Impact of hepatitis C virus infection on all-cause and liver-related mortality in a large community-based cohort of inner city residents

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TITLE PAGE

Title: Impact of hepatitis C virus infection on all-cause and liver-related mortality in a large community-based cohort of inner city residents

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ABSTRACT (246 words)

The aim of this study was to measure the impact of HCV infection on mortality in a cohort of inner city residents. CHASE is a community-based study of inner city residents followed retrospectively and prospectively through linkages with provincial virology and mortality databases. We identified participants having received HCV antibody testing, evaluated cause-specific mortality rates and factors associated with all cause and liver-related mortality using Cox Proportional Hazards models. Overall, 2,332 participants received HCV antibody testing (recent non-injection drug use - 81%). The prevalence of HCV and HIV were 64% (1,495 of 2,332) and 21% (485 of 2,332). Between January 2003 and December 2007, there were 180 deaths (192 per 10,000 py; 95% CI: 165, 222), with 21% HIV-related, 20% drug-related and 7% liver-related. Mortality was associated with age >50 years [adjusted hazard ratio (AHR) 2.80 vs. <40 years (referent group); 95% CI 1.93, 4.07, $P<0.001$] and HIV infection (AHR 3.81; 95% CI 2.72, 5.34, $P<0.001$), but not positive HCV antibody status (AHR 1.19; 95% CI 0.83, 1.72, $P=0.35$). Liver-related mortality was associated with age >50 years [AHR 18.49 vs. <40 years (referent group); 95% CI 2.27, 150.41, $P<0.001$] and positive HCV antibody status (AHR 7.69; 95% CI 0.99, 59.98, $P=0.052$). This study demonstrates a high rate of mortality in this population, particularly those with HIV. HCV-infected inner city residents >50 years of age were at significant risk of liver-related mortality. Continued surveillance of this population infected with HCV in the 1970s and 1980s is important.

Keywords: hepatitis C virus, injection drug use, illicit drug use, mortality, HIV

Chronic infection with hepatitis C virus (HCV) is associated with progressive liver disease, cirrhosis, liver cancer and end-stage liver disease (1-5). HCV has been demonstrated to increase the risk of all cause mortality (6), but the majority of studies suggest little impact of HCV infection on all cause mortality (7-12). Among those with HCV infection, an increased risk of liver-related mortality (6, 8, 11, 12) and excess mortality when compared to the general population (13, 14) have been observed.

However, our understanding of the impact of HCV infection on mortality is limited to a few cohort studies in selected populations (6-12, 15) and community-based evaluations comparing mortality among individuals diagnosed with HCV and the general population (13, 14). Many studies are limited in that they are restricted to a small number of post-transfusion (7, 8, 11) and clinic-based (6) cohorts involving patients with more advanced disease which may not be representative of the broader HCV-infected population. Other studies are limited to the long-term follow-up of small numbers of HCV infected individuals (9, 10), restrict analyses to liver-related causes of death (7, 10, 11) and often do not include illicit drug users or patients infected with HIV (7, 8, 10, 11).

The majority of people infected with HCV are illicit drug users although little is known about the impact of HCV on mortality in this population. Drug overdose, suicide, serious bacterial infections and HIV infection are major competing causes of death in illicit drug users (13, 14, 16-24). This could influence the natural history of HCV infection, because illicit drug users often die of other causes and the impact of HCV on mortality might not be properly estimated. Although a number of studies have investigated mortality among illicit drug users (16, 18, 22-28), these have

often been conducted in populations of HCV/HIV-infected injection drug users (IDUs) (25), are restricted to analyses of overall and HIV-related mortality (16, 18, 26-28) or are restricted to descriptions of major causes of death in this population and do not evaluate the impact of HCV infection on mortality (15, 16, 18).

In light of the lack of research on HCV and mortality, we investigated the contribution of HCV infection on all-cause and disease-specific mortality, including identifying factors associated with all cause and liver-related mortality, in a large community-based inner city cohort in Vancouver, consisting mainly of illicit drug users.

METHODS

Study Population

The Community Health and Safety Evaluation (CHASE) cohort was designed to evaluate the uptake of health services and health outcomes in the Downtown Eastside of Vancouver, Canada. In an effort to collect a representative sample of residents in this community, venues for recruitment were selected based on census track data from a total population of approximately 16,000 people. Individuals were informed of the project through community-based agency staff, postings in local agencies, door-to-door initiatives, and through word of mouth. Surveys were administered in a variety of settings, including ten community-based agencies, two community health clinics, single room occupancy hotels and social housing buildings, and a large space that operates as a needle exchange. All those included in the study had to have their names and personal health numbers verified through the British Columbia Ministry of Health database, ensuring that the participants all had the potential to be linked successfully to virology testing and health indicator databases.

Between January 2003 and June 2004, 2,913 participants completed a one-time interviewer administered survey (collecting information on demographics, health service utilization, self-reported HIV and HCV testing and recent drug use) and consented to have specific laboratory, treatment records and health-related information accessed through data linkages using their names, date of birth and/or personal health card numbers. Study participants received CDN\$10 to complete the survey. The University of British Columbia/Providence Health Care Research Ethics Board approved this study.

Data Collection

Participants were followed retrospectively and prospectively through health-related database linkages.

HCV and HIV serologic testing results from 1991 to 2007 were obtained from database linkages performed with the British Columbia Centre for Disease Control and the University of British Columbia Virology Department (laboratories responsible for all Provincial virology testing). Further, HIV antiretroviral prescriptions from 1996 to 2007 were obtained from database linkages performed with the British Columbia HIV/AIDS drug treatment program, which contains information on all HIV participants in the Province having received antiretroviral therapy.

The underlying causes of mortality from 2003 (the year of study recruitment) to 2007 were obtained from the British Columbia Vital Statistics database that captures information on all deaths in the Province. Causes of death were coded and recorded according to the *International Classification of Diseases* (ICD), 10th edition. Causes of death were also grouped according to drug-related, HIV-related and liver-related causes. Drug-related deaths included mental and behavioral disorders due to psychoactive substance use (F11-16, F19), accidental poisoning by drugs (X40-44), suicide by drugs (X60-64), assault by drugs and medicaments (X85), poisoning by drugs or medicaments undetermined if accidental or intentional (Y10-14) and adverse effects of drugs and medicaments (Y40-574, Y577-79, Y598, Y880). Deaths related to HIV infection included those with any ICD-10 of HIV (B20-24). Deaths related to liver disease included those

due to viral hepatitis (B15-19), liver cancer (C22), alcoholic liver disease (K70) and non-alcoholic liver disease (K71-77).

Statistical Analysis

Among individuals with HCV antibody testing in this cohort, we compared causes of mortality among HCV antibody positive and negative participants from January 2003 to December 2007. The rates of mortality were computed using person-years of observation. Person-years at risk were calculated for each person as the as time from date of questionnaire administration to either the date of death or December 31, 2007. Mortality incidence rates were determined by person-time methods. Confidence intervals for incidence rates were calculated using the Poisson exact method.

In a second analysis, we evaluated factors associated with overall and liver-related mortality. Variables examined in statistical analyses included age, sex, ethnicity, housing status, recent methadone maintenance treatment, self-reported health service access, having a regular doctor, self-reported recent non-injection (crack, cannabis, opioids, methamphetamine and benzodiazepines) and injection drug use and HIV and HCV status. Unstable housing was defined as homeless or staying in a temporary shelter or residing in a single-room occupancy room. Recent injection and non-injection drug use (in the previous six months) were evaluated as any drug use vs. none. HCV status was determined based on testing for HCV antibodies. HIV status was determined by a composite of HIV serology (HIV antibody and RNA testing) and HIV antiretroviral medication usage. Factors associated with overall and liver-related mortality were assessed by Cox Proportional Hazards Analysis. For the Cox proportional hazards analysis, HIV

was taken to be a time dependent covariate with the using the midpoint in time between positive and negative tests in seroconvertors, and the date of the first positive test for those who had no previous negative tests. Given that no liver related deaths occurred when a participants HCV status was unknown, HCV was examined using the person's last known status and was not time dependent. Multivariable Cox proportional hazards regression was preformed, with all covariates entered into the model initially, and subject to backwards elimination. Covariates were sequentially eliminated subjected to a likelihood ratio test, with the covariate with the largest likelihood ratio test p-value eliminated at each step, until all covariates had reached statistical significance. Statistically significant differences were assessed at $p < 0.05$; p-values are two-sided.

RESULTS

Participant characteristics

Between 1991 and 2007, 2,332 participants received testing for HCV antibodies. Compared to participants not having received testing for HCV antibodies (n=581), those having received testing for HCV antibodies were younger (mean age 42.0 vs. 44.4, $P<0.001$), more often female (31% vs. 23%, $P<0.001$), of Aboriginal ethnicity (32% vs. 26%, $P=0.009$), had received methadone maintenance treatment in the 6 months prior to their interview (22% vs. 7%, $P<0.001$), reported having a regular doctor (68% vs. 60%, $P<0.001$), were HIV positive (21% vs. 6%, $P<0.001$) and had used illicit non-injection (81% vs. 66%, $P<0.001$) or injection drugs (42% vs. 22%, $P<0.001$) in the 6 months prior to their interview. There were no differences with respect to unstable housing (61% vs. 63%, $P=0.41$) or those reporting usually or always having access to healthcare (83% vs. 81%, $P=0.31$), respectively.

The characteristics of participants having received testing for HCV antibodies stratified by HCV antibody status are shown in Table 1. Among this group with HCV testing results, 21% (485 of 2,332) were infected with HIV and 64% (1,495 of 2,332) were HCV antibody-positive. Compared to those who were HCV antibody-negative, HCV antibody-positive participants were more often female ($P=0.002$), lived in unstable housing ($P<0.001$), had received methadone maintenance treatment in the 6 months prior to their interview ($P<0.001$), reported having a regular doctor ($P<0.001$) and had used illicit non-injection ($P<0.001$) or injection drugs ($P<0.001$) in the 6 months prior to their interview. There were no differences in the mean age ($P=0.386$), Aboriginal ethnicity ($P=0.134$) or those reporting usually or always having access to healthcare ($P=0.523$) between HCV antibody-positive and negative participants, respectively.

Overall and cause-specific mortality

Between January 2003 and December 2007, 180 deaths were observed over 9,365 person-years (py) of follow-up for an overall mortality rate of 192 per 10,000 py (95% CI: 165, 222). In HCV antibody positive participants (n=1,495), 134 deaths were observed (mortality rate: 224 per 10,000 py; 95% CI: 187, 265) and the mean age at the time of death was 44.6 years. Among HCV antibody negative participants (n=837), 46 deaths were observed (mortality rate: 137 per 10,000 py; 95% CI: 100, 182) and the mean age at the time of death in was 49.5 years. HCV antibody-positive participants demonstrated a statistically significant younger mean age at the time of death when compared to HCV antibody-negative participants (44.6 vs. 49.5 years, $P=0.002$).

The causes of death according to ICD-10 code by HCV antibody status are shown in Table 2. Among HCV positive participants, the major causes of death included those due to infection (n=41, 31%), external causes (n=31, 23%), other causes (n=19, 14%) and respiratory system (n=14, 10%). Among HCV negative participants, the major causes of death included those due to neoplasms (n=12, 26%), respiratory system (n=7, 15%), external causes (n=7, 15%) and circulatory system (n=6, 13%).

HIV-, drug- and liver-related deaths by antibody status are shown in Table 2. Among HCV positive participants, deaths were HIV-related in 26% (mortality rate: 58 per 10,000 py; CI: 41, 81), drug-related in 22% (mortality rate: 48 per 10,000 p-y; CI: 32, 69), liver-related in 8% (mortality rate: 18 per 10,000 p-y; CI: 9, 33) and other causes in 44% (mortality rate: 98 per

10,000 p-y; CI: 75, 127). Among HCV antibody positive participants, liver-related deaths (n=11) included viral hepatitis (n=5), liver cancer (n=2), alcoholic liver disease (n=3) and non-alcoholic liver disease (n=1). Among HCV negative participants, deaths were HIV-related in 4% (mortality rate: 6 per 10,000 p-y; CI: 1, 21), drug-related in 15% (mortality rate: 21 per 10,000 p-y; CI: 8, 43), liver-related in 2% (mortality rate: 3 per 10,000 p-y; CI: 0, 17), and other causes in 78% (mortality rate: 107 per 10,000 p-y; CI: 75, 148).

The incidence of drug-, HIV-, liver- and other cause-related deaths in the inner city of Vancouver stratified by age is shown in Figure 1 and Table 3.

Factors associated with overall and liver-related mortality

Factors associated with overall mortality in univariate analysis included age >50 years, injection drug use, HIV positive status, HIV unknown status and HCV antibody positive status (Table 4). However, in Cox Proportional Hazards analysis, age >50 years [adjusted hazard ratio (AHR) 2.80; 95% CI 1.93, 4.07; $P<0.001$] and HIV positive status (AHR 3.81; 95% CI 2.72, 5.34; $P<0.001$) were associated with overall mortality. Positive HCV antibody status was not associated with all cause mortality, when adjusting for age and HIV status (AHR 1.19; 95% CI 0.83, 1.72; $P=0.35$).

Factors associated with liver-related mortality in adjusted Cox Proportional Hazards analysis were HCV infection (AHR 7.69; 95% CI 0.99, 59.98; $P=0.052$) and age >50 years (AHR 18.49 vs. <40 years (referent); 95% CI 2.27, 150.41; $P<0.001$; age 40-50 AHR 3.79 vs. <40 years (referent); 95% CI 0.42, 33.91; $P=0.234$).

DISCUSSION

We have demonstrated several important findings with respect to the impact of HCV on mortality in this large community-based cohort of inner city residents tested for HCV antibodies in Vancouver, consisting primarily of illicit drug users. First, we observed a high rate of mortality, despite a high proportion reporting good health care access, including access to a regular doctor. Second, we have demonstrated that HIV infection continues to drive the high rate of mortality in this population, while HCV infection drives mortality rates related to liver disease. Third, among those that died, the causes of death differed between HCV positive and negative individuals, with the former dying more often of HIV-, drug- and liver-related causes. Lastly, among HCV positive inner city residents <50 years of age the major causes of death were due to HIV and drug-related causes, but liver-related mortality also became a major cause of mortality among participants >50 years of age.

The crude overall mortality rate in this cohort of inner-city residents tested for HCV infection (192 per 10,000 py) was extremely high at approximately four times the age-standardized mortality for the Province of British Columbia (50 per 10,000 py) (29). Further, the mortality rate observed in this study was higher than the weighted average all-cause mortality rate [136 per 10,000 py (95% CI; 105, 167)] in a large systematic review of all cause mortality among IDU cohorts (22). This is despite the fact that this represents a community-based cohort of inner city residents receiving testing for HCV antibodies (only 42% reported recent injecting) and that a high proportion reported good health access and a regular doctor. Further, this occurred in a setting where many of the barriers to health access are removed given that healthcare in the Province of British Columbia (including treatment for HIV infection) is government subsidized.

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The mean age at the time of death was five years younger among HCV positive participants (45 years) than HCV negative participants (50 years). The young age at the time of death in both HCV negative and positive inner city residents in this cohort is a striking finding, given that the mean age at the time of death in British Columbia over the same period was 73 years of age (29).

In multivariate analyses, HCV was not statistically associated with excess mortality. HIV infection and age >50 years were the primary factors associated with an increased risk of overall mortality. The impact of HIV infection on mortality was expected and is consistent with studies among injection drug users (23, 24, 26, 27). The absence of an effect of HCV on all cause mortality is consistent with post-transfusion cohorts (7, 8, 11), veterans with community-acquired HCV infection (10) and a hospital-based cohort of IDUs (24). However, several large community-based studies in the United Kingdom (6) and Australia (13) have demonstrated excess mortality attributed to HCV. Given the young age of the CHASE cohort (mean age was 42 years) and the decades required for the progression of advanced liver disease, longer term follow-up may be required in order to observe an effect of HCV on overall mortality in our cohort. Further, HIV infection and illicit drug use may be altering the natural history of HCV in this cohort of inner city residents.

HCV infection was associated with an increased risk of liver-related mortality. This finding is consistent with a number of studies of post-transfusion cohorts (7, 8, 11), veterans with community-acquired HCV infection (10), IDU-based cohorts (23, 24), community-based cohorts (6) and community-based linkage studies (13, 14).

Among those who died, HCV positive participants more often died of HIV-related (26%), drug-related (22%) and liver-related (8%) causes. Our results are consistent with data from cohorts in Australia and the Netherlands demonstrating that the proportions of deaths attributable to HIV-, drug- and liver-related causes are higher among HCV antibody positive drug users when compared to HCV negative drug users (9, 23). The proportion of deaths attributable to these causes is also consistent with a study of the natural history of HCV among HCV antibody-positive IDUs (15). Among HCV antibody-positive illicit drug users in these studies (9, 15, 23), deaths attributed to HIV-related, drug-related and liver-related causes ranged from 29-40%, 19-28% and 0-9%, respectively.

HIV- and drug-related causes of mortality were the major causes of death in age groups <50 years, but liver-related mortality became a competing cause of mortality among those >50 years of age. These data are consistent with two large, community-based linkage studies in New South Wales, Australia (13) and Scotland (14). This reflects the fact that at younger ages, HCV positive illicit drug users are dying of causes other than HCV. However, participants who live beyond 50 years of age are at significant risk of liver-related mortality, and are likely at lower risk for death due to causes more common among younger participants (e.g., overdose). It will be important to continue the surveillance of cohorts of HCV-infected IDUs and watch this population as IDUs infected in the 1970s and 1980s continue to age. This also may be an important group to follow clinically and it will be particularly important to assess IDUs >50 years of age for more advanced liver disease.

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There are several strengths of the CHASE study that permit an evaluation of mortality. The health service database linkage system in place in British Columbia is unique, allowing for long-term retrospective and prospective monitoring of longitudinal health service outcomes through data linkages of a highly marginalized group of inner city residents having received testing for HCV infection in Vancouver. This is important because the study did not rely on self-reported outcomes. Also, this study was specifically designed to evaluate health service utilization and health outcomes in this community, with mortality being an a priori primary endpoint for this study.

This study also has several limitations. First, given this is an observational cohort, no conclusions about causality can be made. Second, socio-demographic and select behavioural risk data was only collected at baseline. Thus, we were unable to determine the impact of changing behavioural characteristics on all-cause mortality for the study period (e.g. ongoing injection drug use). Third, not all participants with HCV antibody testing were tested for HCV RNA and therefore this study did not account for participants who may have spontaneously cleared their HCV infection or those who were among the few who accessed HCV treatment during this period of observation (30). Fourth, we could not determine the actual year that the infection occurred, and the associations found between HCV and mortality would be expected to strengthen as the cohort is followed longer.

Given the significant burden of disease in this population, strategies are needed to enhance HCV assessment and treatment for those at greatest risk of disease progression. Multidisciplinary clinics offering such services need to educate patients about the risks of liver-related morbidity

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3 and mortality and the availability of treatment, while increasing capacity for HCV assessment
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5 and treatment, particularly among those at greatest risk for disease progression. A coordinated
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7 approach will be required if we are to reduce HCV-related morbidity among IDUs and reduce the
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9 future burden of HCV infection.
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15 Our study demonstrates a high rate of mortality among inner city residents receiving testing for
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17 HCV antibodies associated with a range of competing risk factors including HIV infection.
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19 Although liver disease was not found to be one of the leading causes of overall mortality in this
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21 study, liver-related mortality was associated with HCV infection especially in those over 50 years
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23 old. These findings have important public health implications and this population will need to be
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25 closely followed over the next decade as ageing cohorts of IDUs infected with HCV in the 1970s
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27 and 1980s will be at heightened risk for liver-related mortality.
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Table 1. Characteristics of participants having received HCV antibody testing up to 2007 in a large, community based cohort in the inner city of Vancouver (n=2,332)

Characteristics	Overall (n=2,332) n (%)	HCV antibody positive (n=1,495) n (%)	HCV antibody negative (n=837) n (%)
Mean age (SD)	42.0 (9.2)	41.9 (8.3)	42.2 (10.7)
Male sex	1619 (69%)	1005 (67%)	614 (74%)
Aboriginal ethnicity	743 (32%)	493 (33%)	250 (30%)
Unstable housing	1433 (61%)	959 (64%)	474 (57%)
Methadone maintenance therapy*	521 (22%)	489 (33%)	32 (4%)
Usually/always has health access	1942 (83%)	1251 (84%)	691 (83%)
Have a regular doctor	1580 (68%)	1059 (71%)	521 (62%)
Illicit drug use*	1880 (81%)	1305 (87%)	575 (69%)
Injection drug use*	988 (42%)	879 (59%)	109 (13%)
Alcohol use*			
None	1160 (50%)	811 (54%)	349 (42%)
1-5 drinks per day	368 (16%)	222 (15%)	146 (17%)
≥5 drinks per day	804 (34%)	462 (31%)	342 (41%)
HIV infection			
Yes	485 (21%)	452 (30%)	33 (4%)
No	1530 (66%)	892 (60%)	638 (76%)
Unknown	317 (14%)	151 (10%)	166 (20%)

*in the six months prior to the participant's interview

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Table 2. Causes of death stratified by HCV antibody status among 2,332 inner city residents having received HCV antibody testing in Vancouver (2003-2007).

ICD-10		Overall (n=2332)	%	Mortality rate, per 10000 py	(95% CI)	HCV antibody positive (n=1495)	%	Mortality rate, per 10000 py	(95% CI)	HCV antibody negative (n=837)	%	Mortality rate, per 10000 py	(95% CI)
Person-years		9365				5995				3370			
Deaths due to all causes		180		192	165, 222	134		224	187, 265	46		137	100, 182
A00-B99	Infection	44	24%	47	34, 63	41	31%	68	49, 93	3	7%	9	2, 26
C00-D48	Neoplasms	19	11%	20	12, 32	7	5%	12	5, 24	12	26%	36	18, 62
E00-E90	Endocrine	2	1%	2	0.3, 8	0	0%	0	.	2	4%	6	1, 21
F00-F99	Mental and behavioural	6	3%	6	2, 14	5	4%	8	3, 19	1	2%	3	0.1, 17
G00-G99	Nervous system	4	2%	4	1, 11	2	1%	3	0.4, 12	2	4%	6	1, 21
I00-I99	Circulatory system	13	7%	14	7, 24	7	5%	12	5, 24	6	13%	18	7, 39
J00-J99	Respiratory system	21	12%	22	14, 34	14	10%	23	13, 39	7	15%	21	8, 43
K00-K93	Digestive system	10	6%	11	5, 20	8	6%	13	6, 26	2	4%	6	1, 21
R00-R99*	Other	23	13%	25	16, 37	19	14%	32	19, 49	4	9%	12	3, 30
V00-Y98	External	38	21%	41	29, 56	31	23%	52	35, 73	7	15%	21	8, 43
B20-B24	HIV-related	37	21%	40	28, 54	35	26%	58	41, 81	2	4%	6	1, 21
	Drug-related†	36	20%	38	27, 53	29	22%	48	32, 69	7	15%	21	8, 43
	Liver-related	12	7%	13	7, 22	11	8%	18	9, 33	1	2%	3	0.1, 17
B15-B19	Viral hepatitis	5	3%	5	2, 12	5	4%	8	3, 19	0	0%	0	.
C22	Liver cancer	2	1%	2	0, 8	2	1%	3	0.4, 12	0	0%	0	.
K70	Alcoholic liver disease	4	2%	4	1, 11	3	2%	5	1, 15	1	2%	3	0.1, 17
K71-K77	Non-alcoholic liver disease	1	1%	1	0.0, 6	1	1%	2	0.0, 9	0	0%	0	.
Other causes‡		95	53%	101	82, 124	59	44%	98	75, 127	36	78%	107	75, 148

*Includes unknown causes of death. †Drug related deaths included mental and behavioural disorders due to psychoactive substance use (F11-16, F19), accidental poisoning by drugs (X40-44), suicide by drugs (X60-64), assault by drugs and medicaments (X85), poisoning by drugs or medicaments undetermined if accidental or intentional (Y10-14) and adverse effects of drugs and medicaments (Y40-574, Y577-79, Y598, Y880), ‡all causes that were other than HIV-, drug- or liver-related causes of death.

Table 3. Incidence of drug-, HIV-, liver- and other cause-related deaths among 2,332 inner city residents having received HCV antibody testing in Vancouver (2003-2007) stratified by age and HCV antibody status at most recent testing.

	py	Deaths	Mortality rate, per 10000 py	(95% CI)	HIV- related deaths	HIV- related mortality rate, per 10000 py	(95% CI)	Drug- related deaths	Drug- related mortality rate, per 10000 py	(95% CI)	Liver- related deaths	Liver- related mortality rate, per 10000 py	(95% CI)	Other causes of death	Other- cause mortality rate, per 10000 py	(95% CI)
Overall																
Age (years)																
<40	3928	56	143	108, 185	15	38	21, 63	15	38	21, 63	1	3	0.1, 14	25	64	41, 94
40-50	3773	67	178	138, 225	17	45	26, 72	13	34	18, 59	4	11	3, 27	33	87	60, 123
>50	1663	57	343	260, 444	5	30	10, 70	8	48	21, 95	7	42	17, 87	37	222	157, 307
HCV antibody positive																
Age (years)																
<40	2461	45	183	133, 245	14	57	31, 95	12	49	25, 85	1	4	0.1, 23	18	73	43, 116
40-50	2637	57	216	164, 280	16	61	35, 99	12	46	24, 79	4	15	4, 39	25	95	61, 140
>50	896	32	357	244, 504	5	56	18, 130	5	56	18, 130	6	67	25, 146	16	179	102, 290
HCV antibody negative																
Age (years)																
<40	1467	11	75	37, 134	1	7	0.2, 38	3	20	4, 60	0	0	.	7	48	19, 98
40-50	1136	10	88	42, 162	1	9	0.2, 49	1	9	0.2, 49	0	0	.	8	70	30, 139
>50	767	25	326	211, 481	0	0	.	3	39	8, 114	1	13	0.3, 73	21	274	169, 419

Table 4. Cox proportional hazards analysis of factors associated with mortality among 2,332 inner city residents having received HCV antibody testing in Vancouver (2003-2007)

Variable	py	Deaths	Unadjusted hazard ratio (95% CI)	P-value	Adjusted hazard ratio (95% CI)	P-value
Age						
<40	3928	56	1	-	-	-
40-50	3773	67	1.24 (0.87, 1.77)	0.23	1.30 (0.91, 1.85)	0.15
>50	1663	57	2.41 (1.67, 3.49)	<0.001	2.80 (1.93, 4.07)	<0.001
Sex						
Male	6522	126	1	-	-	-
Female	2843	54	0.99 (0.72, 1.36)	0.94	-	-
Ethnicity						
Other	6398	119	1	-	-	-
Aboriginal ethnicity	2967	61	1.11 (0.81, 1.51)	0.52	-	-
Housing						
Stable	3566	77	1	-	-	-
Unstable	5792	103	0.83 (0.62, 1.11)	0.20	-	-
Methadone maintenance therapy (in the previous 6 months)						
No	7265	130	1	-	-	-
Yes	2099	50	1.34 (0.96, 1.85)	0.082	-	-
Illicit drug use (in previous 6 months)						
No	1807	43	1	-	-	-
Yes	7557	137	0.77 (0.54, 1.08)	0.13	-	-
Injection drug use (in previous 6 months)						
No	5417	89	1	-	-	-
Yes	3948	91	1.40 (1.05, 1.88)	0.023	-	-
Alcohol consumption (in previous 6 months)						
None	4646	95	1	-	-	-
1-5 drinks per day	1456	32	1.08 (0.72, 1.61)	0.72	-	-
≥5 drinks per day	3263	53	0.79 (0.57, 1.11)	0.18	-	-
HIV status						
Negative	6250	74	1	-	1	-
Positive	1857	80	3.67 (2.68, 5.04)	<0.001	3.81 (2.72, 5.34)	<0.001
Unknown	1258	26	1.74 (1.11, 2.72)	0.015	1.53 (0.98, 2.40)	0.062
HCV status						
Negative	3370	46	1	-	1	-
Positive	5995	134	1.65 (1.18, 2.30)	0.004	1.19 (0.83, 1.72)	0.35

py, person-years observation.

Figure 1. Incidence of drug-, HIV-, liver- and other cause-related deaths among 2,332 inner city residents having received HCV antibody testing in Vancouver (2003-2007) by age strata.