

RESEARCH ARTICLE

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# A cross-sectional, population-based study measuring comorbidity among people living with HIV in Ontario

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## Abstract

**Background:** As people diagnosed with HIV and receiving combination antiretroviral therapy are now living longer, they are likely to acquire chronic conditions related to normal ageing and the effects of HIV and its treatment. Comorbidities for people with HIV have not previously been described from a representative population perspective.

**Methods:** We used linked health administrative data from Ontario, Canada. We applied a validated algorithm to identify people with HIV among all residents aged 18 years or older between April 1, 1992 and March 31, 2009. We randomly selected 5 Ontario adults who were not identified with HIV for each person with HIV for comparison. Previously validated case definitions were used to identify persons with mental health disorders and any of the following physical chronic diseases: diabetes, congestive heart failure, acute myocardial infarction, stroke, hypertension, asthma, chronic obstructive lung disease, peripheral vascular disease and end-stage renal failure. We examined multimorbidity prevalence as the presence of at least two physical chronic conditions, or as combined physical-mental health multimorbidity. Direct age-sex standardized rates were calculated for both cohorts for comparison.

**Results:** 34.4% (95% confidence interval (CI) 33.6% to 35.2%) of people with HIV had at least one other physical condition. Prevalence was especially high for mental health conditions (38.6%), hypertension (14.9%) and asthma (12.7%). After accounting for age and sex differences, people with HIV had significantly higher prevalence of all chronic conditions except myocardial infarction and hypertension, as well as substantially higher multimorbidity (prevalence ratio 1.30, 95% CI 1.18 to 1.44) and combined physical-mental health multimorbidity (1.79, 95% CI 1.65 to 1.94). Prevalence of multimorbidity among people with HIV increased with age. The difference in prevalence of multimorbidity between the two cohorts was more pronounced among women.

**Conclusion:** People living with HIV in Ontario, especially women, had higher prevalence of comorbidity and multimorbidity than the general population. Quantifying this morbidity at the population level can help inform healthcare delivery requirements for this complex population.

**Keywords:** Human immunodeficiency syndrome, Primary health care, Chronic disease, Comorbidity, Multimorbidity

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## Background

The accumulation of chronic conditions over the lifespan is a significant and rising burden on individuals and healthcare systems. In Canada, 33% of community dwelling individuals report having at least one of 7 common chronic conditions [1]. There is strong evidence that the management of chronic diseases is most effectively and economically provided in well-supported primary care settings [2,3]. The community-based management of these chronic conditions consumes substantial healthcare resources [4], and the bulk of this management occurs in primary care [5,6].

As people with Human immunodeficiency syndrome (HIV) on combination antiretroviral therapy (ART) are now living longer, they are likely to acquire additional chronic conditions related to normal aging as well as from the effects of HIV and its treatment [7,8]. While the literature regarding what factors contribute to the prevalence of specific conditions is evolving, it is clear that multimorbidity, the presence of several of these conditions, is increasingly the norm for people with HIV [9]. Early in the era of HIV, it was considered a deadly, acute condition, requiring a specialist focus on care [10-12]. However, with ART HIV becomes a chronic condition, and a generalist perspective may now have a more major role as comorbidities increase [13-17]. In order to determine the best way to integrate primary and specialist care [18], we require a full understanding of the complex health needs of this population.

The specific objectives of this study are to describe the prevalence of comorbidities and their multimorbidity for people living with HIV and to compare this prevalence to an age and sex adjusted general population. In Ontario, Canada, administrative data for over 13 million multiethnic residents is routinely collected at the time of care in a single-payer health system. These data can be used to measure the prevalence of chronic disease [19]. To our knowledge, this is the first study to use a population-based approach to measure the types and numbers of chronic diseases associated with HIV. As a result, this study will inform the complex healthcare needs of this population.

## Methods

### Study design

We conducted a retrospective observational study to examine the demographic and clinical characteristics of people living with HIV in Ontario compared with those in the general Ontario population. We analyzed the administrative databases held at the Institute for Clinical Evaluative Sciences (ICES) from the province of Ontario, Canada comprising data on almost 13 million individuals (2008). These data are made available to accredited researchers through a data sharing agreement with the Ontario Ministry of Health and Long-Term

Care and are individually linked using an anonymous identification number in accordance with the provincial Personal Health Information Protection Act. The study was approved by the Ottawa Hospital Research Ethics Board and the Sunnybrook Health Sciences Centre Research Ethics Board.

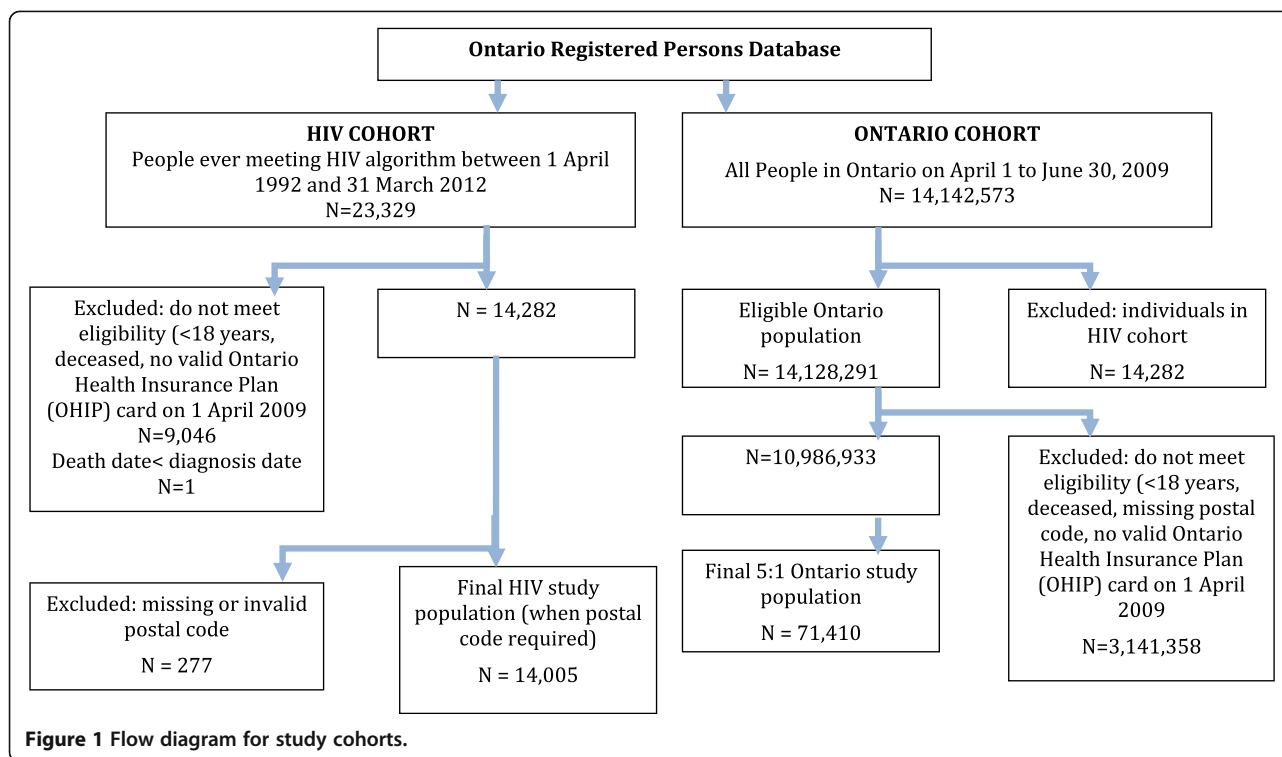
### Study population

We identified eligible individuals from the Registered Persons Database (RPDB), an electronic registry of all Ontarians eligible for health coverage that captures patient demographic information, including age, sex, postal code and mortality data (see flow diagram Figure 1). We used data from the Ontario Health Insurance Plan (OHIP) billing claims system, which records claims for about 95% of physician services conducted in the province, to obtain an HIV cohort. We applied a previously validated algorithm to people 18 years of age and older and living in Ontario between April 1, 1992 and April 1, 2009 [20]. Briefly, this algorithm requires 3 physician claims (International Classification of Diseases, Ninth Revision (ICD-9) code for HIV infection (042, 043, 044)) over a 3-year period and has a sensitivity and specificity of 96.2% (95% CI 95.2% - 97.9%) and 99.6% (95% CI 99.1% - 99.8%), respectively for identifying people living with HIV and receiving HIV care. As a comparison, a cohort of individuals 18 years or older, living in Ontario on April 1, 2009, and not in the HIV cohort was created using a computerized random number generator in a 5:1 ratio to the HIV cohort. For both cohorts, individuals without a valid health card, age or sex value and those without valid postal codes were excluded.

### Variables

All variables for patients in the HIV and Ontario cohorts were captured using identical methods. Age, sex and postal code on April 1, 2009 were obtained from the RPDB. To broadly describe the populations, we used postal codes at the neighborhood level linked to 2006 Statistics Canada census data to assign income quintiles, marginalization quintiles and rurality scores. We used Matheson's Canadian Marginalization Index [21] to assign marginalization quintiles for four components of marginalization (1 lowest to 5 highest): dependency, residential instability, material deprivation, and ethnic concentration and present these as a summary score. Rurality was assigned categorically into major urban areas (score 0 to 9), non-major urban areas (10 to 44), and rural areas (45 or higher) according to the Rurality Index of Ontario [22].

Using OHIP billing claims data, the Canadian Institute for Health Information (CIHI) Discharge Abstract Database, which supplies information on acute care hospitalizations and the CIHI National Ambulatory Care Reporting System, which captures information on visits to



emergency departments, we applied additional previously validated algorithms in both cohorts to identify the status (i.e. presence or absence) of the following physical comorbidities on April 1, 2009: diabetes, congestive heart failure, acute myocardial infarction, hypertension, asthma, chronic obstructive lung disease, stroke, end stage renal disease and peripheral vascular disease [19,23-26]. People with mental health conditions between April 1, 2007 and April 1, 2009 were broadly captured using an algorithm previously validated to identify people receiving mental health services in the primary care setting [27].

Disease count was used to measure the prevalence of multimorbidity [28]. Multimorbidity was defined as the presence of two or more listed physical chronic conditions, and physical-mental health comorbidity was defined as a combination of mental health condition and any physical chronic health condition. In patients in the HIV cohort, this multimorbidity is in addition to HIV as their index condition.

We used the Ontario Drug Benefits claims database to identify individuals in the cohorts who were prescribed drugs paid for by the public system which covers those aged 65 and older and those receiving social assistance (Ontario Works, Ontario Disability Support Program, or the subsidized Trillium program).

#### Statistical analysis

We used descriptive statistics to describe the demographic characteristics of the two cohorts. For our descriptive

analyses, age was treated as both a continuous variable and a categorical variable. Sex, age group, income quintiles, rurality categories and use of Ontario Drug Benefits were described as categorical variables, and the marginalization composite score as a continuous variable. These characteristics were compared between the cohorts using two-sample t-tests for continuous variables and chi-squared tests for categorical variables. We calculated the prevalence of individual physical and mental health comorbidities, multimorbidity, and physical-mental health comorbidity in the HIV cohort, together with 95% confidence intervals (CI).

We used direct standardization to calculate age and sex standardized prevalence rates for both populations. The Canadian 1991 population was used as the reference standard [29]. We present the comparative ratio of these rates together with 95% confidence interval, calculated using the formula provided by Breslow and Day [30]. We also compare the prevalence of comorbidity and multimorbidity with age between the HIV and Ontario cohorts for both men and women. All statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, North Carolina).

#### Results

Table 1 provides for descriptive purposes the demographic characteristics of people in the HIV cohort compared to the Ontario cohort. The sex and age distributions differed substantially between the HIV and Ontario

**Table 1 Demographic characteristics of HIV and Ontario cohorts (April 1, 2009)**

		HIV cohort n = 14,005	Ontario cohort n = 71410	p-value
<b>Age (years)</b>	Mean (SD)	45.36 (10.77)	46.65 (17.79)	<.001
<b>Age group (n, %)</b>	18-35 years	2,355 (16.8%)	21,600 (30.2%)	<.001
	36-50 years	7,798 (55.7%)	21,895 (30.7%)	
	51-65 years	3,283 (23.4%)	16,575 (23.2%)	
	>65 years	569 (4.1%)	11,340 (15.9%)	
<b>Sex (n, %)</b>	Male	11,270 (80.5%)	34,862 (48.8%)	<.001
<b>Income quintile (1 lowest, 5 highest)</b>	Missing	131 (0.9%)	302 (0.4%)	<.001
	1	4,441 (31.7%)	13,918 (19.5%)	
	2	2,875 (20.5%)	14,224 (19.9%)	
	3	2,280 (16.3%)	14,053 (19.7%)	
	4	2,085 (14.9%)	14,554 (20.4%)	
	5	2,193 (15.7%)	14,359 (20.1%)	
<b>Marginalization index</b>	Mean (SD)	3.35 (0.74)	2.97 (0.78)	<.001
<b>Rurality group</b>	Missing	41 (0.3%)	596 (0.8%)	
	Major urban	41 (0.3%)	596 (0.8%)	
	Non-major urban	12,563 (89.7%)	52,020 (72.8%)	<.001
	Rural	1,006 (7.2%)	13,341 (18.7%)	
<b>ODB claim</b>	Yes	395 (2.8%)	5,453 (7.6%)	
		8,789 (62.8%)	21,509 (30.1%)	<.001

populations; people with HIV were more often male (80.5% vs. 48.8%,  $p < 0.001$ ) and less likely to be in the youngest (18–35 years) or oldest (>65 years) age groups (16.8% vs. 30.2% and 4.1% vs. 15.9% respectively,  $p < 0.001$ ). Overall, people with HIV were poorer (lowest income quintile 31.7% vs 19.5%,  $p < 0.001$ ), lived in more marginalized neighborhoods (marginalization index 3.35 (SD 0.74) vs. 2.97 (SD 0.7),  $p < 0.001$ ), were more likely to live in urban settings (89.7% vs. 72.8%,  $p < 0.001$ ) and were more likely to have obtained provincial drug benefits than those in the Ontario cohort (62.8% vs. 30.1%,  $p < 0.001$ ).

The prevalence of individual comorbidities and of multimorbidity among individuals in the HIV cohort are presented in Table 2. More than one-third (38.6%, 95% CI 37.8% to 39.4%) of people with HIV had a mental health condition diagnosed within the previous 2 years. One-third (34.4%, 95% CI 33.6% to 35.2%) had at least one physical chronic condition in addition to their HIV. Comorbidities with especially high prevalence included hypertension (14.9%), asthma (12.7%), diabetes (8.3%) and chronic obstructive pulmonary disease (7.9%). The prevalence of multimorbidity (at least two physical conditions) was 10.8% (95% CI 10.3% to 11.3%), and of physical-mental health comorbidity was 15.5% (95% CI 14.9% to 16.1%).

Table 3 presents the age and sex standardized prevalence rates for the two cohorts (standardized to the 1991 Canadian population), along with the prevalence rate

ratios and 95% confidence intervals. After accounting for age and sex differences, people in the HIV cohort were more likely to have at least one chronic condition than those in the Ontario cohort (prevalence ratio 1.13, 95% CI 1.07 to 1.20). People with HIV had significantly higher prevalence of all chronic conditions except myocardial infarction and hypertension, which were not significantly different from the general population. Individuals with HIV had substantially higher multimorbidity (prevalence ratio 1.30, 95% CI 1.18 to 1.44) and physical-mental health comorbidity (1.79, 95% CI 1.65 to 1.94) than the Ontario population.

Figure 2 shows the prevalence of comorbidity and multimorbidity, for men and women respectively, by age group for the HIV and Ontario cohorts. Prevalence of multimorbidity increased with age in all groups and was higher for women than men. Men in the HIV cohort only had higher prevalence of at least one chronic condition and multimorbidity than men in the Ontario cohort in the younger age groups. In contrast, multimorbidity prevalence among women with HIV was consistently higher than among Ontario women in all age groups, and this gap appeared to widen slightly with age.

## Discussion

Our study quantifies the substantial comorbidity prevalence among people living with HIV in Ontario. Mental

**Table 2 Comorbidities and multimorbidity prevalence of people living with HIV in Ontario (April 1, 2009)**

Comorbidity N = 14,005	Prevalence		
	(n)	(%)	95% CI
Mental health condition	5,401	38.6%	(37.8% to 39.4%)
<b>Physical conditions:</b>			
Myocardial infarction	174	1.2%	(1.1% to 1.4%)
Congestive heart disease	233	1.7%	(1.5% to 1.9%)
Chronic obstructive pulmonary disease	1,106	7.9%	(7.5% to 8.3%)
End stage renal disease	223	1.6%	(1.4% to 1.8%)
Peripheral vascular disease	72	0.5%	(0.4% to 0.6%)
Asthma	1,780	12.7%	(12.2% to 13.3%)
Diabetes	1,167	8.3%	(7.9% to 8.8%)
Hypertension	2,093	14.9%	(14.4% to 15.5%)
Stroke	173	1.2%	(1.1% to 1.4%)
At least one physical condition	4820	34.4%	(33.6% to 35.2%)
Physical-mental health multimorbidity	2,174	15.5%	(14.9% to 16.1%)
Multimorbidity (at least two physical conditions)	1,508	10.8%	(10.3% to 11.3%)

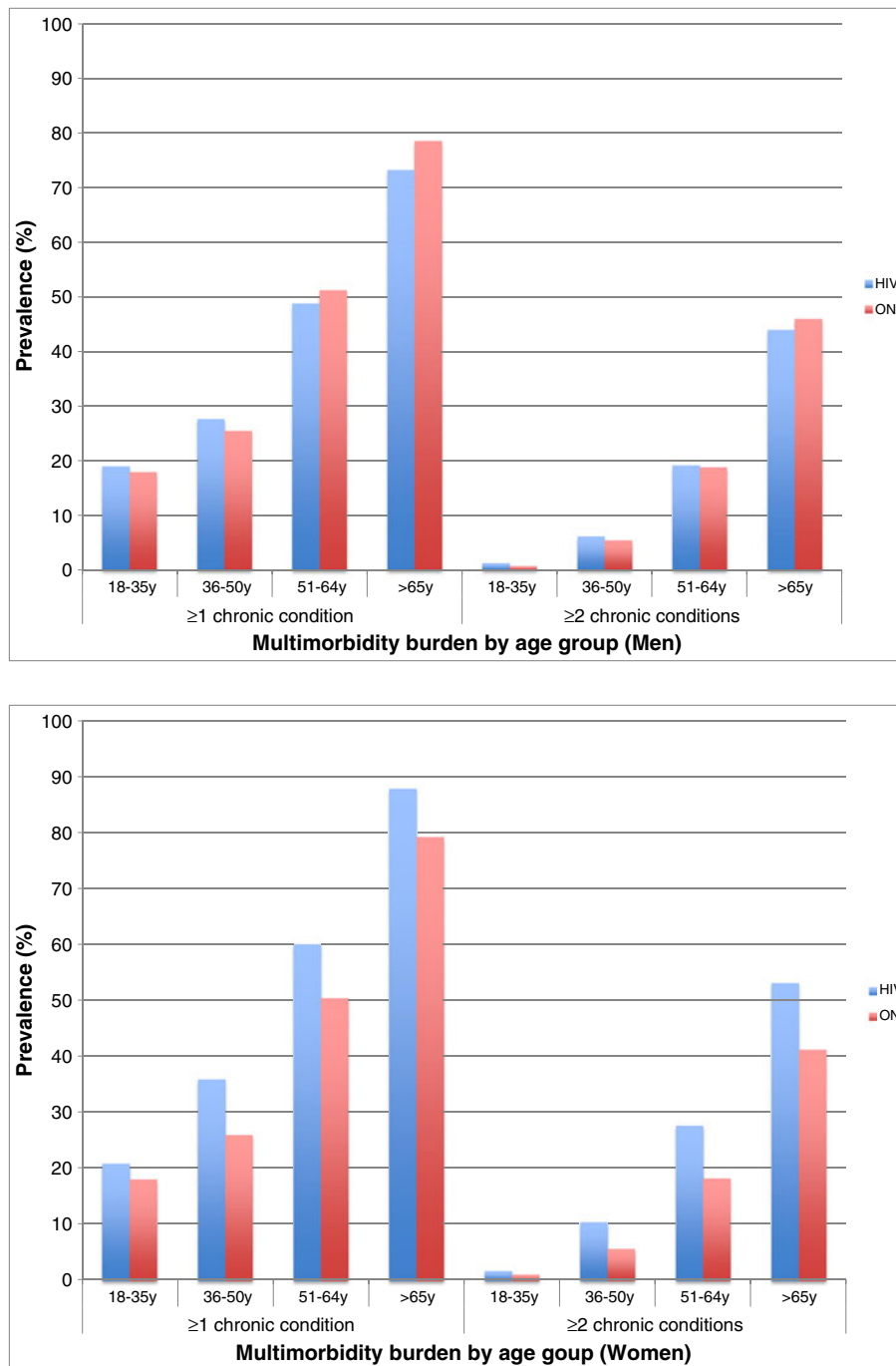
health conditions and individual physical comorbidities were more prevalent among people with HIV than among the general population, as were multimorbidity and physical-mental health comorbidity. In addition, as is seen in the general population, our study confirms the accumulation of multiple chronic conditions with age for both men and women with HIV. Women had higher multimorbidity than men across all groups, which is consistent with the Canadian general population [1].

Furthermore, while men with HIV had slightly lower comorbidity and multimorbidity than Ontario men in most age groups, women with HIV had consistently higher comorbidity and multimorbidity prevalence than women without HIV.

To our knowledge, this is the first study to use a population-based approach to measure the types and numbers of chronic diseases associated with HIV; most studies have been conducted in clinical cohorts of people living

**Table 3 Comparison of comorbidities and multimorbidity prevalence between HIV and Ontario cohorts (standardized by age and sex to Canadian 1991 population)**

	HIV cohort N = 14,005		Ontario cohort N = 71,410		HIV:ON	
	n	Prevalence (%)	n	Prevalence (%)	Prevalence ratio	(95% CI)
Mental health condition	5401	40.55	15935	21.99	1.84	(1.75,1.94)
<b>Physical conditions:</b>						
Acute myocardial infarction	174	1.19	949	1.06	1.12	(0.78,1.60)
Congestive heart failure	233	3.35	1428	1.49	2.26	(1.74,2.92)
Chronic obstructive lung disease	1106	8.33	4621	5.33	1.56	(1.39,1.76)
End stage renal disease	223	1.96	631	0.76	2.57	(1.92,3.44)
Peripheral vascular disease	72	0.63	248	0.29	2.15	(1.35,3.40)
Asthma	1780	15.90	8448	12.13	1.31	(1.20,1.43)
Diabetes	1167	9.65	6730	8.13	1.19	(1.06,1.33)
Hypertension	2093	19.33	16886	20.29	0.95	(0.88,1.04)
Stroke	173	1.55	891	1.01	1.53	(1.15,2.03)
At least one physical condition	4820	38.72	26907	34.23	1.13	(1.07,1.20)
Physical-mental health multimorbidity	2174	16.98	7443	9.49	1.79	(1.65,1.94)
Multimorbidity (at least two physical conditions)	1508	14.49	9417	11.13	1.30	(1.18,1.44)



**Figure 2** Morbidity prevalence by age group among men and women with HIV versus the Ontario general population.

with HIV. While the prevalence of comorbidity in people with HIV is clearly high, there have been inconsistencies regarding which conditions are more or less common in people with HIV. For instance, Butt et al. [31] found that HIV was associated with a decreased risk of diabetes, but that increasing age had a greater effect on diabetes rates in those with HIV than in the general population. Crothers et al. [32] found HIV to be an independent risk factor for

COPD even after adjusting for smoking status and other risk factors. In their very large, almost exclusively male study comparing HIV positive with non HIV positive veterans, Goulet et al. [33] found that those with HIV had lower risk of hypertension, diabetes, vascular disease and psychiatric disorders, and higher rates of renal and liver disease than their HIV negative cohort. In their study of ART-experienced patients, Guaraldi et al. [8] found that

those who were HIV positive had higher rates of diabetes, bone fracture and renal failure, but no difference in cardiovascular disease and hypertension. It is likely that the prevalence of individual comorbidities is a result of the complex interplay of aging, behavioral risk factors such as smoking (known to be higher among those with HIV), genetic risk factors, HIV severity, and ART history [8,9,34-36].

This study offers the unique strength of presenting the multimorbidity of people with HIV from a broad, multi-ethnic population of men and women from a variety of socioeconomic groups. Our findings are consistent with the literature highlighting that multimorbidity is common for people with HIV [7,8,33,34]. However, previously published prevalences of multimorbidity vary depending on the population base of the study, as clinical cohorts of people with HIV are often limited to certain demographic populations or at-risk groups. For example, our study showed that women with HIV have excess multimorbidity, which is consistent with Salter's study of HIV positive injection drug users, but not with Guaraldi's study of poly-pathology in ART-experienced people with HIV enrolled in a metabolic clinic. As men have historically represented a larger but decreasing proportion of people living with HIV, it is possible that Ontario men who were infected earlier in the epidemic were sicker and had higher mortality, resulting in a healthier cohort of older HIV-positive men within our population. However, because our population base isn't limited by the definition of any high risk cohort and presents the clinical experience of people currently living with HIV our data is likely to be a robust estimate of the prevalence of comorbidities in the population.

In addition, previous studies have varied with respect to definitions for multimorbidity, such as specific diseases included, methods of clustering conditions, and numbers of conditions required to meet multimorbidity criteria. [5,37-40]. It is likely that broadening our comorbidity measures would have resulted in higher prevalence of multimorbidity [7,33]. Finally, in finding that almost 50% of people with HIV who have at least one comorbidity also have a mental health diagnosis, our study is the first to our knowledge to quantify the relationship between these conditions. Barnett et al. [37] found that those living in the most deprived areas had the highest prevalence of physical-mental health comorbidity at 11.0%, which is lower than the prevalence found in our HIV population, despite their higher deprivation compared to the Ontario general population.

There are several limitations to our study. First, we did not identify those who were unaware of their HIV status, estimated to be 26% of prevalent infections in Canada [41], or those not accessing health care. Furthermore, there are some settings in Ontario, most notably

community health centres, that are not included in administrative data and so HIV patients in these setting were not included in the study. Community health centres are estimated to provide primary care for about 1% of the Ontario population [42], thus our findings are unlikely to be substantially affected by missing these individuals. Second, we were initially concerned that providers, especially those who have high-volume HIV practices or those who receive incentives for providing HIV care, would have preferentially identified HIV diagnosis codes for services received over other codes for chronic conditions. This potential bias would result in under ascertainment of chronic conditions in the HIV population compared to the general population. In light of this ascertainment issue, we are confident in our finding that, compared to the general Ontario population, the prevalence of almost all chronic conditions among those with HIV is higher.

## Conclusion

This population-based study quantifies the substantially higher comorbidity and multimorbidity prevalence among people living with HIV relative to the general population, and the high contribution of mental health diagnoses to these conditions. This additional burden of disease increasingly defines the care needs of this population [43,44]. Strategies for chronic disease management, including for people with HIV, must be expanded with a view to multimorbidity [18,37,43,45,46]. Particular attention should be paid to the complex care needs defined by the comorbidity burden on women with HIV. By contributing to quantifying this increasing burden with age, our results can inform policy direction around HIV health services delivery. Future work will be directed at understanding how these complex patients access the healthcare system, and how providers are meeting the healthcare needs of this population.

## Abbreviations

HIV: Human immunodeficiency syndrome; RPDB: Registered Persons Database; OHIP: Ontario Health Insurance Program; SAS: Statistical analysis system.

## Competing interests

The authors declare that they have no competing interests.

## Authors' contributions

CK designed the study and oversaw its implementation, performed the analysis, was the primary author and approved the final version of the manuscript. JW and JY were involved in the data analysis, participated in the editing of the manuscript and approved the final version of the manuscript. DGM, MT, RG and WH contributed to the concept of the study, oversaw its implementation, helped guide the analysis and participated in the writing and approved the final version of the manuscript. All authors read and approved the final manuscript.

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