Social Determinants of Health in HIV/HCV Co-infection Compared to HIV Infection Only: Results from the "Positive Spaces, Healthy Places" Study

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Authors Contribution

Sean Rourke conceived the project, contributed to the design of the study, oversaw data collection, guided the data analysis, and was the principal writer of the manuscript. He is responsible for the integrity of the work as a whole. Michael Sobota conceived the study, oversaw data collection, contributed to interpretation of data, and revised the manuscript drafts. Ruthann Tucker conceived the study, contributed to the design of study and interpretation of data, and revised the manuscript. Saara Greene, Laverne Monette, Jay Koornstra, and Steve Byers conceived the study, contributed to the design of the study, oversaw data collection, and reviewed the manuscript. Tsegaye Bekele conducted the data analysis and participated in all phases of the writing. Katharine Gibson participated in the design of the study, participated in drafting the manuscript, and reviewed the manuscript. Colleen Price participated in the conception of the study, contributed to interpretation of the data, and reviewed the manuscript. James Watson participated in the design of the study and collection of data, contributed to the interpretation of data, and reviewed the manuscript. Stephen Hwang, Dale Guenter, and James Dunn conceived the project, participated in the design of the study, contributed to the data interpretation, and revised the article. Michael Wilson contributed to the interpretation of the data, drafted the article, and reviewed the manuscript. Amrita Ahluwalia oversaw data collection and revised manuscript drafts. Jean Bacon contributed to the design of the study, drafted the manuscript, and reviewed the article. All of the authors approved the final version of the manuscript.

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INTRODUCTION

The availability and accessibility of highly active antiretroviral therapy (HAART) has extended the lifespan and improved the health and well-being of thousands of people living with HIV and AIDS in Canada.(1) The high levels of mortality once associated with HIV-infection, and specifically with full-blown AIDS, have been significantly reduced.(2) With this increasing lifespan has come the potential for more medication-related toxicities,(3) and the emergence of co-infections, which increase the complexity of the health-related and health care needs of people living with HIV/AIDS. Hepatitis C (HCV) has become an increasingly common co-infection among people living with HIV/AIDS. As many as 35% of HIV-infected individuals are dually infected with HCV (4) (5) , and HCV is one of the leading causes of death among people living with HIV.(1) (6) Approximately 17,000 Canadians – including more than 5,000 people in Ontario -- are estimated to be co-infected with HIV and HCV.(7) (8)

HIV and HCV share similar routes of transmission (9) and, as with HIV, HCV is becoming epidemic in vulnerable and marginalized populations. (10) The strongest predictor for co-infection worldwide and in Canada is injection drug use (IDU). (8) (11) In Ontario, 98% of people who are co-infected with HIV and HCV are injection drug users.(12) Injection drug use is most prevalent, in turn, among Aboriginal Peoples and current and former prisoners. (8) (13)

While incarceration and injection drug use are known to be key risk factors for HCV co-infection among people living with HIV/AIDS, less attention has been given to other potential social or environmental risk factors or determinants of health. These other risk factors should not be overlooked as they may provide a way to mitigate the significant clinical impact of HCV on the health of people with HIV, including heightened risk of severe liver disease, (14) liver decompensation, (15) a higher probability of progression to an AIDS-defining event, (16) lower health-related quality of life, (17) and increased mortality (15) (16). A recent study revealed that individuals with HIV/HCV co-infection use and access significantly more health care services than individuals with HIV infection alone.(18) However, this study also argues that this increased health care utilization may not be able to adequately account for the morbidity associated with HCV among people living with HIV and AIDS.

In addition to examining the health consequences of HIV/HCV co-infection, researchers are now exploring socio-demographic and environmental risk factors for HCV and HIV co-infection. Two large studies conducted in the United States each revealed that individuals with HIV who are co-infected with HCV are more likely to be African American and are generally older than individuals who are infected with HIV alone.(19) (20) This latter finding is consistent with another US study, which found that older age was significantly associated with HCV co-infection.(21) The Swiss HIV Cohort Study found that HCV seropositivity was associated with lower income and education, female sex, and younger age. (16)

Our current study expands upon these findings, and seeks to determine the range of social determinants of health associated with HCV co-infection among people living with HIV/AIDS in Ontario. Specific focus is given to housing, as this factor has not been adequately addressed in the literature but is suspected to be associated with HCV co-infection. Housing can be conceptualized as an intermediate structural factor, which links together broader societal processes and influences with an individual's immediate social and physical environment.(22) Housing provides physical security and protection from the elements, and plays a central role in determining an individual's physical and social risk environment.(23) (24) It is being increasingly recognized that it can also provide a source of identity and belonging. (22) (23) (25) Furthermore, housing can create a physical or social space in which social ties and positive social relations are fostered and maintained. (22) (25) If housing is inadequate or not available, the physical security, psychological benefits, and social interactions it provides may be jeopardized, leading individuals to places of increased vulnerability for their health and risks for STIs, (26) including HIV/AIDS and HCV.(24) (27) (28)

Previous research has demonstrated that both objective and subjective indicators of housing status are significantly associated with health outcomes among people living with HIV/AIDS. (22)] Housing status has also been shown to influence HIV risk factors, many of which are shared risk factors for infection with HCV.(24) A study which focused on housing transience found that transient individuals were more likely to exhibit drug-related HIV risk behaviour.(29) Another study which examined HIV risk behaviors over time demonstrated that there was a dose response relationship between housing status and HIV risk, and that the odds of specific HIV-related risk behaviors increased when housing status worsened and decreased when housing improved. (30) Among people with HIV, homelessness and unstable housing have also been associated with HCV co-infection, (31) stress and anxiety, (32) depression (33) and lower physical health functioning. (34) However, many of these studies have either not examined HCV and HIV co-infection as a primary outcome, or have not explored both subjective and objective housing indicators as risk factors for HIV/HCV co-infection. Therefore, there is a need to determine whether or not housing is associated with HCV co-infection among people with HIV/AIDS and, if it is, to elucidate which features of housing, and which other determinants of health are most influential and could be targeted in HIV/HCV co-infection prevention programs, policies, and interventions to lower the burden of illness for those infected with both HIV and HCV.

The objectives of the current study, therefore, are: (1) To examine and determine which sociodemographic, clinical, psychosocial, and housing characteristics are associated with HIV/HCV co-infection; and (2) To explore different subjective and objective housing markers / indicators in this sample, and determine whether they are associated with an increased risk of HIV/HCV co-infection. We are particularly interested in exploring the individual risks associated with HIV/HCV, but also the most significant factors that may be overriding risk factors for HIV/HCV.

METHODS

Participants

The *Positive Spaces Healthy Places* study recruited a sample of people living with HIV/AIDS who were principally affiliated with or connected to a community-based AIDS service organization in Ontario. To ensure the representativeness of the study sample, participants were recruited using a wide range of access points, including homeless shelters, agencies serving women, families, and youth, Aboriginal organizations, transitional housing providers, and supportive housing agencies. Efforts were made to include harder-to-reach populations such as injection drug users and street involved communities (individuals who live in and out of hostels and homeless shelters). A total of 602 participants were enrolled in the study; 374 from Greater Toronto Area (GTA), 94 from South and South Western Ontario, 94 from Eastern Ontario, and 40 from Northern Ontario.

All participants were screened for eligibility and informed consent was obtained prior to administering the questionnaire. All consent and survey/questionnaire administration was conducted by peer research assistants (PRAs) -- people living with HIV trained by the study team -- to reflect the study's strong commitment to Community-Based Research (CBR) (35) and the Greater Involvement of People Living with HIV (GIPA) Principle. (36) Participants were eligible for the PSHP study if they were HIV-positive, 18 years or older, able to provide informed consent, and lived in Ontario. This study was funded by the Canadian Institutes of Health Research, the Ontario Ministry of Health and Long Term Care, the Ontario AIDS Network, the Wellesley Institute, and the Ontario HIV Treatment Network. Ethics approval for this study was obtained from the Research Ethics Board of McMaster University, Hamilton, Canada.

Participants were interviewed at baseline and at one-year follow-up. Of the 602 participants enrolled in the study, 509 (85%) completed the one-year follow-up. Of these

509 individuals 482 were eligible for analysis. Twenty-seven (28) reported a past history of HCV infection but were clear of the infection at the time of the interview and were excluded from the analysis. Of the 482 remaining participants, 95 (20%) self-identified as HCV-positive at the time of interview. We did not have laboratory confirmation of HCV infection.

Eligible individuals had similar characteristics to those who were excluded, except for past history of incarceration (24% versus 43%, p=0.02). There were no significant differences in age, gender, sexual orientation, ethnicity, employment, housing status, or AIDS diagnosis between participants who indicated that their HCV had resolved and participants whose HCV remained active.

Data Collection

The study survey was comprised of demographic questions and standardized survey instruments selected by the PSHP study team. At one year after baseline data collection, the questionnaire was supplemented with questions on whether or not the participants had been tested for HCV, and if they still had this infection. Both the baseline and one-year follow-up questionnaire was administered face-to-face by peer research assistants and took approximately 60 to 90 minutes to complete. This study uses data from the one year follow-up interviews only, as data on HCV infection was not collected at baseline.

Measures

The primary outcome in this study is HCV co-infection, as determined by self-reported HCV status at the time of the one-year follow-up interview. Participants were asked to indicate whether or not their infection was active at the time of interview, or had been cleared.

The detailed survey and questionnaires captured a wide array of social determinants of health, including sociodemographics (i.e., age, gender, income, employment status, race, ethnicity), clinical markers of HIV status (recent CD4 and plasma viral load counts, length of HIV disease, presence of AIDS-defining conditions, and receipt of antiretroviral therapy), and health care utilization (use of family doctor, HIV specialist, psychiatrist, mental health counselor/ psychologist, addiction counselor, or needle exchange program). Information on mental health and substance use was also collected, using the CES-D depression scale, the Alcohol Use Disorders Identification Test (AUDIT), and the Drug Abuse Screening Test (DAST-20). The CES-D is a self-report scale consisting of 20 items that assess the presence of depressive symptoms in the general population, including somatic symptoms, positive affect, negative affect, and interpersonal problems. Individuals who have a score of 16 or greater can be classified as "clinically depressed". The CES-D has been validated and is reported to have high test-retest reliability. (37) The AUDIT has been found to have high internal consistency (38) (39) (40) and high test-retest reliability. (40) The DAST-20 has also been validated and shown to have acceptable internal consistency and test-retest reliability.(41) (42) (43) The survey also included items to gauge participants' level of satisfaction with their housing condition and its meaningful dimensions (e.g., housing as a reflection of social identity and pride, a place of refuge, a site for exercise of control, a source of social status).(25) Respondents were asked to rate on a Likert scale their level of satisfaction with several aspects of their housing or residence and neighborhood. Two of the items, "Satisfaction with overall residence" and "I feel that my home provides a good location for me", were dichotomized into "very satisfied/satisfied" versus "neutral/dissatisfied/very dissatisfied" and "strongly agree/agree" versus "neutral/ disagree/ strongly disagree", respectively. Respondents were also asked about whether they had ever been homeless, how often they had moved in the year prior to survey administration (as an indicator of housing transience), and whether or not they lived in supportive housing.

Statistical Analysis

All analyses were performed using SPSS 16.0 (SPSS Inc., Chicago, IL). Data analyses were conducted in two stages. In the first stage, means and standard deviations were calculated for continuous variables for HIV/HCV co-infected and HIV infected only groups, and compared using t-tests and Wilcoxon rank-sum tests (Table I). Frequencies were calculated for categorical variables and compared using Pearson's χ^2 tests and non-parametric chi-square tests. Fisher's exact test was used for contingency tables in which 25% of the expected cell frequencies were less than five.

In the second stage, predictor variables that were significantly associated with HCV/HIV co-infection were entered into a hierarchical multivariate logistic regression model in a series of four blocks. First, demographic variables (sexual orientation, Aboriginal status, education, and income) were entered into the model as a block. In the second block, the only significant HIV disease marker (HIV treatment) was entered. In the third step, mental health and addiction variables (depression and non-medicinal drug use) were entered. Finally, housing variables (history of homelessness, housing location, and region of residence) were entered.

After examining the correlation matrix between predictor variables (results not shown here) , we allowed only income (among income and employment variables) and history of homelessness, location of home, and living outside of GTA (among housing variables) to enter the hierarchical logistic regression model to reduce the degrading effects of collinearity. McFadden R square values were calculated (Table III) and provided as indicators of the goodness of fit of the regression model at each stage of the hierarchical analysis. All reported p-values are two-tailed.

RESULTS

Characteristics of the 482 study participants included in this analysis are presented in Table 1.

Sociodemographics: Compared to those infected with HIV only, a greater proportion of those with HCV co-infection were heterosexual (57% versus 30%, p<0.001), Aboriginal (20% versus 10%, p<0.001), have less than a high school education (41% versus 16%, p<0.001), and were unemployed (87% versus 72%, p<0.001). Co-infected individuals had a significantly lower average monthly income.

HIV Disease Markers: Co-infected individuals were less likely to be receiving HIV treatment (32% versus 64%, p<0.001). Other markers of HIV disease (CD4 count, time since HIV diagnosis, AIDS diagnosis) were not significantly different among those with HIV and those with HIV/HCV.

Mental Health and Addiction: HCV co-infected participants reported significantly higher level of use of non-medicinal drugs (73% versus 30%, p<0.001) and significant level of depression (i.e., CESD >=16) (64% versus 43%). Although hazardous alcohol use was slightly higher among HCV co-infected participants, the difference did not reach statistical significance.

Housing Characteristics: Individuals with HCV co-infection reported higher prevalence of history of homelessness s (16% versus 4%, p<0.001), perceived housing-related discrimination (16% versus 9%, p=0.04), moving two or more times in the past 12 months (14% versus 5%, p<0.001), and dissatisfaction with location of their home (40% versus 30%, p=0.03). A greater proportion of those co-infected were living outside the Greater Toronto Area (72% versus 34%, p<0.001).

Health Care Utilization: Individuals with HCV co-infection reported higher level of utilization of addictions counseling services (28% versus 4%, p<0.001) and needle exchange services (24% versus 3%, p<0.001). Differences in utilization of services of a family doctor, HIV specialist, psychiatrist, mental health counselor or psychologist were not statistically significant.

Insert Table I and II about here

To explore the relative and unique contributions of the social determinants of health on HIV/HCV co-infection, we fitted a hierarchical logistic regression model (see Table II). Four sets of predictor variables (i.e., sociodemographic, clinical, addiction and mental health, and housing variables) were entered into the model. When sociodemographic variables were entered into the model, the McFadden R squared value was 0.113. Of the four sociodemographic variables that were entered into the model, only sexual orientation (adjusted OR=2.24; 95% CI: 1.29- 3.91) and education (adjusted OR=2.48; 95% CI: 1.37-4.49) were significantly associated with HCV/HIV co-infection. When HIV treatment variable was added to the model, the McFadden R squared value increased only by 0.016 and HIV treatment was not significantly associated with HCV co-infection (adjusted OR=1.69; 95% CI: 0.91-3.14). When depression and non-medicinal drug use were entered as the third block, the McFadden R squared value increased by 0.134, but only non-

medicinal drug use remained significantly associated with HCV/HIV co-infection (adjusted OR=4.45; 95 % CI: 2.53-7.81). Among the three housing variables entered as the last block, only living outside of the Greater Toronto Area remained significantly associated with HCV co-infection status (adjusted OR=2.82; 95% CI: 1.60-4.98). Adding the fourth block of housing variables increased the McFadden R squared value by 0.034, yielding a final model with a McFadden R squared value of 0.297.

DISCUSSION

Our study, unlike many others that studied specific populations such as prisoners or injection drug users, is based on data drawn from a population-based cohort of individuals living with HIV or HIV/HCV co-infection with a wide variety of sociodemographic and health characteristics. Our findings suggest that education, sexual orientation, harmful substance use, and place of primary residence each play a potentially significant and independent role in distinguishing between individuals with HIV infection only, and individuals who are co-infected with HCV. Sexual orientation was strongly correlated with gender ($r=0.651$, $p<0.001$) in our sample with 90% of females identifying as heterosexual and 82% of males identifying as gay or bisexual. Therefore, the significant association between sexual orientation and HCV co-infection, we believe, is also a reflection of the difference between the two genders.

Aboriginal status was also significantly associated with HIV/HCV co-infection in the bivariate analysis, but not in the multivariate model. This may be because some of the other variables in the model, especially harmful substance use, were more significantly associated with co-infection and may have masked any potential effects of Aboriginal status. Overall, individuals who were living in better social and economic conditions (as reflected by the social determinants of health variables included in this study) were less likely to be co-infected with HIV and HCV. Although some of these effects became non-significant in the multivariate regression model, sexual orientation, education, and region of residence still influenced the likelihood of being HIV/HCV co-infected, as evidenced by their significant and sizeable effect sizes.

All of the housing characteristics except one -- place of residence -- were not significantly associated with HCV co-infection in the multivariate regression model. However, being homeless at least once, having experienced housing-related discrimination, and not having a home in a good location were each significantly associated with HCV co-infection in bivariate analyses. Therefore, housing variables cannot be overlooked as potential predictors of co-infection with HCV, although they may not be the most significant ones.

Living in the Greater Toronto Area was the only housing characteristic significantly related to HCV co-infection. This finding reinforces epidemiological data for the province of Ontario, which indicates that the prevalence of HIV/HCV co-infection is significantly lower in the Greater Toronto Area than in the three other study regions.

We hypothesize that lower rates of HIV/HCV co-infection are a reflection of two factors: lower rates of HIV infection in the IDU population in the Greater Toronto Area than in other parts of the province and better availability of health care, housing, employment, and social support services in this area compared to the rest of the province. In this study, individuals who were not receiving HIV treatment were significantly more likely to be co-infected with HIV and HCV. The number of people who were co-infected but not accessing HIV treatment may be due to lack of access, to confusion about practice guidelines for treatment of people with HIV/HCV co-infection and changing knowledge about the safety (i.e., toxicity) of antiretroviral therapies for people with HCV. Living in the GTA may provide people with HIV/AIDS with better access to treatment or interventions, which may in turn lead to greater usage of these services and lower risks for HCV co-infection. Living in the Greater Toronto Area may also affect several housing-related characteristics which may not be significant on their own but, when combined with other factors, may be a predictor of HIV/HCV co-infection.

In addition to potentially being influenced by geography, use of HIV treatment may also be related to whether or not an individual is co-infected with HCV. This could be problematic due to the risk of increased HIV transmission (44) by people whose HIV is not treated and the risk of developing resistance to antiretroviral therapies (45) when HAART treatment is not initiated or is stopped. Concerted efforts may be required to ensure that people with HIV/HCV co-infection receive and are able to adhere to effective treatments for both conditions.

Finally, non-medicinal drug use was significantly associated with an increased prevalence of HIV/HCV co-infection. It is unclear from our study whether the substance use predated or was a consequence of HIV or HIV/HCV co-infection. Regardless of the direction of this relationship, more treatment, support and interventions for harmful substance use are needed -- in addition to what is already being done -- to prevent further transmission of HIV and HCV from those already infected.

Our results provide compelling evidence that people with HIV/HCV co-infection face multiple vulnerabilities and risks -- many of which are rooted in the social determinants of health. This study supports the growing body of knowledge that health is shaped not only by physiological or biological factors, but also by “upstream” or fundamental causes, including broader social, political, and economic structures.(22) Education and region of residence were two “upstream” factors in this study which were significantly associated with HCV co-infection. This study also supports the results of other studies which have found that individuals with both HIV and HCV have different sociodemographic and housing-related characteristics than those who are infected with HIV alone.(19) (20) (31) (46) (47) Our findings are consistent with those from a British Columbia-based study, which found that individuals who were co-infected with HIV and HCV were more likely to be female, Aboriginal, have less than a high school education, live in unstable housing, and be unemployed. (46) Notably, our study did not find a significant association between housing instability and HIV/HCV co-infection, but instead found an

association between region of residence and co-infection, which was not assessed in the British Columbia study.

There are limitations to our study. Our sample is a subset of the *Positive Spaces Healthy Places Study*, whose objective was to examine the impact of housing on quality of life, and which included participants who were primarily affiliated with or were receiving services from AIDS service providing agencies. Therefore, the sample may not be representative of all people living with HIV/AIDS in the province. All data, including clinical measures, are self-reported and were collected through face-to-face interviews and may be subject to recall and socially desirable response biases. HCV infection status was determined through self-report, and this information was therefore not as reliable as if it had been obtained through laboratory diagnosis. Due to the cross-sectional nature of the study, we are unable to draw conclusions about the cause and effect or direction of association between housing and other characteristics and co-infection with HCV. Finally, missing data on completed surveys (e.g., CD4 cell count) may have reduced the power to detect a significant model.

Findings from this study contribute to existing evidence that certain sociodemographic, health-related, and housing characteristics are associated with HCV co-infection among people living with HIV/AIDS. This study suggests that living in areas where access to health services and housing is poor may have an impact on whether or not an individual becomes co-infected with HCV and HIV. Therefore, future HIV/HCV co-infection prevention efforts should consider the potential to influence sociodemographic and housing factors as a way to reduce risk. Housing in particular represents one potential risk factor for HIV/HCV co-infection which is amenable to modification, but further research is required to identify the specific aspects or features of housing associated with lower risk of HIV/HCV co-infection.

More social, health and housing supports should be explored as an option for HIV and HIV/HCV prevention. Housing is now seen as a key factor in helping people reduce/manage the drug addictions that increase their risk of both HIV and HIV/HCV co-infection. In the United States, studies are being conducted which examine housing as a prevention option, including the Housing and Health Study and the Chicago Housing for Health Partnership HIV Sub-Study.(48) Similar research is now being conducted in Ontario, and we will be able to comment on the findings soon. Further prospective research is needed to explore how specific risks or vulnerabilities contribute to the acquisition of HIV or HCV infection, and to shape programs and policies which can prevent new infections.