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The measurement of Health Adjusted Life Expectancy (HALE) on a population-based observational cohort of HIV-positive and negative men and women in British Columbia

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Abstract

Background—We sought to understand whether people living with HIV (PLHIV) ever on highly active antiretroviral therapy (HAART) follow a pattern where morbidity is compressed into the last years of life or lessened as people age. Our objective was to estimate Health Adjusted Life Expectancy (HALE) among adults living with and without HIV, and examine dependency between causes of comorbidities.

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Contributors

RSH, OE, ABC, WZ, SJ, VDL, and JSGM conceived the study, interpreted the findings, and drafted the manuscript. WZ conducted the statistical analyses with help from RSH, VDL, SJ, and OE. RSH, OE, VDL, RB, JS and JSGM helped with data acquisition. All authors contributed to study design, interpretation of the results, and drafting of the manuscript. RSH, WZ, OE and VDL gathered and revised the data, and were involved in data analysis and revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

Methods—In this retrospective, population-based cohort study, the prevalence of select comorbidities was determined by age and sex using case-finding algorithms. Deaths were obtained from a vital event registry. Comorbid-specific HALE was estimated from 20 years of age by HIV status and sex. For each comorbidity, a healthy state was defined as the proportion of life expectancy comorbid-free, and was adjusted on the probability of occurrence of other different comorbidities. Lastly, the sensitivity of HALE estimates in our study was assessed to the sequencing of select comorbidities for the dependent comorbidity adjustments.

Findings—Our sample consisted electronic health records from 9,310 HIV-infected and 510,313 uninfected adults over the period 1 April 1996 to 31 December 2012 in British Columbia (BC), Canada. These individuals contributed a total of 49,605 deaths and 5,576,841 person-years over the study period. At exact age 20 years, HALE was approximately 31 years among men living with HIV and 27 years among women living with HIV. In the HIV-negative population, HALE was around 58 years for men and 63 for women. These results appear independent of ordering. However, PLHIV, particularly women living with HIV, had much shorter overall life expectancies than their HIV-negative counterparts in the general population, and thus spent less time in a healthy state.

Interpretation—While we observed limited differences in the levels of morbidity compression by HIV status, PLHIV – especially women living with HIV – spent less time in a healthy state. Expanded service delivery interventions to address complex care needs of aging PLHIV are critical to addressing shorter life expectancies, and improving their healthy states.

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INTRODUCTION

Life expectancy in high-income countries has steadily increased since the 20th century due to changes in fertility patterns, advances in medicine, and improved living conditions (1). This positive shift in years lived underscores the need for better investigative methods to measure longevity and morbidity (2), and to better understand changes in health status over a person's life course (3). To this end, Health Adjusted Life Expectancy (HALE), developed by Sullivan (4), is an important way to compartmentalize states of health by characterizing the number of years a person can expect to live in good and ill health, while considering age-specific mortality, morbidity, and disability.

Three competing theories help explain the relationship between life expectancy and the length of the healthy state: compression of morbidity, expansion of morbidity, and dynamic equilibrium (5, 6). Compression of morbidity assumes that therapeutic and preventive efforts will compress chronic diseases to a shorter period later in life, resulting in reduced periods of disease (5). In contrast, the expansion of morbidity attributes advances in medicine to decreased fatality rates, thus increasing prevalence rates (5, 7). Dynamic equilibrium, however, suggests that while decreased mortality rates lead to an increase in milder chronic diseases, severe chronic diseases will be reduced, resulting in a better quality of life (6).

While these theories highlight the interplay of mortality and morbidity at both individual and population levels, there is an urgent need to determine this relationship within the aging population living with HIV. Thus, we sought to understand whether this cohort of HIV-

positive and negative men and women follow a pattern where morbidity is compressed into the last years of life or lessened as a function of aging. The objective of this study was to estimate HALE, adjusting for co-dependencies between select comorbidities, among persons living with HIV (PLHIV) and those living without HIV in British Columbia (BC), Canada.

METHODS

Study design

The Comparative Outcomes and Service Utilization Trends (COAST) study is a retrospective cohort of adults (≥ 20 years) including all known PLHIV and a 10 percent random sample of the general population of BC, and with longitudinal data spanning from April 1, 1996 to December 31, 2012. COAST is based on de-identified health-related data arising from a unique linkage between the BC Centre for Excellence in HIV/AIDS (BCCfE) and Population Data BC – the British Columbia electronic repository of administrative health records held by the BC Ministry of Health and other provincial agencies for research (8–12). In this study, our combined dataset for individuals in COAST included: physician billings, hospital discharge abstracts, cancer-related diagnoses, and death. In addition, the BCCfE, which centrally manages all antiretroviral prescriptions in the province, provided data on antiretroviral therapy, viral load, and clinical manifestations, such as AIDS defining illness, comorbidities, and mortality (13).

Study population

Two cohorts of persons aged 20 years and over were created for this study. The PLHIV cohort was constructed from all adults known to be living with HIV in BC who have had a record of at least one detectable HIV plasma viral load and ever been prescribed Highly Active Antiretroviral Therapy (HAART) in BC between April 1, 1996 and December 31, 2012. The HIV-negative cohort was constructed from a 10% random sample of all adults in the total BC population meeting the age criterion between April 1, 1996 and December 31, 2012, and with no known HIV diagnosis determined using previously reported algorithm (14). Persons were followed until the end of the study period.

Statistical analysis

The primary outcome variable in our analysis was HALE. This measure estimates the number of healthy years an individual is expected to live at birth by subtracting the years of ill health from overall life expectancy (4). In addition to HALE, we estimated the prevalence of five comorbidities, which were used to estimate HALE. Due to their prevalence among PLHIV, we considered cardiovascular, respiratory, liver, and renal diseases, and non-AIDS defining cancers. All comorbidities were predefined using International Classification of Diseases (ICD) 9 and 10 codes and directly standardized to 1991 Canadian population.

HALE is composed of two sets of partial measures: age-specific death rates and age-specific rates of population morbidity (5). Age-specific death rates allowed us to measure mortality and life expectancy for select age groups, while age-specific rates of population morbidity (defined by cumulative prevalence of the five comorbidities noted above) allowed us to measure the extent of morbidity for these conditions in our two study populations. These

two measures were combined mathematically using an abridge life table approach developed by Sullivan (5) to estimate the HALE and proportion of time spent in a healthy state. HALE was reported at 20 years of age for men and women with corresponding standard error.

We examined the relationship between life expectancy and the length of the healthy state by constructing a measure the proportion of time spent in an unhealthy state. This measure was defined as the ratio of (LE-HALE)/LE and in this case the relative expansion of unhealthy state occurs when this ratio increases and compression of unhealthy state occurs when this ratio decreases (15).

We also considered the dependency of the five select comorbidities in our calculation of HALE. As Colin and colleagues (16) note, if we did not consider that study participants may have more than one of these select comorbidities, we could potentially over estimate person years lived with disability (PYLD) across all five select morbidities in our estimation of HALE. Therefore, for each comorbidity pair, we estimated the ratio of the prevalence of people with two conditions to the product of the two total prevalence rates for each of the conditions. We do this cumulatively in each adjusting step. The resulting dependent comorbidity factors were used to adjust for dependent comorbidity in summation of PYLD across all five comorbidities and in the calculation of HALE. We examined the sensitivity of the HALE estimates in our study to the sequencing of these five select comorbidities for the dependent comorbidity adjustments (16).

Data are presented within categories as frequencies [n (%)] or as median and 25 and 75 percentiles. Confidence intervals and rates were reported to one significant digit. All data were analyzed using SAS software, version 9.3 (SAS Institute, Inc., Cary, North Carolina). HALE and prevalence estimates were programmed using spreadsheets developed in Microsoft Excel for Mac 2011, Version 14.5.9 (Microsoft Corporation, Redmond, Washington). In the following presentation of results, all differences between PLHIV and HIV-negative controls were significant at $p < 0.0001$ unless otherwise specified.

Ethical approval was obtained from the University of British Columbia/ Providence Health Care (#H09-02905) and Simon Fraser University (#2013s0566) research ethics boards.

Role of source of funding—The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

Our sample consisted of 9,310 PLHIV aged 20 years and older on HAART and 510,313 adults who were uninfected with HIV followed from April 1, 1996 to December 31, 2012. Baseline characteristics of the study population are noted in Table 1. Compared to HIV-negative men and women in our sample, PLHIV were more likely to be men, to live in metro-Vancouver, and to have been followed for a shorter period. Rates of mortality, crude and directly adjusted to the Canadian population, were significantly higher among both men and women living with HIV.

Table 2 highlights the directly age-adjusted prevalence of five select individual comorbidities among PLHIV and those uninfected. As noted here, men and women living with HIV, compared to their HIV negative counterparts, exhibited higher prevalence rates for renal and liver diseases. Among PLHIV with liver disease, Hepatitis C accounts for 24.8% (2,024 out of 8,145) of person years lived with liver disease in men and 54.3% (1,003 out of 1,799) among women. In contrast, among HIV-negative men and women, only 5.8% (3,348 out of 53,460) and 5.0% (2,226 out of 44,845) of person years lived due to liver disease can be attributed to Hepatitis C (data not shown).

As note in Appendix Table A1, there is considerable variation in the distribution of paired select individual co-morbidities. Among PLHIV, these individual comorbidities are more likely to be paired with liver and renal diseases, while they are more likely to be paired with cardiovascular diseases amongst HIV-negative individuals. Individuals with only one cause or select individual morbidity ranges from a quarter to half in men and women, indicating that unadjusted HALE measures would greatly over estimate disability.

A total of 49,605 deaths and 5,576,841 person-years were accumulated during this study. A greater proportion of deaths occurred within the cohort of PLHIV ever on HAART (21.0% or 1,958 out of 9,310) than in the non-infected cohort (9.3% or 47,647 out of 510,313). Life expectancy at exact age 20 years between those ever on HAART and those uninfected was 33.7 (0.1, standard error) vs. 60.5 (0.1) years for men; and 29.1 (0.1) vs. 65.4 (0.1) years for women. Among PLHIV, women had a significantly lower life expectancy at this exact age than men [29.1 (0.1) vs. 33.7 (0.1) years].

Table 3 provides a sensitivity analysis of HALE based on all-cause disease prevalence by using different adjusting orders (see Table A2 in the Appendix on the ordering). As noted here, there is considerable difference between unadjusted and adjusted HALE measures. However, the ordering of comorbidities makes little difference in the estimate of HALE and suggests that the level of contraction is similar by gender and HIV status. As noted in this Table and graphically in Figure 1, although men and women living with HIV spent a similar proportion of their life in a healthy state, the years lived in this state were much shorter for PLHIV compared to their HIV-negative counterparts. This was especially noticeable among women living with HIV.

DISCUSSION

We sought to understand whether individuals living with HIV ever on HAART in BC, compared to their HIV-negative counterparts, followed a pattern where morbidity was compressed into the last years of life or lessened as people aged. The level of compression was based on the proportion of time spent in a healthy state. After adjusting for dependency between comorbidities using the approach proposed by Colin and colleagues (16), we found little difference in the proportion of time spent in a healthy state for both PLHIV and their HIV-negative counterparts. However, the time spent in this state was considerably less for men and women living with HIV. Furthermore, much of the pairwise dependency could be attributed to liver and renal diseases among PLHIV and cardiovascular disease among their HIV-negative counterparts.

Consistent with previous work (17–21), our findings highlight that burden of disease was higher for PLHIV on HAART than those in the HIV-negative population. For example, Kendall and colleagues (17) found that PLHIV in Ontario, particularly women, had a significantly higher prevalence of almost all chronic conditions. Additionally, Goulet and colleagues (20) found that in their primarily male cohort, those living with HIV experienced higher rates of liver and renal disease than those who were uninfected. While these and other studies present findings on the range of comorbidities and risk factors impacting the lives of PLHIV, we add to the literature by integrating HALE measures to generate insight into how a substantially higher burden of comorbidity can directly impact PLHIV's health life expectancy, compared to their HIV-negative counterparts.

To our knowledge, this study is the first to characterize the length of the health state for both PLHIV and HIV-negative individuals, and show differentially shortened life expectancy among women living with HIV as compared to their male counterparts. In our sensitivity analysis, we observed similar levels of compression of chronic diseases, resulting in reduced periods of disease in both positive and negative men and women. Like their HIV-negative counterparts, we thus saw a compression of comorbidities in the last few years of life for PLHIV. The shortened life among women living with HIV has previously been observed in Canada. Other national or international studies have either found longer life expectancies among women than men or have found no sex-related differences (22).

We also argue that the substantial differences in health life expectancies may be attributed to previous history of injection drug use among PLHIV. Studies have highlighted the impact of liver-related illnesses and Hepatitis C on morbidity and mortality rates amongst PLHIV who inject drugs or have a history of injection drug use (e.g. 23–25). Lesko and colleagues observed higher rates of end-stage renal and liver diseases amongst PLHIV who inject drugs as compared to non-injecting PLHIV (26). While the increased burden of liver and renal disease impacting PLHIV in our sample may be due to current or previous use of injection drugs, these diseases could be mitigated through access to direct-acting antiviral (DAA) regimens and tenofovir alafenamide (TAF) based antiretroviral regimens (27). Although current costs of DAAs and TAF-based antiretroviral regimens limit use, access strategies being implemented at the provincial level may successfully expand use of these regimens, reducing future infections in persons living with HIV (28).

Our study has several strengths and limitations that should be noted. In terms of strengths, the large and population-based nature of the COAST study from which our analytic sample was defined, allowed us to assess small differences in the outcomes of interest. The cohort of PLHIV included the vast majority of all known PLHIV in BC on HAART due to our case ascertainment method, which included everyone in the BCCfE's registry. The cohort of HIV-negative persons was comprised of individuals from the same time-period and universal health care system as the HAART group, which helped minimize selection bias that can be introduced by using such a comparator. Government funded health care is available to all BC residents if they are a Canadian citizen, landed immigrant, government-assisted refugee, post-secondary international student with a study permit, or temporary worker with a work permit for six months or longer. Additionally, antiretroviral therapy, laboratory monitoring, and medical care for PLHIV and those not infected do not generally require any co-

payments or deductibles in BC, which may be present in some other Canadian jurisdictions or elsewhere. Therefore, potential biases that could result from multiple health care payers and differential access to health care services in the ascertainment of comorbidities in this study are minimized.

In terms of limitations, our results may have been impacted by loss to follow-up. However, we believe loss to follow-up was minimized by using large, population-based administrative data sources, as well as the extensive data linkage that we performed across the multiple data sources included in the COAST study. Our ascertainment of comorbidities may also have been impacted by the reliance on administrative data rather than self- or physician-reported records. Additionally, we did not assess the burden of mental health comorbidities, which are also likely higher among PLHIV (16). We are also limited by our ability to ascertain outcomes that occurred outside of BC. However, these limitations likely impacted the HIV-positive and negative cohorts equally. Finally, we would expect to see differences between these populations decrease if we limited our analysis to more recent years or to those who initiated HAART without any previous antiretroviral therapy use. In this paper, to ensure robustness of our results, we focussed on everyone who has ever started HAART, as well as the entire time-period when these drugs were available in the province.

In conclusion, our results demonstrate that PLHIV spend proportionally about the same amount of time in a health state as their HIV-negative counterparts in British Columbia. However, PLHIV, especially women, have much shorter overall life expectancies than their HIV-negative general population counterparts, and thus spend notably less time in a healthy state. As life expectancy for many PLHIV is increasingly comparable to HIV-negative populations (27), we demonstrated here that it remains imperative to address the challenges this population faces in achieving a healthy state to improve quality of life over the life course.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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All inferences, opinions, and conclusions drawn in this paper are those of the authors, and do not reflect the opinions or policies of the Data Stewards or funders.

Declaration of interests

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References

- Centers for Disease Control and Prevention (CDC) Trends in aging—United States and worldwide. *MMWR Morb Mortal Wkly Rep.* 2003; 52(6):101–6. [PubMed: 12645839]
- Salomon JA, Wang H, Freeman MK, Vos T, Flaxman AD, Lopez AD, et al. Healthy life expectancy for 187 countries, 1990–2010: a systematic analysis for the Global Burden Disease Study 2010. *Lancet.* 2012; 380(9859):2144–62. [PubMed: 23245606]
- Christensen K, Doblhammer G, Rau R, Vaupel JW. Ageing populations: the challenges ahead. *Lancet.* 2009; 374(9696):1196–208. [PubMed: 19801098]
- Sullivan DF. A single index of mortality and morbidity. *HSMHA Health Reports.* 1971; 86(4):347–54. [PubMed: 5554262]
- Nusselder WJ, van der Velden K, van Sonsbeek JL, Lenior ME, van den Bos GA. The elimination of selected chronic diseases in a population: the compression and expansion of morbidity. *American Journal of Public Health.* 1996; 86(2):87–94. [PubMed: 8561251]
- Manton KG. Changing concepts of morbidity and mortality in the elderly population. *Milbank Memorial Fund Quarterly.* 1982; 60(2):183–244.
- Kramer M. The rising pandemic of mental disorders and associated chronic diseases and disabilities. *Acta Psychiatrica Scandinavica.* 1980; 62(285):382–97. [PubMed: 7468297]
- British Columbia Ministry of Health. Data Extract. MOH: Population Data BC; 2014. Medical Services Plan (MSP) Payment Information File. <http://www.popdata.bc.ca/data>
- British Columbia Ministry of Health. Data Extract. MOH: Population Data BC; 2014. Consolidation File (MSP Registration & Premium Billing). <http://www.popdata.bc.ca/data>
- British Columbia Ministry of Health. Data Extract. MOH: Population Data BC; 2014. Discharge Abstract Database (Hospital Separations). <http://www.popdata.bc.ca/data>
- British Columbia Cancer Agency. Data Extract. BC Cancer Agency: Population Data BC; 2014. BC Cancer Agency Registry Data. <http://www.popdata.bc.ca/data>
- BC Vital Statistics Agency. Data Extract. BC Vital Statistics Agency; 2014. Vital Statistics Deaths. Population Data BC. 2014 <http://www.popdata.bc.ca/data>
- BC Centre for Excellence in HIV/AIDS. Drug Treatment Program. 2014. <http://www.cfenet.ubc.ca/drug-treatment-program/>
- Nosyk B, Colley G, Yip B, Chan K, Heath K, Lima VD, et al. Application and validation of case-finding algorithms for identifying individuals with human immunodeficiency virus from administrative data in British Columbia, Canada. *PLoS One.* 2013; 8(1):e54416. [PubMed: 23382898]
- van Baal PHM, Hoogenveen RT, de Wit G, Boshuizen HC. Estimating health-adjusted life expectancy conditional on risk factors: results for smoking and obesity. *Population Health Metrics.* 2006; 4(14)doi: 10.1186/1478-7954-4-14
- Mathers CD, Iburg KM, Begg S. Adjusting for dependent comorbidity in the calculation of healthy life expectancy. *Population Health Metrics.* 2006; 4(4)doi: 10.1186/1478-7954-4-4
- Kendall CE, Wong J, Taljaard M, Glazier RH, Hogg W, Younger J, et al. A cross-sectional, population-based study measuring comorbidity among people living with HIV in Ontario. *BMC Public Health.* 2014; 14:161. [PubMed: 24524286]
- Hasse B, Ledergerber B, Furrer H, Battegay M, Hirschel B, Cavassini M, et al. Morbidity and aging in HIV-infected persons: the Swiss HIV cohort study. *Clinical Infectious Diseases.* 2011; 53(11):1130–9. [PubMed: 21998280]

19. Guaraldi G, Orlando G, Zona S, Menozzi M, Carli F, Garlassi E, et al. Premature age-related comorbidities among HIV-infected persons compared with the general population. *Clinical Infectious Diseases*. 2011; 53(11):1120–6. [PubMed: 21998278]
20. Goulet JL, Fultz SL, Rimland D, Butt A, Gibert C, Rodriguez-Barradas M, et al. Aging and infectious diseases: do patterns of comorbidity vary by HIV status, age, and HIV severity? *Clinical Infectious Diseases*. 2007; 45(12):1593–601. [PubMed: 18190322]
21. Salter ML, Lau B, Go VF, Mehta SH, Krik GD. HIV infection, immune suppression, and uncontrolled viremia are associated with increased multimorbidity among aging injection drug users. *Clinical Infectious Diseases*. 2011; 53(12):1256–64. [PubMed: 21976463]
22. Samji H, Cescon A, Hogg RS, Modur SP, Althoff KN, Buchacz K, et al. Closing the gap: increases in life expectancy among treated HIV-positive individuals in the United States and Canada. *PLoS One*. 2013; 8(12):e81355. [PubMed: 24367482]
23. Monto A, Currie S, Wright TL. Liver disease in injection drug users with Hepatitis C, with and without HIV coinfection. *Journal of Addictive Diseases*. 2008; 27(2):49–59.
24. Buskin SE, Barash EA, Scott JD, Aboulafia DM, Wood RW. Hepatitis B and C infection and liver disease trends among human immunodeficiency virus-infected individuals. *World Journal of Gastroenterology*. 2011; 17(14):1807–16. [PubMed: 21528052]
25. Parashar S, Collins AB, Montaner JS, Hogg RS, Milloy MJ. Reducing rates of preventable HIV/AIDS-associated mortality among people living with HIV who inject drugs. *Current Opinion in HIV/AIDS*. 2016; 11(5):507–13.
26. Lesko CR, Moore RD, Tong W, Lau B. Association of injection drug use with incidence of HIV-associated non-AIDS-related morbidity by age, 1995–2014. *AIDS*. 2016; 30:1447–55. [PubMed: 26990627]
27. Lima VD, Rozada I, Grebely J, Hull M, Lourenco L, Nosyk B, et al. Are interferon-free direct-acting antivirals for the treatment of HCV enough to control the epidemic among people who inject drugs? *PLOS One*. 2015; 10(12):e0143836. [PubMed: 26633652]
28. Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. HIV Outpatient Study Investigators. *New England Journal of Medicine*. 1998; 338(13):853–60. [PubMed: 9516219]

RESEARCH IN CONTEXT

Evidence before this study

Health Adjusted Life Expectancy (HALE) is one index used to capture morbidity and mortality factors of a population, and can thus be utilized to understand the impacts of HIV and comorbid conditions on an aging population living with HIV. However, examining all causes of comorbidity in the measure of HALE, without considering people with more than one condition, would overestimate the severity of the time a population is spent in an unhealthy state. We conducted a systematic review of the scientific literature by searching PubMed, CINAHL (Ebscohost), Global Health (Ovid), EMBASE (Ovid), and the Cochrane Central Register of Controlled Trials databases for studies published up to November 30, 2016. Our search terms included “healthy life expectancy” or “health-adjusted life expectancy” and “comorbidity” or “morbidity.”

Added value of this study

Using data from the Comparative Outcomes and Service Utilization Trends (COAST) study, we estimated HALE, adjusting for potential dependent comorbidities for select conditions among persons living with HIV (PLHIV) and those living without HIV (HIV-negative) in the British Columbian population. To our knowledge, this is the first study to characterize the length of the health state for both PLHIV and HIV-negative individuals, as well as the impact of dependent comorbidities on HALE’s measurement. Age-specific morbidity rates were calculated by dividing the number of people with select comorbidities by the number of person-years over the study period, and reported by age group and gender. Due to their prevalence among PLHIV, we elected to consider the following key comorbid conditions: cardiovascular disease, respiratory disease, liver disease, renal disease, and non-AIDS defining cancers. Over half of comorbidities reported are paired or dependent with another condition. In the case of PLHIV, we found comorbidities were mostly paired with liver and renal diseases, while paired with cardiovascular diseases in the HIV-negative population. The ordering of comorbidity pairs has limited impact on the estimation of HALE, however these adjusted HALE measures are noticeably higher, and the time spent in an unhealthy state is much shorter than the unadjusted measures.

Implications of all available evidence

After adjusting for co-dependencies, we observed limited differences in the levels of morbidity compression between PLHIV and their HIV-negative counterparts, however, men and women living with HIV had lower life expectancies and measures of HALE. Our findings highlight the urgent need to better address PLHIV’s complex care needs through expanded service delivery targeted at comorbidities and chronic-disease management.

Figure 1.

Life expectancy at exact age 20 years taking into adjustment for all cause disease prevalence, broken down by gender, HIV status, and the length of healthy and unhealthy states.

Table 1

Baseline characteristics of the study population, by HIV status.

Variable	PLHIV (n= 9,310)	HIV– (n= 510,313)
Gender		
Male	7,702 (82.7%)	256,440 (50.0)
Female	1,680 (17.3%)	253,873 (50.0)
Age (in years)		
Median (25th–75th percentile)	40 (34–47)	36 (24–50)
Years since enrolment		
Median (25th–75th percentile)	9 (4–14)	13 (5–17)
Residence		
Metro Vancouver	4,732 (50.8%)	86,470 (16.9%)
Other	4,529 (48.7%)	410,729 (80.5%)
Unknown	49 (0.5%)	13,114 (2.6%)
Deaths		
Male	1606 (82.0%)	24,394 (51.2%)
Female	352 (18.0%)	23,253 (48.8%)
Crude Death Rate (per 1,000 person-years)		
Male	29.1	9.0
Female	33.6	8.3
Adjusted Death Rate (per 1,000 person-years)		
Male	30.0	8.3
Female	36.5	5.8

Legend: PLHIV, persons living with HIV; HIV–, HIV negative

Table 2

Relative risk of the age-adjusted prevalence of select individual co-morbidities among British Columbians, by gender and HIV status.

Co-morbidity	Group	Adjusted Prevalence (per cent)	Relative risk (95% CI)
MALES			
Cancers	PLHIV	3.2	1.6 (1.6, 1.7)
	HIV–	1.9	
Cardiovascular diseases	PLHIV	5.5	0.7 (0.7, 0.8)
	HIV–	7.3	
Liver diseases	PLHIV	13.2	7.3 (7.3, 7.3)
	HIV–	1.8	
Renal diseases	PLHIV	6.3	5.1 (5.1, 5.2)
	HIV–	1.2	
Respiratory diseases	PLHIV	4.4	0.9 (0.9, 0.9)
	HIV–	4.8	
FEMALES			
Cancers	PLHIV	1.6	0.8 (0.8,0.8)
	HIV–	1.8	
Cardiovascular diseases	PLHIV	2.8	0.5 (0.5, 0.5)
	HIV–	5.2	
Liver diseases	PLHIV	14.5	9.8 (9.8, 9.9)
	HIV–	1.5	
Renal diseases	PLHIV	9.8	10.2 (10.1,10.2)
	HIV–	1.0	
Respiratory diseases	PLHIV	7.7	1.3 (1.3, 1.3)
	HIV–	5.8	

Legend: CI, Confidence interval; PLHIV, persons living with HIV; HIV–, HIV negative; all significantly different at the $p > 0.0001$.

Table 3

Sensitivity analysis of HALE based on all-cause disease prevalence by using different adjusting order, by gender and HIV status.

Order based first on	Group	HALE, years (SE)	Proportion of time spent in an unhealthy state
MALES			
All cause, unadjusted	PLHIV	24.4 (0.17)	0.28
	HIV–	47.4 (0.04)	0.22
All cause, adjusted			
Cancers	PLHIV	31.5 (0.10)	0.06
	HIV–	58.1 (0.02)	0.04
Cardiovascular diseases	PLHIV	31.8 (0.16)	0.06
	HIV–	58.1 (0.02)	0.04
Liver diseases	PLHIV	31.7 (0.09)	0.06
	HIV–	57.7 (0.02)	0.04
Renal diseases	PLHIV	31.8 (0.09)	0.06
	HIV–	58.0 (0.02)	0.04
Respiratory diseases	PLHIV	32.0 (0.08)	0.05
	HIV–	58.2 (0.02)	0.04
FEMALES			
All cause, unadjusted	PLHIV	20.0 (0.17)	0.31
	HIV–	51.9 (0.04)	0.21
All cause, adjusted			
Cancers	PLHIV	26.9 (0.19)	0.08
	HIV–	63.3 (0.02)	0.03
Cardiovascular diseases	PLHIV	27.8 (0.16)	0.05
	HIV–	63.3 (0.02)	0.03
Liver diseases	PLHIV	28.3 (0.10)	0.03
	HIV–	62.7 (0.02)	0.04
Renal diseases	PLHIV	26.9 (0.19)	0.08
	HIV–	63.2 (0.02)	0.03
Respiratory diseases	PLHIV	28.3 (0.10)	0.03
	HIV–	63.4 (0.02)	0.03

Legend: SE, Standard error; PLHIV, persons living with HIV; HIV–, HIV negative; HALE, healthy life expectancy; LE, life expectancy; The proportion of time spent in an unhealthy state was defined as the ratio of (LE-HALE)/LE.