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The impact of HIV/HCV co-infection on health care utilization and disability: results of the ACTG Longitudinal Linked Randomized Trials (ALLRT) Cohort

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SUMMARY. HIV/hepatitis C virus (HCV) co-infection places a growing burden on the HIV/AIDS care delivery system. Evidence-based estimates of health services utilization among HIV/HCV co-infected patients can inform efficient planning. We analyzed data from the ACTG Longitudinal Linked Randomized Trials (ALLRT) cohort to estimate resource utilization and disability among HIV/HCV co-infected patients and compare them to rates seen in HIV mono-infected patients. The analysis included HIV-infected subjects enrolled in the ALLRT cohort between 2000 and 2007 who had at least one CD4 count measured and completed at least one resource utilization data collection form ($N = 3143$). Primary outcomes included the relative risk of hospital nights, emergency department (ED) visits, and disability days for HIV/HCV co-infected *vs* HIV mono-infected subjects. When controlling for age, sex, race, history of AIDS-defining events, current CD4 count and current HIV RNA, the relative risk of hospitalization, ED visits, and disability days for subjects with HIV/HCV co-infection compared to those with HIV mono-infection were 1.8 (95% CI: 1.3–2.5), 1.7 (95% CI: 1.4–2.1), and 1.6 (95% CI: 1.3–1.9) respectively. Programs serving HIV/HCV co-infected patients can expect approximately 70% higher rates of utilization than expected from a similar cohort of HIV mono-infected patients.

Keywords: health services research, hepatitis C/economics, HIV infections/economics, outcomes research, resource allocation.

INTRODUCTION

Approximately 15–30% of HIV-infected patients in the United States are co-infected with hepatitis C virus (HCV) [1]. Compared to patients with HCV mono-infection, HIV/HCV co-infected patients have higher rates of progression of liver disease [2,3] and greater medication-related hepatotoxicity [4]. Treating HCV co-infection in HIV-infected patients is difficult [5–7], but because individuals with HIV/HCV co-infection have higher rates of morbidity and mortality than HIV mono-infected patients [8–10], the potential benefits of HCV therapy are large [11].

As survival with HIV infection has improved, liver-related mortality has become an increasingly important cause of death among HIV-infected patients, and HIV/HCV co-infection has placed an increasing burden on the health care delivery system [12–14].

Because many patients with HIV/HCV co-infection have poor access to care and rely on government programs such as Medicaid and state AIDS Drug Assistance Programs

Abbreviations: ALLRT, ACTG Longitudinal Linked Randomized Trial; ED, emergency department; HCV, Hepatitis C Virus; IQR, interquartile range.

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(ADAPs) [15], co-infection represents a particular challenge to policy makers seeking to provide adequate care to HIV-infected patients while operating within budget constraints. Accurate estimates of resource utilization attributable to HIV/HCV co-infection are needed to inform resource allocation [16].

We used data from HIV-infected subjects in the ACTG Longitudinal Linked Randomized Trials (ALLRT) cohort to assess and compare health care utilization and disability among HIV/HCV co-infected and HIV mono-infected patients [17].

METHODS

Data

ACTG Longitudinal Linked Randomized Trials is a multicentre, prospective cohort study of HIV-infected subjects who were antiretroviral treatment naïve or experienced and enrolled into selected ACTG trials that provided randomized antiretroviral treatment regimens or strategies [17]. All subjects provided written informed consent. ALLRT enrolment began in 2000 and has since been ongoing. At baseline, subjects report demographic information, including history of injection drug use and history of AIDS-defining events (ADEs). Laboratory analyses at study entry include CD4 count and HIV RNA. HCV antibody testing was used to identify HCV co-infection, though its timing evolved over the 2000–2007 study period. HCV AB testing at ALLRT entry was introduced in the year 2002. Subjects who enrolled prior to 2002 had HCV AB testing at their next ALLRT visit. In 2006, HCV AB testing expanded to include repeat testing every 96 weeks. Subjects who ever had a positive HCV AB were considered HCV infected for the analysis.

ACTG Longitudinal Linked Randomized Trials study visits are at 16-week intervals. At each study visit, subjects provide an interval history of ADEs, as well as samples for laboratory analyses including CD4 count and HIV RNA. Subjects also complete an annual study form asking them to recall the preceding 4 months and to report: (i) the number of nights they stayed in a hospital (hospital nights), (ii) the number of visits they made to an emergency department (ED visits), (iii) the number of days they spent in bed, and (iv) the number of days they felt forced to reduce their usual daily activities owing to illness. We analysed data from the ALLRT cohort to compare self-reported rates of: (i) hospital nights, (ii) ED visits, and (iii) disability days in patients with HIV/HCV co-infection and HIV mono-infection. The analysis included ALLRT subjects who enrolled between 2000 and 2007 with known HCV status who provided at least one CD4 count and completed at least one study form reporting health care utilization (N = 3143). Data for the analysis were collected on subjects through June 30, 2007.

Primary outcomes

Incidence of hospital nights and incidence of emergency department visits

Responses were provided as count data (0, 1–2, 3–5, 6–10, 11–16, >16 nights or visits). For responses of '>16 nights or visits', subjects provided free text entry of the exact number of nights/visits in the prior 4 months. To provide a conservative estimate, and because some intervals did not have an integer mid-point, we used the lower limit of the interval to estimate the number of nights spent in the hospital and the number of ED visits in the preceding 4 months. For responses >16, we used the exact number of nights or visits provided in the free text answer field. Each completed study form represented 4 months of contributed follow-up time. We report observed and adjusted rates in terms of the number of hospital nights and the number of ED visits per 100 person-years with each study form contributing 4 months of follow-up time.

Incidence of disability day

Subjects responded to two questions soliciting information about their level of disability: (i) 'During the past 4 months, how many days did you cut down on your usual daily activities, such as your job, housework, or school?'; and (ii) 'During the past 4 months, how many days did you stay in bed because you were not feeling well?' Both questions were adapted with a longer recall period (4 months *vs* 4 weeks) from previously validated measures of health-related quality of life including the 38-item HIV-adapted Medical Outcomes Study measure and the HIV Cost and Services Utilization Study (HCSUS) measure [18–21]. We performed analyses on each outcome separately. To provide a single measure of disability defined as days spent either in bed or with reduced daily activities, we combined responses from the two questions to obtain a single measure of disability days. Because the number of days spent in bed should be a subset contained entirely within the number of days forced to cut back on usual daily activities, we used the larger number from the two responses as the estimate of the number of disability days in the preceding 4 months. We also report this rate per 100 person-years.

Current CD4 count and HIV RNA

To calculate CD4-stratum-specific rates, we treated CD4 count as a time-varying covariate such that subjects could contribute time to multiple CD4 count strata (≤100/μL, 101–200/μL, 201–350/μL, and >350/μL). Each completed study form contributed 4 months of follow-up time to the CD4 stratum corresponding to the CD4 count at the mid-point of the 4-month interval. We used linear interpolation between the CD4 count when the subject completed the study form and the prior 16-week CD4 count to estimate the CD4 count at the mid-point of the 4-month interval. Current HIV RNA was taken from the same time point as the measurement of resource utilization.

Analyses

We first calculated observed rates of hospital nights, ED visits, and disability days for HIV mono-infected and HIV/HCV co-infected subjects stratified by current CD4 count. We next constructed Poisson regression models of each outcome with HCV serostatus as the predictor of interest, using backward elimination to construct the most parsimonious model. Candidate covariates included age, sex, race, history of injection drug use (ever *vs* never), history of ADE, current CD4 count (≤100/μL, 101–200/μL, 201–350/μL, *vs* >350/μL), current HIV RNA (≤400 *vs* >400 copies/mL), and year in which the data were collected (2-year intervals). Covariates significant at the $P < 0.05$ threshold were included in the final model. We also constructed models that included the cross product of CD4 stratum and HCV serostatus to test for possible effect modification of the impact of HCV co-infection on different CD4 counts.

We report the relative risk of each outcome for patients with HIV/HCV co-infection *vs* HIV mono-infection. We also used the final model to estimate adjusted, CD4-stratum-specific incidences of hospital nights, ED visits, and disability days.

RESULTS

The analysis included 3143 subjects of whom 372 (11.8%) had HIV/HCV co-infection (Table 1). Overall, 83% of the cohort were men and 50% of subjects were non-white. The median baseline CD4 count was 244/μL [interquartile range (IQR) 104–408], and median HIV RNA was 4.6 $\log_{10}$ copies/mL (IQR 3.9–5.3 $\log_{10}$ copies); these were similar among HIV/HCV co-infected and HIV mono-infected subjects. Subjects with HIV/HCV co-infection were somewhat older and more frequently non-white than HIV mono-infected subjects (Table 1).

In subjects with HIV/HCV co-infection, observed follow-up time ranged from 92 person-years in the CD4 ≤100/μL stratum to 332 person-years in the CD4 >350/μL stratum. In subjects with HIV mono-infection, follow-up time ranged from 868 person-years in the CD4 ≤100/μL stratum to 2602 person-years in the CD4 >350/μL stratum (Table 2).

In every CD4 stratum, observed incidences of hospitalization, ED visits, and disability days were higher in HIV/HCV co-infected patients than in HIV mono-infected patients, with larger differences seen in subjects with CD4 ≤350/μL *vs* CD4 >350/μL (Table 2).

In adjusted analyses, HCV serostatus, as well as age, sex, history of ADE, current CD4 count, and current HIV RNA were all significantly associated with resource utilization (Table 3). Reporting a history of injection drug use was not associated with higher resource utilization or disability. In the final model, controlling for age, sex, race, history of ADE, current CD4 count, and current HIV RNA, HIV–HCV co-infection was associated with significantly higher rates of hospital nights, ED visits, and disability days. Relative rates were the following: 1.8 (95% CI 1.3–2.5) for hospital nights, 1.7 (95% CI 1.4–2.1) for ED visits, and 1.6 (95% CI 1.3–1.9) for disability days (Table 3). When we analysed separately the incidence of days spent in bed and days spent with reduced daily activities, HIV–HCV co-infection remained significantly associated with each outcome. Relative rates were 1.2 (95% CI 1.1–1.4) for days spent in bed, and 1.3 (95% CI 1.1–1.4) for days with reduced daily activities. Tests for an interaction between HCV serostatus and current CD4 count revealed no clinically relevant effect size and were not statistically significant.

Choosing men, non-white, 40-year-old HIV/HCV co-infected subjects with HIV RNA <400 copies/mL and no history of ADEs as a representative group of HIV/HCV co-infected patients, adjusted CD4-stratum-specific rates of hospital nights ranged from 294/100 person-years with CD4

Table 1 Baseline characteristics

Characteristic	Cohort overall (n = 3143)	HIV/HCV Co-infected (n = 372)	HIV mono-infected (n = 2771)
Age, mean (SD), years	40 (9.2)	43 (7.7)	40 (9.3)
Male, no. (%)	2619 (83)	293 (79)	2326 (84)
Race no. (%)			
White	1579 (50)	137 (37)	1442 (52)
African-American	875 (28)	155 (42)	720 (26)
Hispanic	603 (19)	70 (19)	533 (19)
Other	86 (3)	10 (3)	76 (3)
CD4 count, median/μL (IQR)	244 (104–408)	251 (115–427)	244 (100–405)
HIV RNA, $\log_{10}$ median copies/mL (IQR)	4.6 (3.9–5.3)	4.6 (3.6–5.1)	4.6 (3.9–5.3)
History of ADE, no. (%)	669 (21)	72 (19)	597 (22)
History of injection drug use, no. (%)	304 (9.7)	191 (51%)	113 (4)

ALLRT, ACTG Longitudinal Linked Randomized Trials; HCV, hepatitis C virus; SD, standard deviation; IQR, interquartile range; ADE, AIDS-defining event.

Table 2 Follow-up time observed and unadjusted incidence rates of hospital nights, ED visits, and disability days in the ALLRT cohort

	Person-years observed		Hospital nights/100 PY (95% CI)		ED visits/100 PY (95% CI)		Disability days/100 PY (95% CI)	
Current CD4	HIV/HCV	HIV	HIV/HCV	HIV	HIV/HCV	HIV	HIV/HCV	HIV
≤100/μL	92	868	170 (143–197)	90 (84–96)	32 (20–43)	28 (24–32)	832 (773–891)	425 (295–555)
101–200/μL	141	873	70 (56–83)	33 (29–37)	25 (17–33)	13 (11–16)	289 (261–317)	218 (158–279)
201–350/μL	178	1616	34 (25–42)	12 (10–14)	28 (20–36)	8.6 (7.2–10)	189 (169–210)	155 (100–210)
>350/μL	332	2602	8.7 (5.6–12)	7.6 (6.5–8.7)	11 (7.6–15)	6.1 (5.2–7.1)	161 (147–175)	134 (99–169)

ALLRT, ACTG Longitudinal Linked Randomized Trials; PY, person-years; ED, emergency department; 95% CI, 95% confidence interval; HIV/HCV, HIV/hepatitis C virus co-infected.

Table 3 Adjusted relative risk of resource utilization and disability days in HIV/HCV co-infected *vs* HIV mono-infected subjects

	Hospital nights		ED visits		Disability days	
Variable	RR	95% CI	RR	95% CI	RR	95% CI
HCV serostatus	1.8	1.3–2.5	1.7	1.4–2.1	1.6	1.3–1.9
Age (per 10 years)	1.1	1.0–1.3	1.0	0.9–1.1	1.2	1.1–1.3
Female	1.5	1.1–2.1	1.3	1.1–1.6	1.1	0.9–1.4
White race	0.9	0.7–1.1	0.9	0.8–1.1	1.8	1.5–2.1
History of ADE*	2.9	1.9–4.3	1.7	1.3–2.4	1.6	1.2–2.2
Current HIV RNA <400 copies/mL*	0.4	0.4–0.6	0.5	0.5–0.6	0.7	0.6–0.8
Current CD4 (*vs* CD4 >350/μL)*						
≤100/μL	5.2	3.7–7.3	2.4	1.9–3.0	2.9	2.4–3.6
101–200/μL	2.3	1.7–3.0	1.4	1.2–1.8	1.4	1.2–1.7
201–350/μL	1.4	1.0–2.0	1.1	1.0–1.3	1.3	1.1–1.5

HCV, hepatitis C virus; ED, emergency department; RR, relative risk; 95% CI, 95% confidence interval; ADE, AIDS-defining event; *treated as a time-updated covariate.

≤100/μL to 57/100 person-years with CD4 >350/μL (Fig. 1). Adjusted incidence of ED visits for patients with HIV/HCV co-infection was 166, 100, 77, and 69/100 person-years for patients with CD4 counts ≤100/μL, 101–200/μL, 201–350/μL, and >350/μL, respectively. Adjusted incidence of disability days for patients with HIV/HCV co-infection was 1350, 669, 596, and 466/100 person-years for patients with CD4 counts ≤100/μL, 101–200/μL, 201–350/μL, and >350/μL, respectively.

DISCUSSION

As patients live longer with HIV infection and AIDS-related complications decline, co-morbidities such as HCV co-infection play a larger role in determining long-term outcomes and place a substantial demand on the health care delivery system [12–14,22]. This analysis provides evidence that in a cohort of HIV-infected patients in the United States, co-infection with HCV is associated with greater resource utilization, independent of the effect of HCV co-infection on CD4 count or HIV RNA.

In every CD4 stratum, observed incidence of hospital nights, ED visits, and disability days was higher in HIV/HCV co-infected patients than in HIV mono-infected patients. In the light of high absolute rates of resource utilization, especially at lower CD4 counts, HIV/HCV co-infection likely results in a substantial burden on health care delivery resources. For example, in a setting where 20% of HIV-infected patients have HIV/HCV co-infection, a program serving 10 000 men, non-white, HIV-infected patients with suppressed viral load and CD4 counts between 200 and 350/μL could expect approximately 700 additional hospital nights per year than would be expected from a similar cohort with only HIV mono-infection.

These findings are important for policy makers and program administrators planning budgets for HIV care in the current environment of resource constraints. While past research has investigated the relative increase in mortality

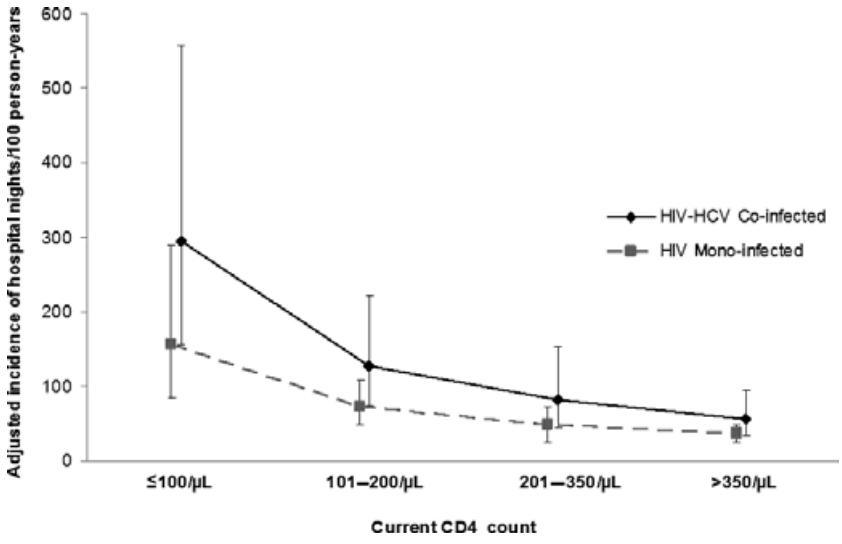

Fig. 1 Adjusted CD4-stratum-specific incidence of hospital nights for male, non white patients aged 40 years with HIV/HCV co-infection, HIV RNA < 400 copies/mL, and no history of AIDS defining events compared to similar patients with HIV mono-infection. Error bars represent 95% confidence intervals.

attributable to HCV co-infection, it has not translated findings into estimates of resource utilization [8–10,23–25]. Knowledge of the impact of HCV co-infection on resource consumption makes realistic projections possible, thereby avoiding unanticipated shortfalls and financial crises. Further, although treating HCV co-infection in HIV-infected patients is difficult [5–7], understanding increased resource utilization associated with HCV co-infection informs the potential economic benefits of its treatment. Such fully informed projections are particularly important for Medicaid and for Health Resources Services Administration (HRSA)–funded programs, such as ADAPs and local health programs, which play a central role in providing health services for HIV/HCV co-infected patients in the United States [16,26,27]. Overall, we find that programs serving HIV/HCV co-infected patients can expect 1.6–1.8 times higher rates of hospital nights, ED visits, and disability days in the HIV/HCV co-infected patients than in a similar group of HIV mono-infected patients.

There are several limitations to this study. First, the data set does not include HCV RNA levels. For the purpose of analysis, we assume that patients with positive HCV antibody have chronic HCV infection. Data indicate, however, that approximately 30% of those with HCV antibodies have negative HCV RNA, indicating that they have cleared their HCV infection [23,28,29]. To the extent that we misclassified some patients with positive HCV antibody and negative HCV RNA as chronically HCV infected, however, we likely underestimated the true effect of HCV co-infection on resource utilization. Reported findings, therefore, represent a conservative estimate.

Second, as with any non-randomized study design, the reported findings may reflect residual confounding by an unmeasured patient characteristic that correlates both with the likelihood of HCV co-infection and resource utilization rates. The possibility that HCV co-infection is a proxy marker for a more risky lifestyle is raised by data from the Strategies for Management of Anti-Retroviral Therapy (SMART) study, suggesting that most excess mortality seen in HIV/HCV co-infected patients is because of non-liver, non-ADE-related causes [9]. While we cannot exclude residual confounding in the results, this analysis did evaluate the effect of a history of injection drug use, but it was not additionally associated with resource utilization in models that included HCV status. To the extent that HCV co-infection is a marker for excess risk, much of that risk is likely correlated with having a history of injection drug use [9]. Most importantly, the biologic mechanism by which HIV/HCV co-infection increases resource utilization is beyond the scope of this study. More relevant from a policy and planning perspective is the finding that a cohort of patients with HIV/HCV co-infection will have substantially elevated rates of resource utilization compared to a similar cohort of HIV mono-infected patients. Parameters commonly employed to project resource utilization, such as CD4 count and history of ADEs, do not accurately capture expected resource consumption from patients with HIV/HCV co-infection [30].

Third, the generalizability of these findings may be limited because the cohort is comprised entirely of subjects who enrolled in ACTG clinical trials. While subjects come from diverse backgrounds (50% non-white and 17% women), their resource utilization patterns may differ from those on the parent ACTG studies who did not enter the ALLRT cohort, or from patients who are not in a research study setting. Patients enrolled in ALLRT, however, are not enrolled in clinical trials throughout the course of their follow-up [17]. While all subjects began the study as part of a randomized ACTG clinical trial, many remained enrolled only in ALLRT when their parent study closed and were thus enrolled in an observational study for the majority of their follow-up time.

In the current environment of increasing resource constraints for public programs, efficient planning becomes increasingly important [31]. HIV/HCV co-infection is a growing cause of morbidity and mortality among HIV-infected patients in the United States and places a disproportionate burden on public programs that often face difficult resource allocation decisions. Policy makers can use these results to project the impact that HIV/HCV co-infection will have on their budgets and make appropriate funding adjustments. By doing so, they can take an important step towards ensuring uninterrupted, high-quality medical services for both HIV mono-infected and HIV/HCV co-infected patients.

REFERENCES

1 Sherman KE, Rouster SD, Chung RT, Rajicic N. Hepatitis C virus prevalence among patients infected with human immunodeficiency virus: a cross-sectional analysis of the US adult AIDS Clinical Trials Group. *Clin Infect Dis* 2002; 34: 831–837.

2 Graham CS, Baden LR, Yu E *et al.* Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis. *Clin Infect Dis* 2001; 33: 562–569.

3 Deng LP, Gui XE, Zhang YX, Gao SC, Yang RR. Impact of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis. *World J Gastroenterol* 2009; 15: 996–1003.

4 Sulkowski MS, Thomas DL, Chaisson RE, Moore RD. Hepatotoxicity associated with antiretroviral therapy in adults infected with human immunodeficiency virus and the role of hepatitis C or B virus infection. *JAMA* 2000; 283: 74–80.

5 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: 2839–2848.

6 Chung RT, Andersen J, Volberding P *et al.* Peginterferon Alfa-2a plus ribavirin versus interferon alfa-2a plus ribavirin for chronic hepatitis C in HIV-coinfected persons. *N Engl J Med* 2004; 351: 451–459.

7 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: 438–450.

8 Backus LI, Phillips BR, Boothroyd DB *et al.* Effects of hepatitis C virus coinfection on survival in veterans with HIV treated with highly active antiretroviral therapy. *J Acquir Immune Defic Syndr* 2005; 39: 613–619.

9 Tedaldi E, Peters L, Neuhaus J *et al.* Opportunistic disease and mortality in patients coinfected with hepatitis B or C virus in the strategic management of antiretroviral therapy (SMART) study. *Clin Infect Dis* 2008; 47: 1468–1475.

10 Weber R, Sabin CA, Friis-Moller N *et al.* Liver-related deaths in persons infected with the human immunodeficiency virus: the D:A:D study. *Arch Intern Med* 2006; 166: 1632–1641.

11 Berenguer J, Alvarez-Pellicer J, Martin PM *et al.* Sustained virological response to interferon plus ribavirin reduces liver-related complications and mortality in patients coinfected with human immunodeficiency virus and hepatitis C virus. *Hepatology* 2009; 50: 407–413.

12 Walensky RP, Paltiel AD, Losina E *et al.* The survival benefits of AIDS treatment in the United States. *J Infect Dis* 2006; 194: 11–19.

13 Palella FJ Jr, Baker RK, Moorman AC *et al.* Mortality in the highly active antiretroviral therapy era: changing causes of death and disease in the HIV outpatient study. *J Acquir Immune Defic Syndr* 2006; 43: 27–34.

14 Grant WC, Jhaveri RR, McHutchison JG, Schulman KA, Kauf TL. Trends in health care resource use for hepatitis C virus infection in the United States. *Hepatology* 2005; 42: 1406–1413.

15 Fleming CA, Tumilty S, Murray JE, Nunes D. Challenges in the treatment of patients coinfected with HIV and hepatitis C virus: need for team care. *Clin Infect Dis* 2005; 40(Suppl 5): S349–S354.

16 Carbaugh A, Kates J, Crutsinger-Perry B, Ginsburg B, Murray PC. National ADAP Monitoring Project Annual Report. Menlo Park, CA: Henry J. Kaiser Family Foundation, April, 2009.

17 Smurzynski M, Collier AC, Koletar SL *et al.* AIDS clinical trials group longitudinal linked randomized trials (ALLRT): rationale, design, and baseline characteristics. *HIV Clin Trials* 2008; 9: 269–282.

18 Bozzette SA, Hays RD, Berry SH, Kanouse DE. A Perceived Health Index for use in persons with advanced HIV disease: derivation, reliability, and validity. *Med Care* 1994; 32: 716–731.

19 Bozzette SA, Hays RD, Berry SH, Kanouse DE, Wu AW. Derivation and properties of a brief health status assessment instrument for use in HIV disease. *J Acquir Immune Defic Syndr Hum Retrovirol* 1995; 8: 253–265.

20 Shaprio M, Bozzette SA, Morton S, Frankel S, Berry SH. HIV Cost and Services Urilization Study: Studying Health Care Issues in a National Probability Sample. In: Association for Health Services Research 13th Annual meeting, Atlanta GA, June 1996.

21 Wu AW, Hays RD, Kelly S, Malitz F, Bozzette SA. Applications of the Medical Outcomes Study health-related quality of life measures in HIV/AIDS. *Qual Life Res* 1997; 6: 531–554.

22 Martin-Carbonero L, Soriano V, Valencia E, Garcia-Samaniego J, Lopez M, Gonzalez-Lahoz J. Increasing impact of chronic viral hepatitis on hospital admissions and mortality among HIV-infected patients. *AIDS Res Hum Retroviruses* 2001; 17: 1467–1471.

23 Rockstroh J, Peters L, Soriano V *et al.* High Hepatitis C Viremia is Associated with an increased Risk for Mortality in HIV/HCV co-infected Individuals (Abstract #101). In: 16th Conference on Retroviruses and Opportunistic Infections. Montreal; 2009.

24 Smit C, van den Berg C, Geskus R, Berkhout B, Coutinho R, Prins M. Risk of hepatitis-related mortality increased among hepatitis C virus/HIV-coinfected drug users compared with drug users infected only with hepatitis C virus: a 20-year prospective study. *J Acquir Immune Defic Syndr* 2008; 47: 221–225.

25 Rockstroh JK, Mocroft A, Soriano V *et al.* Influence of hepatitis C virus infection on HIV-1 disease progression and

response to highly active antiretroviral therapy. *J Infect Dis* 2005; 192: 992–1002.
26 Walensky RP, Paltiel AD, Freedberg KA. AIDS Drug Assistance Programs: highlighting inequities in human immunodeficiency virus-infection health care in the United States. *Clin Infect Dis* 2002; 35: 606–610.
27 McColl W, Schmid C. The AIDS Drug Assistance program: Securing HIV/AIDS Drugs for the Nation's Poor and Uninsured. New York: AIDS Action and the AIDS Institute, 2009.
28 Alter MJ, Kruszon-Moran D, Nainan OV *et al.* The prevalence of hepatitis C virus infection in the United States, 1988 through 1994. *N Engl J Med* 1999; 341: 556–562.
29 Armstrong GL, Wasley A, Simard EP, McQuillan GM, Kuhnert WL, Alter MJ. The prevalence of hepatitis C virus infection in the United States, 1999 through 2002. *Ann Intern Med* 2006; 144: 705–714.
30 Yehia BR, Fleishman JA, Hicks PL, Ridore M, Moore RD, Gebo KA. Inpatient health services utilization among HIV-infected adult patients in care 2002–2007. *J Acquir Immune Defic Syndr* 2009; 53: 397–404.
31 National Association of State and territorial AIDS Directors. Summary Results: Impact of State General Revenue Cuts in HIV/AIDS and Viral Hepatitis Programs. Menlo Park, CA: Henry J. Kaiser Family Foundation; April, 2009.