

1
2
3
4
5
6
7
8
9

Mortality in a large community-based cohort of inner city residents in Vancouver, Canada

10 Deans GD¹, Raffa JD², Lai C³, Fischer B⁴, Krajden M⁵, Amin J⁶, Walter S⁷, Dore GJ⁶,
11
12 Grebely J^{6*} and Tyndall MW^{8*}
13
14
15

16
17 1) Division of Infectious Diseases, Department of Medicine, University of British Columbia, Vancouver,
18
19 British Columbia, Canada; 2) Department of Statistics and Actuarial Science, University of Waterloo,
20
21 Waterloo, Ontario, Canada; 3) British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital,
22
23 Vancouver, British Columbia, Canada; 4) Centre for Applied Research in Mental Health and Addiction,
24
25 Faculty of Health Sciences, Simon Fraser University, Burnaby, British Columbia, Canada; 5) British
26
27 Columbia Centre for Disease Control, Vancouver, British Columbia, Canada; 6) The Kirby Institute for
28
29 Infection and Immunity in Society, The University of New South Wales, Sydney, New South Wales,
30
31 Australia; 7) Centre for Health Systems and Safety Research, Australian Institute of Health Innovation,
32
33 The University of New South Wales, Sydney, New South Wales, Australia; 8) Division of Infectious
34
35 Diseases, Department of Medicine, University of Ottawa, Ontario, Canada
36
37
38

39
40 *contributed equally to this work
41
42
43
44
45

46
47 **Author Contributions:** Authors CL and MWT designed the original study and wrote the protocol. Authors
48
49 GDD, JDR, JG and MWT designed the mortality sub-study. Authors GDD, JDR and JG drafted the primary
50
51 statistical analysis plan, which was reviewed by CL, BF, MK, JA, SW and GJD. The primary statistical
52
53 analysis was conducted by GDD and reviewed by JG, JDR, MWT, CL, BF, MK, JA, SW and GJD. All authors
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

reviewed data analysis. Author GDD wrote the first draft of the manuscript. All authors contributed to
and have approved the final manuscript.

Confidential

Abstract

Background: The Downtown Eastside of Vancouver, Canada is an inner-city neighbourhood with a high prevalence of injection drug use. This study evaluated mortality rates and excess mortality among the broader community of individuals in this inner city neighbourhood.

Methods: The Community Health and Safety Evaluation is a community-based study of inner city residents recruited in the Downtown Eastside of Vancouver, Canada. Participants were followed retrospectively and prospectively through linkages with provincial virology and mortality databases. Mortality rates and standardized mortality ratios (SMRs) were calculated compared to mortality rates from Vancouver.

Results: Among 2,913 participants, 374 deaths occurred for an all-cause mortality rate of 223 per 10,000 person-years (95% CI 201–247). A high excess risk of mortality was evident overall with an SMR of 7.1 (95% CI 6.4–7.9). Women had greater excess mortality than men with an SMR of 15.4 (95% CI 12.8–18.5) compared to 5.8 (95% CI 5.1–6.6) among men. While crude mortality increased with age, excess mortality was greatest among participants <35 years and those 35–39 years, with SMRs of 13.2 (95% CI 9.4–18.5) and 13.3 (95% CI 10.3–17.1), respectively. Excess risk was also elevated among those with HCV, HIV, and HCV-HIV infection, with SMRs of 5.9 (95% CI 4.9–7.1), 19.2 (12.8–28.9), and 23.0 (19.3–27.4), respectively.

Interpretation: This study demonstrates very high mortality in this inner city population, particularly when compared to the general population. Excess mortality was greater among women, younger participants, and those infected with HCV and/or HIV.

Introduction

The Downtown Eastside (DTES) of Vancouver, Canada is an inner city neighbourhood of more than 16,000 people, including an estimated 4,700 injection drug users (IDUs)^{1,2}. Rising rates of fatal drug overdose and extremely high rates of HIV transmission in the DTES prompted the declaration of a public health emergency in 1997^{3,4}. Since that time, despite intensive study, improvements in social services, and the implementation of several effective public health interventions^{5,6}, the impact on health outcomes and overall mortality at a community level is uncertain. Surveillance of mortality among inner city populations is crucial to document disease trends and implement interventions that can have the biggest health impact.

Previous studies among IDUs in Vancouver's DTES have found that mortality remained high from 1996 to 2005 at approximately 300 deaths per 10,000 person-years⁷, despite evidence of decreased drug-related deaths over the same time period^{8,9}. The most common causes of death among inner city IDUs include drug overdose, liver failure, and complications of HIV¹⁰. Excess mortality among DTES residents when compared to the general population has also been observed^{2,11,12}.

Most studies of mortality in the DTES have examined cohorts of IDUs,^{2,7,10,11} which may not be representative of the broader community. Studies examining excess mortality have largely focused on all-cause mortality among specific populations such as women¹¹ and young IDUs² or have included surrounding neighbourhoods with higher socioeconomic status¹². This study was conducted to evaluate mortality rates and excess mortality for all-cause and cause-specific deaths among inner city residents in Vancouver from 2003 to 2009.

Methods

Study Population

The Community Health and Safety Evaluation (CHASE) cohort was designed to evaluate the uptake of health services and health outcomes in Vancouver's DTES. To collect a representative sample of residents in this community, venues for recruitment were selected based on census tract data. 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 their names and personal health numbers verified through the British Columbia Ministry of Health database to facilitate linkage with virology test results and health indicator databases.

Between January 2003 and December 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 test results, treatment records, and health-related information accessed through data linkages using their name, date of birth, and/or personal health number. Study participants received CDN \$10 to complete the survey. This study was approved by the University of British Columbia/Providence Health Care Research Ethics Board.

Data Collection

Participants were followed retrospectively and prospectively through health-related database linkages. HCV and HIV antibody testing results from 1991 to 2009 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 virology testing in the province.

For all deaths among participants from 2003 (the first year of study recruitment) to 2009, the underlying causes of death 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*, 10th edition (ICD-10). Causes of death were grouped according to ICD-10 chapter headings as well as into drug-related, HIV-related and liver-related causes. Drug-related deaths comprised 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). HIV-related deaths were defined as any ICD-10 of HIV (B20-24), while liver-related deaths comprised those due to viral hepatitis (B15-19), liver cancer (C22), alcoholic liver disease (K70) and non-alcoholic liver disease (K71-77).

Statistical Analysis

Causes of mortality from January 2003 to December 2009 were examined among the overall study population and stratified based on HCV and HIV testing results. Mortality incidence rates were computed using person-time methods. Person-years at risk were calculated for each participant as the

1
2
3 time from the date of questionnaire administration until the first of either the date of death or
4
5 December 31, 2009.
6
7
8
9
10

11 Standardized mortality ratios (SMRs) were calculated to compare death rates in the study population to
12 rates in the population of the Health Service Delivery Area of Vancouver for each cause of death. SMRs
13 were adjusted for sex, 5-year age group, and calendar year of death, with the latter two treated as time-
14 varying. Participants with missing date of birth data (n=7, 0.2%) were excluded from SMR analyses.
15
16 Confidence intervals for incidence rates and SMRs were calculated using the Poisson exact method.
17
18 Trends in rates from 2003 to 2009 were examined using Poisson regression. Statistically significant
19 differences were assessed at $P < 0.05$; P-values are two-sided. Statistical analyses were performed using
20
21 R v2.15 (Vienna, Austria) and STATA v10.1 (College Station, TX, United States).
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Results

Participant Characteristics

A total of 2,913 residents of inner city Vancouver were recruited into the CHASE cohort from 2003-2004. Table 1 shows the cohort characteristics. The mean age was 42.5 years and 29% (n=845) were female. Among participants with available test results during the linkage period (1991-2009), the prevalence of HCV, HIV, and HCV-HIV co-infection was 64% (1,533 of 2,405), 24% (535 of 2,270), and 22%, respectively. Injection or non-injection drug use in the six months prior to survey was reported by 80% (n=2,337). Cohort characteristics stratified by HIV and HCV status are shown in Supplementary Table 1.

Between January 2003 and December 2009, 374 deaths (13% of participants) were reported over 16,778 person-years of observation (Table 2), for an all-cause mortality rate of 223 per 10,000 person-years (95% confidence interval [CI] 201–247). Among those with HCV, HIV, HCV/HIV, and neither HCV nor HIV, the mortality rates were 167 (95% CI 138–203), 641 (95% CI 426–964), 515 (95% CI 432–613) and 107 (95% CI 79–143) per 10,000 person-years, respectively (Table 3). Compared to the population of Vancouver, significant excess mortality was evident overall with an SMR of 7.1 (95% CI 6.4–7.9, Table 2). Significantly higher excess risk was observed in those with HCV (SMR 5.9; 95% CI 4.9–7.1), HIV (SMR 19.2; 95% CI 12.8–28.9), and HCV/HIV (SMR 23.0; 19.3–27.4) compared to those without HCV or HIV (SMR 3.5; 95% CI 2.6–4.7, Table 3).

Causes of death by ICD-10 chapter heading for the overall study population and stratified by HCV and HIV status are shown in Tables 2 and 3, respectively (corresponding data for participants with incomplete testing are in Supplementary Table 2). Overall, the most common causes of death were

1
2
3 infection (26%, n=97), external causes (17%, n=62), respiratory disease (12%, n=44), and neoplasm (11%,
4 n=42). Infection and external causes were also common causes of death among participants with HCV,
5 HIV, and HCV/HIV infection. Infection-related deaths were predominantly related to HIV/AIDS (80%,
6 n=78). Excess mortality due to respiratory deaths was related chiefly to pneumonia (49%, n=22) and
7 chronic lower respiratory diseases (31%, n=15). The highest cause-specific SMRs overall were other
8 causes, infection, respiratory disease, and mental and behavioural; the same four causes accounted for
9 much of the greatest excess risk among the HCV-, HIV-, and HCV/HIV-infected as well. Deaths classified
10 as "other causes" included the ICD-10 code for "other ill-defined and unspecified causes of mortality"
11 (n=34) and deaths with missing data regarding cause of death (n=6).
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27

28 Mortality rates and excess mortality related to drug use, liver disease, and HIV/AIDS are shown in Tables
29 4 and 5. Fourteen percent of deaths were drug-related (n=53). The overall drug-related mortality rate
30 was 32 per 10,000 person-years (95% CI 24–41), representing a considerable excess risk of drug-related
31 mortality (SMR 12.0; 95% CI 9.1–15.7). Among those with HCV, HIV and HCV/HIV, the rates of drug-
32 related mortality were high at 35 (95% CI 23–53), 56 (95% CI 14–223), and 86 (95% CI 56–132) per
33 10,000 person-years, respectively. The excess risk of drug-related mortality was significantly elevated in
34 those with HCV-, HIV- and HCV/HIV-infection, with SMRs of 12.6 (95% CI 8.3–19.1), 23.1 (95% CI 5.8–
35 92.3), and 33.7 (95% CI 22.0–51.7), respectively.
36
37
38
39
40
41
42
43
44
45
46
47
48
49

50 Liver-related mortality accounted for 22 deaths with the HCV and HCV/HIV strata accounting for 13 and
51 5 respectively [4 deaths occurred among those with incomplete testing data (Supplementary Table 3)].
52 These deaths were attributed to viral hepatitis (n=9), alcoholic liver disease (n=7), non-alcoholic liver
53
54
55
56
57
58
59
60

1
2
3 disease (n=3), and hepatocellular carcinoma (n=3). Liver-related SMRs were 5.9, 9.6, and 12.1 in the
4
5 overall, HCV-infected and HCV/HIV-infected groups, respectively.
6
7
8
9

10
11 The rate of HIV-related mortality per 10,000 person-years was 46 (95% CI 37–58) overall, 362 (95% CI
12
13 210–624) in those with HIV alone and 262 (95% CI 205–334) among those with HCV/HIV-infection.
14
15 Excess HIV-related mortality was markedly elevated overall and in the HIV- and HCV/HIV-infected groups
16
17 with SMRs of 24.9 (95% CI 20.0–31.1), 199.8 (95% CI 116.0–344.1), and 142.8 (95% CI 111.8–182.5),
18
19 respectively.
20
21
22
23
24
25
26

27 Women in the cohort had very similar rates of mortality compared to men (Table 4). However, women
28
29 had significantly greater excess mortality than men for all causes (SMR 15.4 [95% CI 12.8–18.5] vs. 5.8
30
31 [95% CI 5.1–6.6]) and for drug-, liver-, and HIV-related deaths (Table 4).
32
33
34
35
36
37

38 While crude mortality increased with age, excess mortality was greatest among participants <35 and
39
40 those between 35 and 39, with SMRs of 13.2 (95% CI 9.4–18.5) and 13.3 (95% CI 10.3–17.1) respectively;
41
42 participants aged 45 to 49 years and those ≥ 50 had SMRs of 6.0 (4.7–7.6) and 5.3 (4.5–6.3)
43
44 (Supplementary Table 4). Liver-related mortality trended upwards with age, but was associated with a
45
46 relatively stable excess risk across age groups (Figure 1). In contrast, drug-related deaths and excess
47
48 mortality tended to peak at age 35 to 39 years. HIV-related mortality rates were greatest among 45 to
49
50 49-year-olds with a secondary peak at age 35 to 39, while HIV-related SMRs trended downward overall
51
52 with age.
53
54
55
56
57
58
59
60

1
2
3 The annual rates of mortality over the period from 2003 to 2009 did not show a significant linear trend
4
5 (Figure 2; $P=0.57$). Numeric fluctuation in the all-cause and HIV-related death rates from 2003 to 2004
6
7 occurred during enrolment, when participant numbers were lower, resulting in wider 95% confidence
8
9 intervals.
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Confidential

Interpretation

This large study of inner city residents in Vancouver, Canada, demonstrates several important findings.

Very high mortality, particularly when compared to the general population standardized by age, sex, and year of death, was evident for all-cause and cause-specific mortality. Excess mortality was greater among women, among participants infected with HCV and/or HIV, and among younger individuals.

Major causes of death included HIV, drug-related deaths and unknown causes.

The all-cause mortality rate was very high (223 per 10,000 person-years) and associated with considerable excess mortality compared to the general population (SMR 7.1). This is much greater than the SMR of 1.2 reported by the British Columbia Vital Statistics Agency for the local health area that contains the DTES,¹² likely because the latter includes wealthier neighbourhoods outside the inner city that decrease the observed mortality rates. The SMR observed in this study of inner city residents is closer in magnitude to those of exclusively IDU populations. Previous studies of mortality among IDUs observed SMRs in the range of 10 to 15^{13,14}, while excess mortality among users of opiates and opioid substitution therapy has been in the range of 5 to 13¹⁵⁻¹⁷.

Most of the causes of death associated with the greatest excess mortality, including infection, other causes, and mental and behavioural, were consistent with major causes of death identified in other studies^{14,15,18-23}. Of note was the elevated excess respiratory mortality (primarily due to pneumonia). A study among problem drug users entering treatment in Rome, Italy found a similar SMR of 10.2 for respiratory death²³. This is consistent with the observation that pneumonia is a significant cause of morbidity and hospitalization among IDUs²⁴⁻²⁶.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

The very high rate of drug-related death and considerable excess drug-related mortality is consistent with prior findings among IDUs in Vancouver¹⁰ and other populations of drug users^{13,15,23,27,28}. Liver-related mortality, which accounted for 6% of deaths, was associated with an SMR of 5.9. Comparatively greater SMRs were obtained in studies among persons on opioid substitution therapy (SMR 17.0)¹⁶ and among HBV and HCV-infected individuals (SMRs 10.0 and 15.8, respectively)²⁹. Population differences such as age, proportion with viral hepatitis infection, and pattern of alcohol use may account for such differences in risk. Mortality related to HIV/AIDS was associated with very high rates and SMRs, particularly among participants known to be HIV-infected, among whom 77 of 149 deaths (52%) were HIV-related. In studies of IDUs, deaths due to HIV and AIDS accounted for 34 to 38 percent of deaths among HIV-infected persons^{10,14}.

Sex differences were evident in the all-cause mortality results; while men and women had very similar rates of death (220 and 230 per 10,000 person-years, respectively), women had significantly greater excess mortality with an SMR of 15.4 (95% CI 12.8–18.5) compared to 5.8 (95% CI 5.1–6.6) for men. SMRs for specific causes of death followed similar patterns, with women having greater excess mortality than men for drug-, liver-, and HIV-related deaths. In a meta-analysis of mortality among opioid users, men had higher crude mortality rates than women but women had greater SMRs¹⁸. A similar pattern in the SMRs for all-cause mortality has been observed in a cohort of Vancouver IDUs^{2,11}. The greater excess mortality among women likely reflects the fact that women in the general population tend to have lower mortality rates than men for many major causes of death.

1
2
3 The increase in crude mortality rate from the youngest age group to the oldest is consistent with
4 expected increases in diseases of aging including malignancy and cardiovascular disease. The lower
5
6 excess mortality among older participants could be explained by concurrent increases in these age-
7
8 related conditions in the general population and by survivorship bias. Liver-related mortality trended
9
10 upward with age, which has been observed previously in the HCV-infected subset of this cohort³⁰.
11
12 Among younger inner city residents, liver-related death contributed minimally to mortality while among
13
14 persons aged 50 years or older, liver-related causes of death were similar in rate to drug- and HIV-
15
16 related causes.
17
18
19
20

21
22
23
24
25
26 This study has several limitations. This is an observational cohort and no conclusions should be drawn
27
28 with regard to causality given the possibility of unmeasured confounding variables. Data regarding HCV
29
30 and HIV infection in this cohort are derived from tests ordered for clinical indications as systematic
31
32 testing was not performed; HCV results were unknown in 17% and HIV results in 22%, but those with
33
34 unknown testing had similar demographic characteristics and mortality rates as those who were
35
36 uninfected with HCV and HIV. Linked HCV test results did not always include HCV RNA results and
37
38 spontaneous clearance may have occurred among some of those presumed HCV-infected, leading to an
39
40 underestimation of the observed overall effect of HCV infection on mortality. While the linked mortality
41
42 records capture all deaths reported within the province of British Columbia, any deaths that went
43
44 unreported or occurred in other jurisdictions would lead to an overestimation of person-years of follow-
45
46 up and an underestimation of mortality.
47
48
49
50

51
52
53
54
55 The significant excess mortality and the leading causes of death observed in this study confirm the need
56
57 for comprehensive, multidisciplinary services to support this high risk population and optimize health
58
59
60

1
2
3 outcomes, particularly among youth and women. Screening, follow-up, and appropriate treatment for
4
5 HIV and HCV infection are clearly important tools to reduce the risk of HIV-related mortality and
6
7 transmission and to prevent HCV-related health sequelae. Measures including mental health care,
8
9 improved access to housing, and harm reduction services are also important to address the drug-related
10
11 deaths. Every health system interaction must be used as an opportunity to engage members of this
12
13 population, including women and youth, into the types of comprehensive care needed to address their
14
15 diverse health conditions. Further investment into programs improving inner city health care (including
16
17 HIV, HCV, mental health, and addiction services) will be crucial for addressing the considerable
18
19 morbidity and mortality among inner city populations throughout Canada.
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1: Characteristics of participants in a large, community-based cohort in the inner city of Vancouver (2003-2009).

	Overall (n = 2913) n (%)
Mean age, years (SD)	42.5 (10.1)
Female sex	845 (29)
Aboriginal ethnicity	895 (31)
Unstable housing*	1801 (62)
Jail time*	610 (21)
Alcohol use*	1490 (51)
Injection or non-injection drug use*	2337 (80)
Injection drug use*	1114 (38)
Overdose*	205 (7)
Methadone treatment*	561 (19)
HCV infection†	
Yes	1533 (53)
No	872 (30)
Unknown	508 (17)
HIV infection†	
Yes	535 (18)
No	1735 (60)
Unknown	643 (22)

*In the six months prior to survey, self-reported. †Based on all linked laboratory test results (1991-2009). Characteristics for HCV+, HIV+, HCV+/HIV+, HCV-/HIV- and unknown HCV and/or HIV status participants are shown in Supplementary Table 1.

Table 2: Causes of death by ICD-10 chapter heading among a large, community-based cohort in the inner city of Vancouver (2003-2009).

ICD-10	Description	Overall (n = 2913)		
		Observed deaths	Rate* (95% CI)	SMR (95% CI)
	All-cause	374	223 (201–247)	7.1 (6.4–7.9)
A00-B99	Infection	97	58 (47–71)	20.2 (16.5–24.6)
C00-D48	Neoplasm	42	25 (18–34)	2.7 (2.0–3.7)
E00-E90	Endocrine	4	2 (1–6)	2.4 (0.9–6.3)
F00-F99	Mental and behavioural	13	8 (4–13)	11.1 (6.4–19.0)
G00-G99	Nervous system	8	5 (2–10)	7.0 (3.5–14.0)
I00-I99	Circulatory system	41	24 (18–33)	4.1 (3.0–5.5)
J00-J99	Respiratory system	44	26 (20–35)	12.1 (9.0–16.3)
K00-K93	Digestive system	20	12 (8–18)	7.3 (4.7–11.3)
N00-N99	Genitourinary	4	2 (1–6)	7.3 (2.7–19.4)
R00-R99	Other†	39	23 (17–32)	37.8 (27.6–51.7)
V00-Y98	External	62	37 (39–47)	6.5 (5.0–8.3)

*Rate per 10,000 person-years. †Includes unknown causes of death. SMR standardized mortality ratio.

Table 3. Causes of death by ICD-10 chapter heading stratified by HCV and HIV status among a large, community-based cohort in the inner city of Vancouver (2003-2009).

ICD-10	Description	HCV+ (n = 1068)			HIV+ (n = 70)			HCV+/HIV+ (n = 465)			HCV-/HIV- (n = 693)		
		Observed deaths	Rate* (95% CI)	SMR (95% CI)	Observed deaths	Rate* (95% CI)	SMR (95% CI)	Observed deaths	Rate* (95% CI)	SMR (95% CI)	Observed deaths	Rate* (95% CI)	SMR (95% CI)
	All-cause	106	167 (138–203)	5.9 (4.9–7.1)	23	641 (426–964)	19.2 (12.8–28.9)	126	515 (432–613)	23.0 (19.3–27.4)	44	107 (79–143)	3.5 (2.6–4.7)
A00-B99	Infection	10	16 (8–29)	5.4 (2.9–10.1)	13	362 (210–624)	130.3 (75.7–224.5)	68	278 (219–352)	107.7 (84.9–136.6)	4	10 (4–26)	3.5 (1.3–9.4)
C00-D48	Neoplasm	9	14 (7–27)	1.8 (0.9–3.4)	0	-	-	6	25 (11–55)	4.1 (1.9–9.2)	11	27 (15–48)	2.9 (1.6–5.3)
E00-E90	Endocrine	0	-	-	2	56 (14–223)	50.0 (12.5–200.0)	0	-	-	0	-	-
F00-F99	Mental and behavioural	4	6 (2–17)	10.2 (3.8–27.2)	1	28 (4–200)	37.7 (5.3–267.5)	6	25 (11–55)	50.5 (22.7–112.4)	1	2 (0–17)	3.7 (0.5–26.6)
G00-G99	Nervous system	2	3 (1–13)	5.4 (1.4–21.6)	0	-	-	2	8 (2–33)	18.8 (4.7–75.3)	3	7 (2–23)	11.5 (3.7–35.5)
I00-I99	Circulatory system	14	22 (13–37)	4.4 (2.6–7.5)	1	28 (4–198)	4.1 (0.6–28.8)	3	12 (4–38)	3.5 (1.1–10.9)	7	17 (8–36)	2.9 (1.4–6.1)
J00-J99	Respiratory system	19	30 (19–47)	16.4 (10.4–25.7)	1	28 (4–198)	11.6 (1.6–82.2)	8	33 (16–65)	24.5 (12.3–49.0)	5	12 (5–29)	6.0 (2.5–14.3)
K00-K93	Digestive system	8	13 (6–25)	8.4 (4.2–16.7)	0	-	-	3	12 (4–38)	10.4 (3.4–32.2)	1	2 (0–17)	1.5 (0.2–10.6)
N00-N99	Genitourinary	0	-	-	0	-	-	0	-	-	1	2 (0–17)	8.4 (1.2–59.4)
R00-R99	Other†	12	19 (11–33)	30.4 (17.3–53.6)	1	28 (4–198)	46.9 (6.6–333.1)	12	49 (28–86)	89.9 (51.1–158.3)	6	15 (7–32)	23.8 (10.7–53.1)
V00-Y98	External	28	44 (31–64)	7.6 (5.2–11.0)	4	111 (42–297)	21.2 (8.0–56.5)	18	74 (46–117)	13.9 (8.8–22.1)	5	12 (5–29)	2.2 (0.9–5.2)

*Rate per 10,000 person-years. †Includes unknown causes of death. SMR standardized mortality ratio. Causes of death for participants with unknown HCV and/or HIV status are shown in Supplementary Table 2.

Table 4: Causes of death related to viral hepatitis and liver disease, HIV infection, and drug use among a large, community-based cohort in the inner city of Vancouver (2003-2009).

ICD-10	Description	Sex	Overall (n = 2913)		
			Observed deaths	Rate* (95% CI)	SMR (95% CI)
	All-cause		374	223 (201–247)	7.1 (6.4–7.9)
		Men	263	220 (195–248)	5.8 (5.1–6.6)
		Women	111	230 (191–277)	15.4 (12.8–18.5)
	Drug-related†		53	32 (24–41)	12.0 (9.1,15.7)
		Men	36	30 (22–42)	9.3 (6.7–12.9)
		Women	17	35 (22–57)	30.3 (18.8–48.7)
	Liver-related‡		22	13 (9–20)	5.9 (3.9–8.9)
		Men	15	13 (8–21)	4.5 (2.7–7.4)
		Women	7	15 (7–30)	17.9 (8.5–37.6)
B20-B24	HIV-related		78	46 (37–58)	24.9 (20.0–31.1)
		Men	54	45 (35–59)	18.7 (14.4–24.5)
		Women	24	50 (33–74)	96.8 (64.9–144.5)

*Rate per 10,000 person-years. †Consists of 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). ‡Consists of viral hepatitis, liver cancer, alcoholic and non-alcoholic liver disease. SMR standardized mortality ratio. Causes of death related to viral hepatitis and liver disease, HIV infection, and drug use for participants with unknown HCV and/or HIV status are shown in Supplementary Table 3.

Table 5. Causes of death related to viral hepatitis and liver disease, HIV infection, and drug use in subgroups stratified by HCV and HIV status, among a large, community-based cohort in the inner city of Vancouver (2003-2009).

ICD-10	Description	Sex	HCV+ (n = 1068)			HIV+ (n = 70)			HCV+/HIV+ (n = 465)			HCV-/HIV- (n = 693)		
			Observed deaths	Rate* (95% CI)	SMR (95% CI)	Observed deaths	Rate* (95% CI)	SMR (95% CI)	Observed deaths	Rate* (95% CI)	SMR (95% CI)	Observed deaths	Rate* (95% CI)	SMR (95% CI)
	All-cause		106	167 (138-203)	5.9 (4.9-7.1)	23	641 (426-964)	19.2 (12.8-28.9)	126	515 (432-613)	23.0 (19.3-27.4)	44	107 (79-144)	3.5 (2.6-4.7)
		Men	75	169 (135-233)	4.8 (3.8-6.0)	18	794 (500-1261)	17.1 (10.8-27.2)	77	501 (401-627)	16.9 (13.5-21.1)	34	112 (80-156)	3.0 (2.2-4.2)
		Women	31	164 (115-233)	13.1 (9.2-18.6)	5	378 (157-908)	34.4 (14.3-82.7)	49	538 (407-712)	54 (41-71)	10	93 (50-173)	7.6 (4.1-14.2)
	Drug-related†		22	35 (23-53)	12.6 (8.3-19.1)	2	56 (14-223)	23.1 (5.8-92.3)	21	86 (56-132)	33.7 (22.0-51.7)	4	10 (4-26)	3.8 (1.4-10.2)
		Men	16	36 (22-59)	10.5 (6.4-17.1)	2	88 (22-535)	27.8 (7.0-111.3)	11	72 (40-129)	21.2 (11.7-38.2)	4	13 (5-35)	4.3 (1.6-11.5)
		Women	6	32 (14-71)	26.9 (12.1-59.9)	0	-	-	10	110 (59-204)	96.8 (52.1-180.0)	0	-	-
	Liver-related‡		13	21 (12-35)	9.6 (5.6-16.5)	0	-	-	5	20 (9-49)	12.1 (5.0-29.1)	0	-	-
		Men	9	20 (11-39)	7.4 (3.8-14.2)	0	-	-	2	13 (3-52)	5.6 (1.4-22.3)	0	-	-
		Women	4	21 (8-56)	28.2 (10.6-75.1)	0	-	-	3	33 (11-102)	54.4 (17.6-168.8)	0	-	-
B20-B24	HIV-related		0	-	-	13	362 (210-624)	199.8 (116.0-344.1)	64	262 (205-334)	142.8 (111.8-182.5)	0	-	-
		Men	0	-	-	10	441 (237-820)	177.0 (95.2-329.0)	43	280 (208-377)	108.0 (80.1-145.6)	0	-	-
		Women	0	-	-	3	227 (73-703)	349.9 (112.8-1100.0)	21	231 (150-354)	420.7 (274.3-645.2)	0	-	-

*Rate per 10,000 person-years. †Consists of 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). ‡Consists of viral hepatitis, liver cancer, alcoholic and non-alcoholic liver disease. SMR standardized mortality ratio.

Figure 1: (A) Mortality rates and (B) standardized mortality ratios among a large, community-based cohort in the inner city of Vancouver (2003-2009), stratified by age group.

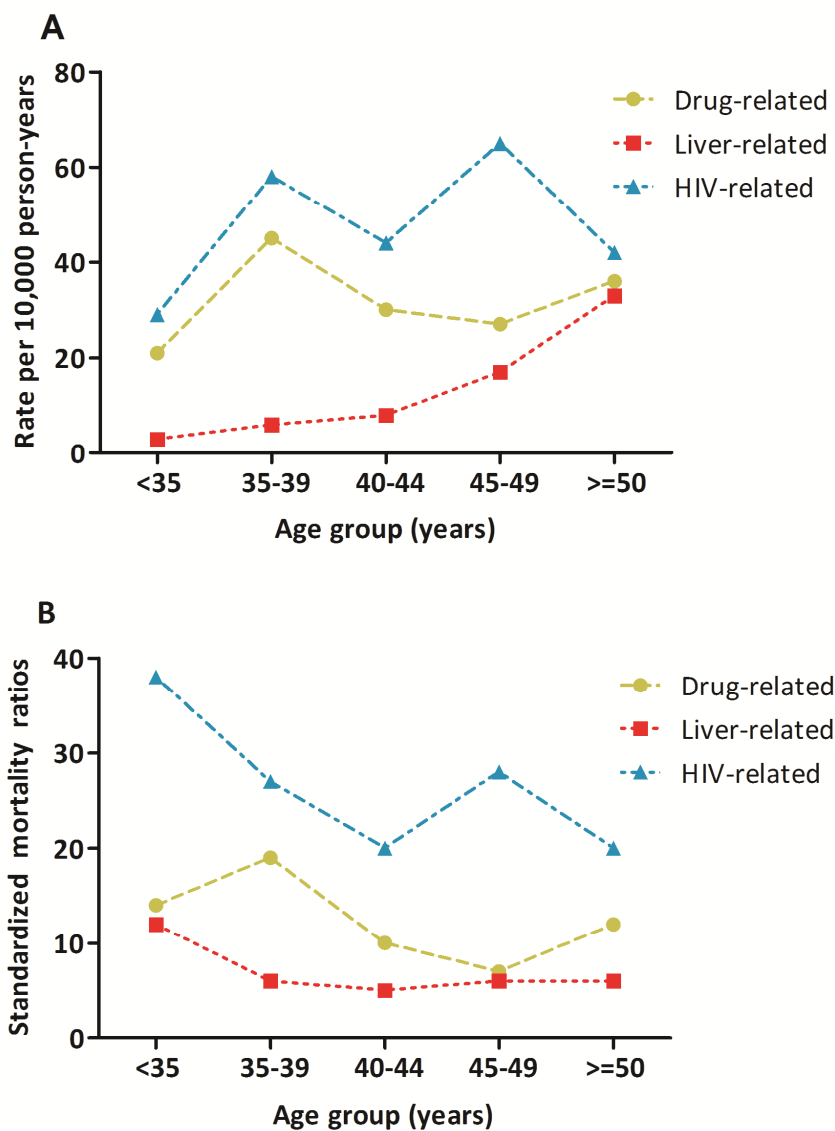
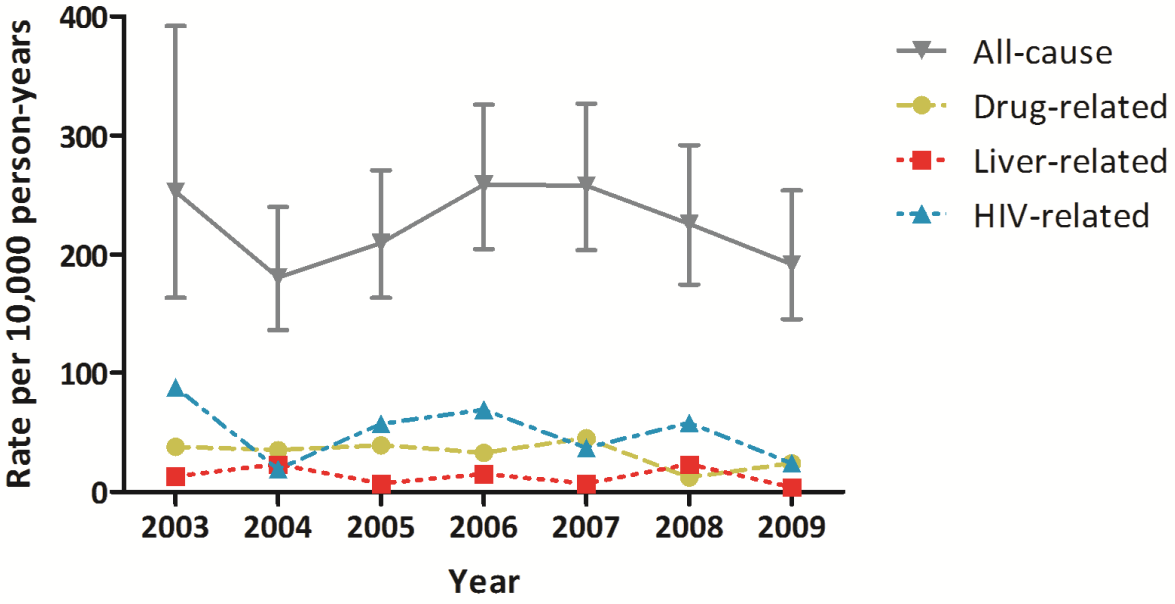


Figure 2: Mortality rates among a large, community-based cohort in the inner city of Vancouver (2003-2009), stratified by year. Bars=95% CI.



Confidential

References

1. 2005/6 Downtown Eastside community monitoring report: City of Vancouver; 2007.
2. Miller CL, Kerr T, Strathdee SA, Li K, Wood E. Factors associated with premature mortality among young injection drug users in Vancouver. *Harm reduction journal* 2007;4:1.
3. Strathdee SA, Patrick DM, Currie SL, et al. Needle exchange is not enough: lessons from the Vancouver injecting drug use study. *AIDS* 1997;11:F59-65.
4. Wood E, Kerr T, Spittal PM, Tyndall MW, O'Shaughnessy MV, Schechter MT. The health care and fiscal costs of the illicit drug use epidemic: the impact of conventional drug control strategies. *B C Med J* 2003;45:128-34.
5. Wood E, Tyndall MW, Montaner JS, Kerr T. Summary of findings from the evaluation of a pilot medically supervised safer injecting facility. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne* 2006;175:1399-404.
6. Kerr T, Small W, Buchner C, et al. Syringe sharing and HIV incidence among injection drug users and increased access to sterile syringes. *American journal of public health* 2010;100:1449-53.
7. Drug situation in Vancouver: Urban Health Research Institute of the British Columbia Centre for Excellence in HIV/AIDS; 2009.
8. Buxton J. Vancouver drug use epidemiology: Canadian Community Epidemiology Network on Drug Use; 2005.
9. Marshall BD, Milloy MJ, Wood E, Montaner JS, Kerr T. Reduction in overdose mortality after the opening of North America's first medically supervised safer injecting facility: a retrospective population-based study. *Lancet* 2011;377:1429-37.
10. Tyndall MW, Craib KJ, Currie S, Li K, O'Shaughnessy MV, Schechter MT. Impact of HIV infection on mortality in a cohort of injection drug users. *J Acquir Immune Defic Syndr* 2001;28:351-7.
11. Spittal PM, Hogg RS, Li K, et al. Drastic elevations in mortality among female injection drug users in a Canadian setting. *AIDS care* 2006;18:101-8.
12. Selected vital statistics and health status indicators: British Columbia Vital Statistics Agency; 2010.
13. Evans JL, Tsui JI, Hahn JA, Davidson PJ, Lum PJ, Page K. Mortality among young injection drug users in San Francisco: a 10-year follow-up of the UFO study. *American journal of epidemiology* 2012;175:302-8.
14. Solomon SS, Celentano DD, Srikrishnan AK, et al. Mortality among injection drug users in Chennai, India (2005-2008). *AIDS* 2009;23:997-1004.
15. Hulse GK, English DR, Milne E, Holman CD. The quantification of mortality resulting from the regular use of illicit opiates. *Addiction* 1999;94:221-9.
16. Gibson A, Randall D, Degenhardt L. The increasing mortality burden of liver disease among opioid-dependent people: cohort study. *Addiction* 2011;106:2186-92.
17. Cornish R, Macleod J, Strang J, Vickerman P, Hickman M. Risk of death during and after opiate substitution treatment in primary care: prospective observational study in UK General Practice Research Database. *BMJ* 2010;341:c5475.
18. Degenhardt L, Bucello C, Mathers B, et al. Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies. *Addiction* 2011;106:32-51.
19. Degenhardt L, Hall W, Warner-Smith M. Using cohort studies to estimate mortality among injecting drug users that is not attributable to AIDS. *Sexually transmitted infections* 2006;82 Suppl 3:iii56-63.
20. Degenhardt L, Singleton J, Calabria B, et al. Mortality among cocaine users: a systematic review of cohort studies. *Drug and alcohol dependence* 2011;113:88-95.

21. Ferreros I, Lumbreras B, Hurtado I, Perez-Hoyos S, Hernandez-Aguado I. The shifting pattern of cause-specific mortality in a cohort of human immunodeficiency virus-infected and non-infected injecting drug users. *Addiction* 2008;103:651-9.
22. O'Kelly FD, O'Kelly CM. The natural history of injecting drug use: a 25-year longitudinal study of a cohort of injecting drug users in inner city Dublin. *Irish journal of medical science* 2012.
23. Bargagli AM, Sperati A, Davoli M, Forastiere F, Perucci CA. Mortality among problem drug users in Rome: an 18-year follow-up study, 1980-97. *Addiction* 2001;96:1455-63.
24. Boschini A, Smacchia C, Di Fine M, et al. Community-acquired pneumonia in a cohort of former injection drug users with and without human immunodeficiency virus infection: incidence, etiologies, and clinical aspects. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America* 1996;23:107-13.
25. Palepu A, Tyndall MW, Leon H, et al. Hospital utilization and costs in a cohort of injection drug users. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne* 2001;165:415-20.
26. O'Donnell A, Pappas L. Pulmonary complications of intravenous drug abuse. Experience at an inner-city hospital. *Chest* 1988;94:251-3.
27. Bird SM, Hutchinson SJ, Goldberg DJ. Drug-related deaths by region, sex, and age group per 100 injecting drug users in Scotland, 2000-01. *Lancet* 2003;362:941-4.
28. Copeland L, Budd J, Robertson JR, Elton RA. Changing patterns in causes of death in a cohort of injecting drug users, 1980-2001. *Archives of internal medicine* 2004;164:1214-20.
29. Walter SR, Thein HH, Amin J, et al. Trends in mortality after diagnosis of hepatitis B or C infection: 1992-2006. *Journal of hepatology* 2011;54:879-86.
30. Grebely J, Raffa JD, Lai C, et al. Impact of hepatitis C virus infection on all-cause and liver-related mortality in a large community-based cohort of inner city residents. *Journal of viral hepatitis* 2011;18:32-41.

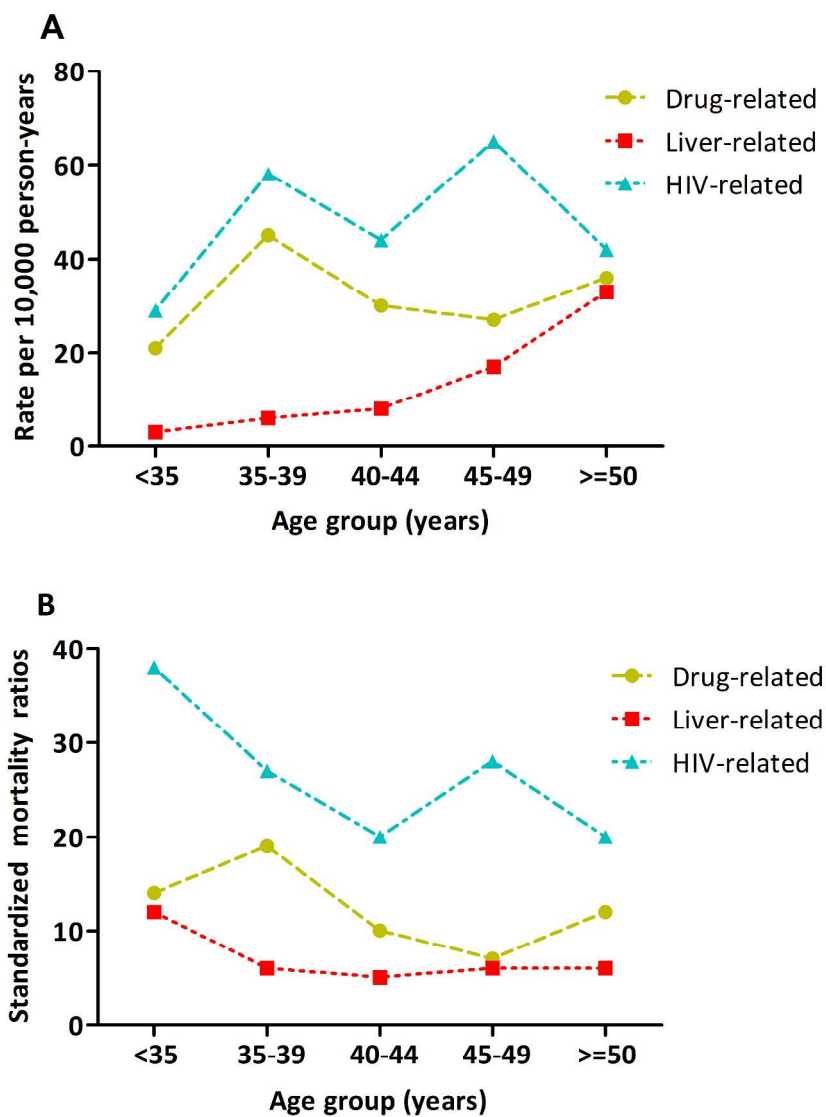


Figure 1: (A) Mortality rates and (B) standardized mortality ratios among a large, community-based cohort in the inner city of Vancouver (2003-2009), stratified by age group.
1343x1759mm (72 x 72 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

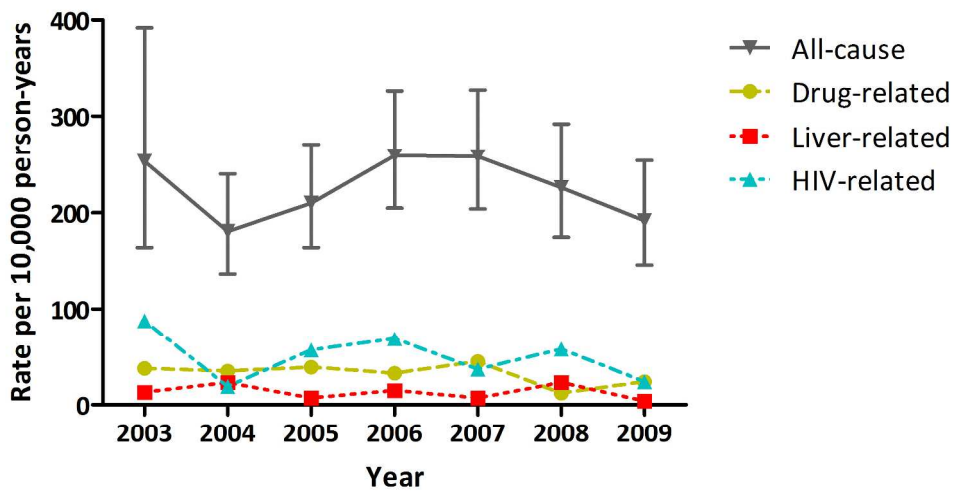


Figure 2: Mortality rates among a large, community-based cohort in the inner city of Vancouver (2003-2009), stratified by year. Bars=95% CI.
1151x633mm (72 x 72 DPI)

Supplementary Table 1. Characteristics of participants stratified by HCV and HIV status, in a large, community-based cohort in the inner city of Vancouver (2003-2009).

	HCV+ (n = 1068) n (%)	HIV+ (n = 70) n (%)	HCV+/HIV+ (n = 465) n (%)	HCV-/HIV- (n = 693) n (%)	Unknown HCV and/or HIV status (n = 617) n (%)
Mean age, years (SD)	42.4 (8.6)	42.5 (10.3)	40.7 (7.7)	41.6 (10.6)	44.9 (12.5)
Female sex	319 (30)	24 (34)	176 (38)	183 (26)	143 (23)
Aboriginal ethnicity	327 (31)	29 (41)	181 (39)	213 (31)	145 (24)
Unstable housing*	704 (66)	34 (49)	280 (60)	404 (58)	379 (61)
Jail time*	277 (26)	20 (29)	108 (23)	111 (16)	94 (15)
Alcohol use*	495 (46)	28 (40)	213 (46)	403 (58)	351 (57)
Injection or non-injection drug use*	952 (89)	59 (84)	445 (96)	489 (71)	392 (64)
Injection drug use*	582 (54)	33 (47)	312 (67)	82 (12)	105 (17)
Overdose*	90 (8)	9 (13)	58 (12)	30 (4)	18 (3)
Methadone treatment*	306 (29)	10 (14)	188 (40)	31 (5)	26 (4)
HCV infection†					
Yes	1068 (100)	-	465 (100)	-	-
No	-	37 (53)	-	693 (100)	142 (23)
Unknown	-	33 (47)	-	-	475 (77)
HIV infection†					
Yes	-	70 (100)	465 (100)	-	-
No	935 (88)	-	-	693 (100)	107 (17)
Unknown	133 (12)	-	-	-	510 (83)

*In the six months prior to survey, self-reported. †Based on all linked laboratory test results (1991-2009).

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

Supplementary Table 2. Causes of death by ICD-10 chapter heading stratified by HCV and HIV status among a large, community-based cohort in the inner city of Vancouver (2003-2009).

ICD-10	Description	Unknown HCV and/or HIV status (n = 617)		
		Observed deaths	Rate* (95% CI)	SMR (95% CI)
	All-cause	75	213 (170-267)	4.9 (3.9-6.2)
A00-B99	Infection	2	6 (1-23)	1.8 (0.5-7.3)
C00-D48	Neoplasm	16	45 (28-74)	3.3 (2.1-5.5)
E00-E90	Endocrine	2	6 (1-23)	3.7 (0.9-15.0)
F00-F99	Mental and behavioural	1	3 (0-20)	2.7 (0.4-19.1)
G00-G99	Nervous system	1	3 (0-20)	2.7 (0.4-18.9)
I00-I99	Circulatory system	16	45 (28-74)	4.7 (2.9-7.7)
J00-J99	Respiratory system	11	31 (17-56)	9.0 (5.0-16.2)
K00-K93	Digestive system	8	23 (11-45)	10.3 (5.2-20.6)
N00-N99	Genitourinary	3	9 (3-26)	14.2 (4.6-44.1)
R00-R99	Other†	8	23 (11-45)	34.5 (17.2-68.9)
V00-Y98	External	7	20 (9-42)	3.3 (1.6-7.0)

*Rate per 10,000 person-years. †Includes unknown causes of death. SMR standardized mortality ratio.

Confidential

Supplementary Table 3. Causes of death related to viral hepatitis and liver disease, HIV infection, and drug use in subgroups stratified by HCV and HIV status, among a large, community-based cohort in the inner city of Vancouver (2003-2009).

ICD-10	Description	Sex	Unknown HCV and/or HIV status (n = 617)		
			Observed deaths	Rate* (95% CI)	SMR (95% CI)
	All-cause		75	213 (170–267)	4.9 (3.9–6.2)
		Men	59	218 (169–281)	4.6 (3.6–6.0)
		Women	16	197 (120–321)	6.5 (4.0–10.5)
	Drug-related†		4	11 (4–30)	4.3 (1.6–11.6)
		Men	3	11 (4–34)	3.6 (1.2–11.3)
		Women	1	12 (2–87)	10.1 (1.4–71.4)
	Liver-related‡		4	11 (4–30)	4.1 (1.5–10.9)
		Men	4	15 (6–39)	4.6 (1.7–12.3)
		Women	0	-	-
B20-B24	HIV-related		1	3 (0–20)	1.5 (0.2–10.9)
		Men	1	4 (1–26)	1.6 (0.2–11.6)
		Women	0	-	-

*Rate per 10,000 person-years. †Consists of 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). ‡Consists of viral hepatitis, liver cancer, alcoholic and non-alcoholic liver disease. SMR standardized mortality ratio.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

Supplementary Table 4. Causes of death related to viral hepatitis and liver disease, HIV infection, and drug use among a large, community-based cohort in the inner city of Vancouver (2003-2009), stratified by age group.

Cause of death	Age group	Observed deaths, n	Rate per 10,000 person-years (95% CI)	SMR (95% CI)
All-cause	Overall	374	223 (201–247)	7.1 (6.4–7.9)
	<35	34	89 (64–125)	13.2 (9.4–18.5)
	35-39	60	193 (150–248)	13.3 (10.3–17.1)
	40-44	76	210 (168–263)	9.0 (7.2–11.3)
	45-49	65	222 (174–283)	6.0 (4.7–7.6)
	>=50	139	420 (355–495)	5.3 (4.5–6.3)
Drug-related	Overall	53	32 (24–41)	12.0 (9.1,15.7)
	<35	8	21 (11–42)	14.3 (7.2–28.6)
	35-39	14	45 (27–76)	19.0 (11.3–32.1)
	40-44	11	30 (17–55)	10.5 (5.8–18.9)
	45-49	8	27 (14–55)	7.2 (3.6–14.5)
	>=50	12	36 (21–64)	12.2 (6.9–21.5)
Liver-related	Overall	22	13 (9–20)	5.9 (3.9–8.9)
	<35	1	3 (0–19)	11.9 (1.7–84.8)
	35-39	2	6 (2–26)	5.5 (1.4–22.1)
	40-44	3	8 (3–26)	4.8 (1.5–14.9)
	45-49	5	17 (7–41)	6.0 (2.5–14.3)
	>=50	11	33 (18–60)	6.0 (3.3–10.9)
HIV-related	Overall	78	46 (37–58)	24.9 (20.0–31.1)
	<35	11	29 (16–52)	38.2 (21.1–69.0)
	35-39	18	58 (36–92)	27.3 (17.2–43.3)
	40-44	16	44 (27–72)	19.9 (12.1–32.4)
	45-49	19	65 (41–102)	28.5 (18.1–44.6)
	>=50	14	42 (25–71)	19.8 (11.7–33.5)