Published in final edited form as:

Sex Health. 2017 August ; 14(4): 345–354. doi:10.1071/SH16151.

Retrospective study of hepatitis C outcomes and treatment in HIV co-infected persons from the Australian HIV Observational Database

Rainer Puh^{A,I}, Stephen T. Wright^{A,B}, Jennifer F. Hoy^{C,D}, David J. Templeton^{A,E}, Nicolas Durier^{F,G}, Gail V. Matthews^A, Darren Russell^H, and Matthew G. Law^A

^AThe Kirby Institute, University of New South Wales, Sydney, NSW 2052, Australia ^BSchool of Mathematical and Physical Sciences, University of Technology, Sydney, NSW 2007, Australia

^CThe Alfred Hospital, Melbourne, Vic. 3004, Australia ^DDepartment of Medicine, Monash University, Melbourne, Vic. 3800, Australia ^ERPA Sexual Health, Sydney Local Health District, Sydney, NSW 2050, Australia ^FTREAT Asia, amfAR-The Foundation for AIDS Research, Bangkok 10110, Thailand ^HCairns Sexual Health Service, Cairns, Qld 4870, Australia

Abstract

Background—The widespread availability of direct-acting antivirals (DAAs) is expected to drastically improve the treatment uptake and cure rate of hepatitis C virus (HCV). In this paper, rates of and factors associated with HCV treatment uptake and cure in the HIV co-infected population in Australia were assessed before access to DAAs.

Methods—The medical records of patients in the Australian HIV Observational Database who were reported to be HCV antibody positive from 1999 to 2014 were reviewed for HCV treatment data. Patients with detectable HCV RNA were included in this analysis. Logistic regression models were applied to identify factors associated with treatment uptake and HCV sustained virological response (SVR) 24 weeks' post treatment.

^ICorresponding author. rpuhr@kirby.unsw.edu.au.

^GCurrent address: Dreamlopmnts enterprise, Bangkok 10400, Thailand.

Conflicts of interest

Jennifer Hoy's institution received reimbursement for her time on Advisory Boards for ViiV Healthcare and Gilead Sciences, and from AbbVie for her involvement in the OsteoRenal Exchange.

Gail Matthews has received research funding from Gilead Sciences, AbbVie, Bristol-Myers Squibb, Merck Sharp & Dohme and Janssen-Cilag. She has received speaker payments from Gilead Sciences, AbbVie and Bristol-Myers Squibb. She has received travel support from Bristol-Myers Squibb and AbbVie.

Matthew Law has received unrestricted grants from Boehringer Ingelheim, Gilead Sciences, Merck Sharp & Dohme, Bristol-Myers Squibb, Janssen-Cilag, ViiV HealthCare and consultancy and presentation fees from Gilead Sciences.

The Australian HIV Observational Database is funded as part of the Asia Pacific HIV Observational Database, a program of The Foundation for AIDS Research, amfAR, and is supported in part by grant no. U01-AI069907 from the U.S. National Institutes of Health, with funding provided by the National Institute of Allergy and Infectious Diseases, Eunice Kennedy Shriver National Institute of Child Health & Human Development and the National Cancer Institute, and by unconditional grants from Merck Sharp & Dohme, Gilead, Bristol-Myers Squibb, Boehringer Ingelheim, Roche, Pfizer, GlaxoSmithKline and Janssen-Cilag. The Kirby Institute is funded by the Australian Government Department of Health and Ageing, and is affiliated with the Faculty of Medicine, The University of New South Wales. The content is solely the responsibility of the authors and the views expressed in this publication do not necessarily represent the position of the Australian Government or the official views of the U.S. National Institutes of Health.

Results—The median follow-up time of those with chronic HCV/HIV co-infection was 103 months (interquartile range 51–166 months). Of 179 HCV viraemic patients, 79 (44.1%) began treatment. In the adjusted model, a higher METAVIR score was the only significant factor associated with treatment uptake (odds ratio (OR) 8.87, 95% confidence interval (CI) 2.00–39.3, $P = 0.004$). SVR was achieved in 37 (50%) of 74 treated patients. HCV genotypes 2/3 compared with 1/4 remained the only significant factor for SVR in an adjusted multivariable setting (OR 5.44, 95% CI 1.53–19.4, $P = 0.009$).

Conclusions—HCV treatment uptake and SVR have been relatively low in the era of interferon-containing regimens, in Australian HIV/HCV coinfecting patients. With new and better tolerated DAAs, treatment of HCV is likely to become more accessible, and identification and treatment of HCV in co-infected patients should become a priority.

Additional keywords

hepatitis; C; HCV/HIV; co-infection; HCV treatment; uptake; sustained; virological; response; HIV

Introduction

The global burden of those infected with hepatitis C virus (HCV) eclipses that of those infected with HIV, an estimated 80 million versus 31–35 million persons.^{1,2} Many of these HCV-infected persons are also co-infected with HIV due to shared modes of transmission.² The risk of HCV disease progression is higher in those with HIV co-infection compared with those mono-infected with HCV.^{3,4} Although successful HCV treatment can “cure” the disease and may substantially reduce disease progression and reduce HCV-related and all-cause mortality,^{5–7} treatment uptake is low. Large European cohorts report between 25% and 30% of co-infected patients initiate HCV therapy.^{8,9} The majority of US studies report 15% or less.¹⁰

In Australia, an estimated 13% of people living with HIV also have HCV.¹¹ The burden of disease associated with HCV infection is increasing in the general population. HCV infection is now the most frequent indication for liver transplantation in Australia and, in addition, hospital rates for HCV-related liver disease and liver cancer have increased significantly in recent years.^{12,13} The uptake of treatment for those with chronic HCV in Australia is low. Twenty-six per cent of people with chronic HCV have ever received therapy, with an estimated 2% on treatment in 2014.¹³ Along with the toxicity of interferon-based treatment, it has been argued that the major impediments to treatment uptake are: low referral rates for HCV treatment assessment and suboptimal infrastructure for treatment delivery. At an individual level, recent studies identified factors related to drug and alcohol use were major influences on the deferral of treatment.^{12,14} To date, only limited data have been published on the uptake of HCV treatment in HIV co-infected populations.

The widespread availability of second and third generation interferon-free, direct-acting antiviral (DAA) regimens is expected to drastically improve treatment uptake and cure rates of HCV.¹⁵ In contrast to interferon-based treatments, DAAs are as effective in HIV/HCV co-infected as in HCV mono-infected patients.¹⁶ The objective of this paper was to assess rates

of and factors associated with HCV treatment uptake and cure in the HIV co-infected population in the era of interferon-containing regimens. This is important to establish new treatment targets, changes in treatment uptake, and inform future policy.

Methods

Patient selection

All analyses were based on patients recruited to the Australian HIV Observational Database (AHOD). In brief, AHOD is an observational cohort study of HIV-infected patients seen at 29 clinical sites around Australia. Data are transferred electronically to the Kirby Institute at the University of New South Wales, Sydney, every 6 months for aggregation, quality control and analysis. Core data variables include: sex, date of birth, date of most recent visit, HIV exposure, hepatitis B virus surface antigen status, hepatitis C virus antibody status, CD4 and CD8 counts, HIV viral load, antiretroviral treatment data, AIDS-defining illnesses and date and cause of death.¹⁷ Small sites with only a few cases of HIV/HCV co-infection were not considered.

Ethics approval was obtained from the University of New South Wales Human Research Ethics Committee and all other relevant institutional review boards, and written informed consent was obtained from all patients.

Information on HCV treatment uptake and outcomes was collected retrospectively for HIV/HCV co-infected patients (HIV/HCV co-infected patients were identified based on positive HCV antibody test results collected in AHOD from December 1999 to March 2014) from patient medical records using a standardised case report form. Smaller sites with only a few cases of HIV/HCV co-infection were not included in this substudy due to resource constraints. In addition to routinely collected AHOD data, other data collected included: HCV viral load, HCV genotype, liver fibrosis stage by METAVIR score, HCV treatment data, liver disease progression [cirrhosis, hepatocellular carcinoma (HCC) or end-stage liver disease (ESLD)]; intravenous drug use, alcohol and smoking status. METAVIR scores were derived from biopsy or Fibroscan[®], with values of 9.5 kPa or higher resulting in a METAVIR score of F3 or higher. All data was evaluated at the last visit for untreated patients or at treatment start for those starting HCV treatment, where 'at treatment start' was defined as the closest measurement to the start of HCV treatment in a period of 90 days prior and up to 7 days after the actual start date. Data collection stopped on 31 December 2014, so that the data period spans from 1998 to 2014. Treatment uptake was defined as patients commencing treatment for their HCV infection and all treatment regimens were considered. Sustained virological response (SVR) was defined as at least one negative HCV RNA test 6 months after ending HCV treatment.

Statistical analysis

Differences between HCV-negative, HCV-untreated and HCV-treated patients were assessed using Pearson's χ^2 test or Fisher's exact test for categorical variables, the Kruskal–Wallis test for three-way comparisons and the Mann–Whitney U-test for two-way comparison of metric variables. We identified factors associated with HCV treatment uptake and SVR by

applying univariate logistic regressions. Variables assessed for both analyses were: gender, age, body mass index (BMI), alcohol consumption, smoking, injecting drug use, year last seen, CD4 count, HIV viral load, on antiretroviral therapy (ART) at HCV treatment start, presence of AIDS-defining illnesses, cirrhosis before HCV treatment start, time since HCV diagnosis, HCV viral load, HCV genotype and METAVIR score; additionally for SVR only, other variables included: time treated for HCV, year of HCV treatment, multiple HCV treatments and HCV treatment regimen. For simplification purposes, all continuous variables were grouped in reasonable classes. For both analyses, characteristics with *P* values less than 0.1 in univariate analysis were included in a multivariate model. All statistical tests were performed two-sided and *P* values of below 0.05 were considered statistically significant.

Results

Patient characteristics

Of the 2793 eligible AHOD patients (71.7% of the total AHOD cohort), 2137 were HCV antibody negative and 290 were HCV antibody positive (11.9% of tested population). In 366 patients, HCV status was unavailable. Thirty-five (12%) of the HCV antibody-positive patients had undetectable HCV viral loads. In 179 (61.7% of HCV antibody-positive) patients, HCV RNA was detectable. For 60 of the HCV antibody positive, patient files were unavailable; for 16 other patients, HCV RNA was not tested (Fig. 1). Among all HCV antibody-positive patients, the proportion with chronic hepatitis C infection (defined as detectable HCV RNA) was 68.8%. For patients with chronic HCV, the median follow-up time from entry into AHOD was 103 months (IQR 51–166 months). Genotype distribution of chronic HCV patients was: genotype 1: 61.3%; genotype 2: 5.1%; genotype 3: 32.1%; and genotype 4: 1.5%. Male patients accounted for 95.3% of the study population, and the median age of all patients at last visit or at treatment start was 47 years, both comparable with the AHOD population (92% male, median age at last visit 48 years). Characteristics of HCV-negative, HCV-untreated and HCV-treated patients are shown in Tables 1 and 2. Differences in age, HIV viral load and the number on antiretroviral therapy can be explained by the fact that ‘at last visit’ is on average 4.8 years later than ‘at treatment start’. Significant differences between treated and untreated patients were also observed in the number of patients with elevated liver markers, alanine transaminase (ALT, *P* = 0.013) and aspartate transaminase (AST, *P* = 0.047), as well as METAVIR scores (*P* = 0.008), which is indicative of treatment of patients with advanced liver fibrosis.

Treatment uptake

Of the 179 known HCV viraemic patients, 79 (44.1%) began treatment during the study period. Twelve of these patients were HCV treatment experienced. Among untreated patients, 9% were HCV RNA negative, suggesting spontaneous clearance had occurred (Fig. 1).

On univariate analysis (Table 3), treatment uptake was increased among those who had stopped smoking (OR 2.40; 95% CI 1.06–5.42, *P* = 0.035) and those with a METAVIR score of F3 or higher (OR 5.71; 95% CI 1.84–17.7, *P* = 0.003). Treatment uptake was lower among those who started ART before HCV treatment (OR 0.36, 95% CI 0.17–0.74, *P* =

0.006). In the adjusted multivariable analysis, only a METAVIR score of F3–F4 versus F0–F2 remained significantly associated with treatment uptake (AOR 8.87, 95% CI 2.00–39.3, $P = 0.004$), with a borderline significant association of HCV genotypes 2 and 3 (vs 1 and 4) (AOR 4.68, 95% CI 0.99–22.2, $P = 0.052$).

Sustained virological response

Complete treatment information was available for 74 of the 79 (93.7%) patients who started HCV treatment. Treatment types included interferon (IFN) monotherapy ($n = 7$, 9.5%), interferon and ribavirin (IFN/RBV) ($n = 20$, 27.0%), pegylated interferon and ribavirin (pegIFN/RBV) ($n = 33$, 44.6%), pegIFN/RBV with boceprevir/telaprevir ($n = 5$, 6.8%) and direct acting antiviral drugs ($n = 6$, 8.1%). Overall, SVR was achieved in 37 of the 74 treated patients (50%, Fig. 1). Four patients stopped treatment due to adverse events or side-effects. The highest treatment success was observed for treatments commenced after 2007 [success rate (SVR) of 61.1%]. Success rates for HCV genotype 1 and 4 (32.4%) were worse than genotypes 2 and 3 (69.0%).

On univariate logistic regression, only the HCV genotype had a significant effect on SVR (Table 4). Patients with HCV genotypes 2 or 3 had an odds of HCV SVR 4.6-fold higher than those with genotypes 1 or 4 (95% CI 1.60–13.5, $P = 0.002$). On multivariable analysis, HCV genotypes 2 or 3 were the only significant factor associated with SVR (AOR 5.44, 95% CI 1.53–19.4, $P = 0.009$).

Discussion

Forty-four per cent of HIV/HCV co-infected AHOD patients with detectable HCV RNA and available patient files initiated HCV therapy between 1998 and 2014. Anti-HCV treatment uptake was associated with a METAVIR score of F3 or greater, and non-significantly associated with genotype 2 and 3. SVR rates were 32.4% for genotype 1 and 4, and 69.0% for genotypes 2 and 3. HCV genotype was the only factor in our analyses that was associated with SVR.

We found a higher proportion of patients in our study had taken up HCV treatment than has been reported for other large cohort studies such as EuroSIDA (25.3%),⁸ the Swiss HIV Cohort Study (30.2%)⁹ and other European studies (25–40.8%).^{14,18,19} Treatment uptake in Australian co-infected patients was also substantially higher than the 15% or less in the majority of US studies.¹⁰ This may reflect improving treatment options for HCV over time, with our data being more recent than these other studies. Additionally, in Australia, engagement in HIV care for people living with HIV is generally high. The Australian treatment and care cascades for HIV and HCV¹³ exceeds their US counterparts,^{20–22} though comparability of such cascades is limited due to differences in time periods, data sources and methods used to calculate the elements of the cascade.²³ Furthermore, the distribution of HCV genotype differs in the AHOD population from other studies, with lower numbers of genotype 4, possibly leading to different treatment strategies. We found a borderline significant association of genotype 2 and 3 with increased treatment uptake, a finding also reported in a recent Scandinavian study.¹⁴ This may be due to the fact that genotypes 2 and 3 have a better treatment response to interferon-based therapy. It is also worth noting that the

expected availability of interferon-free HCV therapy potentially influenced the decision to start treatment in the later stages of our study, especially for those patients with genotype 1. The only factor associated with treatment uptake was a METAVIR score of F3 or higher. However, this result should be interpreted with caution due to a large number of missing values.

Reported cure rates of 32.4% for genotype 1 and 4, and 69.0% for genotype 2 and 3 are in line with findings from the Swiss HIV Cohort Study (35.2% and 68.4%)⁹ and other European studies (31–37.5% and 62.5–87%, respectively),^{14,19} and comparable to randomised controlled trials (between 17–29% and 44–62%).^{24,25} For pegylated interferon treatment, SVR rates of HIV/HCV co-infected patients are lower than those among HCV mono-infected patients.²⁶ SVR outcomes in mono-infected patients in Australia were 59.5% overall; 49.5% for genotype 1 and 69.6% for genotypes 2 and 3.²⁷ With the arrival of DAAs, these differences are likely to diminish.¹⁶

Among the strengths of this study is the long follow-up time of patients, with a mean follow-up time of 8.5 years per patient along with prospectively collected clinical data. However, some limitations need to be considered when interpreting the results of this study. First, the HCV treatment data was reviewed retrospectively from patient files, and so are subject to the biases and missing data that this entails. Patient files were, however, reviewed by a single person at all but one site (STW), and a standardised case report form was used to limit inconsistencies in data collection. Second, we did not collect data on contraindications to HCV treatment, so we are unable to determine if patients who did not receive treatment were, in fact, ineligible due to comorbidities or psychosocial issues.

With the new and more potent and better-tolerated DAAs now available in Australia (as of 1 April 2016), rates of treatment initiation and SVR are likely to increase significantly. In particular, Australian primary care physicians will now be able to provide interferon-free HCV therapy without referral into tertiary centres, except in cases where patients have advanced disease. This unique situation, together with a concerted effort in identifying HIV/HCV co-infection, gives clinicians a real opportunity to eliminate HCV/HIV co-infection in Australia.

Acknowledgments

AHOD Collaborators

Asterisks indicate steering committee members in 2015.

New South Wales: D. Ellis, Coffs Harbour Medical Centre, Coffs Harbour; M. Bloch, S. Agrawal, T. Vincent, Holdsworth House Medical Practice, Sydney; D. Allen, Holden Street Clinic, Gosford; D. Smith, K. Allardice, Lismore Sexual Health & AIDS Services, Lismore; D. Baker*, E. Odgers, East Sydney Doctors, Surry Hills; D.J. Templeton*, C.C. O'Connor, S. Phan, RPA Sexual Health, Camperdown; E. Jackson, K. McCallum, Blue Mountains Sexual Health and HIV Clinic, Katoomba; N. Ryder, G. Sweeney, Tamworth Sexual Health Service, Tamworth; D. Cooper, A. Carr, K. Macrae, K. Hesse, St Vincent's Hospital, Darlinghurst; R. Finlayson, S. Gupta, Taylor Square Private Clinic, Darlinghurst; R. Varma, J. Shakeshaft, Nepean Sexual Health and HIV Clinic, Penrith; K. Brown, S. Idle, N. Arvela, Illawarra Sexual Health Service, Warrawong; C. Thng, H. Lu, Sydney Sexual Health Centre, Sydney; D. Couldwell, Western Sydney Sexual Health Clinic; D.E. Smith*, V. Furner, D. Smith, T. Errington, Albion Street Centre; S. Fernando, Clinic 16 – Royal North Shore Hospital; A. Cogle*, National Association of People living with HIV/AIDS; C. Lawrence*, National Aboriginal Community Controlled Health

Organisation; B. Mulhall*, Department of Public Health and Community Medicine, University of Sydney; M. Law*, K. Petoumenos*, R. Puhr*, Erin Ogilvie*, M. Boyd*, The Kirby Institute, University of NSW.

Northern Territory: M. Gunathilake, R. Payne, Communicable Disease Centre, Royal Darwin Hospital, Darwin.

Queensland: M. O'Sullivan, S. White, Gold Coast Sexual Health Clinic, Miami; D. Russell, J. Joslin, C. Cashman, Cairns Sexual Health Service, Cairns; D. Sowden, K. Taing, K. McGill, Clinic 87, Sunshine Coast-Wide Bay Health Service District, Nambour; D. Orth, D. Youds, Gladstone Road Medical Centre, Highgate Hill; D. Rowling, N. Latch, E. Warzywoda, Sexual Health and HIV Service in Metro North, Brisbane; B. Dickson*, CaraData.

South Australia: W. Donohue, O'Brien Street General Practice, Adelaide.

Victoria: R. Moore, S. Edwards, S. Boyd, Northside Clinic, North Fitzroy; N.J. Roth*, H. Lau, Prahran Market Clinic, South Yarra; T. Read, J. Silvers*, W. Zeng, Melbourne Sexual Health Centre, Melbourne; J. Hoy*, K. Watson*, M. Bryant, S. Price, The Alfred Hospital, Melbourne; I. Woolley, M. Giles*, T. Korman, J. Williams*, Monash Medical Centre, Clayton.

Western Australia: D. Nolan, G. Guelfi, Department of Clinical Immunology, Royal Perth Hospital, Perth.

New Zealand: G. Mills, C. Wharry, Waikato District Hospital, Hamilton; N. Raymond, K. Bargh, Wellington Hospital, Wellington.

Coding of Death Form (CoDe) reviewers: D. Sowden, J. Hoy, L. Wray, K. Morwood, T. Read, N. Roth, I. Woolley, K. Choong, C. O'Connor.

References

1. Gower E, Estes C, Blach S, Razavi-Shearer K, Razavi H. Global epidemiology and genotype distribution of the hepatitis C virus infection. *J Hepatol.* 2014; 61(1, Suppl):S45–57. DOI: 10.1016/j.jhep.2014.07.027 [PubMed: 25086286]
2. Sievert W, Altraif I, Razavi HA, et al. A systematic review of hepatitis C virus epidemiology in Asia, Australia and Egypt. *Liver Int.* 2011; 31(Suppl 2):61–80. DOI: 10.1111/j.1478-3231.2011.02540.x [PubMed: 21651703]
3. Soto B, Sanchez-Quijano A, Rodrigo L, et al. Human immunodeficiency virus infection modifies the natural history of chronic parenterally-acquired hepatitis C with an unusually rapid progression to cirrhosis. *J Hepatol.* 1997; 26:1–5. DOI: 10.1016/S0168-8278(97)80001-3
4. Danta M, Semmo N, Fabris P, et al. Impact of HIV on host-virus interactions during early hepatitis C virus infection. *J Infect Dis.* 2008; 197:1558–66. DOI: 10.1086/587843 [PubMed: 18419344]
5. Berenguer J, Alvarez-Pellicer J, Martín PM, et al. Sustained virological response to interferon plus ribavirin reduces liver-related complications and mortality in patients coinfecting with human immunodeficiency virus and hepatitis C virus. *Hepatology.* 2009; 50:407–13. DOI: 10.1002/hep.23020 [PubMed: 19575364]
6. Berenguer J, Rodríguez E, Miralles P, et al. Sustained virological response to interferon plus ribavirin reduces non-liver related mortality in patients coinfecting with HIV and hepatitis C virus. *Clin Infect Dis.* 2012; 55:728–36. DOI: 10.1093/cid/cis500 [PubMed: 22610932]
7. Limketkai BN, Mehta SH, Sutcliffe CG, et al. Relationship of liver disease stage and antiviral therapy with liver-related events and death in adults coinfecting with HIV/HCV. *JAMA.* 2012; 308:370–8. DOI: 10.1001/jama.2012.7844 [PubMed: 22820790]
8. Grint D, Peters L, Schwarze-Zander C, et al. Temporal changes and regional differences in treatment uptake of hepatitis C therapy in EuroSIDA. *HIV Med.* 2013; 14:614–23. DOI: 10.1111/hiv.12068 [PubMed: 23869664]
9. Kovari H, Ledergerber B, Cavassini M, et al. High hepatic and extrahepatic mortality and low treatment uptake in HCV-coinfecting persons in the Swiss HIV cohort study between 2001 and 2013. *J Hepatol.* 2015; 63:573–80. DOI: 10.1016/j.jhep.2015.04.019 [PubMed: 25937433]
10. Oramasionwu CU, Moore HN, Toliver JC. Barriers to hepatitis C antiviral therapy in HIV/HCV co-infected patients in the United States: a review. *AIDS Patient Care STDS.* 2014; 28:228–39. DOI: 10.1089/apc.2014.0033 [PubMed: 24738846]

11. Cowie, B.Dore, G., Sasadeusz, J., editors. Co-infection: HIV & viral hepatitis: a guide for clinical management. Sydney: Australian Society for HIV Medicine (ASHM); 2010.
12. Gidding HF, Law MG, Amin J, et al. Predictors of deferral of treatment for hepatitis C infection in Australian clinics. *Med J Aust.* 2011; 194:398–402. [PubMed: 21495939]
13. The Kirby Institute. Annual surveillance report 2015. Sydney: National Centre in HIV Epidemiology and Clinical Research, University of New South Wales; 2015. HIV/AIDS, viral hepatitis and sexually transmissible infections in Australia.
14. Stenkvist J, Weiland O, Sönnernborg A, Blaxhult A, Falconer K. High HCV treatment uptake in the Swedish HIV/HCV co-infected cohort. *Scand J Infect Dis.* 2014; 46:624–32. DOI: 10.3109/00365548.2014.921932 [PubMed: 24984040]
15. Poordad F. Big changes are coming in hepatitis C. *Curr Gastroenterol Rep.* 2011; 13:72–7. DOI: 10.1007/s11894-010-0153-9 [PubMed: 21063814]
16. Shafraan SD. HIV coinfecting have similar SVR rates as HCV monoinfected with DAAs: it's time to end segregation and integrate HIV patients into HCV trials. *Clin Infect Dis.* 2015; 61:1127–34. DOI: 10.1093/cid/civ438 [PubMed: 26060286]
17. The Australian HIV Observational Database. Rates of combination antiretroviral treatment change in Australia, 1997–2000. *HIV Med.* 2002; 3:28–36. DOI: 10.1046/j.1464-2662.2001.00094.x [PubMed: 12059948]
18. Medrano J, Resino S, Vispo E, et al. Hepatitis C virus (HCV) treatment uptake and changes in the prevalence of HCV genotypes in HIV/HCV-coinfected patients. *J Viral Hepat.* 2011; 18:325–30. DOI: 10.1111/j.1365-2893.2010.01309.x [PubMed: 20456635]
19. Beisel C, Heuer M, Otto B, et al. German cohort of HCV mono-infected and HCV/HIV co-infected patients reveals relative under-treatment of co-infected patients. *AIDS Res Ther.* 2014; 11:16.doi: 10.1186/1742-6405-11-16 [PubMed: 25006340]
20. Bradley H, Hall HI, Wolitski RJ, et al. Vital signs: HIV diagnosis, care, and treatment among persons living with HIV—United States, 2011. *MMWR Morb Mortal Wkly Rep.* 2014; 63:1113–7. [PubMed: 25426654]
21. Mugavero MJ, Amico KR, Horn T, Thompson MA. The state of engagement in HIV care in the United States: from cascade to continuum to control. *Clin Infect Dis.* 2013; 57:1164–71. DOI: 10.1093/cid/cit420 [PubMed: 23797289]
22. Yehia BR, Schranz AJ, Umscheid CA, Lo Re V 3rd. The treatment cascade for chronic hepatitis C virus infection in the United States: a systematic review and meta-analysis. *PLoS One.* 2014; 9:e101554.doi: 10.1371/journal.pone.0101554 [PubMed: 24988388]
23. Medland NA, McMahon JH, Chow EP, Elliott JH, Hoy JF, Fairley CK. The HIV care cascade: a systematic review of data sources, methodology and comparability. *J Int AIDS Soc.* 2015; 18:20634.doi: 10.7448/IAS.18.1.20634 [PubMed: 26626715]
24. Carrat F, Bani-Sadr F, Pol S, et al. Pegylated interferon alfa-2b vs standard interferon alfa-2b, plus ribavirin, for chronic hepatitis C in HIV-infected patients: a randomized controlled trial. *JAMA.* 2004; 292:2839–48. DOI: 10.1001/jama.292.23.2839 [PubMed: 15598915]
25. Torriani FJ, Rodriguez-Torres M, Rockstroh JK, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection in HIV-infected patients. *N Engl J Med.* 2004; 351:438–50. DOI: 10.1056/NEJMoa040842 [PubMed: 15282351]
26. Monje-Agudo P, Castro-Iglesias A, Rivero-Juárez A, et al. Impact of HIV infection on sustained virological response to treatment against hepatitis C virus with pegylated interferon plus ribavirin. *Eur J Clin Microbiol Infect Dis.* 2015; 34:1929–36. DOI: 10.1007/s10096-015-2434-6 [PubMed: 26155784]
27. Gidding HF, Law MG, Amin J, et al. Hepatitis C treatment outcomes in Australian clinics. *Med J Aust.* 2012; 196:633–7. DOI: 10.5694/mja12.10014 [PubMed: 22676878]

Fig. 1. Analysis eligibility diagram. AHOD, Australian HIV observational database; HCV, hepatitis C virus; HCV AB, hepatitis C virus antibody; SVR, sustained virological response.

Table 1

Characteristics of HIV mono-infected and HIV/HCV co-infected patients at last visit for those who did not have treatment for HCV or at the time of HCV treatment initiation

	HCV negative	HCV untreated	HCV treated	<i>P</i>
Total patients	2137	100	79	
Gender				
Female	95 (4.4)	8 (8)	3 (3.8)	0.454 ^A
Male	2038 (95.4)	92 (92)	76 (96.2)	
Transgender	4 (0.2)	0 (0)	0 (0)	
Age (years)				
Median (IQR)	49 (41–56)	49 (42–55)	44 (40–51)	0.001 ^B
HIV exposure group				
Homosexual contract	1798 (84.4)	50 (50)	60 (76.0)	–
Homosexual contact and IDU	45 (2.1)	15 (15)	8 (10.1)	
IDU	12 (0.6)	18 (18)	7 (8.9)	
Heterosexual contact	228 (10.7)	11 (11)	1 (1.3)	
Receipt of blood (products)	6 (0.3)	3 (3)	2 (2.5)	
Other/missing	42 (2.0)	3 (3)	1 (1.3)	
HBV surface antigen test				
<i>n</i>	1888	89	70	
Positive	89 (4.7)	3 (3.4)	1 (1.4)	0.506 ^A
Smoking				
<i>n</i>	771	37	32	
Current	219 (28.4)	20 (54.1)	10 (31.3)	0.005 ^A
CD4 count (cells/mm ³)				
<i>n</i>	1307	60	57	
Median (IQR)	580 (420–780)	499 (260–780)	494 (336–640)	0.009 ^B
HIV viral load (copies/mL)				
<i>n</i>	1246	52	56	
Median (IQR)	38 (20–50)	40 (19–392)	50 (40–750)	<0.001 ^B
Ever on ART	1997 (93.4)	93 (93)	66 (83.5)	0.005 ^A
AIDS	432 (20.2)	27 (27)	18 (22.8)	0.225 ^A

ART, antiretroviral treatment; HBV, hepatitis B virus; HCV, hepatitis C virus; IDU, injecting drug use; IQR, interquartile range. Data are presented as *n* (%) unless otherwise stated

^AFisher's exact test.

^BKruskal–Wallis test.

Table 2

Hepatitis C virus (HCV)-specific characteristics of HIV/HCV co-infected patients at last visit for those who did not have treatment for HCV or at the time of HCV treatment initiation

	HCV untreated	HCV treated	<i>P</i>
Total patients	100	79	
HCV genotype			
1	47 (68.1)	37 (54.4)	0.297 ^A
2	2 (2.9)	5 (7.4)	
3	19 (27.5)	25 (36.8)	
4	1 (1.4)	1 (1.5)	
HCV viral load (log ₁₀ (copies/mL))			
<i>n</i>	66	44	
Median (IQR)	6.1 (5.3–6.8)	5.85 (5.33–6.6)	0.394 ^B
ALT (U/L)			
<i>n</i>	28	28	
Median (IQR)	55 (36–82)	101 (62–181)	0.004 ^B
Elevated (>55 U/L)	13 (46.4)	22 (78.6)	0.013
AST (U/L)			
<i>n</i>	22	21	
Median (IQR)	47 (35–83)	77 (51–121)	0.038 ^B
Elevated (>55 U/L)	8 (36.7)	14 (66.7)	0.047
F-score			
F0	16 (47.1)	4 (18.2)	0.008 ^A
F1	9 (26.5)	3 (13.6)	
F2	5 (14.7)	5 (22.7)	
F3	0 (0)	5 (22.7)	
F4	4 (11.8)	5 (22.7)	
Transient elastography (kPa)			
<i>n</i>	32	11	
Median (IQR)	6.2 (5.1–7.8)	6.1 (4.7–14.2)	0.707 ^B
Biopsy			
None	1 (14.3)	6 (31.6)	0.227 ^A
Mild	5 (71.4)	8 (42.1)	
Moderate	1 (14.3)	2 (10.5)	
Severe	0 (0)	3 (15.8)	
ESLD	0	1	
HCC before treatment start	3	0	

ALT, alanine transaminase; AST, aspartate transaminase; ESLD, end-stage liver disease; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; IQR, interquartile range. Data are presented as *n* (%) unless otherwise stated

^AFisher's exact test.

$B_{\text{Mann-Whitney U-test}}$.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 3

Factors associated with HCV treatment uptake

Predictor	Treatment		Univariate analysis			Multivariable analysis		
	No (n)	Yes (n (%))	OR (95% CI)	P	P (Overall)	OR (95% CI)	P	P (Overall)
Total patients	100	79 (44.1)						
Gender								
Female	8	3 (27.3)	1					
Male	92	76 (45.3)	2.20 (0.56–8.59)	0.255				
Genotype								
1/4	48	38 (44.2)	1			1		
2/3	21	30 (58.8)	1.80 (0.89–3.63)	0.099		4.68 (0.99–22.2)	0.052	
Unknown	31	11 (26.2)						
Age group at diagnosis (years)								
<35	38	23 (37.7)	1					
35–50	50	51 (50.5)	1.69 (0.88–3.22)	0.115	0.128			
>50	12	5 (29.4)	0.69 (0.21–2.21)	0.530				
Injecting drug use								
Current	3	2 (40)	1					
Past	29	24 (45.3)	1.16 (0.18–7.46)	0.874	0.959			
Never	60	46 (43.4)	1.08 (0.17–6.63)	0.937				
Unknown	8	7 (46.7)						
Alcohol consumption								
Current	12	10 (45.5)	1					
Past	24	17 (41.5)	0.85 (0.30–2.41)	0.760	0.920			
Never	45	37 (45.1)	0.99 (0.38–2.54)	0.978				
Unknown	19	15 (44.1)						
Smoking								
Current	39	26 (40)	1			1		
Past	15	24 (61.5)	2.40 (1.06–5.42)	0.035	0.059	0.98 (0.18–5.23)	0.984	1.000
Never	36	23 (39.0)	0.96 (0.47–1.97)	0.908		1.00 (0.22–4.49)	0.997	
Unknown	10	6 (37.5)						

Predictor	Treatment		Univariate analysis			Multivariable analysis		
	No (n)	Yes (n (%))	OR (95% CI)	P	P (Overall)	OR (95% CI)	P	P (Overall)
Cirrhosis before treatment start								
No	96	74 (43.5)	1					
Yes	4	5 (55.6)	1.01 (0.26–3.91)	0.985				
Time since diagnosis (years)								
<10	58	35 (37.6)	1					
10–19	29	33 (53.2)	1.89 (0.98–3.62)	0.056	0.162			
20	13	10 (43.5)	1.27 (0.51–3.21)	0.607				
Unknown	0	1 (100)						
HCV viral load (copies/mL)								
<1 million	30	24 (44.4)	1					
1 million–5 million	15	10 (40)	0.83 (0.32–2.18)	0.711	0.373			
>5 million	24	10 (29.4)	0.52 (0.21–1.30)	0.161				
Unknown/not detectable	31	35 (53.0)						
CD4 count (cells/mm ³)								
<350	30	17 (36.2)	1					
350–500	21	19 (47.5)	1.60 (0.68–3.77)	0.286	0.515			
>500	43	35 (44.9)	1.44 (0.68–3.02)	0.340				
Unknown	6	8 (57.1)						
HIV viral load (copies/mL)								
Undetectable	68	50 (42.4)	1					
400–10 000	4	7 (63.6)	2.38 (0.66–8.57)	0.185	0.360			
>10 000	12	12 (50)	1.36 (0.56–3.28)	0.493				
Unknown	16	10 (38.5)						
Past AIDS defining illness								
No	73	61 (45.5)	1					
Yes	27	18 (40)	0.80 (0.40–1.59)	0.519				
On ART at start of treatment								
No	15	26 (63.4)	1			1		
Yes	85	53 (38.4)	0.36 (0.17–0.74)	0.006		0.22 (0.12–3.69)	0.642	
METAVIR score								

Predictor	Treatment		Univariate analysis			Multivariable analysis		
	No (n)	Yes (n (%))	OR (95% CI)	P	P (Overall)	OR (95% CI)	P	P (Overall)
F0, F1, F2	30	14 (31.8)	1			1		
F3, F4	6	16 (72.7)	5.71 (1.84–17.7)	0.003		8.87 (2.00–39.3)	0.004	
Unknown	64	49 (43.4)						
BMI								
<18.5	2	2 (50)	1					
18.5–25	29	27 (48.2)	0.93 (0.12–7.08)	0.945	0.906			
25–30	16	16 (50)	1.00 (0.13–8.00)	1				
>30	4	2 (33)	0.50 (0.04–6.68)	0.600				
Unknown	49	32 (39.5)						
Last seen (year)								
Before 2006	9	2 (18.2)	1					
2006–2010	12	13 (52)	4.87 (0.87–27.3)	0.071	0.196			
After 2010	79	63 (44.4)	3.59 (0.75–17.2)	0.110				
Unknown	0	1 (100)						

ART, antiretroviral treatment; BMI, body mass index; CI, confidence interval; HCV, hepatitis C virus; OR, odds ratio

Table 4

Factors associated with hepatitis C virus sustained virological response

Predictor	SVR		Univariate analysis			Multivariable analysis		
	No (n)	Yes (n (%))	OR (95% CI)	P	P (Overall)	OR (95% CI)	P	P (Overall)
Total patients	37	37 (50)						
Gender								
Female	1	1 (50)	1					
Male	36	36 (50)	1 (0.06–16.6)	1				
Genotype								
1/4	23	11 (32.4)	1			1		
2/3	9	20 (69.0)	4.65 (1.60–13.5)	0.002		5.44 (1.53–19.4)	0.0094	
Unknown	5	6 (54.5)						
Age group at treatment (years)								
<35	2	4 (66.7)	1					
35–50	23	26 (53.1)	0.57 (0.09–3.38)	0.532	0.349			
>50	12	7 (36.8)	0.29 (0.04–2.02)	0.212				
Injecting drug use								
Current	1	1 (50)	1					
Past	12	9 (42.9)	0.75 (0.04–13.7)	0.846	0.472			
Never	18	26 (59.1)	1.44 (0.08–24.6)	0.800				
Unknown	6	1 (14.3)						
Alcohol consumption								
Current	7	3 (30)	1					
Past	7	7 (50)	2.33 (0.30–2.41)	0.332	0.301			
Never	15	21 (58.3)	3.27 (0.38–2.54)	0.123				
Unknown	8	6 (42.9)						
Smoking								
Current	11	12 (52.2)	1					
Past	13	11 (45.8)	0.78 (0.25–2.44)	0.664	0.905			
Never	11	10 (47.6)	0.83 (0.25–2.72)	0.763				
Unknown	2	4 (66.7)						

Predictor	SVR		Univariate analysis			Multivariable analysis		
	No (n)	Yes (n (%))	OR (95% CI)	P	P (Overall)	OR (95% CI)	P	P (Overall)
Cirrhosis before treatment start								
No	34	36 (51.4)	1					
Yes	3	1 (25)	0.31 (0.03–3.18)	0.327				
Duration of infection (years)								
<10	27	30 (52.6)	1					
10–19	7	7 (50)	0.90 ^A (0.28–2.90)	0.862	0.866			
20	1	0 (0)	0.30 ^A (0.00–28.6)	0.605				
Unknown	2	0 (0)						
HCV viral load before treatment start (copies/mL)								
<1 million	10	12 (54.5)	1					
1 million–5 million	3	5 (62.5)	1.39 (0.26–7.30)	0.698	0.450			
>5 million	6	3 (33.3)	0.42 (0.08–2.11)	0.290				
unknown/not detectable	18	17 (48.6)						
CD4 count before treatment start (cells/mm ³)								
<350	8	7 (46.7)	1					
350–500	9	10 (52.6)	1.27 (0.33–4.93)	0.730	0.912			
>500	17	15 (46.9)	1.01 (0.29–3.45)	0.989				
Unknown	3	5 (62.5)						
HIV viral load before treatment start (copies/mL)								
Undetectable	22	24 (52.2)	1			1		
400–10 000	7	0	0.06 ^A (0.00–1.38)	0.079	0.213	0.07 (0.00–2.65)	0.150 ^A	0.342
>10 000	6	6 (50)	0.92 ^A (0.26–3.27)	0.896		1.18 (0.21–6.70)	0.849 ^A	
Unknown	2	7 (77.8)						
AIDS defining illness								
No	28	29 (50.9)	1					
Yes	9	8 (47.1)	0.85 (0.29–2.54)	0.782				
On ART at start of treatment								
No	14	10 (41.6)	1					
Yes	23	27 (54)	1.64 (0.61–4.40)	0.322				
Year of start of treatment								

Predictor	SVR		Univariate analysis			Multivariable analysis		
	No (n)	Yes (n (%))	OR (95% CI)	P	P (Overall)	OR (95% CI)	P	P (Overall)
<2001	3	1 (25)				1		
2001–2004	7	8 (53.3)	3.43 (0.29–40.9)	0.330	0.060	0.09 (0.00–40.8)	0.436 ^A	0.237
2005–2007	15	6 (28.6)	1.20 (0.10–14.0)	0.884		0.04 (0.00–15.9)	0.293 ^A	
>2007	12	22 (61.1)	5.50 (0.51–58.8)	0.159		0.16 (0.00–56.8)	0.545 ^A	
Time treated (months)								
<3	3	0 (0)	1					
3–9	15	15 (50)	7.00 ^A (0.21–230)	0.275	0.514			
>9	19	21 (52.5)	7.72 ^A (0.23–250)	0.249				
Unknown	0	1 (100)						
Total Patients	37	37 (50)						
Multiple treatment episodes								
No	33	29 (46.8)	1					
Yes	4	8 (66.7)	2.28 (0.62–8.35)	0.215				
HCV treatment regimen								
IFN	4	3 (42.9)	1					
IFN/RBV	10	10 (50)	1.33 (0.24–7.56)	0.745	0.964			
pegIFN/RBV	15	18 (54.5)	1.60 (0.31–8.30)	0.576				
pegIFN/RBV+DAA	3	2 (40)	0.89 (0.09–9.16)	0.921				
Trial	3	3 (50)	1.33 (0.15–11.9)	0.797				
Unknown	2	1 (33.3)						
METAVIR-score								
F0, F1, F2	5	8 (61.5)	1					
F3, F4	9	6 (40)	0.42 (0.09–1.91)	0.259				
Unknown	23	23 (50)						
BMI (kg/m ²)								
<18.5	1	1 (50)	1					
18.5–25	14	13 (48.1)	0.93 (0.05–16.4)	0.960	0.908			
25–30	6	9 (40)	1.50 (0.08–28.9)	0.788				
>30	1	1 (50)	1.00 (0.02–50.4)	1				

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

ART, antiretroviral treatment; BMI, body mass index; CI, confidence interval; HCV, hepatitis C virus; OR, odds ratio; SVR, sustained virological response; IFN, interferon; RBV, ribavirin; pegIFN, pegylated interferon

^A Firth correction.