RESEARCH: Neighbourhood level material deprivation is independently associated with response to combination antiretroviral therapy in the Canadian HIV Observational Cohort Collaboration (CANOC)

Alison R. McClean PharmD[1,2], Jason Trigg MA[1], Monica Ye MSc[1], Taylor McLinden PhD[1], Katherine W. Kooij MD, PhD[1,3], Nic Bacani BSc[1], Christian Hui MSW[4,8], Paul Sereda BA[1], Ann N. Burchell PhD[5,6], Sharon Walmsley MD, MSc[7,8], Deborah Kelly PharmD[9], Nimâ Machouf PhD[10], Julio Montaner MD[1,2], Mona Loutfy MD MPH[6,12], Robert S. Hogg PhD[1,2] on behalf of the CANOC Collaboration†

1. British Columbia Centre for Excellence in HIV/AIDS, Vancouver, BC, Canada,
2. University of British Columbia, Vancouver, BC, Canada
3. Simon Fraser University, Burnaby, BC, Canada,
4. Ryerson University, Toronto, ON, Canada
5. St. Michael's Hospital, Toronto, ON, Canada,
6. University of Toronto, Toronto, ON, Canada,
7. University Health Network, Toronto, ON, Canada,
8. CIHR Canadian HIV Trials Network, Vancouver, BC, Canada,
9. Memorial University of Newfoundland, St. John's, NL, Canada,
10. Clinique de Médecine Urbaine du Quartier Latin, Montreal, QC, Canada,
11. Maple Leaf Medical Clinic, Toronto, ON, Canada,

Corresponding author: Alison McClean, PharmD

Email: alisonmcclean@alumni.ubc.ca

Tel: 250-819-1378

†The CANOC Collaboration is listed in the acknowledgements.

Funding: CANOC is funded by the Canadian Institutes of Health Research (CIHR) through a Centres Grant (CIHR#02684); two Operating Grants (CIHR#134047, CIHR#136882); a Foundation Grant (CIHR#143342); in collaboration with the CIHR Canadian HIV Trials Network (CTN#242). The funders had no role in study design, data collection, analysis, interpretation, and decision to publish.

Declaration: ARM, JT, MY, TM, KWK, NB, CH, PS, DK, NM, ANB, and RSH have no conflicts to disclose. SW has served on advisory boards, attended speaking engagements, meetings, symposiums, and conducted clinical studies for ViiV Health Care, GSK, Gilead and Merck. JM has received support from the BC Ministry of Health and the Public Health Agency of Canada and institutional grants have been provided by Gilead and Merck. ML has received grants from ViiV Health Care, AbbVie, and Gilead. All conflicts are outside this work.

ABSTRACT

Introduction

Socioeconomic status (SES) has been associated with adverse health outcomes, including higher viral loads (VL) and lower CD4 cell counts (CD4) among people living with HIV (PLWH). However, indicators of SES may be absent from traditional clinical and administrative datasets. This study explored the relationship between neighbourhood level material deprivation, a proxy of SES, and immunologic and virologic response to combination antiretroviral therapy (cART) among PLWH in Canada.

Methods

Response to cART was defined as positive if the CD4 cell count increased ≥50 cells/mm^3 (CD4+) and VL decreased to ≤50 copies/mL (VL+) within 6 months of treatment initiation. Response was further categorized as concordant positive (CD4+/VL+), concordant negative (CD4-/VL-) or discordant (CD4+/VL- or CD4-/VL+). Adjusted multinomial regression was used to quantify the relationship between neighbourhood level material deprivation and immunologic and virologic response. Interactions between neighbourhood level material deprivation and age at baseline, sex at birth, and province were examined as well.

Results

This study included 10 133 PLWH, of which 3379 (33.3%) participants lived in materially deprived neighbourhoods. The majority of individuals (n 6277, 62.0%) demonstrated a concordant positive (CD4+/VL+) response to cART. After adjustment for confounding, living in a materially deprived neighbourhood was associated with concordant negative

response (adjusted OR 1.34, 95%CI 1.13-1.60). The association between neighbourhood level material deprivation and immunologic and virologic response to cART was significantly affected by variations in province but not by age or sex.

Interpretation

This study supports an association between neighbourhood level SES and response to cART even in the context of universal healthcare in Canada.

Keywords: HIV, material deprivation, CD4, viral load, treatment response

INTRODUCTION

For people living with HIV (PLWH), combination antiretroviral therapy (cART) has improved HIV-related morbidity and mortality by reducing HIV viral load (VL) and increasing the number of CD4+ T-lymphocyte cells (CD4) (1). Response to cART can be assessed as positive if an individual experiences an increase in CD4 count ≥50 cells/mm^3 (CD4+) and a decrease in VL ≤50 copies/mL (VL+) within 6 months of treatment initiation (2–5). Treatment response can be further categorized as concordant positive (CD4+/VL+), concordant negative (CD4-/VL-) or discordant (CD4+/VL- or CD4-/VL+). Concordant positive responses are preferable whereas concordant negative and discordant responses are associated with increased risk of mortality and opportunistic infection (2,3).

In general, individuals of lower socioeconomic status (SES) have been disproportionately affected by HIV and indicators of adverse SES have been associated with suboptimal HIV treatment-related outcomes, including higher VL and lower CD4 counts, at the individual level (6–9). For example, when comparing PLWH who are employed to those who are not, employment predicted significantly higher CD4 counts (10) and education (above the high school level) has been associated with VL <400 copies/mL (11). After adjustment for demographic characteristics and cART adherence, it has also been shown that either being unemployed or not having completed a university education was significantly associated with VL ≥50 copies/mL (Burch et al., 2014). Nevertheless, adherence to cART may be an important mediator in the relationship between material deprivation and immunologic and virologic response (11,13).

Although one's socioeconomic circumstances play an important role in health outcomes, SES can be challenging to assess using standard clinical and administrative databases in the Canadian context. Geographic proxies for individual level data, such as neighbourhood level material and social deprivation indexes, have been developed to address this gap (14). Previous studies have demonstrated an association between neighbourhood level socioeconomic circumstances and specific morbidities (e.g. coronary artery disease, myocardial infarction, end stage renal disease) and mortality (15–19). The objective of this research was to examine the relationship between neighbourhood level material deprivation and concordant positive, concordant negative, and discordant responses to cART. Further, this study addressed the question of whether differences in the magnitude of this effect varied by age at baseline, sex at birth, or province of enrolment.

METHODS

The Canadian HIV Observational Cohort (CANOC) is a longitudinal cohort study of 13 040 PLWH who have initiated cART. CANOC consists of eleven sites spanning five provinces (British Columbia, Saskatchewan, Ontario, Quebec, Newfoundland and Labrador) and contains data from January 1, 2000 to December 31, 2016. In addition to living with HIV, CANOC inclusion criteria requires participants to (1) be antiretroviral therapy naïve at entry into cohort, (2) have initiated cART consisting of at least three antiretroviral medications on or after January 1, 2000, (3) be 18 years or older at cART initiation, (4)

be a Canadian resident, and (5) have at least one HIV VL and CD4 count within one year of cART initiation.

Study specific inclusion criteria included having a valid postal code, known sex at birth, at least 6 months of follow up time, and sufficient data to determine immunologic and virologic response. Demographic and clinical data were extracted from medical files at individual sites and collated at the British Columbia Centre for Excellence in HIV/AIDS (BC-CfE). Ethics approval was obtained at participating sites and from the harmonized University of British Columbia-Simon Fraser University Research Ethics Board at Providence Health Care Research Institute (H07-02684). More information regarding CANOC has been published elsewhere (20).

The main exposure, neighbourhood level material deprivation, was derived from an index built using Canadian census data to approximate individual level SES by geographic area (14). The basic geographic unit of the index are dissemination areas (DA) and the score is constructed at the DA level using individuals' postal code information (21). Factor scores are built around the DA using average household income, proportion unemployed of those over 15 years, and high school education rate from the 2006 version of the Canadian census. If information was missing at the DA level, data were taken from the census subdivision (CSD) level. Index scores range from -8 to +8 where a lower score indicates less deprivation and a higher score indicates more; a value of 0 corresponds to the Canadian average. A dichotomous variable was thus created—i.e. residence in a materially deprived neighbourhood (index >0) or not (index <0).

Based on research published elsewhere, response to cART was categorized as concordant positive (CD4+/VL+), concordant negative (CD4-/VL-), or discordant (CD4+/VL- or CD4-/VL+) based on whether CD4 increased ≥50 cells/mm^3 (CD4+) and VL decreased ≤50 copies/mL (VL+) within 6 months of treatment initiation (2,5). Baseline characteristics between groups with and without neighbourhood level material deprivation were compared using chi-square tests and Kruskal Wallis tests, where appropriate. To examine the relationship between neighbourhood level material deprivation and immunologic and virologic response category, univariable and multivariable multinomial regression modelling was used. Concordant positive (CD4+/VL+) was used as the reference category. Multivariable models were adjusted for a pre-defined list of potential confounders, including age at baseline, sex at birth, province of enrolment, era of cART initiation, and whether people had injected drugs (ever). Subanalyses, where an interaction term was introduced between neighbourhood level material deprivation and age at baseline, sex at birth, or province of enrolment, were conducted to examine whether the strength of the association between living in a materially deprived neighbourhood, or not, and immunologic and virologic response category was affected by each of these potential effect modifiers. Individuals enrolled in CANOC in Newfoundland and Labrador were excluded from the provincial subanalysis due to small cell counts (<5 individuals) in some of the categories. All analyses were run with SAS® Proprietary Software version 9.4 (Cary, NC, USA); a p-value of <0.05 was considered statistically significant.

RESULTS

From 13 040 CANOC participants, 10 133 (77.7%) were eligible for this study (Table 1). Individuals were excluded if they did not have at least 6 months of follow up (n 873, 6.7%), sufficient VL and CD4 data to determine response (n 1192, 9.1%), known sex at birth (n <5), or a valid postal code (n 839, 6.4%). Overall, 6277 (62.0%) of study participants exhibited a concordant positive response whilst 718 (7.1%) were concordant negative. The remaining 2078 (20.5%) and 1060 (10.5%) individuals exhibited CD4+/VL- and CD4-/VL+ discordant responses to cART, respectively. Of those included, 6754 (66.7%) individuals did not live in a materially deprived neighbourhood whilst 3379 (33.3%) did. The largest proportions of study individuals were male (84.6%) and white (43.5%) and the median baseline age was 40 years old (Q1, Q3 32, 47). The median baseline CD4 count was 250 cells/mm^3 (Q1, Q3 140, 380) and median baseline viral load was 4.85 $\log_{10}$copies/mL (Q1, Q3 4.34, 5.17).

In the univariable multinomial regression model, individuals living in a materially deprived neighbourhood were more likely to exhibit a concordant negative (OR 1.74, 95%CI 1.48-2.03) or discordant (CD4+/VL- OR 1.21, 95%CI 1.09-1.34; CD4-/VL+ OR 1.19 95%CI 1.04-1.37) response to cART (Table 2). After adjustment for sex at birth, province of enrolment, whether individuals had ever injected drugs, era of entry into cohort, and age at baseline, neighbourhood level material deprivation was significantly associated with concordant negative response (OR 1.34, 95%CI 1.13-1.60).

The interaction term fit between age at baseline and neighbourhood level material deprivation was not significant for any immunologic and virologic response category

(Table 3), which indicates the relationship between neighbourhood level material deprivation and immunologic and virologic response was not significantly affected by variation in age. The effect modification of sex at birth was approaching significance (p-value 0.0820). To further investigate neighbourhood level material deprivation and sex at birth, a 4-level exposure that combines material deprivation and sex at birth was put into the model and adjusted by the same confounders as the main model. Compared to male sex and no neighbourhood level material deprivation, female sex and no neighbourhood level deprivation showed an OR of 1.63 (95%CI 1.25-2.12), female sex and neighbourhood level deprivation demonstrated an OR of 1.59 (95%CI 1.20-2.11), but male sex and neighbourhood level material deprivation only showed an OR of 1.49 (95%CI 1.23-1.80) for concordant negative responders.

The interaction term fit between province and neighbourhood level material deprivation was statistically significant (p-value 0.0338; referent no deprivation and residence in BC). Residence in a materially deprived neighbourhood in BC increased the odds of having a concordant negative response (OR 1.82, 95%CI 1.43-2.31). Residence in a non-materially deprived neighbourhood in Saskatchewan increased the risk of concordant negative (OR 6.09, 3.58-10.37) and CD4+/VL- discordant (OR 1.78, 1.05-3.04) response while residence in a materially deprived Saskatchewan neighbourhood was associated with an increased risk of all three response categories (CD4-/VL- OR 7.20, 95% CI 4.79, 10.84; CD4+/VL- OR 2.38, 95%CI 1.62, 3.49; CD4-/VL+ OR 2.25, 95%CI 1.41, 3.60). Within Ontario, residence in either type of neighbourhood was significantly associated with experiencing a CD4-/VL+ discordant response (non-deprived OR 1.25, 1.04-1.51;

deprived OR 1.42, 1.08-1.88). Individuals from Quebec had higher odds of CD4-/VL+ discordance if they lived in a non-deprived neighbourhood (OR 1.31, 95%CI 1.03-1.66).

INTERPRETATION

Among PLWH in Canada who initiated cART between 2000 and 2016, those living in a materially deprived neighbourhood at initiation were least likely to achieve viral suppression and/or an increase in CD4 cells within 6 months of cART initiation (i.e. concordant negative or discordant response). The association between concordant negative response and neighbourhood level material deprivation was robust and persisted with adjustment for individual level factors such as birth sex, province of enrolment, ever injecting drugs, era of entry into cohort, and age at baseline. Specifically, the odds of experiencing a concordant negative response to cART—as compared to achieving a concordant positive response— is statistically significantly and independently increased for individuals living in a materially deprived neighbourhood. Because concordant negative and discordant responses have been associated with increased risk of mortality, this research provides further insights into the previously reported association between neighbourhood level education and income and increased mortality risk (2,22,23). Lower income and education rates at the neighbourhood level have been associated with higher mean community viral load (24) and there is evidence of associations between higher neighbourhood SES and viral suppression (13,25,26). Furthermore, individuals living in a neighbourhood with higher rates of deprivation may be more likely to experience CD4 counts <200 cells/μL (27).

The magnitude and direction of the association between neighbourhood material deprivation and treatment response is not affected by age. We did find evidence of effect modification between sex at birth and neighbourhood level material deprivation, showing a stronger association between neighbourhood level material deprivation and unfavourable treatment response in males. In females, neighbourhood context did not appear to affect treatment response. However, females were more likely to have experienced concordant negative response than males regardless of neighbourhood level material deprivation. The provincial subanalysis demonstrated that neighbourhood level material deprivation significantly increased the odds of experiencing concordant negative response to cART in BC, whereas this association was less pronounced in Ontario, Quebec, or Saskatchewan. Individuals from Saskatchewan were more likely to have concordant negative or discordant response regardless of whether their neighbourhood was materially deprived. These results suggest that the impact of neighbourhood setting on immunologic and virologic response to cART likely varies by geographic location of residence. It is worth noting that CANOC relies on clinic-based data in some provinces (SK, ON, QC) and population-based data in others (BC) and this may account for part of the observed provincial differences. Another possible explanation could be that although the current exposure, neighbourhood level material deprivation, has only two categories (i.e. deprived and non-deprived), the contrast between deprived and non-deprived may be more pronounced in some provinces. Readers should be cautious when interpreting these results. Firstly, the study lacked individual level data with regards to indicators of SES (i.e. employment, income, and

education attainment). By definition, the neighbourhood level material deprivation index requires making generalizations about an individual based on a larger group, which may be liable to the ecological fallacy. Additionally, due to CANOC study design and available data, it was not possible to adjust for adherence which is likely related to both SES and response to cART (11,13,27). The generalizability of the results of this study beyond the Canadian context may be limited due to the use of a context specific definition of neighbourhood level material deprivation. However, conclusions regarding an association between neighbourhood level SES and treatment response are likely generalizable to other settings with universal access to cART. Despite these limitations, CANOC remains a large pan-provincial observational cohort following over 13 000 PLWH.

In conclusion, this study provides additional evidence that SES may affect treatment response to cART among PLWH with access to universal healthcare in Canada. To the best of our knowledge, this study is the first to examine the associations between neighbourhood level material deprivation and immunologic and virologic response to cART in the Canadian context. Future studies with access to traditional individual-level indicators of SES (e.g. income, education, employment) could explore whether the associations reported here are consistent across studies. Further inquiry could examine whether SES impacts cART treatment failure in the Canadian context.

ACKNOWLEDGEMENTS

We would like to thank all of the study participants who allowed their data to be a part of the CANOC Collaboration.

We would also like to acknowledge all of CANOC's affiliated researchers:

The nominated Principal Investigator: Robert Hogg (British Columbia Centre for Excellence in HIV/AIDS; Simon Fraser University); Site Principal Investigators: Zabrina Brumme (British Columbia Centre for Excellence in HIV/AIDS), Ann N. Burchell (Ontario HIV Treatment Network (OHTN); University of Toronto; OHTN Cohort Study (OCS)], Curtis Cooper (University of Ottawa; OCS), Deborah Kelly (Memorial University of Newfoundland), Abigail Kroch (Ontario HIV Treatment Network; University of Toronto), Marina Klein (Montreal Chest Institute Immunodeficiency Service Cohort; McGill University), Mona Loutfy (University of Toronto; Maple Leaf Medical Clinic; OCS), Nima Machouf (CMU du Quartier Latin), Julio Montaner (British Columbia Centre for Excellence in HIV/AIDS; University of British Columbia), Kate Salters (British Columbia Centre for Excellence in HIV/AIDS; University of British Columbia), Rejean Thomas (Clinique Médicale l'Actuel), Stephen Sanche (University of Saskatchewan), Sharon Walmsley (University Health Network; University of Toronto); Alexander Wong (University of Saskatchewan); Co-Principal Investigators: Tony Antoniou (St Michael's Hospital; University of Toronto; Institute for Clinical Evaluative Sciences), Ahmed Bayoumi (St Michael's Hospital; University of Toronto), Mark Hull (British Columbia Centre for Excellence in HIV/AIDS), Bohdan Nosyk (British Columbia Centre for Excellence in HIV/AIDS; Simon Fraser University); Co-Investigators: Angela Cescon (Northern Ontario School of Medicine), Michelle Cotterchio (Cancer Care Ontario;

University of Toronto), Charlie Goldsmith (Simon Fraser University), Silvia Guillemi (British Columbia Centre for Excellence in HIV/AIDS; University of British Columbia), P. Richard Harrigan (British Columbia Centre for Excellence in HIV/AIDS; University of British Columbia), Marianne Harris (St Paul's Hospital), Sean Hosein (Community AIDS Treatment Information Exchange (CATIE)), Sharon Johnston (Bruyere Research Institute; University of Ottawa), Claire Kendall (Bruyere Research Institute; University of Ottawa), Clare Liddy (Bruyere Research Institute; University of Ottawa), Viviane Lima (British Columbia Centre for Excellence in HIV/AIDS; University of British Columbia), David Moore (British Columbia Centre for Excellence in HIV/AIDS; University of British Columbia), Alexis Palmer (British Columbia Centre for Excellence in HIV/AIDS; Simon Fraser University), Sophie Patterson (British Columbia Centre for Excellence in HIV/AIDS; Simon Fraser University), Peter Phillips (British Columbia Centre for Excellence in HIV/AIDS; University of British Columbia), Anita Rachlis (University of Toronto; OCS), Sean B. Rourke (University of Toronto; OCS), Janet Raboud (University of Toronto; University Health Network; OCS), Hasina Samji (British Columbia Centre for Excellence in HIV/AIDS), Marek Smieja (McMaster University), Benoit Trottier (Clinique Medicale l'Actuel, Universit e de Montr eal), Chris Tsoukas (McGill University), Mark Wainberg (McGill University; Lady Davis Institute for Medical Research), Collaborators: Chris Archibald (Public Health Agency of Canada Centre for Communicable Diseases and Infection Control), Margaret Kisikaw Piyesis (Canadian Aboriginal AIDS Network), Monique Doolittle-Romas (Canadian AIDS Society), Laurie Edmiston (Canadian Treatment Action Council), Sandra Gardner (OHTN; University of Toronto; OCS), Brian

Huskins (Canadian Treatment Action Council), Jerry Lawless (University of Waterloo), Douglas Lee (University Health Network; University of Toronto; Institute for Clinical Evaluative Sciences (ICES)), Renee Masching (Canadian Aboriginal AIDS Network), Stephen Tattle (Canadian Working Group on HIV & Rehabilitation), Alireza Zahirieh (Sunnybrook Health Sciences Centre); Analysts and Staff: Claire Allen (Regina General Hospital), Nic Bacani (British Columbia Centre for Excellence in HIV/AIDS), Stryker Calvez (Saskatoon HIV/AIDS Research Endeavour (SHARE)), Guillaume Colley (British Columbia Centre for Excellence in HIV/AIDS), Jason Chia (British Columbia Centre for Excellence in HIV/AIDS), Daniel Corsi (The Ottawa Hospital Immunodeficiency Clinic; Ottawa Hospital Research Institute), Erin Ding (British Columbia Centre for Excellence in HIV/AIDS), Louise Gilbert (Immune Deficiency Treatment Centre), Nada Gataric (British Columbia Centre for Excellence in HIV/AIDS), Lucia Light (OHTN), David Mackie (The Ottawa Hospital), Costa Pexos (McGill University), Paul Sereda (British Columbia Centre for Excellence in HIV/AIDS), Susan Shurgold (British Columbia Centre for Excellence in HIV/AIDS), Leah Szadkowski (University Health Network), Chrissi Galanakis (Clinique M edicale L'Actuel), Jason Trigg (British Columbia Centre for Excellence in HIV/AIDS), Monica Ye (British Columbia Centre for Excellence in HIV/AIDS), Benita Yip (British Columbia Centre for Excellence in HIV/AIDS), Jaime Younger (University Health Network), and Julia Zhu (British Columbia Centre for Excellence in HIV/AIDS).

REFERENCES

1. Montaner J, Lima V, Harrigan P, Lourenco L, Yip B, Nosyk B, et al. Expansion of HAART Coverage Is Associated with Sustained Decreases in HIV/AIDS Morbidity,

Mortality and HIV Transmission: The “HIV Treatment as Prevention” Experience in a Canadian Setting. PLoSOne. 2014;9(2):e87872.

2. Moore D, Hogg R, Yip B, Wood E, Tyndall M, Braitstein P, et al. Discordant immunologic and virologic responses to highly active antiretroviral therapy are associated with increased mortality and poor aderence to therapy. J Acquir Immune Defic Syndr. 2005;40(3):288–93.
3. Tan R, Westfall A, Willig J, Mugavero M, Saag M, Kaslow R, et al. Clinical outcomes of HIV-infected antiretroviral-naive patients with discordant immunologic and virologic responses to highly active antiretroviral therapy. J Acquir Immune Defic Syndr. 2008;47(5):553–8.
4. Grabar S, Moing V, Goujard C, Leport C, Kazatchkine M, Costagliola D, et al. Clinical outcome of patients with HIV-1 infection according to immunologic and virologic response after 6 months of highly active antiretroviral therapy. Ann Intern Med. 2000;133:401–10.
5. Kelly C, Gaskell K, Richardson M, Klein N, Garner P, MacPherson P. Discordant immune response with antiretroviral therapy in HIV-1: A systematic review of clinical outcomes. PLoS One. 2016;
6. Burch L, Smith C, Phillips A, Johnson M, Lampe F. Socioeconomic status and response to antiretroviral therapy in high-income countries: a literature review. AIDS. 2016;30(8):1147–62.
7. Sobrino-Vegas P, Rodriguez-Urrego J, Berenguer J, Caro-Murillo A, Blanco J, Viciana P, et al. Educational gradient in HIV diagnosis delay, mortality, antiretroviral treatment initiation and response in a country with universal health care. Antivir Ther. 2012;17:1–8.
8. D’Almeida K, Lert F, Spire B, Dray-Spira R. Determinants of virologic response to antiretroviral therapy: socio-economic status still plays a role in the era of cART. Results from the ANRS-VESPA 2 study, France. Antivir Ther. 2016;21:661–70.
9. Pellowski J, Kalichman S, Matthews K, Adler N. A pandemic of the poor: Social disadvantage and the US HIV epidemic. Am Psychol. 2013;68:197–209.
10. Simoni J, Yard S, Huh D. Prospective prediction of viral suppression and immune response nine months after ART initiation in Seattle, WA. AIDS Care. 2013;25(2):181–5.
11. Shacham E, Nurutdinova D, Onen N, Stamm K, Overton E. The interplay of sociodemographic factors on virologic suppression among a U.S. outpatient HIV clinic population. AIDS Patient Care STDS. 2010;24(4):229–35.
12. Burch L, Smith C, Anderson J, Sherr L, Rodger A, O’Connell R, et al. Socio-economic factors and virologic suppression among people diagnosed with HIV in the United Kingdom: Results from the ASTRA study. J Int AIDS Soc. 2014;17(S3):19533.
13. Eberhart M, Yehia B, Hillier A, Voytek C, Fiore D, Blank M, et al. Individual and community factors associated with geographic clusters of poor HIV care retention and poor viral suppression. J Acquir Immune Defic Syndr. 2015;69(1):S37–43.
14. Pampalon R, Hamel D, Gamache P, Raymond G. A deprivation index for health planning in Canada. Chronic Dis Can. 2009;29(4):178–91.

15. Carlsson A, Li X, Holzmann M, Wandell P, Gasevic D, Sundquist J, et al. Neighbourhood socioeconomic status and coronary heart disease in individuals between 40 and 50 years. Heart. 2016;102(10):775–82.
16. Ross N, Oliver L, Villeneuve P. The contribution of neighbourhood material and social deprivation to survival: A 22-year follow-up of more than 500 000 Canadians. Int J Env Res Public Heal. 2013;10:1378–91.
17. Akrawi D, Li X, Sundquist J, Sundquist K, Zoller B. End stage renal disease risk and neighbourhood deprivation: A nationwide cohort study in Sweden. Eur J Intern Med. 2014;25(9):853–9.
18. Stjarne M, Ponce de Leon A, Hallqvist J, Group S study. Contextual effects of social fragmentation and material deprivation on risk of myocardial infarction- results from the Stockholm Heart Epidemiology Program (SHEEP). Int J Epidemiol. 2004;33(4):732–41.
19. Yen I, Kaplan G. Neighbourhood social environment and risk of death: Multilevel evidence from the Alameda County study. Am J Epidemiol. 1999;149(10):898–907.
20. Palmer A, Klein M, Raboud J, Cooper C, Hosein S, Loutfy M. Cohort Profile: The Canadian Observational Cohort collaboration. Int Jour Epidem. 2011;40(1):25–32.
21. StatCan. Dissemination area reference maps, by census tract. 2006.
22. Joy R, Druyts E, Brandson E, Lima V, Rustad C, Zhang W, et al. Impact of Neighborhood-Level Socioeconomic Status on HIV Disease Progression in a Universal Health Care Setting. Epidemiol Soc Sci. 2008;47(4):500–5.
23. Hogg R, Srathdee S, Craib Math K, O'Shaughnessy M, Montaner J, Schechter M. Lower socioeconomic status and shorter survival following HIV infection. Lancet. 1994;344(8930):1120–4.
24. Castel A, Befus M, Willis S, Griffin A, West T, Hader S, et al. Use of the community viral load as a population- based biomarker of HIV burden. AIDS. 2012;26(3):345–53.
25. Gueler A, Schoeni-Affolter F, Moser A, Bertisch B, Bucher H, Calmy A, et al. Neighbourhood socio-economic position, late presentation and outcomes in people living with HIV in Switzerland. AIDS. 2015;29(2):231–8.
26. Rebeiro P, Howe C, Rogers W, Bebawy S, Turner M, Kheshti A, et al. The relationship between adverse neighborhood socioeconomic context and HIV continuum of care outcomes in a diverse HIV clinic cohort in the Southern United States. AIDS Care. 2018;30(11):1426–34.
27. Shacham E, Lian M, Onen N, Donovan M, Overton E. Are neighborhood conditions associated with HIV management? HIV Med. 2013;14(10):624–32.

Table 1. Sociodemographic and clinical characteristics of people living with HIV stratified by neighbourhood level material deprivation at cART initiation (n 10 133).

	Overall (n 10 133)		Neighbourhood level material deprivation				
			No (n 6754)		Yes (n 3379)		
	N	*col %*	*N*	*col %*	*N*	*col %*	*p-values*
Immune response							
Concordant positive (CD4+/VL+)	6277	61.9	4320	64.0	1957	57.9	<0.0001
Concordant negative (CD-/VL-)	718	7.1	402	6.0	316	9.4	
Discordant response (CD4+/VL-)	2078	20.5	1344	19.9	734	21.7	
Discordant response (CD4-/VL+)	1060	10.5	688	10.2	372	11.0	
Neighbourhood level material deprivation							
No	6754	66.7					
Yes	3379	33.4					
Sex at birth							
Male	8572	84.6	5886	87.2	2686	79.5	<0.0001
Female	1561	15.4	868	12.9	693	20.5	
Province							
BC	4485	44.3	3208	47.5	1277	37.8	<0.0001
SK	309	3.1	103	1.5	206	6.1	
ON	2960	29.2	2328	34.5	632	18.7	
QC	2339	23.1	1110	16.4	1229	36.4	
NL	40	0.4	5	0.07	35	1.0	
People who ever injected drugs							
No	6283	62.0	4296	63.6	1987	58.8	<0.0001
Yes	1923	19.0	985	14.6	938	27.8	
Unknown	1927	19.0	1473	21.8	454	13.4	
MSM							
No	3139	31.0	1746	25.9	1393	41.2	
Yes	5113	50.5	3558	52.7	1555	46.0	
Unknown	1881	18.6	1450	21.5	431	12.8	
AIDS defining illness (ADI)							
No ADI ever	8137	80.3	5430	80.4	2707	80.1	<0.0001
ADI before or at baseline	1116	11.0	749	11.1	367	10.9	
ADI after baseline	546	5.4	322	4.8	224	6.6	

ADI with unknown date	334	3.3	253	3.8	81	2.4	
Era of entry into cohort							
2000-2003	1707	16.9	1142	16.9	565	16.7	0.48
2004-2007	2266	22.4	1539	22.8	727	21.5	
2008-2011	3315	32.7	2193	32.5	1122	33.2	
2012-2016	2845	28.1	1880	27.8	965	28.6	
ART regimen							
NNRTI	4115	40.6	2735	40.5	1380	40.8	0.76
PI	4365	43.1	2926	43.3	1439	42.6	
II	1253	12.4	822	12.2	431	12.8	
Other	400	4.0	271	4.0	129	3.8	
	N	***median (Q1, Q3)***	***N***	***median (Q1, Q3)***	***N***	***median (Q1, Q3)***	
Age at baseline (years)	10133	40 (32, 47)	6754	40 (32, 47)	3379	40 (33, 47)	0.89
CD4 at baseline (cells/mm3)	10133	250 (140, 380)	6754	250 (140, 380)	3379	246 (140, 372)	0.067
Baseline viral load (log10 copies/ml)	10133	4.9 (4.3, 5.2)	6754	4.9 (4.4, 5.2)	3379	4.8 (4.3, 5.2)	0.047
Follow-up time (months)	10133	76.2 (39.9, 116.5)	6754	77.1 (39.6, 118.6)	3379	74.7 (40.4, 113.4)	0.21

BC British Columbia, SK Saskatchewan, ON Ontario, QC Quebec, NL Newfoundland and Labrador

MSM men who have sex with men, ADI AIDS defining illness

cART combination antiretroviral therapy classified by third agent, NNRTI non-nucleoside reverse-transcriptase inhibitor, PI protease inhibitor, II integrase inhibitor

% col column percent Q1, Q3 quartile 1, quartile 3

Table 2. Univariable and multivariable multinomial associations between neighbourhood level material deprivation and immunologic and virologic response category (n 10 133). Concordant positive (CD4+/VL+) was used as the reference category.

	Concordant negative (CD4-/VL-)			Discordant response (CD4+/VL-)			Discordant response (CD4-/VL+)			
	OR	*95% CI*		*OR*	*95% CI*		*OR*	*95% CI*		*p-values*
Univariable model										
Neighbourhood level material deprivation										
No [ref]	1.00			1.00			1.00			<0.0001
Yes	1.74	1.48	2.03	1.21	1.09	1.34	1.19	1.04	1.37	
Multivariable										
Neighbourhood level material deprivation										
No [ref]	1.00			1.00			1.00			0.0036
Yes	1.34	1.13	1.60	1.11	0.99	1.24	1.12	0.97	1.29	
Confounders										
Sex at birth										
Male [ref]	1.00			1.00			1.00			0.015
Female	1.33	1.09	1.62	0.97	0.84	1.12	1.14	0.95	1.37	
Province										
BC [ref]	1.00			1.00			1.00			
SK	4.89	3.49	6.84	2.05	1.49	2.82	1.84	1.25	2.72	
ON	0.94	0.76	1.16	0.93	0.82	1.06	1.23	1.04	1.45	<0.0001
QC	0.82	0.64	1.05	0.97	0.84	1.12	1.17	0.97	1.42	
NL	0.52	0.07	3.92	2.69	1.36	5.31	1.34	0.45	3.99	
Year of entry into cohort										
2000-2003 [ref]	1.00			1.00			1.00			
2004-2007	0.55	0.43	0.69	0.84	0.72	0.98	0.71	0.56	0.88	<0.0001
2008-2011	0.52	0.42	0.65	0.73	0.63	0.84	0.93	0.76	1.13	
2011-2016	0.53	0.42	0.67	0.55	0.47	0.64	1.13	0.92	1.38	
People who ever injected drugs										
No [ref]	1.00			1.00			1.00			<0.0001
Yes	2.77	2.26	3.39	1.52	1.32	1.75	1.39	1.15	1.68	

Unknown	1.14	0.90	1.45	1.00	0.87	1.16	1.13	0.94	1.36	
Age at baseline (10 years)	0.99	0.91	1.07	1.04	0.99	1.10	1.01	0.95	1.08	0.37

CD4+, an increase of ≥50 cells/mm within 6 months of cART initiation 3; VL+, viral suppression ≤50 copies/mL within 6 months of cART initiation

BC British Columbia, SK Saskatchewan, ON Ontario, QC Quebec, NL Newfoundland and Labrador

OR odds ratio, 95% CI 95% confidence interval

Table 3. Multivariable subanalyses exploring the associations between neighbourhood level material deprivation and age at baseline (n 10 133), sex at birth (n 10 133), and province of residence (n 10 093). Concordant positive response (CD4+/VL+) was used as the reference category.

	Concordant negative response (CD4-/VL-)			Discordant response (CD4+/VL-)			Discordant response (CD4-/VL+)			
	OR	*95% CI*		*OR*	*95% CI*		*OR*	*95% CI*		*p-values*
Model A NLMD*age at baseline										
per 10 years increase in deprivation "no"	0.97	0.87	1.07	1.04	0.98	1.10	1.03	0.96	1.12	0.65
per 10 years increase in deprivation "Yes"	1.02	0.79	1.33	1.05	0.90	1.24	0.97	0.79	1.20	
Model B NLMD*sex at birth										
No deprivation and Male [ref]	1.00			1.00			1.00			0.0002
No deprivation and Female	1.63	1.25	2.12	0.92	0.76	1.11	1.21	0.96	1.53	
Yes deprivation and Male	1.49	1.23	1.80	1.09	0.96	1.23	1.15	0.98	1.35	
Yes deprivation and Female	1.59	1.20	2.11	1.12	0.91	1.37	1.20	0.91	1.57	
Model C NLMD*province										
No deprivation and BC [ref]	1.00			1.00			1.00			<0.0001
No deprivation and SK	6.09	3.58	10.37	1.78	1.05	3.04	1.65	0.85	3.21	
No deprivation and ON	1.21	0.95	1.54	0.89	0.77	1.03	1.25	1.04	1.51	
No deprivation and QC	0.99	0.71	1.39	1.00	0.83	1.20	1.31	1.03	1.66	
Yes deprivation and BC	1.82	1.43	2.31	1.08	0.91	1.27	1.22	0.97	1.53	
Yes deprivation and SK	7.20	4.79	10.84	2.38	1.62	3.49	2.25	1.41	3.60	
Yes deprivation and ON	0.88	0.58	1.33	1.13	0.91	1.40	1.42	1.08	1.88	

Yes deprivation and QC	1.19	0.88	1.61	1.02	0.85	1.22	1.23	0.98	1.56

Newfoundland and Labrador were excluded from the provincial subanalyses due to small cell size (<5)

Models are adjusted for pre-defined potential age at baseline (models B, C only), sex at birth (models A, C only), province of enrolment (models A, B only), people who ever injected drugs, and era of entry into cohort

BC British Columbia, SK Saskatchewan, ON Ontario, QC Quebec

NLMD neighbourhood level material deprivation

OR odds ratio, 95% CI 95% confidence interval

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

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3-4
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5-6
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	7-8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	7-8
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-9
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	8-9
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	9
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	8
		(*c*) Explain how missing data were addressed	9
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	NA
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	9
		(b) Give reasons for non-participation at each stage	9
		(c) Consider use of a flow diagram	NA
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9,19-20
		(b) Indicate number of participants with missing data for each variable of interest	19-20
		(c) Summarise follow-up time (eg, average and total amount)	9,20
Outcome data	15*	Report numbers of outcome events or summary measures over time	9-10, 19-24

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	9-10, 19-24 9 NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10,11
Discussion			
Key results	18	Summarise key results with reference to study objectives	11
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	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21	Discuss the generalisability (external validity) of the study results	13
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	2

*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.