

Neighbourhood-level material deprivation and response to combination antiretroviral therapy in the Canadian Observational Cohort (CANOC): a longitudinal cohort study

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Abstract

Background: Socioeconomic status has been associated with higher viral loads and lower CD4 cell counts among people living with HIV. The objective of this study was to evaluate the relation between neighbourhood-level material deprivation and immunologic and virologic response to combination antiretroviral therapy (ART) among people living with HIV in Canada.

Methods: The Canadian Observational Cohort (CANOC) is a longitudinal cohort of people living with HIV, containing data from 2000–2016 from 5 Canadian provinces. We defined response to combination ART as positive if the CD4 cell count increased by 50 cells/mm³ (0.05 cells × 10⁹/L) or more (CD4+) and viral load decreased to 50 copies/mL or less (VL+) within 6 months of treatment initiation. We further categorized response to therapy as concordant positive (CD4+/VL+), concordant negative (CD4-/VL-) or discordant (CD4+/VL- or CD4-/VL+). We used adjusted multinomial logistic regression to quantify the relation between neighbourhood-level material deprivation and immunologic and virologic response.

Results: This study included 8274 people living with HIV, of which 1754 (21.2%) lived in the most materially deprived neighbourhoods. Most individuals (62.2%) showed a concordant positive response to combination ART. After adjustment, living in the most materially deprived neighbourhoods was associated with a CD4-/VL+ discordant response (adjusted odds ratio [OR] 1.31, 95% confidence interval [CI] 1.06–1.62) and a concordant negative response (adjusted OR 1.45, 95% CI 1.13–1.86), using a concordant positive response as the reference. No other deprivation quartile was independently associated with a particular response.

Interpretation: People living with HIV from the most materially deprived neighbourhoods had increased odds of poor immunologic or virologic response to combination ART. These results motivate further study of the specific socioeconomic factors that potentially affect response to combination ART among people living with HIV in Canada.

For people living with HIV, combination antiretroviral therapy (ART) has improved risk of HIV-related morbidity and death by reducing HIV viral load (VL) and increasing the number of CD4 T-lymphocyte cells (CD4).¹ Response to combination ART can be assessed as positive if an individual has an increase in CD4 count of 50 cells/mm³ (0.05 cells × 10⁹/L) or more (CD4+) and a decrease in viral load to 50 copies/mL or less (VL+) within 6 months of treatment initiation.^{2–6} 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 death and opportunistic infection.^{2,3,5}

In general, individuals of lower socioeconomic status have been disproportionately affected by HIV, and indicators of low socioeconomic status have been associated with suboptimal

HIV treatment-related outcomes, including higher viral load and lower CD4 counts, at the individual level.^{7–10} For example,

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when comparing people living with HIV who are employed to those who are not, employment predicted significantly higher CD4 counts,¹¹ and education (above the high school level) has been associated with viral loads of less than 400 copies/mL.¹² After adjustment for demographic characteristics and combination ART adherence, it has also been shown that either being unemployed or not having completed a university education was significantly associated with viral loads of 50 copies/mL or more.¹³ Nevertheless, adherence to combination ART may be an important mediator in the relation between material deprivation and immunologic and virologic response.^{12,14}

Although one's socioeconomic circumstances play an important role in health outcomes, socioeconomic status 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 indices, have been developed to address this gap.¹⁵ Previous studies have shown an association between neighbourhood-level socioeconomic circumstances and specific morbidities (e.g., coronary artery disease, myocardial infarction, end-stage renal disease) and death.^{16–20} The objective of this study was to evaluate the relation between neighbourhood-level material deprivation and concordant positive, concordant negative and discordant responses to combination ART.

Methods

Study design, setting and participants

The Canadian Observational Cohort (CANOC) is a longitudinal cohort study of 13 057 people living with HIV who have initiated combination ART. This study includes 11 sites spanning 5 provinces (British Columbia, Saskatchewan, Ontario, Quebec, Newfoundland and Labrador) and contains data from Jan. 1, 2000, to Dec. 31, 2016. In addition to living with HIV, CANOC inclusion criteria requires participants to have never used antiretroviral therapy before entry into the cohort; have initiated combination ART, consisting of at least 3 antiretroviral medications, on or after Jan. 1, 2000; be 18 years or older at initiation of combination ART; be a Canadian resident; and have at least 1 HIV viral load and CD4 count within 1 year of initiating combination ART.

Study-specific inclusion criteria included having a valid postal code, known sex, 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 BC Centre for Excellence in HIV/AIDS. More information regarding CANOC has been published elsewhere.²¹

Variable definitions

We derived the main exposure, neighbourhood-level material deprivation, from an index built using Canadian census data to approximate individual-level socioeconomic status by geographic area.¹⁵ The basic geographic unit of the index is the dissemination area, and the score is constructed at the level of the dissemination area using individual postal code information.²²

Factor scores are built around the dissemination area using average household income, proportion of unemployed people older than 15 years, and high school education rate from the 2006 Canadian census. Index scores range from –8 to +8, where a lower score indicates less deprivation and a higher score indicates more deprivation; a value of 0 corresponds to the Canadian average. We then grouped neighbourhoods by deprivation quartile from 1 (least deprived) to 4 (most deprived).

In alignment with a systematic review of immunologic and virologic discordant response to combination ART, we used a follow-forward window of 6 months to assess initial treatment response.⁵ We categorized response to combination ART as concordant positive (CD4+/VL+), concordant negative (CD4–/VL–) or discordant (CD4+/VL– or CD4–/VL+) based on whether CD4 increased by 50 cells/mm³ (0.05 cells × 10⁹/L) or more (CD4+) and viral load decreased to 50 copies/mL or less (VL+) within 6 months of treatment initiation based on previous research.^{2,5,6}

AIDS-defining illnesses included non-Hodgkin lymphoma, viral infections (e.g., cytomegalovirus), bacterial infection (e.g., *Mycobacterium avium* complex), HIV-related disease (e.g., HIV encephalopathy), protozoal infections (e.g., *Toxoplasma gondii* encephalitis) and mycotic infection (e.g., esophageal candidiasis).²³

Statistical analysis

We compared baseline characteristics among neighbourhood-level material deprivation quartiles (Q1–Q4) using χ^2 tests and Kruskal–Wallis tests, where appropriate. To evaluate the relation between neighbourhood-level material deprivation quartile and immunologic and virologic response category, we used univariable and multivariable multinomial logistic regression modelling, with a CD4+/VL+ response as the reference category.

Developed from theoretical associations between neighbourhood-level material deprivation and immune and virologic response, we adjusted multivariable models for a predefined list of potential confounders, including province of enrolment, era of combination ART initiation, whether people had ever injected drugs, age at baseline and sex. We included province as a confounder as trends in HIV diagnosis and access to care vary across Canada.^{24,25} Era of entry into cohort was included in the model to adjust for temporal trends in HIV care over time (such as how timing of treatment initiation based on CD4 cell count has changed over time, and different therapies have been available and favoured over time, and 1 study found the all-cause mortality rate was lower among individuals initiating combination ART in 2008–2010 than those initiating it in 2000–2003).²⁶ As people living with HIV who use drugs are at increased risk for morbidity and death compared with those who do not, and individuals who have injected drugs may have reduced immunologic and virologic response to combination ART, we adjusted the multivariable model for history of ever injecting drugs.^{27,28} We also included sex and age.

We did not employ multiple imputation as we lacked information on other known variables to predict the missingness. To decrease the number of individuals excluded from the

study, we conducted an additional analysis using a dichotomized version of the deprivation index.⁶ To achieve the dichotomous score, we first categorized the material deprivation index into 2 groups, where people with a score greater than 0 were considered to live in a deprived area and those with a score less than 0 were considered not to be living in a deprived area. For people who resided in areas covered by only either positive or negative index scores, we were thus able to categorize them despite having insufficient location information to provide a specific index score. Because only partial location information was available for a portion of the cohort, this simplification allowed us to achieve greater coverage for the index.

We conducted all analyses with SAS version 9.4 and considered a *p* value of less than 0.05 statistically significant.

Ethics approval

Ethics approval was obtained at participating sites and from the harmonized University of British Columbia–Simon Fraser University Research Ethics Board at the Providence Health Care Research Institute (H07–02684).

Results

From 13 057 CANOC participants, 8274 (63.4%) were eligible for this study (Table 1). Overall, 5144 (62.2%) of the 8274 study participants exhibited a concordant positive response and 595 (7.2%) were concordant negative. The remaining 1670 (20.2%) and 865 (10.5%) individuals exhibited CD4+/VL– and CD4–/VL+ discordant responses to combination ART, respectively. Of those included, 2908 (35.1%) individuals lived in the least materially deprived neighbourhoods compared with 1754 (21.2%) who lived in the most deprived neighbourhoods. The remaining 3612 participants (43.7%) were evenly distributed among the 2 intermediate material deprivation quartiles. The largest proportions of study individuals were male (*n* = 7118, 86.0%) and from the province of BC (*n* = 4372, 52.8%) with a median baseline age of 40 years (Q1 33, Q3 47). The median baseline CD4 count was 250 cells/mm³ (Q1 140, Q3 390) or 0.25 (Q1 0.14, Q3 0.39) cells × 10⁹/L; the median viral load was 4.9 log₁₀ copies/mL (Q1 4.3, Q3 5.0).

From the 13 057 CANOC participants, we excluded 4783 people living with HIV from the analysis, including 873 without at least 6 months of follow-up, 2788 with incomplete geographic information, 811 with insufficient viral load and CD4 data to determine response and 311 with unknown neighbourhood-level material deprivation or unknown sex. Compared with those included, individuals lacking sufficient CD4 and viral load data were less likely to live in the least deprived neighbourhoods (35.2% v. 23.2%) and were more often females (14.0% v. 29.8%) from Saskatchewan (3.7% v. 15.4%) or BC (52.8% v. 57.7%) who reported ever injecting drugs (20.5% v. 37.0%). Individuals with missing postal code information were more often females (22.4%) from Ontario (16.8% v. 71.0%) with a lower CD4 count at baseline (250 v. 231 cells/mm³ or 0.25 v. 0.23 cells × 10⁹/L) in comparison with the analytic sample.

Although BC had the lowest proportion of individuals excluded for missing data (9.8%), the largest proportion of individuals excluded for missing data in the outcome or exposure variables were from Ontario (*n* = 2130, 54.5%). Among those from Ontario, excluded individuals were more likely to be female (8.5% v. 22.2%) with a lower baseline CD4 cell count (278 v. 230 cells/mm³ or 0.28 v. 0.23 cells × 10⁹/L) who reported ever injecting drugs (5.3% v. 13.0%).

Neighbourhood-level material deprivation and immunologic and virologic response

In the univariable multinomial logistic regression model, participants residing in neighbourhoods of the second least materially deprived quartile had increased odds of a CD4+/VL– discordant response (odds ratio [OR] 1.21, 95% confidence interval [CI] 1.05–1.41) compared with the least deprived quartile. Living in the third neighbourhood-level material deprivation quartile was associated with increased odds of a concordant negative (OR 1.44, 95% CI 1.13–1.83) and CD4+/VL– discordant response (OR 1.19, 95% CI 1.02–1.38). Individuals living in the most materially deprived neighbourhoods were more likely to exhibit a concordant negative (OR 2.33, 95% CI 1.86–2.91) or discordant response (CD4+/VL– OR 1.32, 95% CI 1.13–1.54; CD4–/VL+ OR 1.45 95% CI 1.19–1.76) to combination ART (Table 2).

After adjustment for sex, province of enrolment, whether individuals had ever injected drugs, era of entry into cohort and age at baseline, living in the most materially deprived neighbourhoods was significantly associated with increased odds of a concordant negative response (adjusted OR 1.45, 95% CI 1.13–1.86) and CD4–/VL+ discordant response (adjusted OR 1.31, 95% CI 1.06–1.62). This indicates that the odds of having a concordant negative response to combination ART in the first 6 months is 45% higher for individuals in the most deprived category than those in the least deprived category when all confounders are fixed. Similarly, the odds of having a CD4–/VL+ discordant response for individuals in the most deprived neighbourhoods is 31% higher than those in the least deprived group, adjusting for the aforementioned confounders.

As an example, a 40-year-old male entering the cohort from BC in 2004–2007, who reports having ever injected drugs and who lives in the most materially deprived neighbourhood, would have a 51.2% predicted probability of having a concordant positive response, compared with a 12.8% chance of having a concordant negative response. In comparison, if the same individual lived in the least materially deprived neighbourhood, the predicted probability of a concordant positive and concordant negative response would be 56.5% and 9.7% after adjustment, respectively. No other neighbourhood-level material deprivation quartile was significantly associated with increased odds of a particular immunologic or virologic response category.

The additional analysis using a dichotomized material deprivation index included 10 176 (77.9%) individuals from CANOC. Individuals were excluded for follow-up time of less than 6 months (*n* = 585), insufficient viral load or CD4 cell count (*n* = 1450), and insufficient geographic

Table 1: Sociodemographic and clinical characteristics of people living with HIV, stratified by neighbourhood-level material deprivation quartile at initiation of combination antiretroviral therapy

Characteristic	No. (%) of participants*					p value
	Total n = 8274	Q1 n = 2908	Q2 n = 1818	Q3 n = 1794	Q4 n = 1754	
Response category						< 0.001
Concordant positive (CD4+/VL+)	5144 (62.2)	1925 (66.2)	1125 (61.9)	1106 (61.7)	988 (56.3)	
Concordant negative (CD-/VL-)	595 (7.2)	160 (5.5)	112 (6.2)	132 (7.4)	191 (10.9)	
Discordant (CD4+/VL-)	1670 (20.2)	544 (18.7)	386 (21.2)	372 (20.7)	368 (21.0)	
Discordant (CD4-/VL+)	865 (10.5)	279 (9.6)	195 (10.7)	184 (10.3)	207 (11.8)	
Sex						< 0.001
Male	7118 (86.0)	2716 (93.4)	1564 (86.0)	1488 (82.9)	1350 (77.0)	
Female	1156 (14.0)	192 (6.6)	254 (14.0)	306 (17.1)	404 (23.0)	
Province						< 0.001
British Columbia	4372 (52.8)	1800 (61.9)	1068 (58.8)	749 (41.8)	755 (43.0)	
Saskatchewan	307 (3.7)	36 (1.2)	44 (2.4)	72 (4.0)	155 (8.8)	
Ontario	1389 (16.8)	650 (22.4)	306 (16.8)	251 (14.0)	182 (10.4)	
Quebec	2206 (26.7)	422 (14.5)	400 (22.0)	722 (40.3)	662 (37.7)	
Ever injected drugs						< 0.001
No	4754 (57.5)	1680 (57.8)	1038 (57.1)	1113 (62.0)	923 (52.6)	
Yes	1696 (20.5)	371 (12.8)	371 (20.4)	353 (19.7)	601 (34.3)	
Unknown	1824 (22.0)	857 (29.5)	409 (22.5)	328 (18.3)	230 (13.1)	
AIDS-defining illness						0.14
None	6836 (82.6)	2438 (83.8)	1489 (81.9)	1471 (82)	1438 (82.0)	
Before or at baseline	916 (11.1)	311 (10.7)	218 (12.0)	202 (11.3)	185 (10.6)	
After baseline	444 (5.4)	139 (4.8)	89 (4.9)	105 (5.9)	111 (6.3)	
Unknown date	78 (0.9)	20 (0.7)	22 (1.2)	16 (0.90)	20 (1.1)	
Year of entry into cohort						0.82
2000–2003	1352 (16.3)	466 (16.0)	287 (15.8)	298 (16.6)	301 (17.2)	
2004–2007	1854 (22.4)	670 (23.0)	408 (22.4)	401 (22.4)	375 (21.4)	
2008–2011	2765 (33.5)	978 (33.6)	608 (33.4)	578 (32.2)	601 (34.3)	
2012–2016	2303 (27.8)	794 (27.3)	515 (28.3)	517 (28.8)	477 (27.2)	
Combination ART regimen, classified by third agent						0.004
NNRTI	3240 (39.2)	1192 (41.0)	673 (37.0)	659 (36.7)	716 (40.8)	
PI	3701 (44.7)	1269 (43.6)	854 (47.0)	813 (45.3)	765 (43.6)	
IIN	993 (12.0)	317 (10.9)	231 (12.7)	244 (13.6)	201 (11.5)	
Other	340 (4.1)	130 (4.5)	60 (3.3)	78 (4.4)	72 (4.1)	
Baseline age, yr, median (Q1, Q3)	40 (33, 47)	40 (33, 47)	41 (33, 48)	40 (32, 47)	40 (33, 47)	0.059
Baseline CD4, cells/mm ³ , median (Q1, Q3)†	250 (140, 390)	260 (160, 410)	250 (140, 380)	250 (148, 380)	240 (130, 363)	< 0.001
Baseline viral load, log ₁₀ copies/mL, median (Q1, Q3)	4.9 (4.3, 5.0)	4.9 (4.4, 5.0)	4.9 (4.3, 5.0)	4.83 (4.3, 5.0)	4.82 (4.3, 5.0)	0.008
Follow-up time, mo, median (Q1, Q3)	76 (40, 115)	78 (41, 118)	74 (38, 114)	76 (40, 116)	73 (39, 111)	0.056

Note: ART = antiretroviral therapy, CD4+ = CD4 count increase by ≥ 50 cells/mm³ (0.05 cells × 10⁹/L), IIN = integrase inhibitor, NNRTI = non-nucleoside reverse-transcriptase inhibitor, PI = protease inhibitor, Q = quartile, VL+ = viral load decrease to ≤ 50 copies/mL.
 *Unless indicated otherwise.
 †Baseline median (Q1, Q3) CD4 counts (in cells × 10⁹/L) are as follows: total sample 0.25 (0.14, 0.39); Q1 group 0.26 (0.16, 0.41); Q2 group 0.25 (0.14, 0.38); Q3 group: 0.25 (0.15, 0.38), Q4 group: 0.24 (0.13, 0.36).

Table 2: Univariable and multivariable multinomial logistic regression of neighbourhood-level material deprivation quartile and immunologic and virologic response category (n = 8274)*

Characteristic	Concordant negative (CD4-/VL-)		Discordant (CD4+/VL-)		Discordant (CD4-/VL+)	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Neighbourhood-level material deprivation quartile						
1 (least deprived) [ref]	1.00	1.00	1.00	1.00	1.00	1.00
2	1.20 (0.93–1.54)	1.03 (0.80–1.34)	1.21 (1.05–1.41)	1.16 (0.99–1.35)	1.20 (0.98–1.46)	1.16 (0.95–1.42)
3	1.44 (1.13–1.83)	1.23 (0.95–1.59)	1.19 (1.02–1.38)	1.14 (0.97–1.33)	1.15 (0.94–1.40)	1.09 (0.89–1.35)
4 (most deprived)	2.33 (1.86–2.91)	1.45 (1.13–1.86)	1.32 (1.13–1.54)	1.14 (0.96–1.34)	1.45 (1.19–1.76)	1.31 (1.06–1.62)
Sex						
Male [ref]	1.00	1.00	1.00	1.00	1.00	1.00
Female	2.49 (2.03–3.05)	1.44 (1.15–1.80)	1.32 (1.13–1.55)	1.11 (0.94–1.31)	1.29 (1.05–1.59)	1.15 (0.93–1.42)
Province						
British Columbia [ref]	1.00	1.00	1.00	1.00	1.00	1.00
Saskatchewan	5.94 (4.38–8.05)	4.80 (3.40–6.79)	1.85 (1.37–2.52)	2.11 (1.53–2.92)	2.31 (1.59–3.37)	1.79 (1.20–2.65)
Ontario	0.47 (0.35–0.62)	0.74 (0.55–1.01)	0.69 (0.58–0.81)	0.79 (0.66–0.93)	1.13 (0.93–1.38)	1.28 (1.04–1.56)
Quebec	0.57 (0.45–0.71)	0.80 (0.62–1.04)	0.85 (0.75–0.97)	0.94 (0.81–1.10)	1.06 (0.90–1.26)	1.15 (0.94–1.41)
Year of entry into cohort						
2000–2003 [ref]	1.00	1.00	1.00	1.00	1.00	1.00
2004–2007	0.49 (0.38–0.63)	0.50 (0.38–0.65)	0.86 (0.72–1.02)	0.87 (0.73–1.03)	0.72 (0.56–0.92)	0.71 (0.55–0.92)
2008–2011	0.46 (0.37–0.59)	0.47 (0.37–0.60)	0.72 (0.61–0.85)	0.74 (0.63–0.87)	0.93 (0.74–1.17)	0.92 (0.73–1.15)
2012–2016	0.56 (0.44–0.71)	0.50 (0.38–0.64)	0.53 (0.45–0.63)	0.53 (0.44–0.63)	1.17 (0.94–1.47)	1.16 (0.92–1.46)
Ever injected drugs						
No [ref]	1.00	1.00	1.00	1.00	1.00	1.00
Yes	4.45 (3.67–5.40)	2.97 (2.36–3.72)	1.77 (1.54–2.04)	1.46 (1.25–1.71)	1.36 (1.13–1.65)	1.41 (1.14–1.74)
Unknown	1.25 (0.98–1.59)	1.24 (0.96–1.61)	1.04 (0.90–1.20)	1.02 (0.87–1.18)	1.08 (0.91–1.29)	1.19 (0.98–1.44)
Baseline age (per 10-yr increase)	0.93 (0.86–1.01)	0.98 (0.89–1.07)	1.05 (0.99–1.10)	1.04 (0.98–1.10)	0.97 (0.91–1.04)	0.99 (0.93–1.07)

Note: CD4+, an increase of ≥ 50 cells/mm³ (0.05 cells $\times 10^9$ /L) within 6 months of combination antiretroviral therapy initiation, CI = confidence interval, OR = odds ratio, VL+, viral suppression ≤ 50 copies/mL within 6 months of combination antiretroviral therapy initiation.
 *The concordant positive (CD4+/VL+) group was used as the reference category. Statistical significance ($p < 0.05$) is indicated by a 95% CI that excludes the null value of 1.

information ($n = 846$). Distribution of concordant positive ($n = 6316$, 62.1%), concordant negative ($n = 719$, 7.1%), and CD4+/VL- ($n = 2059$, 20.2%) and CD4-/VL+ ($n = 1082$, 10.6%) discordant responses were consistent with the primary analysis. There were also no significant differences with respect to baseline characteristics. Consistent with the primary analysis, living in a materially deprived neighbourhood was significantly associated with increased odds of concordant negative response in the multivariable model (adjusted OR 1.34, 95% CI 1.13–1.59). There were no other statistically significant associations.

Interpretation

Among people living with HIV in Canada who initiated combination ART between 2000 and 2016, those living in the most materially deprived neighbourhoods were least likely to achieve viral suppression or an increase in CD4 cells within 6 months of combination ART initiation. The association between a concordant negative response and CD4-/VL+ discordant response, and residence in the most materially deprived neighbourhoods, was robust and persisted with adjustment for individual-level factors such as

sex, province of enrolment, ever injecting drugs, era of entry into cohort and age at baseline.

Because concordant negative and discordant responses have been associated with increased risk of death, this research provides further insights into the previously reported association between neighbourhood-level education and income, and increased risk of death.^{2,29,30} Lower income and education rates at the neighbourhood level have been associated with higher mean community viral load³¹ and there is evidence of associations between higher neighbourhood socioeconomic status and viral suppression.^{14,32,33} Furthermore, individuals living in a neighbourhood with higher rates of deprivation may be more likely to experience CD4 counts < 200 cells/mm³ (0.20 cells × 10⁹/L).³⁴

Limitations

The study lacked individual-level data with regard to indicators of socioeconomic status (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.

This study population consisted mainly of male (86.0%) residents of BC (52.8%) who reported no previous history of injecting drugs (57.5%). Although a systematic review and meta-analysis has found no association between sex and immunologic and virologic response, repeating this analysis with another study population may yield different findings.^{35,36} More recent data that account for both the uptake of integrase inhibitors and other advances in HIV care and the ongoing COVID-19 pandemic may also generate different findings. No information was available on hospital admission rates or other health care use in the study population. In addition, our study relied on information from 2000 to 2016, and thus these findings may not be generalizable to more recent circumstances. It is possible that significant improvements in care for people living with HIV may have been made in the last 5 years, which could change the association between neighbourhood-level material deprivation and response to combination ART.

We excluded a large number of individuals from the present study ($n = 4789$, 37.0%) which could have introduced bias. In general, excluded individuals were more often females with lower baseline CD4 counts who had ever injected drugs. If we had included these individuals in the present analysis, the nature of the association between neighbourhood-level material deprivation and achieving viral suppression or CD4 response may have been altered.

Some provinces had very high amounts of missingness (Ontario, 54.5%), whereas others had very little (BC, 9.8%). This can be at least partially explained by the way postal code data were provided to the BC Centre for Excellence in HIV/AIDS; some clinics in Ontario reported only the first 3 digits of the postal code, which limited our ability to ascertain their neighbourhood-level material deprivation quartile. In contrast, the population-based cohort in BC had much more complete data. It cannot be excluded that differences in how the data are collected may have contributed to regional differences in study findings. We believe that the set of variables present in the CANOC data set was not

sufficient to have accurately predicted the missingness and, as a result, we did not use multiple imputation. Of note, although the additional analysis including 77.9% of CANOC participants supported the association between neighbourhood-level material deprivation and concordant negative response to combination ART, this approach has not been validated.

Given the CANOC study design and available data, it was not possible to adjust for adherence, which is likely related to both socioeconomic status and response to combination ART.^{12,14,34,37} Adjusting for adherence may have reduced the strength of the association between neighbourhood-level material deprivation and concordant negative and discordant response to combination ART. It was also not possible to adjust for comorbid conditions that could be associated with adherence and treatment response.

The generalizability of the results of this study beyond the Canadian context may be limited given the use of a context-specific definition of neighbourhood-level material deprivation. However, conclusions regarding an association between neighbourhood-level socioeconomic status and treatment response are likely generalizable to other settings with universal access to combination ART.

Conclusion

This study provides additional evidence that socioeconomic status may affect treatment response to combination ART among people living with HIV with access to publicly funded health care in Canada. In particular, we identified associations between neighbourhood-level material deprivation and immunologic and virologic response to combination ART in the Canadian context. Future studies with access to traditional, individual-level indicators of socioeconomic status (e.g., income, education, employment) could explore whether the associations reported here are consistent across studies. Further inquiry could also evaluate whether socioeconomic status is associated with longer term (i.e., beyond 6 months) combination ART treatment failure in the Canadian context.

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