Astemborski J, et al. Nonstructured treatment interruptions among injection drug users in Baltimore, MD. J Acquir Immune Defic Syndr 2009; 50:360–6.
21. Werb D, Milloy MJ, Kerr T, et al. Injecting drug use and HIV antiretroviral therapy discontinuation in a Canadian setting. AIDS Behav 2013; 17:68–73.
22. Nolan S, Milloy MJ, Zhang R, et al. Adherence and plasma HIV RNA response to antiretroviral therapy among HIV-seropositive injection drug users in a Canadian setting. AIDS Care 2011; 23:980–7.
23. Kerr T, Marshall BD, Milloy MJ, et al. Patterns of heroin and cocaine injection and plasma HIV-1 RNA suppression among a long-term cohort of injection drug users. Drug Alcohol Depend 2012; 124:108–12.
24. Martin LJ, Houston S, Yasui Y, et al. Rates of initial virological suppression and subsequent virological failure after initiating highly active antiretroviral therapy: the impact of Aboriginal ethnicity and injection drug use. Current HIV Research 2010; 8:649–58.
25. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Available at: http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf. Accessed 23 January 23, 2014.
26. WHO, UNODC, UNAIDS Technical Guide. For countries to set targets for universal access to HIV prevention, treatment and care for injecting drug users. Available at: http://apps.who.int/iris/bitstream/10665/77969/1/9789241504379_eng.pdf. Accessed 23 January 2014.
27. Lucas GM, Mullen BA, Weidle PJ, et al. Directly administered antiretroviral therapy in methadone clinics is associated with improved HIV treatment outcomes, compared with outcomes among concurrent comparison groups. Clin Infect Dis 2006; 42:1628–35.
28. Altice FL, Maru DS, Bruce RD, et al. Superiority of directly administered antiretroviral therapy over self-administered therapy among

HIV-infected drug users: a prospective, randomized, controlled trial. Clin Infect Dis 2007; 45:770–8.

29. Altice FL, Bruce RD, Lucas GM, et al. HIV treatment outcomes among HIV-infected, opioid-dependent patients receiving buprenorphine/naloxone treatment within HIV clinical care settings: results from a multisite study. J Acquir Immune Defic Syndr 2011; 56:22–32.

30. Macalino GE, Hogan JW, Mitty JA, et al. A randomized clinical trial of community-based directly observed therapy as an adherence intervention for HAART among substance users AIDS 2007; 21:1473–7.

31. Lucas GM, Mullen BA, McCaul ME, et al. Adherence, drug use, and treatment failure in a methadone-clinic-based program of directly administered antiretroviral therapy. AIDS Patient Care STDS 2007; 8:564–74.

32. Raffa JD, Grebely J, Tossonian H, et al. The impact of ongoing illicit drug use on methadone adherence in illicit drug users receiving treatment for HIV in a directly observed therapy program. Drug Alcohol Depend 2007; 89:306–9.

33. Maru DS, Bruce RD, Walton M, et al. Initiation, adherence, and retention in a randomized controlled trial of directly administered antiretroviral therapy. AIDS Behav 2008; 12:284–93.

34. Gonzalez A, Mimiaga MJ, Israel J, et al. Substance use predictors of poor medication adherence: the role of substance use coping among HIV-infected patients in opioid dependence treatment. AIDS Behav 2013; 17:168–73.

35. Celentano DD, Lucas G. Optimizing treatment outcomes in HIV-infected patients with substance abuse issues. Clin Infect Dis 2007; 45:318–23.

36. Feldman C, Anderson R. HIV-associated bacterial pneumonia. Clin Chest Med 2013; 34:205–16.

37. Grebely J, Raffa JD, Lai C, et al. Low uptake of treatment for hepatitis C virus infection in a large community-based study of inner city residents. J Viral Hepat 2009; 16:352–8.

38. Alavi M, Grebely J, Micallef M, et al. Enhancing Treatment for Hepatitis C in Opioid Substitution Settings (ETHOS) Study Group. Assessment and treatment of hepatitis C virus infection among people who inject drugs in the opioid substitution setting: ETHOS study. Clin Infect Dis 2013; 57:62–9.

39. Lloyd-Smith E, Wood E, Zhang R, et al. Determinants of hospitalization for a cutaneous injection-related infection among injection drug users: a cohort study. BMC Public Health 2010; 10:327.