

HIV and viral hepatitis co-infection in New York City, 2000–2010: prevalence and case characteristics

C. PRUSSING¹, C. CHAN¹, J. PINCHOFF^{1,2}, L. KERSANSKE¹,
K. BORNSCHLEGEL¹, S. BALTER¹, A. DROBNIK¹ AND J. FULD^{1*}

¹*New York City Department of Health and Mental Hygiene, Long Island City, NY, USA*

²*Johns Hopkins Bloomberg School of Public Health, Department of International Health, Baltimore, MD, USA*

*Received 2 April 2014; Final revision 9 July 2014; Accepted 2 August 2014;
first published online 29 August 2014*

SUMMARY

Using surveillance data, we describe the prevalence and characteristics of individuals in New York City (NYC) co-infected with human immunodeficiency virus (HIV) and hepatitis B virus (HBV) and/or hepatitis C virus (HCV). Surveillance databases including persons reported to the NYC Department of Health and Mental Hygiene with HIV, HBV, and HCV by 31 December 2010 and not known to be dead as of 1 January 2000, were matched with 2000–2011 vital statistics mortality data. Of 140 606 persons reported with HIV, 4% were co-infected with HBV only, 15% were co-infected with HCV only, and 1% were co-infected with HBV and HCV. In all groups, 70–80% were male. The most common race/ethnicity and HIV transmission risk groups were non-Hispanic blacks and men who have sex with men (MSM) for HIV/HBV infection, and non-Hispanic blacks, Hispanics, and injection drug users for HIV/HCV and HIV/HBV/HCV infections. The overall age-adjusted 2000–2011 mortality was higher in co-infected than HIV mono-infected individuals. Use of population-based surveillance data provided a comprehensive characterization of HIV co-infection with HBV and HCV. Our findings emphasize the importance of targeting HIV and viral hepatitis testing and prevention efforts to populations at risk for co-infection, and of integrating HIV and viral hepatitis care and testing services.

Key words: Hepatitis B, hepatitis C, HIV/AIDS, public health, surveillance.

INTRODUCTION

As people living with HIV/AIDS are surviving longer with antiretroviral therapy, they are increasingly likely to suffer from the long-term sequelae of related chronic infections, such as viral hepatitis. Hepatitis B virus (HBV) and hepatitis C virus (HCV) are especially important co-infections because of their

shared transmission routes with HIV, interaction with HIV that results in more serious disease, and implications for HIV treatment. All three viruses are bloodborne pathogens and can, therefore, be spread parenterally or perinatally. Both HIV and HBV are sexually transmitted, and there is also evidence that HCV can be transmitted sexually, particularly among HIV-positive men who have sex with men (MSM) [1].

Individuals co-infected with HIV and chronic HBV and/or HCV have worse outcomes than mono-infected individuals. HIV/HBV-infected individuals have higher levels of HBV viraemia, increased

* Author for correspondence: Ms. J. Fuld, Division of Disease Control, New York City Department of Health and Mental Hygiene, 2 Gotham Center, 42-09 28th St. 5th floor, Long Island City, NY 11101, USA
(Email: jfuld@health.nyc.gov)

likelihood of progression to chronic HBV infection, and increased risk of cirrhosis and hepatocellular carcinoma [2, 3]. HIV/HBV infection is also associated with increased hepatotoxicity from antiretroviral drugs [2] and impaired CD4 cell recovery during antiretroviral therapy [4]. Similarly, HIV/HCV infection leads to more aggressive and faster progression of liver disease [1, 5], increased risk of HIV-related kidney disease, and higher risk of cardiovascular disease and diabetes mellitus [5]. HIV/HCV infection is also associated with poor tolerance of and greater risk of hepatotoxicity from antiretroviral therapy [5] and attenuated responses to antiretroviral therapy [6]. Individuals with HIV/HBV infection [7], HIV/HCV infection [8], and HIV/HCV/HBV infection [9] have higher rates of mortality compared to individuals with HIV infection alone.

Multiple clinical cohort and cross-sectional studies have studied the prevalence of and risk factors for HBV and HCV co-infection in groups of people living with HIV/AIDS (PLWHA) throughout the world [7, 10–14]. Another important method for assessing the prevalence of HIV co-infection with HBV and/or HCV and the characteristics of co-infected patients is to match surveillance data for each infection collected by state or local health departments [15–18]. Surveillance data are derived from large, geographically well-defined populations and include all positive tests reported to health departments; therefore, such data are more representative than data from highly specialized clinical studies, which are limited to patients selected for enrolment. As of 2010, HIV was reportable in every state in the USA, and chronic HBV and HCV were reportable in 44 states and 46 states, respectively, and in the District of Columbia [19]. National guidance for both HIV and viral hepatitis surveillance and prevention recommends the use of health department surveillance data to better understand co-infection [20, 21].

This analysis represents the first match of viral hepatitis and HIV surveillance databases using New York City (NYC) surveillance data. NYC has a high prevalence of HIV/AIDS (1.3% of the population diagnosed and living with HIV in NYC *vs.* 0.003% nationally at the end of 2007 [22]), HBV (an estimated prevalence of 1.2% in 2008 *vs.* 0.3–0.5% nationally in 2006 [23]), and HCV (an estimated prevalence of 2.4% in 2010 *vs.* 1.3% nationally from 1999 to 2002 [24]). NYC's large surveillance databases for these three infections provide a rich data source to examine the prevalence and risk factors for co-infections of these

viruses. Linking databases can help identify populations at risk for and/or living with HIV co-infection with HBV and/or HCV so that prevention, screening, and treatment services can be better targeted to those populations.

The objective of this analysis was to better understand HBV and HCV co-infection with HIV in NYC using surveillance data. We characterize the prevalence of HIV/HBV, HIV/HCV, and HIV/HBV/HCV infection among NYC residents, describe the major risk factors for these co-infections, and compare mortality between individuals with these co-infections and HIV mono-infected individuals.

METHODS

In 2010, the NYC Department of Health and Mental Hygiene (DOHMH) implemented Centers for Disease Control and Prevention's (CDC) Program Collaboration and Service Integration (PCSI) initiative to increase data integration and better understand co-infections and syndemics between HIV, HBV, HCV, tuberculosis (TB), and sexually transmitted diseases (STDs) in NYC [25]. As part of this initiative, a retrospective, deterministic cross-match was conducted of HIV, HBV, HCV, TB, and STD surveillance data, and vital statistics mortality data. Individuals within each dataset were matched iteratively against each of the other datasets using SQL and SAS 9.2. Fourteen matching keys, comprised of first name, last name, date of birth and social security number, were used to link records across datasets. The methods of this match are described in detail elsewhere [26].

For the purposes of this analysis, HIV-infected persons were defined as individuals diagnosed with HIV and reported to the DOHMH HIV surveillance registry by 31 December 2010. HBV-infected persons were defined as individuals with a positive hepatitis B surface antigen, hepatitis B e antigen, or hepatitis B virus DNA test reported to the DOHMH by 31 December 2010, who did not meet the case definition for acute hepatitis B [27]. HCV-infected persons were defined as individuals with a positive HCV antibody or RNA test reported to the DOHMH by 31 December 2010, who did not meet the case definition for acute hepatitis C [28]. To be consistent with the CDC/CSTE case definition for hepatitis C, past or present [29], persons with a negative HCV RNA test or no documented HCV RNA test were included. AIDS reporting to the DOHMH began in 1981, while reporting of new and previously diagnosed

cases of HIV infection began on 1 June 2000. HBV has been reportable since serological tests for the virus became available in the 1970s, and mandated reporting of HCV to the DOHMH began in January 2000. All persons known to be dead as of 1 January 2000 were excluded from the match. As changes in treatment and testing recommendations for all three diseases occurred over the study period, a subanalysis excluding those persons known to have died between 1 January 2000 and 31 December 2010 was conducted to estimate the prevalence of reported co-infection with HBV, HCV, and HBV/HCV at the end of the study period.

HIV mono-infected persons were defined as HIV-infected persons who did not match to a report of HBV or HCV; HIV/HBV-infected persons were defined as persons reported to the DOHMH with HIV who matched to a report of HBV; HIV/HCV-infected persons were defined as persons reported to the DOHMH with HIV who matched to a report of HCV; and HIV/HBV/HCV-infected persons were defined as persons reported to the DOHMH with HIV who matched to reports of both HBV and HCV. An individual who matched to 2000–2011 vital statistics mortality data was considered to have died; date of death was obtained from this match. Race/ethnicity data were obtained from HIV, HBV, HCV, TB, and STD surveillance databases. Discrepancies were addressed by using data from the surveillance database considered to be the most complete and accurate. TB data were considered the most complete and accurate, as the TB program manages each case of TB through treatment completion or death. HIV data were considered to be the second most complete, as additional data are obtained for all persons reported with HIV through medical record review. The STD and viral hepatitis databases had less complete data on race/ethnicity and thus were used only to populate missing values.

Information on HIV transmission risk factors and history of incarceration was obtained during the course of the HIV case investigation from providers, patient charts, and/or patient interviews. Recorded HIV transmission risk factors for each individual were classified into a single ‘transmission risk’ category. The mutually exclusive categories were: (1) injection drug use (IDU), (2) MSM, (3) heterosexual sex, and (4) other/unknown (including perinatal transmission) [30]. Individuals with multiple reported risk factors were classified in the transmission category listed first in descending order of the probability of

transmission per act; for example, individuals with both MSM and IDU as reported HIV transmission risk factors were classified into the IDU category.

We calculated the number of deaths between 2000 and 2011 per 1000 HIV-infected persons in each infection group. In order to account for differences in the age distribution between the infection groups, we age-adjusted by direct standardization to the 2000 projected US population [31], using the age distribution of each infection group in 2000. Age-adjusted proportions and confidence intervals were calculated according to CDC’s Statistical Notes on Direct Standardization [32].

Demographics and risk factors were compared between persons with HIV only, HIV/HBV infection, HIV/HCV infection, and HIV/HBV/HCV infection. Pearson’s χ^2 test was used for statistical comparison of categorical variables, and the Wilcoxon–Mann–Whitney test was used for statistical comparison of continuous variables. Statistical significance was defined as $P < 0.05$. All analyses were conducted using SAS v. 9.2. (SAS Institute, USA).

RESULTS

A total of 140 606 HIV-infected persons were reported to the DOHMH by 31 December 2010 and were not known to be dead as of 1 January 2000. Of these, 111 340 (79%) were HIV mono-infected; 6231 (4%) were co-infected with HBV only; 21 093 (15%) were co-infected with HCV only; and 1942 (1%) were co-infected with both HBV and HCV. All groups were predominantly male, particularly the HIV/HBV-infected and HIV/HBV/HCV-infected groups, which were 79% and 76% male, respectively. The age at time of HIV diagnosis was similar for all groups, with a median age of 35 years for the HIV mono-infected and HIV/HBV-infected groups, 36 years for the HIV/HBV/HCV-infected group, and 39 years for the HIV/HCV-infected group. The majority of HIV/HBV-infected individuals were of non-Hispanic black race/ethnicity (58%); the largest proportion of HIV/HCV-infected and HIV/HBV/HCV-infected individuals were non-Hispanic black (43%, 46%, respectively) or Hispanic (42%, 38%) (Table 1).

The distribution of HIV transmission risk categories was significantly different in the co-infected groups compared to the HIV mono-infected group ($P < 0.0001$ for all comparisons). The largest proportion of HIV/HBV-infected persons were in the MSM HIV transmission risk category (38%). IDUs

Table 1. Demographics of HIV mono-infected, HIV/HBV-infected, HIV/HCV-infected, and HIV/HBV/HCV-infected individuals

| | HIV mono-infected | HIV/HBV-infected only | <i>P</i> value* | HIV/HCV-infected only | <i>P</i> value* | HIV/HBV/HCV-infected | <i>P</i> value* |
|---|-------------------|-----------------------|-----------------|-----------------------|-----------------|----------------------|-----------------|
| <i>N</i> | 111 340 | 6231 | — | 21 093 | — | 1942 | — |
| HIV-infected (%) | 79% | 4% | — | 15% | — | 1% | — |
| Male, <i>n</i> (%)† | 76 402 (69%) | 4907 (79%) | <0.0001 | 14 975 (71%) | 0.003 | 1472 (76%) | <0.0001 |
| Median age (years) at HIV diagnosis (IQR)† | 35 (28–43) | 35 (29–42) | <0.0001 | 39 (33–45) | <0.0001 | 36 (30–42) | 0.0192 |
| Age group (years) at HIV diagnosis, <i>n</i> (%)† | | | | | | | |
| <20 | 5902 (5%) | 199 (3%) | <0.0001 | 268 (1%) | <0.0001 | 43 (2%) | <0.0001 |
| 20–29 | 25 095 (23%) | 1541 (25%) | | 3045 (14%) | | 417 (22%) | |
| 30–39 | 39 456 (36%) | 2501 (40%) | | 7657 (36%) | | 787 (41%) | |
| 40–49 | 25 715 (24%) | 1373 (22%) | | 7237 (34%) | | 516 (27%) | |
| 50–59 | 9387 (9%) | 449 (7%) | | 2401 (11%) | | 151 (8%) | |
| ≥60 | 3338 (3%) | 131 (2%) | | 404 (2%) | | 25 (1%) | |
| Race/ethnicity, <i>n</i> (%)‡ | | | | | | | |
| Non-Hispanic white | 22 489 (21%) | 1034 (17%) | <0.0001 | 2951 (14%) | <0.0001 | 298 (15%) | <0.0001 |
| Non-Hispanic black | 49 968 (46%) | 3617 (58%) | | 9011 (43%) | | 888 (46%) | |
| Hispanic | 34 109 (31%) | 1402 (23%) | | 8919 (42%) | | 735 (38%) | |
| Asian/Pacific Islander | 1798 (2%) | 139 (2%) | | 102 (0.5%) | | 15 (1%) | |

IQR, Interquartile range.

* Compared with HIV mono-infected.

† For percent male and age at HIV diagnosis, percentages and χ^2 *P* values were calculated for those with non-missing values of these variables; percent male and age at HIV diagnosis were each unknown for 2% of HIV-infected individuals.

‡ Percentages and χ^2 *P* values were calculated for those for whom race/ethnicity was neither other nor unknown; race/ethnicity was other or unknown for 2% of HIV-infected individuals.

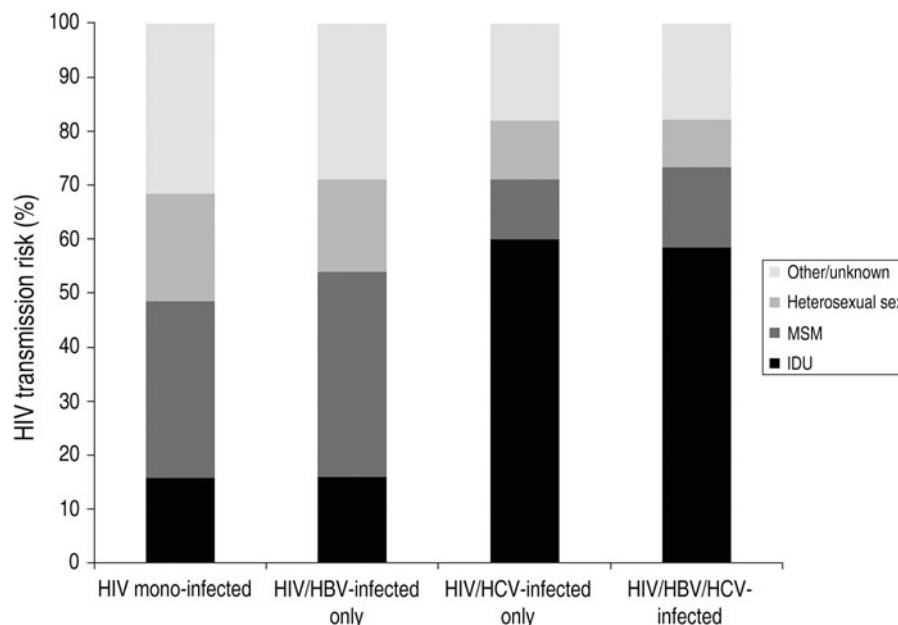


Fig. 1. HIV transmission risk among HIV-infected individuals. MSM, Men who have sex with men; IDU, injection drug use.

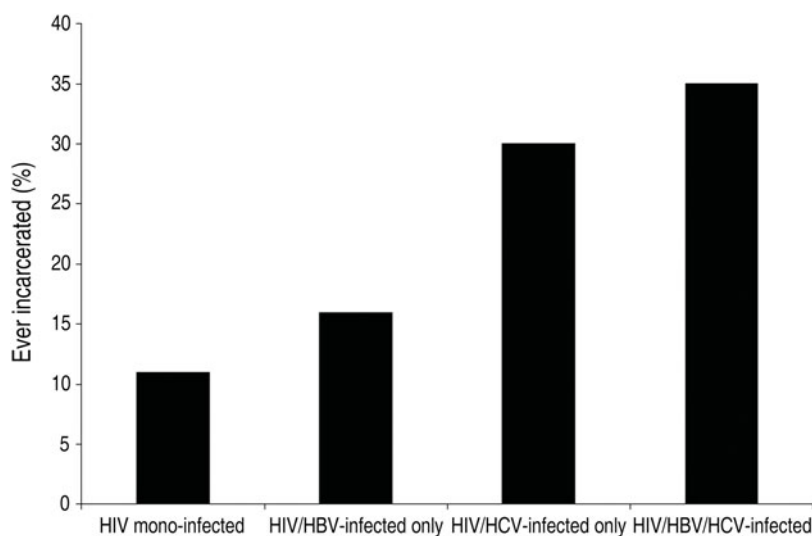


Fig. 2. History of incarceration among HIV-infected individuals.

comprised the greatest proportion of persons HIV/HCV-infected (60%) and HIV/HBV/HCV-infected (59%) (Fig. 1). The proportion of individuals with a history of incarceration was higher in all co-infected groups compared to the HIV mono-infected group ($P < 0.0001$ for all comparisons) (Fig. 2).

The age-adjusted number of deaths per 1000 HIV-infected persons between 2000 and 2011 was 313 [95% confidence interval (CI) 267–358] for HIV/HBV/HCV-infected individuals, compared to 268

(95% CI 256–279) for HIV/HCV-infected individuals, 235 (95% CI 217–254) for HIV/HBV-infected individuals, and 158 (95% CI 156–161) for HIV mono-infected individuals (Fig. 3).

A subanalysis excluded 25 957 individuals reported with HIV who were known to have died between 1 January 2000 and 31 December 2010 to calculate the percentage of HIV-infected persons co-infected with HBV and/or HCV at the end of 2010. Of the remaining 114 649 persons, 94 718 (83%) were HIV

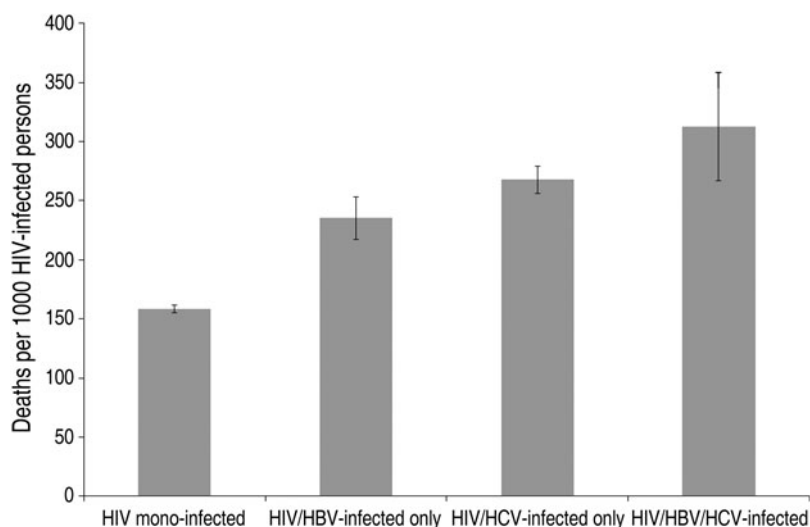


Fig. 3. Age-adjusted mortality from 2000 to 2011 among HIV-infected individuals.

mono-infected; 4634 (4%) were co-infected with HBV only; 14 133 (12%) were co-infected with HCV only; and 1164 (1%) were co-infected with both HBV and HCV.

DISCUSSION

Between 2000 and 2010, 6% of HIV-infected individuals in NYC were co-infected with HBV (including HIV/HBV/HCV-infected individuals), and 16% were co-infected with HCV (including HIV/HBV/HCV-infected individuals). The percentages among those not known to have died by the end of 2010 were slightly lower. Taking into account deaths from 2000 to 2010, these lower proportions could reflect increased mortality of co-infected persons compared to HIV mono-infected persons over the study period, or decreasing reports of HBV and HCV infection among HIV-infected individuals over the study period, or both.

Overall, our findings are consistent with other analyses of HIV co-infection using state and local surveillance data. In Michigan, 1.8% of HIV-infected individuals were co-infected with HBV [17]. HIV/HCV infection estimates range from 2.2% to 23.6% from public health surveillance database matches in Colorado, Connecticut, Oregon, and Michigan [16, 17]. The co-infected proportions we found are lower than estimates from multicenter clinical cohorts, which have reported HBV prevalences of 9–11% among PLWHA in the USA and Europe [7, 12] and HCV prevalences of 20–37% among PLWHA in the USA [10, 11]. These higher estimates are not

surprising, as all members of these cohorts were tested for HBV and HCV, and it is likely that high-risk groups were selected for enrolment. However, as surveillance data include positive tests from sites not generally included in clinical cohorts, such as prisons and jails, drug treatment facilities, and needle exchange programmes, our analysis of the characteristics of this population is more representative of the co-infected population in NYC than analyses from clinical cohort studies.

The largest proportion of HIV/HBV/HCV-infected and HIV/HBV-infected individuals were non-Hispanic black, while the HIV/HCV-infected group had nearly equal proportions of non-Hispanic blacks and Hispanics, together representing nearly 85% of the total population. A majority of cases in all infection categories were male. This is consistent with other studies that have found that male sex, black race, and Hispanic ethnicity are associated with higher risk of HIV co-infection with HBV and HCV [10, 12, 17]. The HIV transmission risk categories of individuals at highest risk for HIV co-infection with HBV or HCV in NYC were also consistent with the transmission routes of and reported risk factors for HBV and HCV [10, 11, 13–16, 18]. The largest proportion of HIV/HBV-infected individuals were MSM, while the largest proportion of HIV/HCV-infected and HIV/HBV/HCV-infected individuals had a history of IDU. Health departments and clinicians should target HIV, HBV, and HCV prevention and screening efforts towards these populations.

We found that the age-adjusted number of deaths per 1000 individuals between 2000 and 2011 was

higher among HIV/HBV-, HIV/HCV-, and HIV/ HBV/HCV-infected individuals compared to HIV mono-infected individuals. As individuals who were diagnosed early in the study period had a longer follow-up period in which death might occur than individuals who were diagnosed late in the study period, the numbers of deaths we reported should not be interpreted as mortality rates in these populations. However, the differences between the infection groups indicate that greater efforts should be made to ensure that co-infected individuals are receiving comprehensive primary care, HIV treatment, evaluation for liver disease, and evaluation for HBV and/or HCV treatment. Given the large proportion of co-infected persons with IDU as an HIV transmission risk factor, services that can prevent morbidity and mortality from drug use such as harm reduction and drug treatment may also prevent deaths in co-infected persons. A high prevalence of prior incarceration among co-infection groups indicates that increased efforts are needed to reach the current and formerly incarcerated population with prevention, diagnosis, and treatment of HIV, HBV, and HCV. Especially with the new availability of effective short-course HCV antiviral treatment, prisons are appropriate settings for providing this needed care [33].

Guidelines from the CDC, the National Institutes of Health (NIH), and the HIV Medicine Association of the Infectious Diseases Society of America recommend that all PLWHA be tested for HCV upon entry to HIV care, with annual follow-up for at-risk PLWHA who are HCV-negative, and that all PLWHA be tested for HBV upon entry to HIV care and vaccinated if susceptible to HBV [34]. HIV healthcare providers and clinics should ensure that screening guidelines for HBV and HCV are followed for all PLWHA, and in particular for high-risk groups. Conversely, HBV- and HCV-infected individuals should be tested regularly for HIV. Our findings also support targeting both primary and secondary HBV and HCV prevention efforts towards PLWHA.

This analysis has several limitations. First, the HIV, HBV, and HCV surveillance databases include only individuals reported to the NYC DOHMH; infected persons not tested for HIV, HBV, or HCV are not represented. In addition, persons with unreported positive tests are not represented, although the amount of under-reporting by laboratories is likely minimal [35]. Second, while we defined persons with a positive HCV antibody test and no HCV RNA test documented as HCV-infected, some persons

with a positive HCV antibody test do not have chronic HCV; the literature suggests that 25–30% of HCV antibody-positive persons are RNA-negative either because of a resolved infection or a false-positive result [36, 37]. Our routine HCV surveillance data from 2000 to 2010 do not include negative HCV RNA tests. Third, deaths among HIV-infected individuals that occurred outside NYC were not included in this analysis, so the proportions of HIV-infected individuals who died shown in [Figure 3](#) may be underestimated. Finally, this analysis was exploratory and did not assess independent risk factors for HIV co-infection with HBV and HCV. Future analyses could use multivariable models to identify which of the identified risk factors were independent.

The strengths of this analysis include its scale and comprehensiveness. All HIV diagnoses and all positive HBV and HCV tests reported to the DOHMH by the end of 2010 were included for analysis. We present estimates of the proportion of HIV-infected individuals co-infected with HBV and HCV in NYC, as well as the demographic and risk groups most at risk for these co-infections and a comparison of mortality between the co-infection groups. Our analysis uses surveillance data, a representative source of population-based data, to assess the prevalence and risk factors of co-infection. Our findings highlight the importance of primary prevention and testing for HIV, HBV, and HCV among high-risk groups. Overall, these findings demonstrate the need for integrating HIV, HBV, and HCV testing and treatment services so that co-infected individuals can be more easily and efficiently identified and treated. Additionally, this analysis reinforces the importance of disease surveillance and provides replicable methods that can be used by other jurisdictions to better understand the local epidemiology of viral hepatitis infection in PLWHA. Matching surveillance databases is an effective and cost-effective method for health departments to determine the burden of co-infection and populations at risk for infection with multiple diseases in their jurisdiction and work with community providers on primary and secondary prevention activities [38, 39].

ACKNOWLEDGEMENTS

The authors thank Sharon Greene for her valuable review and feedback on the epidemiological methods and statistical analyses; James Hadler and Jay K. Varma for helpful feedback on earlier versions of this paper; Elizabeth Terranova, Alex Breskin and Caitlin Falvey for editorial support; and Sonny Ly and Julie Yuan for

matching the data. This project was supported in part by an appointment to the Applied Epidemiology Fellowship Program administered by the Council of State and Territorial Epidemiologists (CSTE) and funded by the Centers for Disease Control and Prevention (CDC) Cooperative Agreement Number 5U38HM 000 414–5.

DECLARATION OF INTEREST

None.

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