BMJ Open

Cohort Profile: the LHIV-Manitoba clinical cohort of people living with HIV in Manitoba, Canada

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-034259
Article Type:	Cohort profile
Date Submitted by the Author:	12-Sep-2019
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Keywords:	HIV & AIDS < INFECTIOUS DISEASES, Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES

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Cohort Profile: the LHIV-Manitoba clinical cohort of people living with HIV in Manitoba, Canada

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ABSTRACT

Purpose: The LHIV-Manitoba cohort was developed as a way to provide a comprehensive source of HIV-related health information in the central Canadian Prairie province of Manitoba. The cohort will provide important information as we aim to better understand local HIV epidemiology and address key knowledge and practice gaps in HIV prevention, treatment, and care programming in the province.

Participants: In total, 890 individuals, aged 18 or older and living or receiving HIV care in Manitoba are enrolled in the cohort. A complete clinical dataset exists for 725 participants, which includes variables on socio-demographic characteristics, comorbidities and co-infections, self-reported HIV exposure categories, and HIV clinical indicators. A limited clinical dataset exists for an additional 165 individuals who were enrolled posthumously. 97.5% of cohort participants' clinical records are linked to provincial administrative health datasets.

Findings to date: The average age of cohort participants is 49.7 years. Approximately three-quarters of participants are male, 42% self-identified as white and 42% as Indigenous. The majority of participants (64%) reported condomless vaginal sex as a risk exposure for HIV. Nearly one-fifth (18%) of participants have an active HCV infection and the cohort's median CD4 count increased from 316 to 518 cells/mm^3 between time of entry into care to end of the first quarter in 2019.

Future plans: The LHIV-Manitoba cohort is an open cohort, and as such, participant enrolment, data collection, and analyses will be continually ongoing. Future analyses will focus on the impact of provincial drug plans on clinical outcomes, determinants of mortality among cohort participants, and deriving estimates for a local HIV care cascade.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This cohort is the first comprehensive source of health data compiled from people living with HIV in Manitoba and will provide important opportunities for understanding clinical care needs, gaps, and outcomes of people living with HIV in the province.
- Cohort enrolment protocols are clinic-based, and as such, this cohort may not be representative of people living with HIV who are sub-optimally engaged in care. One key strategy to circumvent the misinterpretation of analyses derived from cohort data will be to involve Manitoba HIV Program clients and their providers in the analysis, interpretation, and knowledge translation processes.
- Because this cohort is embedded within the Manitoba HIV Program, and stakeholders within government and the community of people with lived experience are actively involved in its development, data from the cohort will be able to facilitate analyses to inform programming and provincial policy on adequately resourcing HIV-related health services.

Word count: 2,652

INTRODUCTION

Annual reports on HIV in Canada consistently highlight heterogeneous, albeit relatively stable, epidemiological trends across the country.[1] At the end of 2016, the Public Health Agency of Canada (PHAC) estimated that 63,110 people were living with HIV in the country and 2,402 people were newly diagnosed in 2017.[1] Nationally, new HIV diagnoses disproportionately occur among Indigenous (First Nations, Inuit, and Métis) populations and people who have immigrated from countries where HIV is endemic.[1] The greatest proportion of prevalent HIV infections in nearly all Canadian provinces are attributed to condomless sex between men; however, notable exceptions include the central Prairie provinces of Saskatchewan and Manitoba, where most incident and prevalent cases are attributable to injection drug use and heterosexual transmission, respectively.[2-4] Rates of new HIV diagnoses per 100,000 population in Manitoba have been consistently higher than the national average, ranging from 9.5 new diagnoses in 2014 to 6.6 in 2016 and 2017.[1 4 5] Despite evidence of unique epidemiology and disproportionately high rates of infection, relatively little research addresses HIV epidemiology in the Canadian Prairies,[6] and there is a specific lack of published research focusing on Manitoba.

Current HIV epidemiological data for Manitoba are primarily derived from surveillance reports produced by PHAC and the provincial health department, Manitoba Health, Seniors and Active Living (MSHAL).[1 2] In 2017, MHSAL reported 89 new cases of HIV in the province with the majority of cases occurring in Winnipeg (81%) and a disproportionately high incidence among women when compared to national rates.[2] While useful for providing basic information about patterns and trends in HIV infection in Manitoba, these reports only provide aggregate-level demographic- and geographic analyses of the previous year's incident infections (new diagnoses and/or cases introduced to, but not acquired in, the province). Without clinical data, these reports are limited in their ability to inform specific research questions or programmatic decisions for HIV care and service delivery in the province.

In 2013, as part of a Canadian Institutes of Health Research-funded program of research, the "Advancing Primary Health Care for Persons Living with HIV in Canada" (LHIV) study provided support for the establishment of a prospective clinical cohort of people living with HIV in Manitoba. This clinical cohort is the first comprehensive source of HIV-specific health data in Manitoba and provides important opportunities to address key knowledge gaps in local HIV epidemiology—including patterns of healthcare utilisation and relevant clinical outcomes—and to understand healthcare needs of people living with HIV in the province. Similar cohorts have been developed and are now are well-established in other Canadian provinces, including British Columbia[7] and Ontario.[8] This article provides an overview of processes and procedures involved in cohort development and maintenance, and describes demographic- and HIV-related characteristics of LHIV-Manitoba cohort participants.

COHORT DESCRIPTION

Study setting

Established in 2007, the Manitoba HIV Program is the primary provider of treatment, care, and support for people living with HIV in the province. The Manitoba HIV Program employs a multidisciplinary care model in which HIV specialist physicians, family physicians, nurses (including nurse practitioners), pharmacists, dieticians, social workers, and other allied service providers provide comprehensive HIV care out of three clinic sites—a hospital-based outpatient

clinic and a community health centre in Manitoba's capital city, Winnipeg, and a nurse-run health access centre in Brandon, a semi-urban city approximately 200 kilometres west of Winnipeg.

Although arising from a research project, the LHIV-Manitoba cohort is strategically embedded within the Manitoba HIV Program and the local study team partners with stakeholders within the Manitoba HIV Program, MHSAL, and the LHIV study's Community Scholar Program,[9] all of whom have been actively involved in the development of the cohort. As such, findings from cohort data are expected to have direct relevance and applicability for both HIV care programming and provincial health policy.

Ethical approval

The LHIV-Manitoba cohort study received ethics approval from the University of Manitoba's Health Research Ethics Board, the local hospital's Research Impact Committee, and the Health Information Privacy Committee (HIPC) of MHSAL. This work has also received support from the Health Information Research Governance Committee of *Nanaandawewigamig*, the First Nations Health and Social Secretariat of Manitoba.

Enrolment procedures

Recruitment began at one clinic site in October 2013 and was fully implemented across all Manitoba HIV Program sites by January 2014. Data collection, linkage to administrative health databases, and data cleaning and analyses began in early 2017. Both enrolment and linkage are ongoing.

The enrolment process is illustrated in **Figure 1**. Inclusion criteria for the cohort are broad: participants must be at least 18 years of age and either living with HIV in Manitoba or receiving HIV care in Manitoba. Individuals who met these criteria but are under the jurisdiction of the Public Guardian and Trustee of Manitoba, or were otherwise unable to make decisions pertaining to their own healthcare, are deemed ineligible for participation in the cohort.

Recruitment and informed consent procedures take place within the Manitoba HIV Program clinics; clients who present to clinic are approached by a nurse or another allied healthcare provider and asked whether they are willing to speak to a research assistant about participating in a research project. If a client is agreeable, a research assistant meets with them to explain the purpose, context, and methods for the LHIV-Manitoba cohort study, and reviews the informed consent form to determine whether the person is interested, willing, and able to participate. Participants have the opportunity to take part in any combination of three separate components of the LHIV-Manitoba cohort: (i) have their clinical data collected; and/or (ii) have their clinical data linked to administrative health data that is routinely collected by the province; and/or (iii) indicate interest in being approached about future HIV research studies. Clients who are not ready to decide immediately can defer their decision to participate in the cohort and request to meet with the research assistant at a later date to reconsider their participation. Study staff keep track of individuals who asked to defer their decision to participant and actively follow-up with them at their next clinic appointment on in a year's time, depending on stated preference.

Study measures, data sources, and data collection

Clinical data are manually extracted from electronic medical records (EMR)—or from paper charts for data clinical information recorded prior to the introduction of EMR to clinic sites—within the Manitoba HIV Program's clinic sites by the first author and two trained extractors, and then entered into an encrypted, password protected Excel spreadsheet for consenting participants. A complete clinical dataset for the LHIV-Manitoba cohort includes variables on participants' socio-demographic characteristics (age, sex, geographic location of residence, self-identified ethnicity), comorbid chronic- and mental health diagnoses, opportunistic- and other co-infections (occurring within 6-months of presentation to HIV care), including Hepatitis C virus (HCV); recorded HIV exposure categories; date and geographic location of first positive HIV test; CD4 count at time of diagnosis, at time of antiretroviral therapy (ART) initiation, and at the end of the second and fourth quarters of each year, beginning in 2017; date of first ART initiation; current ART regimen (collected biannually, beginning in 2017); alcohol and drug use, including injection drug use; and type of prescription pharmaceutical insurance coverage (collected biannually, beginning in 2017).

The study's institutional ethics approvals also allow data from deceased clients of the Manitoba HIV Program to be collected via retrospective chart reviews. A limited dataset is extracted from clinical records of deceased individuals, which comprises a subset of the aforementioned clinical datasets, excluding all comorbidity and co-infection data from clinical records, except for HCV; treatment regimen data; and prescription pharmaceutical insurance data.

For deceased clients and participants who provide consent to data linkage, anonymized, de-identified clinical data are linked to provincial administrative health databases housed at MHSAL. Manitoba's administrative health datasets include individual-level records for nearly all contacts with the provincial healthcare system, including physician visits, hospital admissions, pharmaceutical prescription dispensations, and laboratory testing.[10] Linkage between clinical and administrative datasets is done through matching an individual's unique Personal Health Identification Number (PHIN) within both datasets. Before linked datasets are returned to the study team, MHSAL scrambles PHINs to de-identify the datasets and maintain participant anonymity.[11]

Characteristics of study participants

As of March 31st, 2019, 890 unique individuals are included in the cohort (Figure 1). A complete clinical dataset exists for 725 (81.5%) cohort participants who agreed to have their data reviewed and extracted from clinical records within the Manitoba HIV Program. A limited clinical dataset exists for an additional 165 individuals whose clinical records were reviewed posthumously. Nearly all individual-level clinical data are also linked to provincial administrative health datasets (n=868, 97.5%). At the end of the first quarter of 2019, 676 cohort participants (76.0%) were alive and 214 (24.0%) were deceased.

Select sociodemographic characteristics and outcomes of cohort participants are presented in **Table 1** and compared to the larger Manitoba HIV Program client population. The average age of cohort participants at the end of the first quarter of 2019 (or at time of death, for participants who were deceased by March 31st, 2019), was 49.7 ± 11.9 years. The majority of cohort participants are male (71.2%), over 80% reported being either white (42.4%) or Indigenous (41.6%), while an additional 10.9% self-identified as an ethnicity categorized as

African/Caribbean/black. Geographic distribution of cohort participants is primarily concentrated in Winnipeg (80.8%), while 1.4% of cohort participants live outside of Manitoba.

FINDINGS TO DATE

Analyses from the LHIV-Manitoba cohort are ongoing; a summary of preliminary findings is provided below.

Representativeness and distribution of key outcomes within the LHIV-Manitoba cohort

Given the research and programmatic potential of this cohort, it is of particular interest to understand whether, and to what extent, the demographic profile of cohort participants is representative of the larger Manitoba HIV Program client population (Table 1). Although similar in age structure, compared to the Manitoba HIV Program's client population, cohort participants are significantly more likely to be ≥40 years (78.9% vs. 70.0%, $p<0.05$). Compared to the Manitoba HIV Program, the cohort includes significantly more men (71.2% vs. 64.7%; $p=0.001$) and individuals who self-identify as white (42.3% vs. 30.0%, $p<0.001$) or Indigenous (41.5% vs. 33.0%, $p<0.001$) are greater in the LHIV-Manitoba cohort, while African/Caribbean/black clients are underrepresented (10.9% vs. 15.8%, $p<0.001$). The geographic distribution of cohort participants is similar to that of the larger client population, with the large majority of participants residing in Winnipeg (80.8% vs. 79.6%, $p=0.486$).

HIV-specific clinical indicators, co-infections, and comorbidities

Select clinical indicators, analysed by sex, are presented in **Table 2**. Preliminary findings from cohort participants' clinical data highlight similar trends to those seen in the most recent Manitoba HIV Program annual reports.[12 13] While a substantial proportion of cohort participants presented late to HIV care, with 57.0% having initial CD4 counts ≤350 cells/mm^3, 52.3% of most recent CD4 counts are >500cells/mm^3. In general, the proportion of participants with suppressed viral loads (<200 HIV RNA copies/mL) increased from their initial to most recent clinic visit (50.5% to 83.2%, respectively). Female cohort participants were significantly more likely than male participants to have unsuppressed viral loads (i.e. >200 copies/mL) at presentation to care, but this same difference was not seen when analysing most recent viral load results. Opportunistic infections (OIs) were diagnosed at or within 6-months of presentation to HIV care among 29.1% of participants who were alive at enrolment, and 6.6% presented to care with ≥2 OIs. Prevalence of active HCV co-infection at enrolment is 17.5% among all participants, and slightly higher among female than male participants (19.9% vs. 16.6%). Two-fifths of participants had at least one comorbidity recorded in their clinical records, and 12.8% (n=93) were living with at least two.

HIV exposures among cohort participants

Table 3 presents all HIV exposure categories recorded in participants' clinical files, analysed by sex. Although data in Table 3 are organized according to an HIV "risk hierarchy",[14] we report multiple exposure categories per individual in order to capture some of the complexity that can be missed with conventional hierarchy frameworks.[15] Notably, 41.0% of female participants reported at least two possible HIV exposure categories, while 29.6% of men reported the same. Similar to trends from annual surveillance reports in Manitoba, [2 12 13 16] condomless vaginal sex is the most commonly identified exposure category. Nearly half of male participants (47.6%) reported condomless anal sex with other men as a possible exposure, and 4.4% reported both

condomless anal sex with men and injection drug use. The majority of female participants (92.6%) reported condomless vaginal sex as a possible exposure, and 26.2% reported injection drug use.

STRENGTHS AND LIMITATIONS

Key limitations and challenges experienced throughout the development of the LHIV-Manitoba cohort, and the particular challenges associated with developing clinical cohorts using research dollars, have been described in detail elsewhere.[17] Briefly, a number participants expressed apprehension about the kinds of data that would be collected as a result of their involvement with the cohort, and in response, study staff made a point to spend adequate time to clearly explain the processes through which the study is able to link clinical and administrative data while maintaining confidentiality. Additionally, efficiently implementing study protocols without disrupting existing clinic operations was another substantial challenge; incorporating additional procedures related to cohort enrolment into routine encounters was difficult for healthcare providers who are working within busy HIV clinics. The study team regularly engages with providers to highlight the benefits that the cohort may confer to their own practice, their clients' needs, and the operations of Manitoba HIV Program.

Because enrolment protocols are clinic-based, this cohort may not be representative of people living with HIV who are sub-optimally engaged in care. As enrolment efforts move forward, it will be important for the study team to consider strategies to increase the proportion of participants belonging to demographic subgroups who are currently underrepresented in the cohort. It is of particular interest to the study team to understand whether certain subgroups are less likely to consent to cohort participation, and if so why. While findings from the cohort will still be important for informing care programming and policy decisions for the province, generalizability may be limited, and results must be interpreted accordingly. One key strategy to circumvent the misinterpretation of analyses derived from cohort data will be to involve Manitoba HIV Program clients and their providers in the analysis, interpretation, and knowledge translation processes.

The LHIV-Manitoba cohort is the first comprehensive source of health data compiled from people living with HIV in the province and will provide important opportunities for systematically and comprehensively understanding clinical care needs, gaps, and outcomes of Manitobans living with HIV. Importantly, Manitoba is well-positioned to undertake large, population-based linkage studies given the existence of a single insurer (MHSAL) that is responsible for payment of most health services, and the existence of linkable, population-based administrative health databases through the Manitoba Centre for Health Policy.[18 19] The cohort also identifies common comorbidities such as diabetes and hypertension where further assessment of outcomes offers opportunities for targeted resource allocation for improved management.

Because the clinical cohort is embedded within the Manitoba HIV Program, and stakeholders within MHSAL and the community of people with lived experience have been actively involved in its development, we also expect that data from the cohort will facilitate epidemiological analyses that can inform both HIV care programming and provincial policy on adequately resourcing HIV-related health services. As such, future analyses will focus on the impact of

provincial drug plans on clinical outcomes and determinants of mortality among cohort participants. Additionally, cohort data will be used to generate Manitoba-specific HIV care cascade estimates[20-22] and examine the cascade through an equity lens to understand how different groups of participants experience HIV care and treatment outcomes differently.

Finally, the Manitoba HIV Program embodies a unique care model—comprising both specialist and primary care services—that closely aligns with the Patient Centered Medical Home (PCMH) model of HIV care.[23] As such, findings from the LHIV-Manitoba cohort will be able to speak to the growing body of literature focusing on holistic models of HIV care delivery.[23 24]

Table 1. Sociodemographic characteristics and key outcomes of LHIV-Manitoba cohort participants, as compared to Manitoba HIV Program client population.

	LHIV-Manitoba cohort (*N*=890)		Manitoba HIV Program (*N*=1,357)		*p*-value
	n	%	*n*	%	
Age (years) on March 31st, 2019 or at time of death					
<18	0	0	2	0.2	0.245
18-24	10	1.1	46	3.4	0.001
25-39	178	20.0	358	26.4	0.001
40-64	621	69.8	871	64.2	0.006
≥65	81	9.1	78	5.8	0.003
Mean (SD)	49.7 (11.9)		46.8 (12.1)		0.000
Median (IQR)	49.8 (41.5-57.5)		46.9 (37.9-55.2)		0.000
Sex					
Male	634	71.2	878	64.7	0.001
Female	256	28.8	478	35.2	0.002
Self-identified ethnicity*					
White	376	42.4	407	36.2	0.000
Indigenous (First Nations, Inuit, Métis)	369	41.6	448	39.9	0.000
Sub-Saharan African/Caribbean/black	97	10.9	214	19.1	0.001
Other†	44	5.0	54	4.8	0.307
Region of residence					
Winnipeg	719	80.8	1,080	79.6	0.486
Central and Eastern Manitoba	48	5.4	71	5.2	0.836
Southern Manitoba	37	4.2	67	4.9	0.440
Western Manitoba	35	3.9	64	4.7	0.365
Northern Manitoba	30	3.4	46	3.4	1.000
Out of province	12	1.4	21	1.6	0.705
Unknown/No known address	9	1.0	8	0.6	0.285
Drug coverage at March 31st, 2019‡					

Out-of-pocket expenses associated with drug plan	293	45.4	-	-	
No out-of-pocket expenses associated with drug plan	346	53.6	-	-	-
Not on treatment/Unknown	6	0.9	-	-	
Problematic substance use recorded in clinic file[§]					
Alcohol	292	40.3	-	-	
Drugs (prescription or illegal)	346	47.7	-	-	-
Alcohol and drugs	217	29.9	-	-	
Has a primary care practitioner[§]	627	70.5	-	-	-

[*]Sample sizes may not add up to total participants due to missing data for some variables.
[†]Includes Latin American, East/Southeast Asian, South Asian, West Asian/North African/Middle Eastern.
[‡]Variable only collected for participants alive in the fourth quarter of 2018 (*n*=645).
[§]Variable only collected for participants alive at cohort enrolment (*n*=725).

Table 2. HIV-specific and other clinical indicators among LHIV-Manitoba cohort participants, by sex.

	Male* (*N*=634)		Female* (*N*=256)		Total* (*N*=890)		*p*-value
	n	%	*n*	%	*n*	%	
Initial CD4 count in Manitoba (cells/mm³)							
<200	211	33.8	72	28.7	283	32.3	0.467
200-350	151	24.2	65	25.9	216	24.7	
351-500	117	18.8	47	18.7	164	18.7	
>500	145	23.2	67	26.7	212	24.2	
Mean (SD)	328.2 (248.7)		370.5 (257.1)		340.3 (251.7)		
Median (IQR)	298.5 (116-478.5)		336 (179-517)		316 (129-492)		
Last CD4 count, up to end of 2018 (cells/mm³)							
<200	81	12.8	47	18.6	128	14.5	0.064
200-350	88	14.0	38	15.0	126	14.3	
351-500	130	20.6	38	15.0	168	19.0	
>500	332	52.6	130	51.4	462	52.3	
Mean (SD)	589.3 (303.6)		331.7 (302.0)		542.2 (319.1)		
Median (IQR)	565 (384-768)		256 (99-472)		517.5 (309.5-735.5)		
Initial viral load (copies/mL)							
<200	329	54.7	100	40.3	429	50.5	0.001†
200-999	27	4.5	16	6.5	43	5.1	
1,000 – 99,999	147	24.5	90	36.3	237	27.9	
100,000 – 999,999	80	13.3	36	14.5	116	13.7	
≥1,000,000	18	3.0	6	2.4	24	2.8	
Mean (SD)	125,778.7 (523,975.9)		107,972 (340,114.2)		120,577.2 (477,511.4)		
Median (IQR)	60.9 (0-38,400)		1,875 (0-40.300)		170 (0-38,800)		
Last viral load, up to end of 2018 (copies/mL)							
<200	491	84.4	190	80.2	681	83.2	0.517†
200-999	22	3.8	9	3.8	31	3.8	
1,000 – 99,999	46	7.9	28	11.8	74	9.0	

100,000 – 999,999	18	3.1	8	3.4	26	3.2	
≥1,000,000	5	0.9	2	0.8	7	0.9	
Mean (SD)	40,972 (415,359.2)		27,705 (171,693.3)		37,133.2 (362,048.3)		
Median (IQR)	0 (0-27.9)		0 (0-54.6)		0 (0-32.4)		
Opportunistic infections (OI) ‡§							
None	364	69.9	150	73.5	514	70.9	
Oropharyngeal and/or esophageal candidiasis (thrush)	108	20.7	39	19.1	147	20.3	
Pneumocystis jirovecii pneumonia (PJP)	56	10.8	9	4.4	65	9.0	0.131†
Active tuberculosis	29	5.6	14	6.9	43	5.9	
Mycobacterium avium-intracellulare (MAI)	7	1.3	1	0.5	8	1.1	
Cryptococcal meningitis	4	0.8	1	0.5	5	0.7	
Hepatitis C virus status at cohort enrolment							
No infection	496	78.2	182	71.1	678	76.2	
Active infection (RNA+)	105	16.6	51	19.9	156	17.5	0.085†
Past infection (RNA-/Ab+)	32	5.1	22	8.6	54	6.1	
Unknown	1	0.2	1	0.4	2	0.2	
Comorbidities‡‖							
None	305	58.5	125	61.3	430	59.3	
Asthma/COPD	93	17.9	36	17.7	129	17.8	
Hypertension (HTN)	88	16.9	24	11.8	112	15.5	0.006†
Type II diabetes (DM2)	66	12.7	39	19.1	105	14.5	
Chronic kidney disease (CKD)	33	6.3	7	3.4	40	5.5	
Coronary artery disease (CAD)	33	6.3	3	1.5	36	5.0	

*Sample sizes may not add up to total participants due to missing data for some variables.
†Some expected values <5, so *p*-values must be interpreted with caution.
‡Variable only collected for participants who were alive at cohort enrolment; Male, *n*=521; Female, *n*=204; Total, *n*=725.
§Diagnosed at, or within 6-months of presentation to care with the Manitoba HIV Program. Sum of categories exceeds total sample size because some participants presented with ≥1 OI.
‖Sum of categories exceeds total sample size because some participants presented with ≥1 comorbidity.

Table 3. Self-identified HIV exposure categories among LHIV-Manitoba cohort participants, by sex

	Male* (*N*=634)		Female* (*N*=256)		Total (*N*=890)		*p*-value
	n	%	*n*	%	*n*	%	
Condomless anal sex between males + injection drug use	**28**	**4.4**	**-**	**-**	**28**	**3.1**	**-**
Condomless anal sex between males	**302**	**47.6**	**-**	**-**	**302**	**33.9**	**-**
+ *Recipient of blood/blood product*	3	1.0	-	-	3	0.3	
+ *Condomless vaginal sex*	50	16.6	-	-	50	5.6	
+ *Possible exposure in an HIV-endemic country*	5	1.7	-	-	5	0.6	
+ *Occupational exposure*	2	0.7	-	-	2	0.2	
Injection drug use	**126**	**19.9**	**67**	**26.2**	**193**	**21.7**	**0.039**
+ *Recipient of blood/blood product*	5	4.0	2	3.0	7	0.8	
+ *Condomless vaginal sex*	80	63.5	56	83.6	136	15..3	
+ *Possible exposure in an HIV-endemic country*	1	0.8	0	0	1	0.1	
+ *Occupational exposure*	1	0.8	1	1.5	2	0.2	
Recipient of blood/blood product	**18**	**2.0**	**8**	**0.9**	**26**	**2.9**	**0.248**
+ *Condomless vaginal sex*	11	61.1	6	75.0	17	1.9	
+ *Possible exposure in an HIV-endemic country*	2	11.1	1	12.5	3	0.3	
+ *Occupational exposure*	1	5.6	2	25.0	3	0.3	
Condomless vaginal sex	**331**	**52.2**	**237**	**92.5**	**568**	**63.8**	**<0.001**
+ *Possible exposure in an HIV-endemic country*	35	10.6	40	15.6	75	8.4	
+ *Occupational exposure*	2	0.6	4	1.7	6	0.7	
Occupational exposure	**5**	**0.8**	**4**	**1.6**	**9**	**1.0**	**0.285**
+ *Possible exposure in an HIV-endemic country*	0	0	0	0	0	0	
Possible perinatal acquisition	**1**	**0.2**	**0**	**0**	**1**	**0.1**	**-**
+ *Possible exposure in an HIV-endemic country*	1	100	-	-	1	0.1	
Other/Unknown	**16**	**2.5**	**7**	**2.7**	**23**	**2.6**	**0.864**
Number of potential HIV exposures recorded							
1	446	70.4	151	59.0	597	67.1	
2	172	27.1	102	39.8	274	30.8	<0.001
≥3	16	2.5	3	1.2	19	2.1	

*Sum of categories exceeds total sample size because participants may have ≥1 HIV exposure category reported in clinical file.

Acknowledgements
The authors thank Dr. Christopher Briggs, Dr. Elsabé du Plessis, Nicole Herpai, Stella Leung, Michael Paillé, and Dr. Souradet Shaw for their help with participant enrolment, data collection, and/or data analyses. This work would not be possible without the entire Manitoba HIV Program staff and providers – their support and tireless efforts throughout cohort development and participant recruitment continue to be invaluable. Finally, we also acknowledge and thank our partners at MHSAL's Information Management & Analytics unit and Cadham Provincial Laboratory for their cooperation and support with administrative data extraction.

Collaboration and data sharing statement
Researchers interested in accessing data related to the LHIV-Manitoba cohort should be directed to Dr. Marissa Becker (marissa.becker@umanitoba.ca). All access requests for individual-level data must be accompanied by proposals for the research projects and will be subject to approvals by Health Research Ethics Board at the University of Manitoba, as well as the researchers' home institution. Aggregate and/or deidentified data may be shared with fewer restrictions pending review by the LHIV study team.

Contributors
Study conceptualisation and design: LMM, EC, CEK, MLB. Data collection and acquisition: LMM, LI, KK, YK, MLB. Data analysis: LMM. Data interpretation: LMM, CEK, YK, JFB, MLB. Drafting of the manuscript: LMM. Critical revisions and final approval: EC, LI, CEK, CB, CL, YK, KK, JFB, MLB.

Funding
The LHIV Study is funded by CIHR (funding reference no. TT5-128270). LMM received funding from the CIHR Canada Graduate Scholarship Doctoral Award, the University of Manitoba, and the Canadian Association for HIV Research to support this work.

Competing interests
The authors have no competing interests to report.

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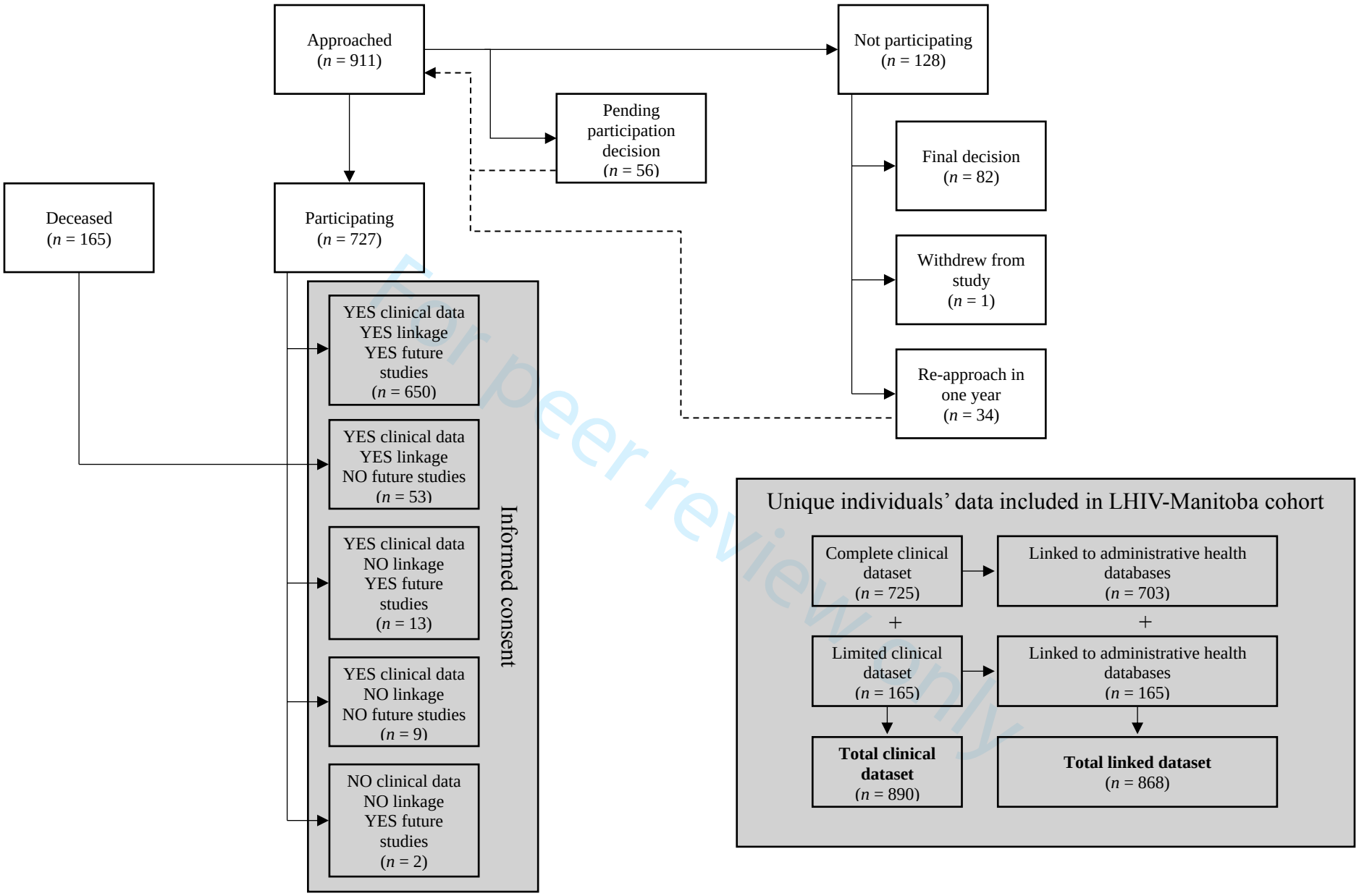

Figure 1. Recruitment, informed consent, and data collection processes for the LHIV-Manitoba cohort

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, explain how loss to follow-up was addressed
		(*e*) Describe any sensitivity analyses
Results		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
		(c) Summarise follow-up time (eg, average and total amount)
Outcome data	15*	Report numbers of outcome events or summary measures over time
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
Discussion		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

BMJ Open

Cohort Profile: the LHIV-Manitoba clinical cohort of people living with HIV in Manitoba, Canada

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2019-034259.R1
Article Type:	Cohort profile
Date Submitted by the Author:	06-Feb-2020
Complete List of Authors:	McClarty, Leigh; University of Manitoba, Centre for Global Public Health, Department of Community Health Sciences Cheuk, Eve; University of Manitoba, Centre for Global Public Health, Department of Community Health Sciences Ireland, Laurie; Nine Circles Community Health Centre Kendall, Claire; Elisabeth Bruyere Research Institute Bibeau, Christine; Community Scholar Loeppky, Carla; Government of Manitoba, Health, Seniors & Active Living Kasper, Ken; University of Manitoba, Internal Medicine Keynan, Yoav; University of Manitoba, Medical Microbiology and Infectious Diseases Blanchard, james; University of Manitoba, Centre for Global Public Health, Department of Community Health Sciences Becker, Marissa ; University of Manitoba, Centre for Global Public Health, Department of Community Health Sciences
Primary Subject Heading:	HIV/AIDS
Secondary Subject Heading:	Epidemiology
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, Epidemiology < INFECTIOUS DISEASES, Public health < INFECTIOUS DISEASES

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Cohort Profile: the LHIV-Manitoba clinical cohort of people living with HIV in Manitoba, Canada

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ABSTRACT

Purpose: The LHIV-Manitoba cohort was developed as a way to provide a comprehensive source of HIV-related health information in the central Canadian Prairie province of Manitoba. The cohort will provide important information as we aim to better understand local HIV epidemiology and address key knowledge and practice gaps in HIV prevention, treatment, and care programming in the province.

Participants: In total, 890 individuals, aged 18 or older and living or receiving HIV care in Manitoba are enrolled in the cohort. A complete clinical dataset exists for 725 participants, which includes variables on socio-demographic characteristics, comorbidities and co-infections, self-reported HIV exposure categories, and HIV clinical indicators. A limited clinical dataset exists for an additional 165 individuals who were enrolled posthumously. 97.5% of cohort participants' clinical records are linked to provincial administrative health datasets.

Findings to date: The average age of cohort participants is 49.7 years. Approximately three-quarters of participants are male, 42% self-identified as white and 42% as Indigenous. The majority of participants (64%) reported condomless vaginal sex as a risk exposure for HIV. Nearly one-fifth (18%) of participants have an active HCV infection and the cohort's median CD4 count increased from 316 to 518 cells/mm^3 between time of entry into care to end of the first quarter in 2019.

Future plans: The LHIV-Manitoba cohort is an open cohort, and as such, participant enrolment, data collection, and analyses will be continually ongoing. Future analyses will focus on the impact of provincial drug plans on clinical outcomes, determinants of mortality among cohort participants, and deriving estimates for a local HIV care cascade.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This cohort is the first comprehensive source of health data compiled from people living with HIV in Manitoba and will provide important opportunities for understanding clinical care needs, gaps, and outcomes of people living with HIV in the province.
- Cohort enrolment protocols are clinic-based, and as such, this cohort may not be representative of people living with HIV who are sub-optimally engaged in care. One key strategy to circumvent the misinterpretation of analyses derived from cohort data will be to involve Manitoba HIV Program clients and their providers in the analysis, interpretation, and knowledge translation processes.
- Because this cohort is embedded within the Manitoba HIV Program, and stakeholders within government and the community of people with lived experience are actively involved in its development, data from the cohort will be able to facilitate analyses to inform programming and provincial policy on adequately resourcing HIV-related health services.

Word count: 3,041

INTRODUCTION

Annual reports on HIV in Canada consistently highlight heterogeneous, albeit relatively stable, epidemiological trends across the country.[1] At the end of 2016, the Public Health Agency of Canada (PHAC) estimated that 63,110 people were living with HIV in the country and 2,402 people were newly diagnosed in 2017.[1] Nationally, new HIV diagnoses disproportionately occur among Indigenous (First Nations, Inuit, and Métis) populations and people who have immigrated from countries where HIV is endemic.[1] The greatest proportion of prevalent HIV infections in nearly all Canadian provinces are attributed to condomless sex between men; however, notable exceptions include the central Prairie provinces of Saskatchewan and Manitoba, where most incident and prevalent cases are attributable to injection drug use and heterosexual transmission, respectively.[2-4] Rates of new HIV diagnoses per 100,000 population in Manitoba have been consistently higher than the national average, ranging from 9.5 new diagnoses in 2014 to 6.6 in 2016 and 2017.[1 4 5] Despite evidence of unique epidemiology and disproportionately high rates of infection, relatively little research addresses HIV epidemiology in the Canadian Prairies,[6] and there is a specific lack of published research focusing on Manitoba.

Current HIV epidemiological data for Manitoba are primarily derived from surveillance reports produced by PHAC and the provincial health department, Manitoba Health, Seniors and Active Living (MSHAL).[1 2] In 2017, MHSAL reported 89 new cases of HIV in the province with the majority of cases occurring in Winnipeg (81%) and a disproportionately high incidence among women when compared to national rates.[2] While useful for providing basic information about patterns and trends in HIV infection in Manitoba, these reports only provide aggregate-level demographic- and geographic analyses of the previous year's incident infections (new diagnoses and/or cases introduced to, but not acquired in, the province). Without clinical data, these reports are limited in their ability to inform specific research questions or programmatic decisions for HIV care and service delivery in the province.

In 2013, as part of a Canadian Institutes of Health Research-funded program of research, the "Advancing Primary Health Care for Persons Living with HIV in Canada" (LHIV) study provided support for the establishment of a prospective clinical cohort of people living with HIV in Manitoba. This clinical cohort is the first comprehensive source of HIV-specific health data in Manitoba and provides important opportunities to address key knowledge gaps in local HIV epidemiology—including patterns of healthcare utilisation and relevant clinical outcomes—and to understand healthcare needs of people living with HIV in the province. Similar cohorts have been developed and are now are well-established in other Canadian provinces, including British Columbia[7] and Ontario.[8] This article provides an overview of processes and procedures involved in cohort development and maintenance, and describes demographic- and HIV-related characteristics of LHIV-Manitoba cohort participants.

COHORT DESCRIPTION

Study setting

Established in 2007, the Manitoba HIV Program is the primary provider of treatment, care, and support for people living with HIV in the province. The Manitoba HIV Program employs a multidisciplinary care model in which HIV specialist physicians, family physicians, nurses (including nurse practitioners), pharmacists, dieticians, social workers, and other allied service providers provide comprehensive HIV care out of three clinic sites—a hospital-based outpatient

clinic and a community health centre in Manitoba's capital city, Winnipeg, and a nurse-run health access centre in Brandon, a semi-urban city approximately 200 kilometres west of Winnipeg. While all three clinic sites follow a multidisciplinary care model and each have links to health promotion programs and resources, some differences in organization exist. For example, the clinic at the community health centre is run by family doctors and each client at that site is assigned to a specific physician and nurse couple. Meanwhile, physicians at the hospital-based clinic are Infectious Disease specialists and all clients of the hospital clinic in Winnipeg and the nurse-run clinic in Brandon are seen by a rotating roster of providers.

Patient and Public Involvement

Although arising from a research project, the LHIV-Manitoba cohort is strategically embedded within the Manitoba HIV Program and the local study team partners with stakeholders within the Manitoba HIV Program and other community clinics, MHSAL, the Manitoba First Nations AIDS Working Group, and the LHIV study's Community Scholar Program,[9] all of whom have been actively involved in the development of the cohort. Study design and enrolment procedures were conducted by researchers and trainees within the LHIV study team. Throughout the development of the cohort, engagement through community forums and meetings with key stakeholders provided information about the objectives of the LHIV-Manitoba cohort and what it meant to be a participant, while actively seeking input about research questions that could be addressed using cohort data. As such, findings from cohort data are expected to have direct relevance and applicability for both HIV care programming and provincial health policy. Dissemination and knowledge translation activities with all key stakeholders, including community members, community-based organisations, and key policy- and decision-makers, will be facilitated by study team members and Manitoba HIV Program staff.

Ethical approval

The LHIV-Manitoba cohort study received ethics approval from the University of Manitoba's Health Research Ethics Board, the local hospital's Research Impact Committee, and the Health Information Privacy Committee (HIPC) of MHSAL. This work has also received support from the Health Information Research Governance Committee of *Nanaandawewigamig*, the First Nations Health and Social Secretariat of Manitoba.

Enrolment procedures

Recruitment began at one clinic site in October 2013 and was fully implemented across all Manitoba HIV Program sites by January 2014. Data collection, linkage to administrative health databases, and data cleaning and analyses began in early 2017. Both enrolment and linkage are ongoing.

The enrolment process is illustrated in **Figure 1**. Inclusion criteria for the cohort are broad: participants must be at least 18 years of age and either living with HIV in Manitoba or receiving HIV care in Manitoba. Individuals who met these criteria but are under the jurisdiction of the Public Guardian and Trustee of Manitoba, or were otherwise unable to make decisions pertaining to their own healthcare, are deemed ineligible for participation in the cohort.

Recruitment and informed consent procedures take place within the Manitoba HIV Program clinics; clients who present to clinic are approached by a nurse or another allied healthcare

provider and asked whether they are willing to speak to a research assistant about participating in a research project. If a client is agreeable, a research assistant meets with them to explain the purpose, context, and methods for the LHIV-Manitoba cohort study, and reviews the informed consent form to determine whether the person is interested, willing, and able to participate. Participants have the opportunity to take part in any combination of three separate components of the LHIV-Manitoba cohort: (i) have their clinical data collected; and/or (ii) have their clinical data linked to administrative health data that is routinely collected by the province; and/or (iii) indicate interest in being approached about future HIV research studies. Clients who are not ready to decide immediately can defer their decision to participate in the cohort and request to meet with the research assistant at a later date to reconsider their participation. Study staff keep track of individuals who asked to defer their decision to participant and actively follow-up with them at their next clinic appointment in a year's time, depending on stated preference.

Study measures, data sources, and data collection

Clinical data are manually extracted from electronic medical records (EMR)—or from paper charts for data clinical information recorded prior to the introduction of EMR to clinic sites—within the Manitoba HIV Program's clinic sites by the first author and two trained extractors, and then entered into an encrypted, password protected Excel spreadsheet for consenting participants. Standardised definitions were developed for each variable to ensure quality and consistency of data abstracted from clinical records. Manitoba HIV Program clinicians who had entered data into clinical records were consulted for instances in which information to be collected was unclear or ambiguous. A complete clinical dataset for the LHIV-Manitoba cohort includes variables on participants' socio-demographic characteristics (age, sex, geographic location of residence, self-identified ethnicity), comorbid chronic- and mental health diagnoses, opportunistic- and other co-infections (occurring within 6-months of presentation to HIV care), including Hepatitis C virus (HCV); recorded HIV exposure categories; date and geographic location of first positive HIV test; CD4 count at time of diagnosis, at time of antiretroviral therapy (ART) initiation, and at the end of the second and fourth quarters of each year, beginning in 2017; date of first ART initiation; current ART regimen (collected biannually, beginning in 2017); alcohol and drug use, including injection drug use; and type of prescription pharmaceutical insurance coverage (collected biannually, beginning in 2017).

The study's institutional ethics approvals also allow data from deceased clients of the Manitoba HIV Program to be collected via retrospective chart reviews. A limited dataset is extracted from clinical records of deceased individuals, which comprises a subset of the aforementioned clinical datasets, excluding all comorbidity and co-infection data from clinical records, except for HCV; treatment regimen data; and prescription pharmaceutical insurance data. Including data from deceased clients provides an important opportunity to explore and better understand determinants of mortality among people living with HIV in Manitoba. This has been identified as an area of particular interest to the Manitoba HIV Program, which, up to now, has not been adequately explored. Furthermore, the inclusion of these data helps to ensure broader generalizability of our findings from the cohort.

For individuals who were enrolled posthumously, and for participants who provide consent to data linkage, anonymized, de-identified clinical data are linked to provincial administrative health databases housed at MHSAL. Manitoba's administrative health datasets include

individual-level records for nearly all contacts with the provincial healthcare system, including physician visits, hospital admissions, pharmaceutical prescription dispensations, and laboratory testing.[10] Linkage between clinical and administrative datasets is done through matching an individual's unique Personal Health Identification Number (PHIN) within both datasets. Before linked datasets are returned to the study team, MHSAL scrambles PHINs to de-identify the datasets and maintain participant anonymity.[11]

Characteristics of study participants

As of March 31st, 2019, 890 unique individuals are included in the cohort (Figure 1). A complete clinical dataset exists for 725 (81.5%) cohort participants who agreed to have their data reviewed and extracted from clinical records within the Manitoba HIV Program. A limited clinical dataset exists for an additional 165 individuals whose clinical records were reviewed posthumously. Nearly all individual-level clinical data are also linked to provincial administrative health datasets (n=868, 97.5%). At the end of the first quarter of 2019, 676 cohort participants (76.0%) were alive and 214 (24.0%) were deceased.

Select sociodemographic characteristics and outcomes of cohort participants are presented in **Table 1** and compared to the larger Manitoba HIV Program client population. The average age of cohort participants at the end of the first quarter of 2019 (or at time of death, for participants who were deceased by March 31st, 2019), was 49.7 ± 11.9 years. The majority of cohort participants are male (71.2%), over 80% reported being either white (42.4%) or Indigenous (41.6%), while an additional 10.9% self-identified as an ethnicity categorized as African/Caribbean/black. Geographic distribution of cohort participants is primarily concentrated in Winnipeg (80.8%), while 1.4% of cohort participants live outside of Manitoba.

FINDINGS TO DATE

Analyses from the LHIV-Manitoba cohort are ongoing; a summary of preliminary findings is provided below.

Representativeness and distribution of key outcomes within the LHIV-Manitoba cohort

Given the research and programmatic potential of this cohort, it is of particular interest to understand whether, and to what extent, the demographic profile of cohort participants is representative of the larger Manitoba HIV Program client population (Table 1). Although similar in age structure, compared to the Manitoba HIV Program's client population, cohort participants are significantly more likely to be ≥40 years (78.9% vs. 70.0%, p<0.05). Compared to the Manitoba HIV Program, the cohort includes significantly more men (71.2% vs. 64.7%; p=0.001) and individuals who self-identify as white (42.3% vs. 30.0%, p<0.001) or Indigenous (41.5% vs. 33.0%, p<0.001) are greater in the LHIV-Manitoba cohort, while African/Caribbean/black clients are underrepresented (10.9% vs. 15.8%, p<0.001). The geographic distribution of cohort participants is similar to that of the larger client population, with the large majority of participants residing in Winnipeg (80.8% vs. 79.6%, p=0.486).

HIV-specific clinical indicators, co-infections, and comorbidities

Select clinical indicators, analysed by sex, are presented in **Table 2**. Preliminary findings from cohort participants' clinical data highlight similar trends to those seen in the most recent Manitoba HIV Program annual reports.[12 13] While a substantial proportion of cohort participants

presented late to HIV care, with 57.0% having initial CD4 counts ≤350 cells/mm^3, 52.3% of most recent CD4 counts are >500cells/mm^3. In general, the proportion of participants with suppressed viral loads (<200 HIV RNA copies/mL) increased from their initial to most recent clinic visit (50.5% to 83.2%, respectively). Female cohort participants were significantly more likely than male participants to have unsuppressed viral loads (i.e. >200 copies/mL) at presentation to care, but this same difference was not seen when analysing most recent viral load results. Opportunistic infections (OIs) were diagnosed at or within 6-months of presentation to HIV care among 29.1% of participants who were alive at enrolment, and 6.6% presented to care with ≥2 OIs. Prevalence of active HCV co-infection at enrolment is 17.5% among all participants, and slightly higher among female than male participants (19.9% vs. 16.6%). Two-fifths of participants had at least one comorbidity recorded in their clinical records, and 12.8% (*n*=93) were living with at least two.

HIV exposures among cohort participants

Table 3 presents all self-reported HIV exposure categories recorded in participants' clinical files, analysed by sex. Although data in Table 3 are organized according to an HIV "risk hierarchy"—through which participants' primary risk exposure categories are assigned according to an established hierarchy of risk factors[14]—we report multiple exposure categories per individual in order to capture some of the complexity that can be missed with conventional hierarchy frameworks.[15] Notably, 41.0% of female participants reported at least two possible HIV exposure categories, while 29.6% of men reported the same. Similar to trends from annual surveillance reports in Manitoba, [2 12 13 16] condomless vaginal sex is the most commonly identified exposure category. Nearly half of male participants (47.6%) reported condomless anal sex with other men as a possible exposure, and 4.4% reported both condomless anal sex with men and injection drug use. The majority of female participants (92.6%) reported condomless vaginal sex as a possible exposure, and 26.2% reported injection drug use.

STRENGTHS AND LIMITATIONS

Key limitations and challenges experienced throughout the development of the LHIV-Manitoba cohort, and the particular challenges associated with developing clinical cohorts using research dollars, have been described in detail elsewhere.[17] Briefly, a number participants expressed apprehension about the kinds of data that would be collected as a result of their involvement with the cohort, and in response, study staff made a point to spend adequate time to clearly explain the processes through which the study is able to link clinical and administrative data while maintaining confidentiality. Additionally, efficiently implementing study protocols without disrupting existing clinic operations was another substantial challenge; incorporating additional procedures related to cohort enrolment into routine encounters was difficult for healthcare providers who are working within busy HIV clinics. The study team regularly engages with providers to highlight the benefits that the cohort may confer to their own practice, their clients' needs, and the operations of Manitoba HIV Program.

Because enrolment protocols are clinic-based, this cohort may not be representative of people living with HIV who are sub-optimally engaged in care. As enrolment efforts move forward, it will be important for the study team to consider strategies to increase the proportion of participants belonging to demographic subgroups who are currently underrepresented in the cohort. It is of particular interest to the study team to understand whether certain subgroups are

less likely to consent to cohort participation, and if so why. While findings from the cohort will still be important for informing care programming and policy decisions for the province, generalizability may be limited, and results must be interpreted accordingly. One key strategy to circumvent the misinterpretation of analyses derived from cohort data will be to involve Manitoba HIV Program clients and their providers in the analysis, interpretation, and knowledge translation processes.

The LHIV-Manitoba cohort is the first comprehensive source of health data compiled from people living with HIV in the province and will provide important opportunities for systematically and comprehensively understanding clinical care needs, gaps, and outcomes of Manitobans living with HIV. Importantly, Manitoba is well-positioned to undertake large, population-based linkage studies given the existence of a single insurer (MHSAL) that is responsible for payment of most health services, and the existence of linkable, population-based administrative health databases through the Manitoba Centre for Health Policy.[18 19] The cohort also identifies common comorbidities such as diabetes and hypertension where further assessment of outcomes offers opportunities for targeted resource allocation for improved management. Furthermore, the Manitoba HIV Program embodies a unique care model—comprising both specialist and primary care services—that closely aligns with the Patient Centered Medical Home (PCMH) model of HIV care.[20] As such, findings from the LHIV-Manitoba cohort will be able to speak to the growing body of literature focusing on holistic models of HIV care delivery.[20 21]

Finally, because the clinical cohort is embedded within the Manitoba HIV Program, and stakeholders within MHSAL and the community of people with lived experience have been actively involved in its development, we also expect that data from the cohort will facilitate epidemiological analyses that can inform both HIV care programming and provincial policy on adequately resourcing HIV-related health services.

FUTURE PLANS

Future analyses using clinical cohort data will focus on areas that have been identified as specific points of interest for the Manitoba HIV Program. Namely, generating a better understanding of the impact of existing provincial drug plans on clinical outcomes and exploring, for the first time in the province, characteristics and determinants of mortality among people living with HIV. Additionally, cohort data is currently being used to generate Manitoba-specific HIV care cascade estimates,[22-24] which will be presented in detail in a forthcoming manuscript. Subsequent work will examine the local HIV care cascade through an equity lens to better understand how different groups of participants experience HIV care and treatment outcomes differently within Manitoba.

Table 1. Sociodemographic characteristics and key outcomes of LHIV-Manitoba cohort participants, as compared to Manitoba HIV Program client population.

	LHIV-Manitoba cohort (*N*=890)		Manitoba HIV Program (*N*=1,357)		*p*-value
	n	%	*n*	%	
Age (years) on March 31st, 2019 or at time of death					
<18	0	0	2	0.2	0.245
18-24	10	1.1	46	3.4	0.001
25-39	178	20.0	358	26.4	0.001
40-64	621	69.8	871	64.2	0.006
≥65	81	9.1	78	5.8	0.003
Mean (SD)	49.7 (11.9)		46.8 (12.1)		0.000
Median (IQR)	49.8 (41.5-57.5)		46.9 (37.9-55.2)		0.000
Sex					
Male	634	71.2	878	64.7	0.001
Female	256	28.8	478	35.2	0.002
Self-identified ethnicity*					
White	376	42.4	407	36.2	0.000
Indigenous (First Nations, Inuit, Métis)	369	41.6	448	39.9	0.000
Sub-Saharan African/Caribbean/black	97	10.9	214	19.1	0.001
Other†	44	5.0	54	4.8	0.307
Region of residence					
Winnipeg	719	80.8	1,080	79.6	0.486
Central and Eastern Manitoba	48	5.4	71	5.2	0.836
Southern Manitoba	37	4.2	67	4.9	0.440
Western Manitoba	35	3.9	64	4.7	0.365
Northern Manitoba	30	3.4	46	3.4	1.000
Out of province	12	1.4	21	1.6	0.705
Unknown/No known address	9	1.0	8	0.6	0.285
Drug coverage at March 31st, 2019‡					

Out-of-pocket expenses associated with drug plan	293	45.4	-	-	
No out-of-pocket expenses associated with drug plan	346	53.6	-	-	-
Not on treatment/Unknown	6	0.9	-	-	
Problematic substance use recorded in clinic file§					
Alcohol	292	40.3	-	-	
Illegal or "street" drugs‖	222	31.6	-	-	-
Alcohol and drugs	148	21.1	-	-	
Has a primary care practitioner§	627	70.5	-	-	-

*Sample sizes may not add up to total participants due to missing data for some variables.
†Includes Latin American, East/Southeast Asian, South Asian, West Asian/North African/Middle Eastern.
‡Variable only collected for participants alive in the fourth quarter of 2018 (*n*=645).
§Variable only collected for participants alive at cohort enrolment (*n*=725).
‖Includes cocaine, crack cocaine, heroin, crystal methamphetamine, other hallucinogens (Lysergic acid diethylamide [LSD, "acid"], γ-Hydroxybutyric acid [GHB], ketamine, 3,4-Methylenedioxymethamphetamine [MDMA, "ecstasy"]), solvents, Talwin & Ritalin, and alkyl nitrates ("poppers").

Table 2. HIV-specific and other clinical indicators among LHIV-Manitoba cohort participants, by sex.

	Male* (*N*=634)		Female* (*N*=256)		Total* (*N*=890)		*p*-value
	n	%	*n*	%	*n*	%	
Initial CD4 count in Manitoba (cells/mm³)							
<200	211	33.8	72	28.7	283	32.3	0.467
200-350	151	24.2	65	25.9	216	24.7	
351-500	117	18.8	47	18.7	164	18.7	
>500	145	23.2	67	26.7	212	24.2	
Mean (SD)	328.2 (248.7)		370.5 (257.1)		340.3 (251.7)		
Median (IQR)	298.5 (116-478.5)		336 (179-517)		316 (129-492)		
Last CD4 count, up to end of 2018 (cells/mm³)							
<200	81	12.8	47	18.6	128	14.5	0.064
200-350	88	14.0	38	15.0	126	14.3	
351-500	130	20.6	38	15.0	168	19.0	
>500	332	52.6	130	51.4	462	52.3	
Mean (SD)	589.3 (303.6)		331.7 (302.0)		542.2 (319.1)		
Median (IQR)	565 (384-768)		256 (99-472)		517.5 (309.5-735.5)		
Initial viral load (copies/mL)							
<200	329	54.7	100	40.3	429	50.5	0.001†
200-999	27	4.5	16	6.5	43	5.1	
1,000 – 99,999	147	24.5	90	36.3	237	27.9	
100,000 – 999,999	80	13.3	36	14.5	116	13.7	
≥1,000,000	18	3.0	6	2.4	24	2.8	
Mean (SD)	125,778.7 (523,975.9)		107,972 (340,114.2)		120,577.2 (477,511.4)		
Median (IQR)	60.9 (0-38,400)		1,875 (0-40.300)		170 (0-38,800)		
Last viral load, up to end of 2018 (copies/mL)							
<200	491	84.4	190	80.2	681	83.2	0.517†
200-999	22	3.8	9	3.8	31	3.8	
1,000 – 99,999	46	7.9	28	11.8	74	9.0	

100,000 – 999,999	18	3.1	8	3.4	26	3.2	
≥1,000,000	5	0.9	2	0.8	7	0.9	
Mean (SD)	40,972 (415,359.2)		27,705 (171,693.3)		37,133.2 (362,048.3)		
Median (IQR)	0 (0-27.9)		0 (0-54.6)		0 (0-32.4)		
Opportunistic infections (OI) [‡§]							
None	364	69.9	150	73.5	514	70.9	
Oropharyngeal and/or esophageal candidiasis (thrush)	108	20.7	39	19.1	147	20.3	
Pneumocystis jirovecii pneumonia (PJP)	56	10.8	9	4.4	65	9.0	0.131[†]
Active tuberculosis	29	5.6	14	6.9	43	5.9	
Mycobacterium avium-intracellulare (MAI)	7	1.3	1	0.5	8	1.1	
Cryptococcal meningitis	4	0.8	1	0.5	5	0.7	
Hepatitis C virus status at cohort enrolment							
No infection	496	78.2	182	71.1	678	76.2	
Active infection (RNA+)	105	16.6	51	19.9	156	17.5	0.085[†]
Past infection (RNA-/Ab+)	32	5.1	22	8.6	54	6.1	
Unknown	1	0.2	1	0.4	2	0.2	
Comorbidities[‡‖]							
None	305	58.5	125	61.3	430	59.3	
Asthma/COPD	93	17.9	36	17.7	129	17.8	
Hypertension (HTN)	88	16.9	24	11.8	112	15.5	0.006[†]
Type II diabetes (DM2)	66	12.7	39	19.1	105	14.5	
Coronary artery disease (CAD)	33	6.3	3	1.5	36	5.0	

[*]Sample sizes may not add up to total participants due to missing data for some variables.
[†]Some expected values <5, so *p*-values must be interpreted with caution.
[‡]Variable only collected for participants who were alive at cohort enrolment; Male, *n*=521; Female, *n*=204; Total, *n*=725.
[§]Diagnosed at, or within 6-months of presentation to care with the Manitoba HIV Program. Sum of categories exceeds total sample size because some participants presented with ≥1 OI.
[‖]Sum of categories exceeds total sample size because some participants presented with ≥1 comorbidity.

Table 3. Self-identified HIV exposure categories among LHIV-Manitoba cohort participants, by sex

	Male* (*N*=634)		Female* (*N*=256)		Total (*N*=890)		*p*-value
	n	%	*n*	%	*n*	%	
Condomless anal sex between males + injection drug use	**28**	**4.4**	**-**	**-**	**28**	**3.1**	**-**
Condomless anal sex between males	**302**	**47.6**	**-**	**-**	**302**	**33.9**	**-**
+ *Recipient of blood/blood product*	3	1.0	-	-	3	0.3	
+ *Condomless vaginal sex*	50	16.6	-	-	50	5.6	
+ *Possible exposure in an HIV-endemic country*†	5	1.7	-	-	5	0.6	
+ *Occupational exposure*	2	0.7	-	-	2	0.2	
Injection drug use	**126**	**19.9**	**67**	**26.2**	**193**	**21.7**	**0.039**
+ *Recipient of blood/blood product*	5	4.0	2	3.0	7	0.8	
+ *Condomless vaginal sex*	80	63.5	56	83.6	136	15..3	
+ *Possible exposure in an HIV-endemic country*†	1	0.8	0	0	1	0.1	
+ *Occupational exposure*	1	0.8	1	1.5	2	0.2	
Recipient of blood/blood product	**18**	**2.0**	**8**	**0.9**	**26**	**2.9**	**0.248**
+ *Condomless vaginal sex*	11	61.1	6	75.0	17	1.9	
+ *Possible exposure in an HIV-endemic country*†	2	11.1	1	12.5	3	0.3	
+ *Occupational exposure*	1	5.6	2	25.0	3	0.3	
Condomless vaginal sex	**331**	**52.2**	**237**	**92.5**	**568**	**63.8**	**<0.001**
+ *Possible exposure in an HIV-endemic country*†	35	10.6	40	15.6	75	8.4	
+ *Occupational exposure*	2	0.6	4	1.7	6	0.7	
Occupational exposure	**5**	**0.8**	**4**	**1.6**	**9**	**1.0**	**0.285**
+ *Possible exposure in an HIV-endemic country*	0	0	0	0	0	0	
Possible perinatal acquisition	**1**	**0.2**	**0**	**0**	**1**	**0.1**	**-**
+ *Possible exposure in an HIV-endemic country*†	1	100	-	-	1	0.1	
Other/Unknown	**16**	**2.5**	**7**	**2.7**	**23**	**2.6**	**0.864**
Number of potential HIV exposures recorded							
1	446	70.4	151	59.0	597	67.1	
2	172	27.1	102	39.8	274	30.8	<0.001
≥3	16	2.5	3	1.2	19	2.1	

*Sum of categories exceeds total sample size because participants may have ≥1 HIV exposure category reported in clinical file.
†*Possible exposure in an HIV-endemic country* is never assigned as a primary exposure category, but is captured as an additional exposure category if an individual was born in, or spent considerable time living/working in an HIV-endemic country and experienced a potentially "risky" event.

FIGURE CAPTIONS

Figure 1. Recruitment, informed consent, and data collection processes for the LHIV-Manitoba cohort.

Acknowledgements
The authors thank Dr. Christopher Briggs, Dr. Elsabé du Plessis, Nicole Herpai, Stella Leung, Michael Paillé, and Dr. Souradet Shaw for their help with participant enrolment, data collection, and/or data analyses. This work would not be possible without the entire Manitoba HIV Program staff and providers – their support and tireless efforts throughout cohort development and participant recruitment continue to be invaluable. We also acknowledge and thank our partners at MHSAL's Information Management & Analytics unit and Cadham Provincial Laboratory for their collaboration and support with administrative data extraction. Finally, the support and guidance we have received from the LHIV Study team, especially the LHIV Community Scholars, and the advisory board at Nine Circles Community Health Centre have been invaluable to the continuation of this work.

Collaboration and data sharing statement
Researchers interested in accessing data related to the LHIV-Manitoba cohort should be directed to Dr. Marissa Becker (marissa.becker@umanitoba.ca). All access requests for individual-level data must be accompanied by proposals for the research projects and will be subject to approvals by Health Research Ethics Board at the University of Manitoba, as well as the researchers' home institution. Aggregate and/or deidentified data may be shared with fewer restrictions pending review by the LHIV study team.

Contributors
Study conceptualisation and design: LMM, EC, CEK, MLB. Data collection and acquisition: LMM, LI, KK, YK, MLB. Data analysis: LMM. Data interpretation: LMM, CEK, YK, JFB, MLB. Drafting of the manuscript: LMM. Critical revisions and final approval: EC, LI, CEK, CB, CL, YK, KK, JFB, MLB.

Funding
The LHIV Study is funded by CIHR (funding reference no. TT5-128270). LMM received funding from the CIHR Canada Graduate Scholarship Doctoral Award, CIHR Michael Smith Foreign Study Supplement, the University of Manitoba, and the Canadian Association for HIV Research to support this work.

Competing interests
The authors have no competing interests to report.

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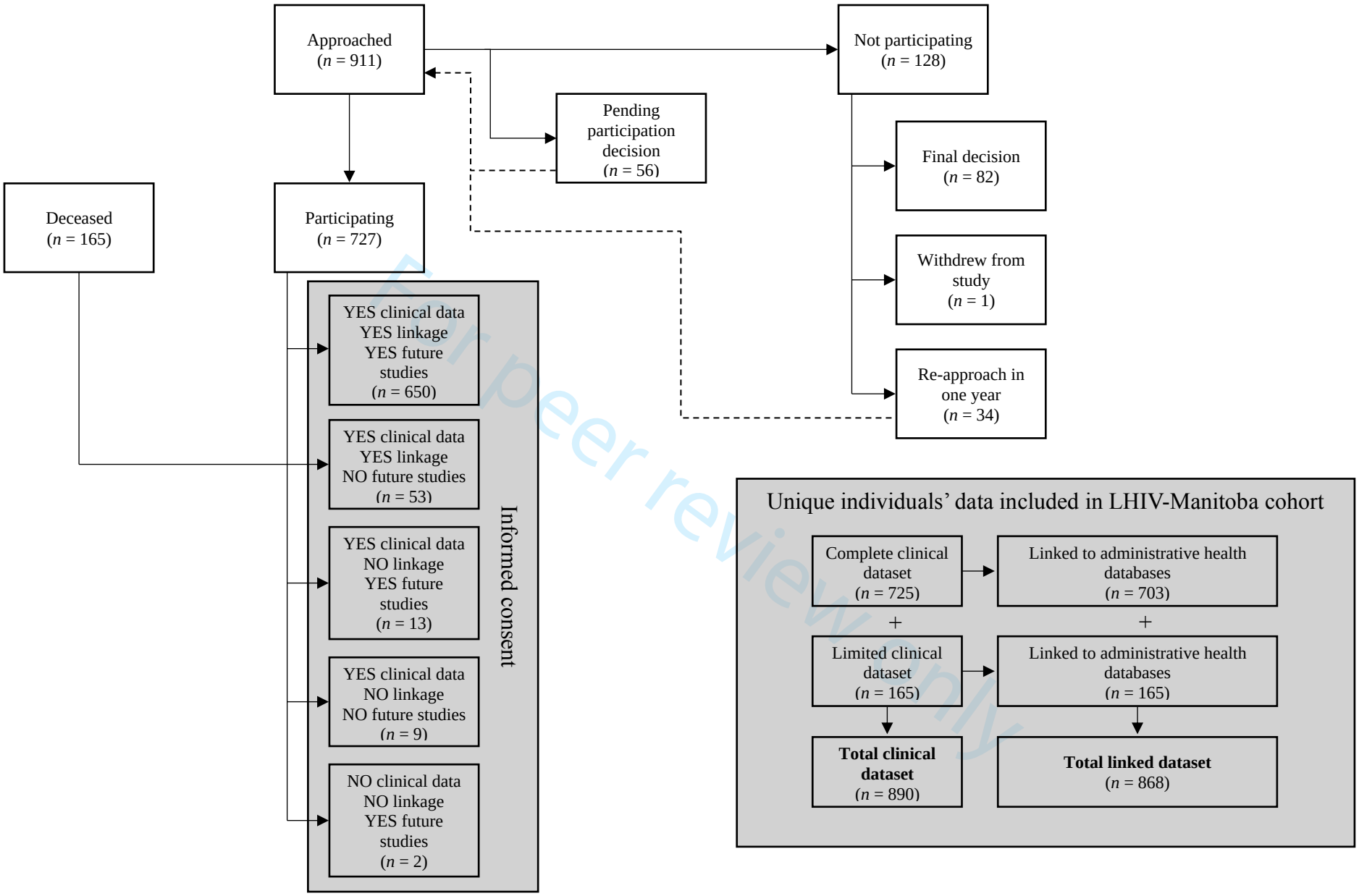

Figure 1. Recruitment, informed consent, and data collection processes for the LHIV-Manitoba cohort

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No.	Comment
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1	See Title
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2	See Abstract
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3	See Introduction section
Objectives	3	State specific objectives, including any prespecified hypotheses	3	Objectives of the cohort, and motivations for its development are outlined in the Introduction section. The cohort profile paper format outlined by BMJ Open does not require that hypotheses are explicitly stated, as this is not meant to be a paper focusing on analyses of the cohort data.
Methods				
Study design	4	Present key elements of study design early in the paper	3-5	This information is provided throughout the paper's Cohort Description section. See specifically the following sub-sections: Study setting; Ethical approval; Enrolment procedures; and Study measures, data sources, and data collection.
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3-5	This information is provided throughout the paper's Cohort Description section.
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4-5	See specifically the Enrolment procedures and Study measures, data sources, and data collection sub-sections.
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	n/a	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5	Variables included in the cohort are outlined in the first paragraph of the Study measures, data sources, and data collection sub-section. Key outcomes of interest are presented in Tables at the end of the paper.
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement).	5	See Study measures, data sources, and data collection sub-section.

		Describe comparability of assessment methods if there is more than one group		
Bias	9	Describe any efforts to address potential sources of bias	7	Specifically, see the first two paragraphs of our Strengths and Limitations section.
Study size	10	Explain how the study size was arrived at	n/a	Recruitment and enrolment procedures are detailed on page 4. This paper describes the development of an open cohort. While we provide information on the current number of participants in the cohort, enrolment is ongoing and as such, the "study size" is dynamic.
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	n/a	BMJ Open specifically indicates that Cohort Profile papers should not include a description of analyses.
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	n/a	BMJ Open specifically indicates that Cohort Profile papers should not include a description of statistical analyses.
		(*b*) Describe any methods used to examine subgroups and interactions	n/a	
		(*c*) Explain how missing data were addressed	n/a	
		(*d*) If applicable, explain how loss to follow-up was addressed	n/a	
		(*e*) Describe any sensitivity analyses	n/a	
Results				
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4	These details are included in Figure 1, which is described in the second paragraph of the Enrolment procedures sub-section.
		(b) Give reasons for non-participation at each stage	4	See Enrolment procedures sub-section and refer to Figure 1.
		(c) Consider use of a flow diagram	Figure 1	Figure 1 attached as separate document, as per BMJ Open submission guidelines. Figure 1 title is included on page 14 of main document.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	5-6	See Characteristics of study participants sub-section and refer to Tables 1-3, included on pages 9-13 of the main document.
		(b) Indicate number of participants with missing data for each variable of interest	n/a	We have not explicitly included this information in the main document because it is not relevant for a Cohort Profile paper. In the footnotes of our Tables, we do note

				which variables have some data missing, but we do not quantify missing data because the authors feel that it is outside the scope of this article and would not meaningfully contribute to our overall messaging.
		(c) Summarise follow-up time (eg, average and total amount)	n/a	As per BMJ Open's guidelines for Cohort Profile papers, we have not provided details about our methods for analyses, and we do not present results from longitudinal analyses in this paper.
Outcome data	15*	Report numbers of outcome events or summary measures over time	n/a	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	n/a	
		(*b*) Report category boundaries when continuous variables were categorized	9-12	Tables 1 and 2 present category boundaries for the following continuous variables: Age (Table 1), CD4 count, viral load (Table 2). The findings presented in these tables are discussed on pages 5-6.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	n/a	
Discussion				
Key results	18	Summarise key results with reference to study objectives	6-8	As per BMJ Open guidelines for Cohort Profile papers, we have provided a brief Findings to Date section, outlining preliminary analyses from the cohort. We also summarize our future analysis plans in the Future Plans section on page 8.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7-8	See Strengths and Limitations section.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	6-8	This are briefly address in our Findings to Date and Strengths and Limitations sections.

Generalisability	21	Discuss the generalisability (external validity) of the study results	6-7	This is addressed in the first sub-section of our Findings to Date section (page 6) and again in the second paragraph of the Strengths and Limitations section (page 7)
Other information				
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15	

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.