Region and Temporal Changes in HIV-related Mortality in British Columbia, 1987-2006

Viviane D. Lima, PhD,1,2 Katherine J. Lepik, MSc,1,3 Wendy Zhang, MSc,1 Katherine A. Muldoon, BSc,1 Robert S. Hogg, PhD,1,4 Julio S.G. Montaner, MD,1,2

ABSTRACT

Background: HIV-related mortality has been declining in Canada; however, little is known about regional differences in HIV-related mortality. The objective of this study was to characterize regional changes in HIV-related mortality from 1987-2006 in British Columbia (BC).

Methods: BC Vital Statistics provided death certificate data for individuals ≥18 years who died of an HIV-related cause in BC between 1987 and 2006. Annual mortality rates were calculated for all BC, five regional health authorities, and two areas within Vancouver. Joinpoint regression analyses measured changes in mortality rates.

Results: There were 3,899 HIV-related deaths in BC from 1987-2006. Over time, HIV-related mortality rates were highest in the densely populated, southern regions, and lowest in the north. In BC, mortality significantly increased from 1987-1994 (annual percent change [APC] 16.3%). In 1994, the trend changed to a significant decrease in mortality from 1994-1998 (APC -20.0%), followed by a sustained reduction from 1998-2006. Four of the five health authorities showed mortality trends similar to the province; however, the north showed significantly increasing mortality from 1987-2006 (APC 6.7%). In Vancouver, the City Centre showed a mortality pattern similar to the province, but the Downtown Eastside had rising mortality rates until 1997, followed by a modest decline.

Conclusion: In most areas of BC, HIV-related mortality declined after the introduction of effective antiretroviral therapy; however, this decline was delayed or absent in some regions. These regional variations may reflect differential access to health care, even in a setting where antiretroviral therapy is provided at no cost to patients.

Key words: Mortality; mortality decline; death rate; HIV; Canada; British Columbia

Population-level declines in HIV-related mortality have been observed in Canada and other resource-rich countries as a result of effective combination antiretroviral therapy.1-6 Similar declines have been observed in resource-limited settings as a result of increased access to antiretroviral therapy in recent years.7,8 Earlier Canadian studies examined localized differences in HIV-related mortality between provinces and large urban centres.9-11 However, little is known about how HIV-related mortality has changed within different regions in a given province. Understanding these regional trends is necessary to guide health service planning for the HIV epidemic. The objective of this study was to characterize changes in HIV-related mortality in British Columbia (BC) between 1987 and 2006 in each of the five provincial health authorities and in two urban local health areas heavily affected by the HIV epidemic.

METHODS

Study design and data sources
We conducted a descriptive, population-based study of HIV-related mortality trends. The BC Vital Statistics Agency provided death certificate data for individuals who died from an HIV-related cause (International Classification of Diseases 10th revision codes B20 to B24) between 1987 and 2006. Individuals were included in the study if they had died in BC and were ≥18 years of age at the time of death. The death records included date and causes of death, age, sex and geographical locators for residence at time of death. Population estimates for BC, broken down by region, age and sex, were obtained from BC Population Estimates (P.E.O.P.L.E. 32) for the years 1987 through 2006.12 Ethical approval to conduct this study was received from the Providence Health Care/University of British Columbia Research Ethics Board.

Author Affiliations
1. British Columbia Centre for Excellence in HIV/AIDS, Vancouver, BC
2. Faculty of Medicine, University of British Columbia, Vancouver, BC
3. Faculty of Pharmaceutical Sciences, University of British Columbia, Vancouver, BC
4. Faculty of Health Sciences, Simon Fraser University, Burnaby, BC

Correspondence and reprint requests: Dr. Julio Montaner, Director, British Columbia Centre for Excellence in HIV/AIDS, St. Paul’s Hospital, 608-1081 Burrard Street, Vancouver, BC V6Z 1Y6, Tel: 604-806-8036, Fax: 604-806-9044, E-mail: jmontaner@cfenet.ubc.ca

Funding: No external funding was received for this research.

Conflict of Interest: Robert Hogg has held grant funding from the National Institutes of Health, the Canadian Institutes of Health Research, the Michael Smith Foundation for Health Research, and Health Canada. He has also received funding from GlaxoSmithKline and Merck Frost Laboratories for participating in continued medical education programmes. Julio Montaner has received grants from, served as an ad hoc advisor to, or spoken at various events sponsored by Abbott, Argos Therapeutics, Bioject Inc, Boehringer Ingelheim, BMS, Gilead Sciences, GlaxoSmithKline, Hoffmann-La Roche, Janssen-Ortho, Merck Frostt, Pfizer, Schering, Serono Inc, TheraTechnologies, Tibotec, Trimeris. He has also held grant funding from the Canadian Institutes of Health Research and the National Institutes of Health. Julio Montaner is a recipient of an Avant-Garde Award from the National Institute of Drug Abuse. Viviane Lima has held fellowship support from the Canadian Institutes of Health Research and the Michael Smith Foundation for Health Research. Katherine Lepik has held fellowship support from the Michael Smith Foundation for Health Research.
REGIONAL AND TEMPORAL CHANGES IN HIV-RELATED MORTALITY

Table 1. Average Annual HIV-related Deaths and Age-/Sex-adjusted HIV-related Mortality Rates per Five-year Interval (by region, 1987-2006)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Authority</td>
<td>Deaths per Year</td>
<td>Rate*</td>
<td>Deaths per Year</td>
<td>Rate*</td>
</tr>
<tr>
<td><strong>Provincial</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>British Columbia</td>
<td>148.0 (45.4)</td>
<td>4.7 (1.3)</td>
<td>304.0 (29.5)</td>
<td>8.3 (0.8)</td>
</tr>
<tr>
<td>Health Authority</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancouver Coastal</td>
<td>106.0 (33.2)</td>
<td>12.8 (3.5)</td>
<td>206.0 (21.8)</td>
<td>21.5 (2.6)</td>
</tr>
<tr>
<td>Vancouver Island</td>
<td>15.0 (4.6)</td>
<td>2.8 (0.8)</td>
<td>37.0 (6.1)</td>
<td>5.8 (1.0)</td>
</tr>
<tr>
<td>Fraser</td>
<td>21.0 (8.7)</td>
<td>2.1 (0.9)</td>
<td>45.0 (7.4)</td>
<td>3.8 (0.5)</td>
</tr>
<tr>
<td>Interior</td>
<td>4.4 (2.3)</td>
<td>0.8 (0.4)</td>
<td>13.2 (2.3)</td>
<td>2.2 (0.4)</td>
</tr>
<tr>
<td>Northern</td>
<td>2.0 (1.5)</td>
<td>0.5 (0.5)</td>
<td>4.0 (2.5)</td>
<td>1.2 (0.8)</td>
</tr>
<tr>
<td>Local Health Area</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>City Centre</td>
<td>62.2 (21.4)</td>
<td>76.3 (24.9)</td>
<td>105.6 (19.8)</td>
<td>106.9 (22.7)</td>
</tr>
<tr>
<td>Downtown Eastside</td>
<td>5.8 (2.5)</td>
<td>11.3 (3.5)</td>
<td>26.6 (11.0)</td>
<td>42.1 (14.3)</td>
</tr>
</tbody>
</table>

* Rates are age- and sex-adjusted and presented per 100,000 population.

Table 2. Joinpoint Regression Results of HIV-related Mortality Rates (by region, 1987-2006)

<table>
<thead>
<tr>
<th>Region</th>
<th>Trend One</th>
<th>Trend Two</th>
<th>Trend Three</th>
</tr>
</thead>
<tbody>
<tr>
<td>Health Authority</td>
<td>Years APC (95% CI)</td>
<td>Years APC (95% CI)</td>
<td>Years APC (95% CI)</td>
</tr>
<tr>
<td><strong>Provincial</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Health Authority</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vancouver Coastal</td>
<td>1987-1994 15.5 (9.9, 21.3)*</td>
<td>1994-1998 -20.9 (-32.7, -7.1)*</td>
<td>1998-2006 -3.7 (-8.0, 0.8)</td>
</tr>
<tr>
<td>Vancouver Island</td>
<td>1987-1994 19.5 (10.2, 29.6)*</td>
<td>1994-1997 -23.4 (-47.2, 11.2)</td>
<td>1997-2006 -2.9 (-8.1, 2.5)</td>
</tr>
<tr>
<td>Fraser</td>
<td>1987-1993 17.3 (11.3, 26.0)*</td>
<td>1993-2006 -7.4 (-17.9, 3.8)*</td>
<td>– – – –</td>
</tr>
<tr>
<td>Interior</td>
<td>1987-1993 23.2 (5.4, 43.9)*</td>
<td>1993-1997 -15.5 (-36.7, 12.7)</td>
<td>1997-2006 4.4 (-1.3, 10.3)</td>
</tr>
<tr>
<td>Northern</td>
<td>1987-2006 6.7 (3.3, 10.2)*</td>
<td>– – – –</td>
<td>– – – –</td>
</tr>
<tr>
<td>Local Health Area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Downtown Eastside</td>
<td>1987-1997 26.1 (16.0, 37.0)*</td>
<td>1997-2006 -5.4 (-8.7, -2.1)*</td>
<td>– – – –</td>
</tr>
</tbody>
</table>

*Significantly different from 0 (p<0.05).

British Columbia Regional Health Boundaries

BC is divided into five regional health authorities: Vancouver Coastal, Vancouver Island, Fraser, Interior, and Northern. These health authorities are responsible for the management and delivery of health services in geographically defined subpopulations of the province.13 Vancouver Coastal, Vancouver Island, and Fraser are comparatively small, densely populated health authorities (with few remote communities). The Interior is geographically large with many urban centres and scattered rural communities. The Northern health authority is a vast region with only one major city and numerous rural and remote communities. Each of these five health authorities is further broken down into several local health areas. Within Vancouver Coastal, two local health areas have been severely affected by the HIV epidemic: Vancouver’s City Centre and Downtown Eastside.14-16

Analyses

Annual age- and sex-adjusted HIV-related mortality rates per 100,000 population were calculated for each health authority and for the two local health areas. Average rates were also calculated for the entire province and entire study period. All rates were calculated using the SAS population rates macro, version 6 (Manitoba Centre for Health Policy and Evaluation, Winnipeg, Manitoba, Canada).

Joinpoint regression was used to identify changes in HIV-related mortality rates over time for each region. Model development began with the assumption that a single trend in mortality would best describe the data. “Joinpoints” (years in which there was a statistically significant change in mortality trend) were added sequentially and retained in the model if their inclusion significantly improved model fit (by the permutation test).17,18 The final model described the best-fit number of distinct trends in HIV-related mortality, the annual percent change in mortality within each trend period and the years in which changes in trend occurred. Joinpoint analyses were carried out using Joinpoint version 3.3 (National Cancer Institute, Bethesda, Maryland, United States).

RESULTS

A total of 3,899 HIV-related deaths were reported in BC between 1987 and 2006, with 2,550 (65.4%) in Vancouver Coastal, 458 (11.8%) in Vancouver Island, 622 (16.0%) in Fraser, 194 (5.0%) in Interior, and 75 (1.9%) in Northern health authorities. Within the Vancouver Coastal health authority, 1,164 (45.6%) HIV-related deaths were reported in the City Centre and 561 (24.9%) were reported in the Downtown Eastside between 1987 and 2006.

Table 1 summarizes the number of HIV-related deaths and HIV-related mortality rates per 100,000 population per five-year interval for all BC, for each health authority and for two local health areas. Throughout the study period, the absolute number of HIV-related deaths and mortality rate remained highest in the most densely populated health authorities (Vancouver Coastal, Fraser, and Vancouver Island) and lowest in the Interior and North. In Vancouver, the City Centre had the greatest number of HIV-related deaths and highest HIV-related mortality rate until 1996. After 1996, HIV-related deaths began to decline in City Centre, but continued to increase in the Downtown Eastside.

Table 2 summarizes the output of the joinpoint regression analyses showing temporal trends in HIV-related mortality rates for the provincial total, each health authority, and the two local health areas. These trends are graphically depicted in Figures 1 and 2. In BC as a whole (Figure 1, Panel A), HIV-related mortality significantly increased between 1987 and 1994 (trend one). In 1994, there
was a change in trend with a significant decrease in HIV-related mortality (trend two). The year 1998 marked the transition to trend three, reflecting a sustained reduction in HIV-related mortality.

As shown in Figure 1, the three-phase pattern of HIV-related mortality observed at the provincial level was mirrored in Vancouver Coastal (Panel B), Vancouver Island (Panel C), and Interior (Panel E), although the mortality declines of trend two did not achieve statistical significance in Vancouver Island and Interior (Table 2). While Fraser (Panel D) showed only a two-phase pattern in HIV-related mortality, trend two showed a steady significant decline from 1993 to 2006. In contrast, the Northern health authority (Panel F) showed a single trend of significantly increasing HIV-related mortality from 1987 to 2006.

In Vancouver, the City Centre (Table 2; Figure 2, Panel A) demonstrated the same three-phase HIV-related mortality trend seen in Vancouver Coastal, with a significant increase until 1994, followed by a statistically significant decline between 1994 and 1998, then a sustained reduction to 2006. In contrast, the Downtown Eastside
(Table 2; Figure 2, Panel B) showed a two-phase trend, with the significant increase in HIV-related mortality persisting until 1997, followed by a gradual but statistically significant decline. Since 1997, HIV-related mortality has remained higher in the Downtown Eastside than in City Centre.

**DISCUSSION**

In BC, there were marked changes in HIV-related mortality during the 20-year period between 1987 and 2006. The three distinct trends in HIV-related death observed at the provincial level mirror the evolving HIV epidemic and advances in antiretroviral therapy. Prior to 1992, there were limited therapeutic options for treating HIV, and HIV-related mortality rose steadily before this time. The introduction of two-drug antiretroviral regimens in 1992 was followed by a decrease in HIV-related mortality, which was consolidated with the widespread availability of combination antiretroviral therapy starting in 1996. Investigators in other resource-rich countries have described a similar three-phase pattern in HIV-related mortality over a comparable date range.

The substantial decline in HIV-related mortality observed at the provincial level has been largely driven by changes taking place in the densely populated, southern regions. Through strength of numbers, the patterns seen in these regions may overshadow trends in local health areas. We found regional variation in the changes in HIV-related mortality over time in BC. In particular, the Northern health authority showed increasing HIV-related mortality rates at a time when HIV deaths were decreasing in the other health authorities. Vast geographic area, low population density, coupled with a relative lack of specialized HIV resources, are some of the factors that may partially explain this phenomenon. It should be noted that while the highest rate of new HIV positive tests was in Vancouver Health Service Delivery Area (30.7 per 100,000 population; 193 cases), the next highest was in the Northern Interior Health Service delivery area (16.0 per 100,000 population; 23 cases), followed by the South Vancouver Island Health Service delivery area (9.9 per 100,000 population; 36 cases). Localized differences are also present within health authorities. The Vancouver Coastal health authority has substantial HIV-focused health care resources in comparison to other regions and has seen impressive overall declines in HIV-related mortality. However, the downturn in HIV-related mortality in the Downtown Eastside, which is known for a high prevalence of homelessness, poverty and illicit drug use, occurred at a later date and has been declining at a slower rate in comparison to the decline in the relatively affluent and adjacent City Centre. This intra-regional difference suggests that despite the availability of specialized HIV-related health care resources in Vancouver, there may be insufficient HIV-related services, such as outreach programs that administer antiretroviral therapy, additional HIV training of local practitioners, and increased HIV testing, to meet the needs of the population in the Downtown Eastside.

**Strengths and limitations**

This study has several strengths, including the 20-year study period and the use of age- and sex-adjusted mortality rates to account for the changing demographic profile of HIV. The use of cause-specific HIV-related mortality data rather than all-cause mortality was an unavoidable limitation because BC has no longitudinal registry of HIV-infected individuals. It was therefore not possible to describe non-HIV-related causes of death in HIV-infected individuals. The accuracy of this reporting of HIV-related causes of death could also vary by region. The sampling strategy relied on cause of death reported on the death certificate, therefore, our data may be subject to some degree of underreporting, including cases where HIV infection was unrecognized at the time of death or an HIV-related cause of death was not disclosed on the death certificate. Finally, caution must be exercised when comparing HIV-related mortality rates across regions, given the substantial differences in HIV prevalence between regions.

**CONCLUSION**

Substantial declines in HIV-related mortality have occurred over the last 20 years in the province of BC. Reductions in HIV-related mortality have occurred in three distinct phases, mirroring advances in antiretroviral therapy. The inter- and intra-regional variations in HIV mortality described here may be due to differential access to health care, even in a health care system where antiretroviral therapy is provided at no cost to patients.

These findings have important implications for health service planning. There is a need for more rigorous and ongoing monitoring of deaths among HIV-infected individuals by region. Further
research is necessary to determine the primary causes and region-specific influences of HIV-related mortality. A greater effort is needed to ensure that the benefit of antiretroviral therapy on HIV mortality is equally felt across BC. Health care programs – such as outreach programs that administer antiretroviral therapy – additional training of local practitioners with support from HIV specialists at major centres, and increased HIV testing targeted to the special needs of each region need to be evaluated as a possible means to overcome the excess HIV-related mortality observed in some regions of BC.

REFERENCES
5. ART-LINC. Mortality of HIV-1-infected patients in the first year of antiretroviral therapy: Comparison between low-income and high-income countries. Lancet 2006;367(9513):817-24.

Received: July 31, 2009
Accepted: May 20, 2010

RÉSUMÉ


Méthode : Dans les statistiques démographiques de la province, nous avons répertorié les personnes ≥18 ans décédées de causes liées au VIH entre 1987 et 2006. Les taux de mortalité annuels ont été calculés pour toute la C.-B., pour les cinq régions régionales de la santé et pour deux secteurs de Vancouver. Des analyses de régression aux points de jonction ont mesuré l’évolution des taux.


Conclusion : Presque partout en C.-B., la mortalité liée au VIH a baissé après l’introduction de traitements antirétroviraux efficaces, mais cette baisse a été retardée ou absente dans certaines régions. Les écarts régionaux pourraient s’expliciter par des inégalités d’accès aux soins de santé, même là où les traitements antirétroviraux sont fournis gratuitement.

Mots clés : mortalité; baisse de mortalité; VIH; Canada; Colombie-Britannique