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# Tobacco Smoking Not Independently Associated with Immune and Virologic Response Among Individuals of the Canadian HIV Observational Cohort (CANOC)

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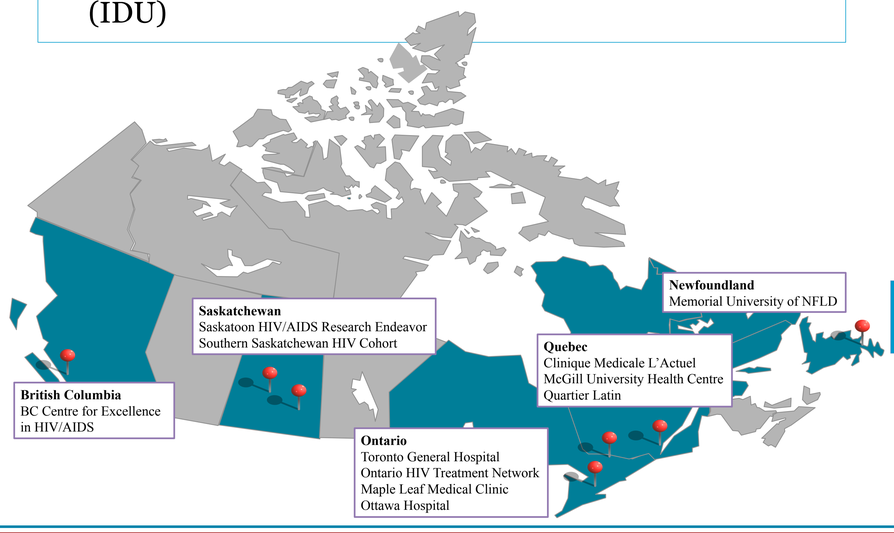
## Background

- In general, combined antiretroviral therapy (cART) reduces viral load (VL) and increases CD4 cell counts (CD4)
- Response to cART can be categorized as complete (CD4+/VL+), incomplete (CD4-/VL-), or discordant (CD4+/VL- or CD4-/VL+)
- There is a higher prevalence of tobacco smoking among people living with HIV (PLWH) compared to the general population[1]
- Some studies have found that smoking tobacco is associated with worse CD4 and VL[2] while others have found no such association[3]

**Hypothesis:** individuals who smoke tobacco will be more likely to achieve incomplete and/or discordant immune/ virologic response

## Methods

- The Canadian HIV Observational Cohort (CANOC) includes individuals initiating cART as ART-naïve between Jan 1, 2000 and Dec 31, 2016
- Any study participants with (1) known sex at birth, (2) follow-up ≥6 months, (3) VL and CD4 data to determine response, (4) tobacco smoking status within 12 months of cART initiation
- Study participants were categorized (CD4+/VL+, CD4-/ VL+, CD4+/VL-, or CD4-/VL-) based on a 6 month time window after cART initiation where
  - ❖ CD4+ corresponds to an increase in 50 cells/ mm3
  - ❖ VL+ corresponds to achieving viral suppression <50 copies/mL
- Univariable and multivariable multinomial regression used to model the relationship between tobacco smoking status and immune and virologic response category
- Pre-specified confounders: sex at birth, baseline age, province, era of entry into cohort, neighborhood level material deprivation, and history of injection drug use (IDU)




## Results

- From 10 972 CANOC participants, 4267 individuals were included in the study (Table 1)
- After adjustment, participants who smoked tobacco were not more likely to achieve incomplete and/or discordant response (Table 2)

**Table 1**. Baseline characteristics (n= 4267).

| | Overall | | Never smoker (N=2405) | | Former smoker (N=546) | | Current smoker (N=1316) | | |
|---|---|---|---|---|---|---|---|---|---|
| | *N* | *col %* | *N* | *col %* | *N* | *col %* | *N* | *col %* | *p-values* |
| **Outcomes** | | | | | | | | | |
| **Immune response** | | | | | | | | | |
| Complete response (CD4+ VL+) | 2692 | 63.1 | 1545 | 64.2 | 365 | 66.9 | 782 | 59.4 | <0.0001 |
| Incomplete response (CD4- VL-) | 237 | 5.6 | 112 | 4.7 | 20 | 3.7 | 105 | 8.0 | |
| Discordant response (CD4+ VL-) | 864 | 20.3 | 489 | 20.3 | 93 | 17.0 | 282 | 21.4 | |
| Discordant response (CD4- VL+) | 474 | 11.1 | 259 | 10.8 | 68 | 12.5 | 147 | 11.2 | |
| **Immune response (VL)** | | | | | | | | | |
| VL- | 1101 | 25.8 | 601 | 25.0 | 113 | 20.7 | 387 | 29.4 | 0.0002 |
| VL+ | 3166 | 74.2 | 1804 | 75.0 | 433 | 79.3 | 929 | 70.6 | |
| **Immune response (CD4)** | | | | | | | | | |
| CD4- | 711 | 16.7 | 371 | 15.4 | 88 | 16.1 | 252 | 19.2 | 0.01 |
| CD4+ | 3556 | 83.3 | 2034 | 84.6 | 458 | 83.9 | 1064 | 80.9 | |
| **Main exposure** | | | | | | | | | |
| **Smoking status at cART initiation** | | | | | | | | | |
| Never | 2405 | 56.4 | | | | | | | |
| Former | 546 | 12.8 | | | | | | | |
| Current | 1316 | 30.8 | | | | | | | |
| **Characteristics** | | | | | | | | | |
| **Sex at birth** | | | | | | | | | |
| Male | 3584 | 84.0 | 1978 | 82.3 | 496 | 90.8 | 1110 | 84.4 | <0.0001 |
| Female | 683 | 16.0 | 427 | 17.8 | 50 | 9.2 | 206 | 15.7 | |
| **Ethnicity** | | | | | | | | | |
| White | 2112 | 49.5 | 1052 | 43.7 | 317 | 58.1 | 743 | 56.5 | <0.0001 |
| African-Caribbean-Black | 533 | 12.5 | 456 | 19.0 | 32 | 5.9 | 45 | 3.4 | |
| Indigenous | 242 | 5.7 | 48 | 2 | 33 | 6.0 | 161 | 12.2 | |
| Asian (East/South) | 263 | 6.2 | 179 | 7.4 | 27 | 5.0 | 57 | 4.3 | |
| Hispanic | 204 | 4.8 | 133 | 5.5 | 20 | 3.7 | 51 | 3.9 | |
| Mixed | 118 | 2.8 | 64 | 2.7 | 17 | 3.1 | 37 | 2.8 | |
| Other | 36 | 0.8 | 23 | 1.0 | 6 | 1 | 7 | 0.5 | |
| Unknown | 759 | 17.8 | 450 | 18.7 | 94 | 17.2 | 215 | 16.3 | |
| **Province** | | | | | | | | | |
| BC | 1597 | 37.4 | 857 | 35.6 | 179 | 32.8 | 561 | 42.6 | <0.0001 |
| SK | 126 | 3.0 | 26 | 1.1 | 15 | 2.8 | 85 | 6.5 | |
| ON | 1409 | 33.0 | 897 | 37.3 | 160 | 29.3 | 352 | 26.8 | |
| QC | 1071 | 25.1 | 595 | 24.7 | 188 | 34.4 | 288 | 21.9 | |
| NL | 64 | 1.5 | 30 | 1.3 | 4 | 0.7 | 30 | 2.3 | |
| **IDU** | | | | | | | | | |
| No | 3374 | 79.1 | 2078 | 86.4 | 458 | 83.9 | 838 | 63.7 | <0.0001 |
| Yes | 656 | 15.4 | 119 | 5.0 | 74 | 13.6 | 463 | 35.2 | |
| Unknown | 237 | 5.6 | 208 | 8.7 | 14 | 2.6 | 15 | 1.1 | |
| **MSM** | | | | | | | | | |
| No | 1394 | 32.7 | 698 | 29.0 | 159 | 29.1 | 537 | 40.8 | <0.0001 |
| Yes | 2641 | 61.9 | 1502 | 62.5 | 374 | 68.5 | 765 | 58.1 | |
| Unknown | 232 | 5.4 | 205 | 8.5 | 13 | 2.4 | 14 | 1.1 | |
| **AIDS defining illness (ADI) at baseline** | | | | | | | | | |
| No ADI ever | 3293 | 77.2 | 1873 | 77.9 | 403 | 73.8 | 1017 | 77.3 | 0.0001 |
| Had ADI before or on baseline | 553 | 13.0 | 275 | 11.4 | 102 | 18.7 | 176 | 13.4 | |
| Had ADI after baseline | 217 | 5.1 | 126 | 5.2 | 19 | 3.5 | 72 | 5.5 | |
| Had ADI with unknown date | 204 | 4.8 | 131 | 5.5 | 22 | 4.0 | 51 | 3.9 | |
| **Era of cART initiation** | | | | | | | | | |
| 2000-2003 | 454 | 10.6 | 343 | 14.3 | 34 | 6.2 | 77 | 5.9 | <0.0001 |
| 2004-2007 | 815 | 19.1 | 528 | 22.0 | 84 | 15.4 | 203 | 15.4 | |
| 2008-2011 | 1514 | 35.5 | 810 | 33.7 | 217 | 39.7 | 487 | 37.0 | |
| 2012-2016 | 1484 | 34.8 | 724 | 30.1 | 211 | 38.6 | 549 | 41.7 | |
| **Neighbourhood level material deprivation** | | | | | | | | | |
| No | 2713 | 63.6 | 1655 | 68.8 | 322 | 59.0 | 736 | 55.9 | <0.0001 |
| Yes | 1275 | 29.9 | 592 | 24.6 | 198 | 36.3 | 485 | 36.9 | |
| Unknown | 279 | 6.5 | 158 | 6.6 | 26 | 4.8 | 95 | 7.2 | |
| | *N* | *median (Q1, Q3)* | *N* | *median (Q1, Q3)* | *N* | *median (Q1, Q3)* | *N* | *median (Q1, Q3)* | |
| **Age at baseline (years)** | 4267 | 40 (32, 47) | 2405 | 39 (32, 47) | 546 | 43 (34, 51) | 1316 | 39 (31, 46) | <0.0001 |
| **CD4 at baseline (cells/ mm3)** | 4267 | 260 (140, 390) | 2405 | 250 (140, 378) | 546 | 253 (110, 390) | 1316 | 280 (150, 420) | 0.0003 |
| **Baseline viral load (log10 copies/ml)** | 4267 | 4.84 (4.33, 5) | 2405 | 4.86 (4.36, 5) | 546 | 4.91 (4.32, 5) | 1316 | 4.78 (4.27, 5) | 0.02 |
| **Follow-up time (months)** | 4267 | 71.6 (37.1, 108.5) | 2405 | 80.0 (44.7, 119.6) | 546 | 63.7 (33.6, 97.9) | 1316 | 59.9 (29.6, 94.5) | <0.0001 |

**Table 2**. Univariable and multivariable multinomial regression modelling immune response using complete response (CD4+ VL+) as reference category (n= 4267).

| | Incomplete response (CD4- VL-) | | | Discordant response (CD4+ VL-) | | | Discordant response (CD4- VL+) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | *Odds Ratio* | *95% CI* | | *Odds Ratio* | *95% CI* | | *Odds Ratio* | *95% CI* | | *p-values* |
| **Unviariable model** | | | | | | | | | | |
| **Smoking status at cART initiation** | | | | | | | | | | |
| Never [ref] | 1.00 | | | 1.00 | | | 1.00 | | | <0.0001 |
| Former | 0.76 | 0.46 | 1.23 | 0.81 | 0.63 | 1.03 | 1.11 | 0.83 | 1.49 | |
| Current | 1.85 | 1.40 | 2.45 | 1.14 | 0.96 | 1.35 | 1.12 | 0.90 | 1.40 | |
| **Multivariable model** | | | | | | | | | | |
| **Smoking status at cART initiation** | | | | | | | | | | |
| Never [ref] | 1.00 | | | 1.00 | | | 1.00 | | | 0.23 |
| Former | 0.68 | 0.41 | 1.13 | 0.78 | 0.60 | 1.01 | 1.06 | 0.78 | 1.42 | |
| Current | 1.17 | 0.84 | 1.64 | 1.00 | 0.83 | 1.21 | 1.05 | 0.82 | 1.33 | |
| **Confounders** | | | | | | | | | | |
| **Sex at birth** | | | | | | | | | | |
| Male [ref] | 1.00 | | | 1.00 | | | 1.00 | | | 0.17 |
| Female | 1.31 | 0.94 | 1.83 | 0.88 | 0.70 | 1.10 | 1.10 | 0.83 | 1.44 | |
| **Province** | | | | | | | | | | |
| BC [ref] | 1.00 | | | 1.00 | | | 1.00 | | | 0.0025 |
| SK | 2.38 | 1.30 | 4.37 | 1.89 | 1.19 | 3.01 | 1.61 | 0.88 | 2.97 | |
| ON | 1.18 | 0.83 | 1.66 | 0.76 | 0.62 | 0.94 | 1.28 | 0.99 | 1.65 | |
| QC | 0.95 | 0.63 | 1.44 | 0.94 | 0.76 | 1.17 | 1.26 | 0.95 | 1.68 | |
| NL | 0.97 | 0.28 | 3.42 | 1.26 | 0.67 | 2.36 | 0.94 | 0.41 | 2.14 | |
| **IDU** | | | | | | | | | | |
| No [ref] | 1.00 | | | 1.00 | | | 1.00 | | | <0.0001 |
| Yes | 2.98 | 2.08 | 4.27 | 1.39 | 1.10 | 1.77 | 1.06 | 0.76 | 1.46 | |
| Unknown | 0.83 | 0.39 | 1.77 | 1.00 | 0.71 | 1.42 | 0.88 | 0.54 | 1.45 | |
| **Era of cART initiation** | | | | | | | | | | |
| 2000-2003 [ref] | 1.00 | | | 1.00 | | | 1.00 | | | <0.0001 |
| 2004-2007 | 0.87 | 0.52 | 1.45 | 0.96 | 0.73 | 1.28 | 0.72 | 0.48 | 1.08 | |
| 2008-2011 | 0.71 | 0.44 | 1.15 | 0.88 | 0.68 | 1.15 | 0.95 | 0.67 | 1.36 | |
| 2012-2016 | 0.83 | 0.51 | 1.33 | 0.63 | 0.48 | 0.83 | 1.16 | 0.82 | 1.65 | |
| **Neighborhood level material deprivation** | | | | | | | | | | |
| No [ref] | 1.00 | | | 1.00 | | | 1.00 | | | 0.0085 |
| Yes | 1.11 | 0.81 | 1.51 | 1.16 | 0.96 | 1.38 | 1.16 | 0.92 | 1.47 | |
| Unknown | 1.32 | 0.76 | 2.31 | 1.47 | 1.06 | 2.03 | 1.98 | 1.38 | 2.85 | |
| **Age at baseline (10 years)** | 0.98 | 0.86 | 1.12 | 1.00 | 0.93 | 1.08 | 1.01 | 0.92 | 1.11 | 0.98 |

## Discussion

- There was an association between tobacco smoking status and immune and virologic response category in the unadjusted model (p-value <0.0001)
- After adjustment, no statistically significant independent association was detected (p-value 0.23)
- More granular data regarding tobacco smoking history (e.g. duration, pack years) may yield different results

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