

COHORT PROFILE

Cohort Profile: Longitudinal Investigations into Supportive and Ancillary health services

Katrina C Duncan,¹ Kate Salters,¹ Jamie I Forrest,¹ Alexis K Palmer,¹ Hong Wang,¹ Nadia O'Brien,¹ Surita Parashar,^{1,2} Angela M Cescon,¹ Hasina Samji,¹ Julio SG Montaner^{1,3} and Robert S Hogg^{1,2*}

¹British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital, Vancouver, BC, Canada, ²Faculty of Health Sciences, Simon Fraser University, Burnaby, BC, Canada and ³Division of AIDS, Department of Medicine, University of British Columbia, Vancouver, BC, Canada

*Corresponding author. Faculty of Health Sciences, Simon Fraser University, Director, HIV/AIDS Drug Treatment Program, BC Centre for Excellence in HIV/AIDS, 608-1081 Burrard Street, Vancouver, BC, Canada V6Z 1Y6. E-mail: bobhogg@cfcenet.ubc.ca

Accepted 13 February 2012

The Longitudinal Investigations into Supportive and Ancillary health services (LISA) study is a cohort of people living with HIV/AIDS who have ever accessed anti-retroviral therapy (ART) in British Columbia, Canada. The LISA study was developed to better understand the outcomes of people living with HIV with respect to supportive services use, socio-demographic factors and quality of life. Between July 2007 and January 2010, 1000 participants completed an interviewer-administered questionnaire that included questions concerning medical history, substance use, social and medical support services, food and housing security and other social determinants of health characteristics. Of the 1000 participants, 917 were successfully linked to longitudinal clinical data through the provincial Drug Treatment Program. Within the LISA cohort, 27% of the participants are female, the median age is 39 years and 32% identify as Aboriginal. Knowledge translation activities for LISA include the creation of plain language summaries, internet resources and arts-based engagement activities such as Photovoice.

How did the study come about?

Since the advent of anti-retroviral therapy (ART), there has been a substantial reduction in HIV-associated morbidity and mortality among people living with HIV/AIDS (PHA) who are accessing treatment.^{1,2} The life expectancy of PHA on treatment now approaches that of HIV-negative individuals, which has led to a reconceptualization of HIV as a manageable chronic condition in high-resource settings.^{1–3}

Increased ART access, however, is not the sole factor determining the health outcomes and life expectancy of PHA. The role of social determinants of health in influencing HIV risk and health outcomes of PHA is increasingly recognized.^{4,5} The widely cited fundamental cause theory posits that social factors,

including socio-economic status and access to social support, are important underlying factors associated with disease and disease progression.⁶ Whereas risk factors and behaviours at the level of the individual play an important role, primordial causes are conceptualized as putting people 'at risk of risks'.⁶ Understanding the role of social determinants of health is integral to understanding why certain individuals and populations have a greater risk of infection, lack access to care, reduced ART uptake and poorer adherence.^{4–6,9,11,29,30,33–35}

In British Columbia (BC), Canada, the number of new HIV infections continues to be highest among men who have sex with men (MSM) (46.9%), heterosexual/non-endemic contacts (26.6%) and people who inject drugs (18.9%).⁷ Notably, HIV prevalence is

particularly elevated in Vancouver's Downtown Eastside, the district with the lowest national life expectancy and per capita income and the highest rates of illicit drug use in Canada.^{8–10} The prevalence of HIV among people who inject drugs in the Downtown Eastside ranges from 17% to 31%¹¹ and is reportedly 26% among female survival sex workers (women who receive goods, such as money, food and shelter in exchange for sex).¹² Outside the Vancouver Coastal Health region, there is an increasing number of PHA in other areas of the province, especially the Vancouver Island, Northern and Fraser Health Authorities.¹³

Within this context, the Longitudinal Investigations into Supportive and Ancillary health services (LISA) study was initiated to examine the experiences of PHA who have ever accessed ART in BC. This work was supported by the Canadian Institutes for Health Research (CIHR). Participants completed an interviewer-administered questionnaire, and their clinical information continues to be followed longitudinally through linkages with the Drug Treatment Program (DTP) (further detailed below).

What does the study cover?

The overall aims of this study are to evaluate the impact of social determinants of health on HIV clinical outcomes and on health-care utilization and to document the experiences of PHA accessing ART across the province. The study objectives are as follows:

- (1) to explore the influence of social determinants of health on timely ART uptake, ART regimen change, adherence, biological mediators (body mass index and co-infections), disease progression (CD4 cell count and viral load), resistance to ART and mortality;
- (2) to investigate the impact of HIV-associated stigma, quality of life, resistance testing, food security, body image and other topics deemed important by our study team (members of the community advisory committee, physicians, community leaders and PHA) on clinical outcomes;
- (3) to provide an opportunity for PHA on ART to voice the challenges and successes of their experiences living with HIV/AIDS; and
- (4) to inform decision makers regarding policy and programme development as well as strategic priority setting.

Where is the study area?

The LISA study was conducted within the province of BC. The Vancouver Coastal Health authority region, which includes Vancouver, Richmond, North and

West Vancouver, Sunshine Coast and BC's Central Coast, contains 55% of all PHA on treatment in BC who would have been eligible to participate in the LISA study. As shown in Figure 1, ~65% of the LISA sample was from the Vancouver Coastal Health authority region.

Ethical approval for the LISA study was obtained from the University of British Columbia/Providence Health Care, Simon Fraser University, the University of Victoria and Vancouver Coastal Health research ethics boards.

Who is in the sample?

Between July 2007 and January 2010, PHA over the age of 19 years residing in BC, Canada who had ever accessed ART were eligible to participate in the LISA study. Recruitment was conducted through letters to patients from ART-prescribing physicians, pharmacists, advertisements at HIV/AIDS service organizations and participant word of mouth. Once screened, eligible participants provided informed consent in writing. Participants completed a 1-h interviewer-administered questionnaire, and were reimbursed CDN\$20 for their involvement.

The financial incentive resulted in an oversampling of hard-to-reach individuals and thus the LISA sample is not reflective of the demographics of all people on treatment by health authority in BC, Canada as we oversampled in certain regions (Figure 1). Particular subpopulations, such as women, people who inject drugs and people identifying as Aboriginal, were monitored during recruitment and purposely oversampled in order to sufficiently power subanalyses. Recruitment ended in January 2010 with a final sample size of 1000. Of the 1000 interviews conducted, 83 participants could not be linked to clinical data from the DTP, described below, and were thus excluded from the final LISA cohort ($n = 917$).

What has been measured?

Clinical data

Clinical data (e.g. CD4 cell count, HIV viral load and treatment adherence) are obtained through longitudinal linkages with the provincial DTP. In BC, ART is distributed centrally through the DTP, housed at the BC Centre for Excellence in HIV/AIDS, at no cost to clinically eligible PHA. PHA are enrolled into the DTP when their physicians first prescribe ART. Physicians enrolling a PHA must complete a drug request enrolment form, which acts as a legal prescription and compiles baseline information, including past HIV-specific drug history, CD4 cell count, plasma HIV RNA viral load, current drug requests and enrolling physician data. Each drug request is reviewed by a qualified practitioner to ensure that the BC Centre for Excellence in HIV/AIDS guidelines are

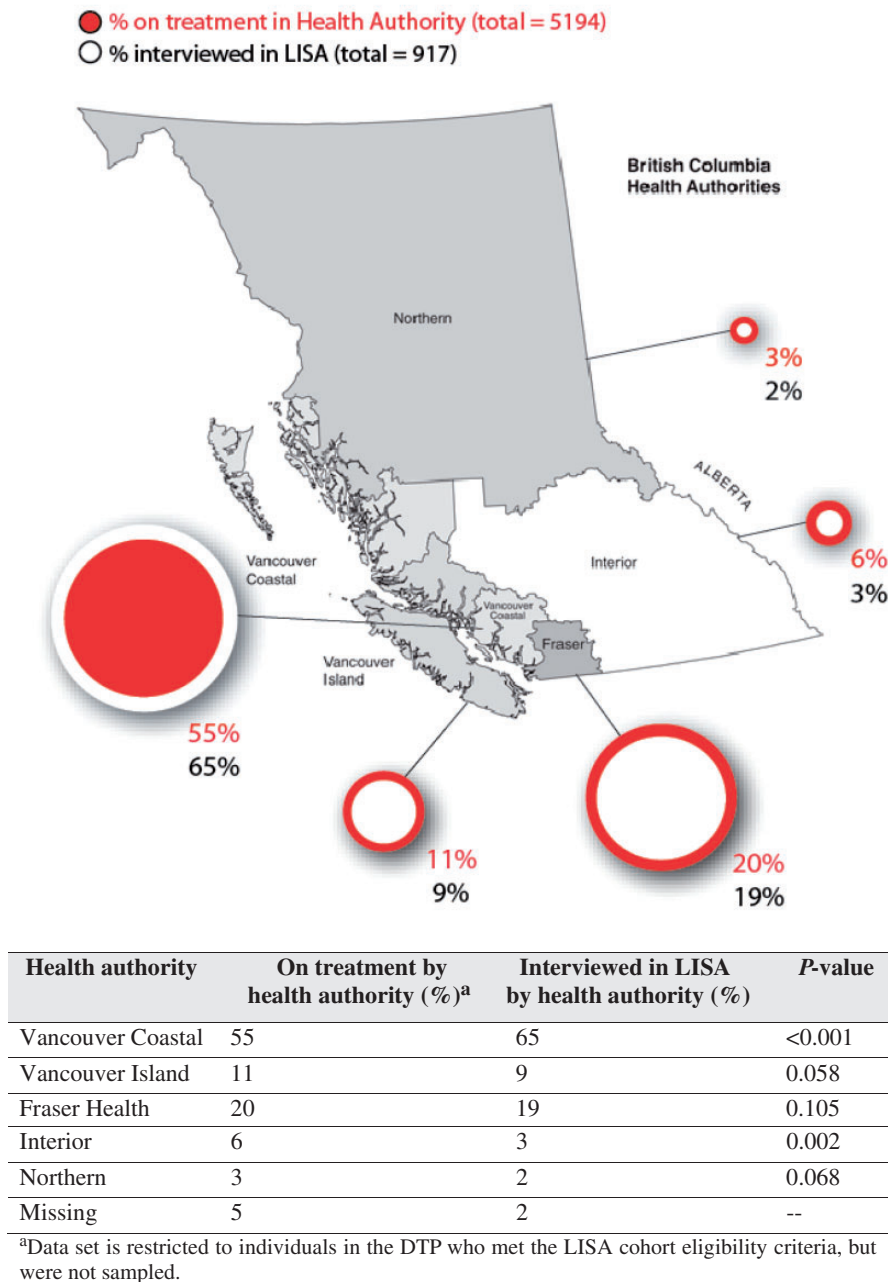


Figure 1 LISA interviews by health authority in British Columbia

met. Prescriptions are renewed or modified as physicians monitor the patient.

The DTP distributes medications in accordance with the BC Therapeutic Guidelines, which have remained consistent with those from the International AIDS Society, USA, between 1996 and at last revision in 2010.¹⁴ At the time of participant recruitment, the committee recommends that PHA initiate therapy when they have CD4 cell count <500 cells/mm³, assuming no other risk factor (i.e. hepatitis C) is present.¹⁵ Moreover, the BC Centre for Excellence in HIV/AIDS recommends that CD4 cell counts and plasma

viral loads be monitored at baseline, at 4 weeks after starting treatment and every 3 months thereafter (for current recommendations, see 2011 Primary Care Guidelines, which differ slightly).¹⁶

Clinical data are transferred to the DTP through a combination of periodic, batched data transfers, real-time electronic data linkages and direct physician reporting. The DTP's clinical data are updated on a daily basis for those cases where a real-time linkage is available or as new data are received in cases of physician report or batched data transfers. Once incorporated into the database, clinical data can be linked to the LISA data.

In June 2007, there were 4017 PHA on ART in BC and in June 2010, there were 5340 PHA on ART in BC. The total sample of individuals in the DTP fluctuates as a result of mortality, people leaving the province, stopping treatment and initiating treatment.

Questionnaire

The LISA questionnaire was administered to 1000 participants throughout BC by trained interviewers. The longitudinal clinical data from the DTP are linked with cross-sectional data from the LISA study allowing for greater insight into the relationship between social and clinical characteristics of PHA. Data were collected at clinics, HIV/AIDS service organizations and by telephone.

An extensive literature review was conducted to determine the domains of interest, the specific variables to be measured, as well as the validated scales used. Validated scales were used to measure a number of social determinants, such as body image,¹⁷ neighbourhood cohesion,¹⁸ quality of life¹⁹ and depressive symptomatology (Centre for Epidemiological Studies Depression Scale, CESD-10).^{20–23} Food insecurity was measured at the individual level using a modified version of the Radimer/Cornell questionnaire.^{24,25} We also included questions that elicited participant perceptions of HIV-associated stigma and discrimination,^{26,27} alcohol use²⁸ and treatment adherence self-efficacy.²⁹

The questionnaire was then reviewed by community partners and piloted with a number of focus groups in Vancouver to ensure its suitability and cultural sensitivity to the populations of interest. This process was iterative, with the study team providing draft questionnaires and community members revising and developing the study instrument.

What has been found?

Key findings to date

Of the 917 LISA cohort participants, the median age of ART initiation is 39 years [interquartile range (IQR): 33–45], 251 (27%) are female and 289 (32%) are of Aboriginal ancestry. Of all LISA participants, 608 (66.5%) reported being food insecure, 703 (76.7%) were unemployed at the time of interview and 476 (51.9%) reported ever being incarcerated (Table 1). The LISA cohort met the intended goal of enriching representation of traditionally hard to reach populations, with over-representation of women, people who inject drugs and people identifying as Aboriginal. The LISA sample and DTP patients who were eligible for the study but did not participate were compared, as shown in Figure 1 and Table 2.

Multiple publications have emerged from the LISA data, which contribute to the growing body of literature on the social determinants of health of PHA. Broader socio-demographic and lifestyle factors collected in the LISA study enrich clinical outcomes by

Table 1 The socio-demographic characteristics of LISA participants ($n = 917$)

Variable	Count, n (%)
In a relationship	214 (23.3)
Stable housing	623 (67.9)
Food insecure	608 (66.5)
Currently unemployed	703 (76.7)
History of violence	683 (74.5)
Ever incarcerated	476 (51.9)
Alcohol use	
Ever used	879 (95.9)
Current use	472 (51.5)
Current drug use	205 (22.4)
Depressive symptoms	524 (57.1)

highlighting social, behavioural and quality of life characteristics. The key findings featured in publication and/or conference presentations include the following.

- (1) In investigating the prevalence and correlates of food insecurity in the LISA cohort, it was found that there is a high prevalence of food insecurity among the LISA cohort (71%) and that food insecurity is associated with a compendium of environmental and behavioural factors.³⁰
- (2) In identifying determinants of access to HIV drug resistance testing and factors associated with testing, we found that resistance testing is greatly underused despite current clinical guidelines. Of those eligible LISA participants, nearly 40% failed to be tested for resistance, the majority of whom were vulnerable populations.³¹
- (3) An examination of knowledge of developing HIV drug resistance showed that younger age, having greater than high school education, discussing medication with physicians, having high provider trust and receiving one-to-one counselling by a pharmacist are predictive of a complete or partial definition of HIV resistance.³²
- (4) An evaluation of the impact of socio-economic factors on neighbourhood perceptions found that food security and stable housing are related to neighbourhood perceptions among individuals on ART. The results point to potential targets for intervention, including improvements in the realm of housing and food security, which may promote treatment success for ART, especially in marginalized communities.³³
- (5) The concept of body image is complex and encompasses an individual's perception of their existential self, physical self and social interpretation of their body by others. Within the LISA

Table 2 Comparison of LISA cohort participants with individuals enrolled in the DTP who were eligible for the LISA study, but not included

Variable	LISA (<i>n</i> = 917)	DTP (excluding LISA) ^a (<i>n</i> = 5194)	<i>P</i> -value [†]
Demographics			
Age (years) when initiating ART, median (IQR)	39 (33–45)	38 (32–45)	0.522
Sex, <i>n</i> (%)			
Female	251 (27.4)	829 (16.0)	<0.001
Male	666 (72.6)	4365 (84.0)	
History of injection drug use, <i>n</i> (%)			
Yes	654 (71.3)	1474 (28.4)	<0.001
No	263 (28.7)	3720 (71.6)	
Self-identified gay or bisexual, <i>n</i> (%)			
Yes	339 (50.9)	1755 (40.2)	<0.001
Either heterosexual or value missing	327 (49.1)	1090 (25.0)	
Aboriginal ancestry, <i>n</i> (%)			
Yes	289 (31.5)	350 (6.7)	<0.001
No	624 (68.1)	2368 (45.6)	
Unknown	4 (0.4)	2476 (47.7)	
Clinical			
Hepatitis-C positive, <i>n</i> (%)			
Yes	613 (66.9)	1494 (28.8)	<0.001
No	246 (26.8)	2678 (51.6)	
Unknown	58 (6.3)	1022 (19.7)	
AIDS at baseline, <i>n</i> (%)			
Yes	114 (12.4)	684 (13.2)	0.541
No	803 (87.6)	4510 (86.8)	
Physician experience, ^{b,c} median (IQR)	72 (20–172)	68 (8–176)	0.026
Adherence >95%, <i>n</i> (%)			
>95	464 (50.6)	2885 (55.5)	<0.001
≤95	446 (48.6)	2072 (39.9)	
N/A ^g	7 (0.8)	237 (4.6)	
Baseline CD4 cell count, ^d median (IQR)	220 (130–350)	240 (130–360)	0.054
Baseline plasma viral load, ^e median (IQR)	87 650 (28 000–100 010)	80 100 (23 800–100 010)	0.434
Viral load testing rate (tests/year) median (IQR)	4 (3–6)	4 (3–5)	<0.001
Total follow-up time (months), median (IQR)	91 (44–144)	82 (28–151)	0.004
Loss to follow-up, <i>n</i> (%)	15 (1.6)	818 (15.8)	<0.001
Crude death rate, <i>n</i> (%)	33 (3.6)	263 (5.1)	0.057
Treatment			
Initiated ART, <i>n</i> (%)			
Before 1996	32 (3.5)	911 (17.5)	<0.001
1996–99	322 (35.1)	1502 (28.9)	
2000–03	181 (19.7)	806 (15.5)	

(continued)

Table 2 Continued

Variable	LISA (<i>n</i> = 917)	DTP (excluding LISA) ^a (<i>n</i> = 5194)	<i>P</i> -value [†]
2004–07	292 (31.8)	1080 (20.8)	
2008–10	90 (9.8)	895 (17.2)	
Years on ART, ^f median (IQR)	6 (2–11)	9 (3– 13)	<0.001

Results presented as median (IQR) or *n* (%).

^aThis cohort refers to the other patients in DTP who are not in LISA cohort but were eligible for the study (were alive in July 2007, started ART before January 2010 and were aged over 19 years by January 2010).

^bNumber of HIV-positive patients whose GP is treating at baseline.

^c253 patients (4%) do not have information about GP experience.

^d158 patients (3%) do not have information about baseline CD4 cell count.

^e1434 patients (23%) do not have information about baseline viral load.

^fFrom first ART date to interview date for LISA participants, from first ARV date to January 31, 2010 for non-LISA participants.

^gAdherence data was unavailable for patients who stopped treatment or had a treatment interruption.

[†]Chi-square test was used to compare categorical variables. Wilcoxon rank sum test was used to compare continuous variables. *P* < 0.05 were taken to be statistically significant.

study, 47% reported negative body image, which highlights that further efforts are needed to address issues of body image among people living with HIV.³⁴

- (6) Housing is a known determinant of health behaviours, including adherence to ART, as well as health outcomes. This study investigated the association between anti-retroviral adherence and use of support services, including the Maximally Assisted Therapy programme, among PHA who are unstably housed in the LISA sample. The findings suggest that in the absence of sustainable housing solutions, Maximally Assisted Therapy and similar programmes may play an important role in supporting treatment adherence in this population.³⁵
- (7) History of violence among women in the LISA sample was quite prominent. Of the 82% who reported ever having experienced violence, 62% reported violence before the age of 16 years, 22% reported recent experiences of violence and 56% of the women reported more than five violent episodes over their lifetime.³⁶
- (8) Treatment interruptions limit therapeutic successes of ART and are associated with higher morbidity and mortality. Our analysis found that older age, male sex and higher CD4 counts may be protective against treatment interruptions.³⁷
- (9) Late initiation may not only affect the clinical and therapeutic success of treatment but may also increase the likelihood of transmission of HIV. A key social determinant of health, stable housing creates an enabling environment that may support timely health-seeking behaviour. Efforts to improve access to stable housing may reduce delays in treatment initiation, thereby improving HIV outcomes.³⁸

- (10) An overwhelming 84.5% of participants reported using at least one agency within the past 3 months (prior to interview). The findings from this study demonstrate that vulnerable groups use supportive services, yet challenges remain in making improvements to their social and clinical status.³⁹
- (11) Disclosure of HIV status to sexual partners has become an increasingly complex issue. An explanatory analysis on factors associated with disclosure found that women were half as likely to disclose as men and gay/lesbian/bisexual individuals were 40% less likely to disclose than heterosexuals.⁴⁰

Knowledge translation and exchange

A key component of the LISA study involves knowledge translation and exchange (KTE). Although the LISA study interviews are complete, the cohort is still active due to ongoing longitudinal linkages with the DTP.

The goals of our KTE and dissemination strategy are: (i) to inform decision makers regarding policy and programme development as well as strategic priority setting; (ii) to disseminate findings to the academic community; and (iii) to engage with community stakeholders who may not be effectively reached through traditional academic and research dissemination methods. Based on the experience and recent KTE literature, which indicates the effectiveness of popular formats to reach key stakeholders,⁴¹ the following diverse methods are used to communicate our research findings to service providers, policy makers and community members in various parts of the province:

- (1) development and dissemination of plain language summaries, information sheets and newsletters;
- (2) website access to research findings;

- (3) provision of travel support for community round tables with policy makers, health authority representatives and affected communities outside Metro Vancouver; and
- (4) arts-based community engagement, including a Photovoice project examining the impact of unstable housing on the health and quality of life of LISA participants.⁴²

In order to facilitate KTE and ensure that the project goals reflect the needs of the community, we invited community members to participate in a community advisory committee. Eleven committee members represent HIV/AIDS service organization memberships throughout the Lower Mainland and Vancouver Island. The members of the community advisory committee contributed to the development of research questions, advised on and helped build community partnerships and continue to assist with KTE of research findings.

What are the main strengths and weaknesses of the study?

With comprehensive data on 917 individuals, the LISA study contributes important information regarding the well-being of individuals accessing ART in BC. The DTP database mainly collects clinical data; therefore, the LISA study provides insight into the more complex socio-economic and demographical characteristics of PHA who have accessed treatment in BC.

Of note, the study is a non-probability sample, which limits the generalizability of our results. Specifically, this study targeted marginalized populations. The modest cash incentive offered for study participation acted as a powerful stimulus for the over-sampling of individuals in need of financial assistance. LISA is not representative of the provincial DTP nor is it representative of all PHA in the province as it is a sample of participants engaged in care who have accessed treatment.

Furthermore, we relied on individuals' self-report of behaviours; therefore, socially desirable responding and recall bias may have affected some of the study's findings. As the study design is cross-sectional, temporal and causal relationships cannot be inferred. In addition, by design the LISA study only includes individuals who have accessed ART, and thus is not representative of PHA who have yet to access therapy. Similar studies including all PHA in the province would be of value.

Finally, we have experienced challenges in attempting to translate research findings into meaningful change. The process from knowledge production to uptake can be slow and is greatly determined by community and government priorities. We aim to continue strengthening our ties with policy decision-makers and community groups to ensure that the knowledge

gained from the LISA study can be used to improve the health and well-being of PHA on treatment in BC.

Can I get a hold of the data? Where can I find out more?

For further information on the LISA study, please contact the principal investigator, Dr Robert Hogg (bobhogg@cfenet.ubc.ca) or the project coordinator, Kate Salters (ksalters@cfenet.ubc.ca). Electronic data are stored in Oracle and accessible through the data manager. We welcome ideas and feedback regarding the use of collected data, including research questions and knowledge translation initiatives.

Funding

Canadian Institutes of Health Research (CIHR) (grant number 53396).

Acknowledgements

The LISA research team are thankful for the cooperation of our various research sites. We are inspired by their amazing dedication to their clients and the communities they serve. We would especially like to thank the participants of the LISA study who trust us with sensitive and intimate information and share their stories in hopes of supporting research projects that will make a difference in their communities. We respectfully listen and interpret their experiences and hope that we are doing them justice. We are also grateful to the contributions of the LISA Community Advisory Committee: Terry Howard, Rosa Jamal, Isabella Kirchner, Sandy Lambert, Kecia Larkin, Steve Levine, Melissa Medjuck, Stacie Migwans, Sam Mohan, Lori Montgomery, Glyn Townson, Michelle Webb and Sarah White, and Study Co-Investigators: Dr Rolando Barrios, Dr David Burdge, Dr Marianne Harris, Dr David Henderson, Dr Thomas Kerr, Dr Julio S.G. Montaner, Dr Thomas Patterson, Dr Eric Roth, Dr Mark Tyndall, Dr Brian Willoughby and Dr Evan Wood. Finally, we thank our colleagues who have provided additional assistance with the data set and article: David Milan, Dragan Lesovski, Anya Shen and Svetlana Draskovic.

Conflict of interest: In the last five years, Dr. Robert Hogg has held grant funding from the National Institutes of Health (NIH), Canadian Institutes of Health Research (CIHR), Social Sciences and Humanities Research Council of Canada (SSHRC) and Merck. Dr Julio Montaner has received grants from Abbott, Biolytical, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, Janssen, Merck and ViiV Healthcare. He is also supported by the Ministry of Health Services and the Ministry of

Healthy Living and Sport within the Province of British Columbia; through a Knowledge Translation Award from the CIHR; and through an Avant-Garde Award (No.1DP1DA026182-01) from the National Institute of Drug Abuse at the US National Institutes of Health. He has also received support from the International AIDS Society, United Nations AIDS Program, World Health Organization, National Institute on Drug Abuse, National Institutes of Health

Research—Office of AIDS Research, National Institute of Allergy & Infectious Diseases, The United States President's Emergency Plan for AIDS Relief (PEPFAR), Bill & Melinda Gates Foundation, French National Agency for Research on AIDS & Viral Hepatitis (ANRS) and Public Health Agency of Canada. He has academic partnerships with the University of British Columbia, Simon Fraser University, Providence.

KEY MESSAGES

- Of all LISA participants, 608 (66.5%) reported being food insecure, 703 (76.7%) were unemployed at the time of interview and 476 (51.9%) reported ever being incarcerated.
- Within the LISA sample, knowledge of HIV resistance and uptake of resistance testing were low.
- Social factors, such as food insecurity, poor body image and unstable housing were common issues. These factors have been found to have a significant impact on clinical outcomes of HIV such as virological suppression, treatment adherence and treatment interruptions.

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