Estimation of an individual-level deprivation index in a cohort of HIV-HCV co-infected Canadians and its relationship with health outcomes

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April 30th 2020

A thesis submitted to McGill University in partial fulfillment of the requirements of the degree of Master of Science

Abstract:

Background: HIV-HCV co-infected individuals are often more deprived than the general population. These factors may lead to disengagement from care. However, deprivation is difficult to measure, and often relies on aggregate data which don't capture individual heterogeneity. We developed an individual-level deprivation index for HIV-HCV co-infected persons that encapsulated social, material, and lifestyle factors.

Methods: We estimated an individual-level deprivation index with data from the Canadian Co-infection Cohort, a national prospective cohort study. We used multiple correspondence analyses and exploratory data analyses to select 9 dichotomous variables at baseline visit: income >$1500/month; education >high school; employment; identifying as gay or bisexual; Indigenous status; injection drug use in last 6 months; injection drug use ever; past incarceration, and past psychiatric hospitalization. We fitted an item response theory model with: severity parameters (how likely an item was reported), discriminatory parameters, (how well a variable distinguished index levels), and an individual parameter (the index). We considered two models: a simple one with no provincial variation and a hierarchical model by province. The Widely Applicable Information Criterion was used to compare the models. Finally, we evaluated the association of the index with non-attendance to a second clinic visit (as a measure of disengagement) using logistic regression.

Results: We analyzed 1547 complete cases of 1842 enrolled participants; 457 (30%) failed to attend a second visit. The hierarchical model was found to have the best fit. Values of the index were similarly distributed across the provinces. Overall, past incarceration, education, and unemployment had the greatest discriminatory parameters. However, in each province different components of the index were associated with being deprived reflecting local epidemiology. For example, Saskatchewan had the highest severity parameter for Indigenous status while Quebec the lowest. A one-unit increase in the index was associated with 17% odds (95% credible interval, 2% to 34%) of not attending a second visit.

Conclusion: We estimated an individual-level deprivation index with weights of variables varying by province. The index was associated with disengagement from care. This index and methodology may be useful in studying health and treatment outcomes that are influenced by social disparities in co-infected Canadians.

Résumé:

Contexte:

Les individus co-infectés par le VIH et le VHC sont plus souvent dans une situation de vie précaire que la population générale. Ces facteurs peuvent mener ces idividus à être privés de soins. Cependant, la privation est difficile à mesurer. De telle mesures sont souvent basées sur des données agrégées qui ne saisissent pas l'hétérogénéité des individus. Nous avons développé un indice de privation au niveau individuel pour les personnes co-infectées par le VIH et le VHC qui englobe les facteurs sociaux, matériels et de style de vie.

Méthodes:

Nous avons estimé un indice de privation au niveau individuel avec les données de la cohorte canadienne de co-infection, une étude prospective de cohorte nationale. Nous avons utilisé plusieurs analyses de correspondance et analyses de données exploratoires pour sélectionner 9 variables dichotomiques lors de la visite de référence: revenu > 1 500 $ / mois; éducation > école secondaire; emploi; s'identifier comme gai ou bisexuel; Statut autochtone; utilisation de drogues injectables au cours des 6 derniers mois; n'avoir jamais fait usage de drogues injectables; incarcération antérieure et hospitalisation psychiatrique antérieure. Nous avons développé un model théorie de la réponse d'item à un élément avec: des paramètres de gravité (quelle est la probabilité qu'un élément ait été signalé), des paramètres discriminatoires (dans quelle mesure une variable distingue les niveaux d'index) et un paramètre individuel (l'indice). Nous avons considéré deux modèles: un simple sans variation provinciale et un modèle hiérarchique par province. Le critère d'information largement applicable (WAIC) a été utilisé pour comparer les modèles ajustés. Enfin, nous avons évalué l'association de l'indice avec la non-fréquentation à une deuxième visite à la clinique (comme mesure de désengagement) en utilisant la régression logistique.

Résultats:

Nous avons analysé 1547 cas complets de 1842 participants inscrits. 457 (30%) n'ont pas assisté à une deuxième visite. Le modèle hiérarchique s'est révélé le mieux adapté. Les valeurs de l'indice étaient réparties de façon similaire entre les provinces. Dans l'ensemble, les incarcérations, l'éducation et le chômage avaient les paramètres discriminatoires les plus élevés. Cependant, dans chaque province, différentes composantes de l'indice étaient associées à une privation reflétant l'épidémiologie locale. Par exemple, la Saskatchewan avait le paramètre de gravité le plus élevé pour le statut autochtone, tandis que le Québec était le plus faible. Une augmentation d'une unité de l'indice était associée à 17% de chances (intervalle crédible de 95%, 2% à 34%) de ne pas assister à une deuxième visite.

Conclusion:

Nous avons estimé un indice de privation au niveau individuel avec des poids de variables variant par province. L'indice était associé au désengagement des soins. Cet indice et cette méthodologie peuvent être utiles pour étudier les résultats en matière de santé et de traitement qui sont influencés par les disparités sociales chez les Canadiens co-infectés.

Preface

In this thesis, I estimate a novel individual-level deprivation index for HIV-HCV co-infected Canadians across the Canadian co-infection cohort and investigate the relationship between the index and a health outcome. First, in Chapter 1 I give a rationale for the research and outline the main objectives of this thesis. Subsequently, in Chapter 2 I introduce why HIV-HCV co-infected patients are an important population for HCV elimination. I review the literature about the social determinants of health that play a role in HIV-HCV co-infected individuals and detail what is known about the material, social, and lifestyle components surrounding co-infection. Additionally, I talk about the notion of deprivation, and the role that it plays in individual health. I then explore the literature on how deprivation and related concepts are measured. I then discuss the relationship between these measures and the techniques in this thesis. In Chapter 3 I describe the methodologies used in this thesis including the study location, population, variable selection, and statistical analyses. The results are presented in Chapter 4 in the form of a manuscript discussing the building and estimation of the index and how it varies in four Canadian provinces. Finally, the results are discussed and contextualized in Chapter 5, with concluding remarks in Chapter 6. References are provided in Chapter 7.

This thesis has been prepared according to the guidelines for a "Manuscript-Based Thesis". The results are given in one manuscript:

Palayew Adam, Alexandra M. Schmidt, Saeed Sahar, Curtis L Cooper, Alexandre Wong, Valérie Martel-Laferrière, Sharon Walmsley, Joseph Cox, and Marina B. Klein – Estimating an individual-level deprivation index for HIV-HCV co-infected persons in Canada.

Contribution of Authors

All non-manuscript chapters of this thesis were written by AP and critically reviewed and revised by MBK and AMS. The manuscript (Chapter 4.2) was written by AP and critically reviewed and revised by all aforementioned individuals and the co-investigators of the CCC. MBK, SS, AMS, and AP contributed to the study conception and design. Data collection, cohort recruitment, was done by MBK, CLC, AW, VML, SW, and JC. The analyses were performed by AP with support from MBK and AMS. AP, AMS, SS, and MBK interpreted the data. The first draft of the manuscript was written by AP, and was revised by all authors who then approved the final submitted manuscript.

Acknowledgements

This work was supported by Fonds de recherche du Québec –Santé; Réseau sida/maladies infectieuses, the Canadian Institute for Health Research (CIHR; grant number FDN-143270); and the CIHR Canadian HIV Trials Network (grant number CTN222). AP is supported by a MSc award from Fonds de recherche du Québec and the Canadian Network for Hepatitis C. MBK is supported by a Tier I Canada Research Chair. In terms of human resources first, I would like to thank the Canadian co-infection cohort (CCC) team. Without them this thesis would not be possible and to Costa Pextos, Leo Wong, Jessica Lumia, Hansi Persi, Roy Nioletscu, Shouao Wang, and Chantal Burelle. Additionally, I would like to acknowledge the participants of the Canadian Co-Infection Cohort (CTN222), the Co-Investigators, Lisa Barrett, Jeff Cohen, Brian Conway, Curtis Cooper, Pierre Côté, Joseph Cox, M. John Gill, Shariq Haider, David Haase, Mark Hull, Valérie Martel-Laferrière, Julio Montaner, Erica E. M. Moodie, Neora Pick, Danielle Rouleau, Aida Sadr, Steve Sanche, Roger Sandre, Mark Tyndall, Marie-Louise Vachon, Sharon Walmsley, Alexander Wong, and the study coordinators/nurses. I would also like to thank my cohort classmates and fellow McGill students who have been a tremendous source of support throughout my thesis. Penultimately, I am in debt to my two supervisors Marina Klein and Alexandra M. Schmidt who have invested countless hours into my development. They have both been tremendous positive forces in my growth as a scientist and helped foster my love for epidemiology. These two top caliber researchers offered me great opportunities to learn and have changed me for the better into the person I am today. Finally, I would like to thank my mother who has been my number one supporter from day 1. She helped me get my first research job when I was 17 and has helped me throughout my scientific journey ever since. I would not be where I am today without her unconditional loving support and her keen insight, and wisdom. Thank you to everyone who made this possible, but especially to the strong women who have made this thesis happen and have supported me through this ride.

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List of Abbreviations/Acronyms

AIDS: Acquired immunodeficiency syndrome

cART: combination antiretroviral therapy

CCC: Canadian Co-infection Cohort

DAAs: Direct acting antivirals

GBMSM: Gay and bisexual men who have sex with men

GHB: Gamma-hydroxybutyrate

HCV: Hepatitis C virus

HIV: Human immunodeficiency virus

HMC: Hamiltonian Monte Carlo

ICC: Item Characteristic Curve

IRT: Item response theory

MCA: Multiple correspondence analysis

MSM: Men who have sex with men

PREP: Pre-exposure prophylaxis

PWID: People who inject drugs

RNA: Ribonucleic acid

SDoH: Social determinants of health

SVR: Sustained virological response

TasP: Treatment as prevention

WAIC: Widely applicable information criteria

WHO: World Health Organization

1. Introduction

1.1 Rationale

Since 2013, HCV treatment has been revolutionized by direct acting antivirals (DAAs), simple and safe all oral therapies which result in over 90% cure rates (1). The availability of DAAs prompted the World Health Organization (WHO) in 2016 to call for the elimination of the hepatitis C virus (HCV) as a public health threat by the year 2030 (2). Elimination of HCV, in this context, is defined as an 80% reduction in the incidence of HCV and a 65% reduction in HCV related mortality relative to 2015 levels by 2030 (3). In the WHO strategy for the elimination of HCV, individuals who are co-infected with human immunodeficiency virus (HIV) are signaled as a priority group due their increased risk of mortality relative to HCV mono-infected individuals (4). However, challenges faced in addressing HCV elimination in this population include that HIV-HCV co-infected individuals are often marginalized, deprived relative to the general population, and tend to have reduced access to health care (5). However, unlike other HCV mono-infected marginalized populations, HIV co-infected populations tend to be more engaged in care due to their HIV care. This provides hope that elimination of HCV in the HIV-HCV co-infected population is possible. That said, co-infected individuals are a heterogeneous population in terms of deprivation -- composed of individuals of lower socioeconomic status who have high rates of injection drug use and of incarceration as well as men who have sex with men (MSM) who tend to be of a higher socioeconomic status, engaging in riskier sexual behaviors, and have high rates of recreational polydrug use (1, 6). Obviously, significant heterogeneity exists within these two broad categories and there are individuals who are co-infected who fit into neither of these groups (7). Measuring this marginalization/deprivation accurately is hard, deprivation is important to quantify if we are to adequately evaluate interventions in this population as deprivation can be a confounder of several health outcomes.

1.2 Objectives

This thesis has two main aims. The first aim of this thesis is to describe the estimation of an individual-level model-based HIV-HCV deprivation index that aggregates traditional socio-economic measures as well as behavior and lifestyle variables that are relevant to co-infected individuals. We will subsequently examine how this index varies in four Canadian provinces: Quebec, Ontario, British Columbia, and Saskatchewan. The second objective of this thesis, is to estimate the relationship of the individual-deprivation index against non-attendance of a second follow-up visit, a proxy for disengagement from care.

2. Literature Review

2.1 HIV mono-infection

2.1.1 Definition and symptoms of HIV mono-infection

HIV is a human retrovirus, and primarily infects CD4+ T cells of the host immune system. HIV is transmitted through bodily fluids, such as blood, semen, vaginal fluids, or breast milk (8). As HIV infection progresses CD4+ cell counts begin to decrease due to the HIV infection (8). Eventually in the context of uncontrolled HIV infection the CD4+ cell count drops under a critical threshold leading to the loss of cell-mediated immunity (9). As time progresses an uncontrolled HIV infection leads to acquired immunodeficiency syndrome (AIDS), the advanced stage of an uncontrolled HIV infection (10). In Canada, the medical community defines AIDS as the presence of an AIDS-defining condition (e.g., opportunistic infection or AIDS defining malignancy such as Kaposi's sarcoma) and a positive HIV serology (11).

2.1.2 Prevalence and incidence of HIV mono-infection

The WHO estimated that in 2016 there were 36.7 million people globally living with HIV and 1 million deaths due to HIV-related illnesses (12). In Canada, approximately 63,110 individuals are living with HIV (13). Since the advent of combination antiretroviral therapies (cART) there has been a substantial decrease in HIV-related morbidity and mortality (14). cART is a combination of medications that are taken each day sometimes multiple times a day for the remainder of a person's life to maintain HIV viral suppression (15). Due to the success of cART, HIV has become in many aspects a chronic and manageable condition. People living with HIV are living longer and healthier lives due to cART (16). This has given rise to a host of new comorbidities and co-infections in people living with HIV (17). As people living with HIV age, they have an excess of outcomes relative to the general population like cardiovascular disease and depressive symptoms (18). Additionally, as people are living longer with HIV the long-term impacts of co-infections such as HCV increasingly contribute to adverse health outcomes and death. Liver disease now surpasses mortality from AIDS defining illnesses (19).

In addition, to the impact of cART on reducing HIV/AIDS related morbidity and mortality it has had an important role in reducing the transmission of HIV (20) lowering HIV incidence – often referred to as treatment as prevention (TasP) (21). TasP is based off the idea that individuals that are on cART and virally suppressed cannot pass on the HIV virus even if they do not use protective measures such as condoms (22). This serves to lower the number of new HIV infections annually and in theory reduces the number of infectious individuals at a population level (20). This fact has been highlighted by civil society campaigns advocating "undetectable equals untransmittable" better known as U=U (23). However, this strategy only works if treatment is substantially scaled up (24). Additionally, there is a new biomedical approach to HIV prevention-- pre-exposure prophylaxis (PREP) using antiretrovirals that can be taken once daily by uninfected people at risk which greatly reduces their chance of acquiring HIV (25). The more people that are on PREP, the fewer susceptible individuals there are in the population reducing the number of new infections and onward spread of HIV. This is particularly helpful in reducing the incidence of HIV in major cities among high risk population like MSM (26).

However, not everyone has access to medications or can adhere to them long term. New infections due to a lack of access or adherence to cART continue to occur resulting in continued deaths due to AIDS related illnesses (27). These deaths are considered to be largely preventable as the medication required to save these lives exists and is readily available to other populations. Socioeconomic status plays an important role in the long-term adherence to these medications and in accessing them in general (28). People of lower socioeconomic status and who are more deprived are less likely to attend medical visits and therefore are less likely to access cART in the first place or adhere to it in the long-term (29).

2.2 HCV mono-infection

2.2.1 Definitions and symptoms of HCV mono-infection

HCV is a positive sense single-stranded ribonucleic acid (RNA) virus whose mature virion is 40-100 nanometers in size (30). HCV is the causal infectious agent of hepatitis C, which is an infectious disease of the liver (31). The initial acute phase of HCV infection tends to be asymptomatic (32). Approximately, 15-25% of individuals spontaneously clear HCV within six months of infection, with the remaining 75-85% of individuals go on to develop a chronic HCV infection (33). Chronic HCV infection is defined as having a detectable HCV RNA (34). Over time, in chronic HCV mono-infection, patients develop complications and advanced liver disease such as cirrhosis, liver failure, encephalopathy, and hepatocellular carcinoma (liver cancer) (32).

2.2.2 Prevalence and incidence of HCV mono-infection

In 2015, the most up-to-date study estimated that there were 71 million people globally who were living with chronic HCV (35). Additionally, there are approximately 399,000 individuals who die each year from HCV-related causes with the projected number of deaths to increase in the following decade if nothing is done, primarily due to complications from cirrhosis and hepatocellular carcinoma (36).

It was estimated in 2011 that there were approximately 332,000 individuals in Canada who were seropositive for HCV and roughly 270,000 individuals who were chronically infected with HCV (37). In this study, a large proportion of these individuals (~43%) had formerly injected drugs or were actively using. In the same study, foreign born Canadians accounted for 35% of all cases. However, there are not good estimates of viremia prevalence in Canada for HCV. Moreover, there is not strong national epidemiological data in general for HCV in Canada, which is a major barrier to HCV elimination.

2.2.3 Risk factors for HCV

HCV is transmitted via exposure to blood, and can be transmitted sexually or vertically, but at a much lower rate (33). As a consequence, the major routes of transmission for HCV infection are in the context of people injecting drugs and nosocomial infections such as through the receipt of contaminated blood products or re-use of needles during vaccination campaigns (38). In Canada prior to 1992 when the routine screening of blood products for HCV was introduced, it was common for HCV to be transmitted via blood transfusion (39). The HCV epidemic in Canada has disproportionately impacted people who inject drugs, Indigenous communities and HIV positive men who have sex with men (40). Currently, the majority of new cases of HCV in Canada are primarily due to active injection drug use where needles and equipment (such as cookers) are being shared (41).

2.2.4 Treatment for HCV mono-infection

Historically, the treatment for HCV relied on toxic interferon based regimens with low tolerability and cure rates that varied by genotype. In 2011, the first DAA was approved by the US Federal Drug Agency making interferon-free treatments a reality. However, when these treatments first came to market they were prohibitively expensive in high income countries like Canada and required provinces to ration treatment (42, 43). Additionally, early treatment had to be used in combination with interferon, which was poorly tolerated reducing uptake further (44). Since 2013 there are new, more effective, and tolerable all oral treatments for HCV, which achieve sustained virologic response (SVR) rates exceeding 90-95% within as little as 8 to 12 weeks of treatment (34, 45). SVR has been shown to be linked to reduced HCV related health outcomes like hepatocellular carcinoma (46). Both of these treatments are far superior to interferon and differ minimally between each other in their SVR rates, duration of treatment, and how many times a day tablets need to be taken (47-49).

It is important to consider that re-infection with HCV is possible, particularly among individuals who are actively using drugs and who are sharing cookers and injecting equipment (50, 51). In this instance, the person who is re-infected with HCV should be treated with DAAs even if they are actively using drugs as there is strong evidence to support that active drug users have similar SVR rates to non-drug users (52).

2.3 HIV-HCV co-infection

2.3.1 Definition, symptoms, and clinical management of HIV-HCV co-infection

HIV is known to accelerate and modify the natural history of HCV infection (53). Instead of the 15-25% of individuals spontaneously clearing HCV in mono-infected populations, co-infected individuals with HIV have a spontaneous clearance rate of approximately 10% meaning that 90% of HIV-HCV co-infected individuals will progress to developing a chronic HCV infection (53). In addition to lower rates of spontaneous clearance, HIV-HCV co-infected individuals experience HCV associated health outcomes at an accelerated rate relative to HCV mono-infected individuals even when their HIV is fully suppressed on cART (54). Currently, in the majority of high income settings, a leading cause of death among HIV infected individuals is end-stage liver disease due in part to the reduction in mortality of HIV-associated outcomes due to cART (55). To manage HIV-HCV co-infection, patients should be on cART so viral suppression can be achieved, and they should be prescribed DAAs as soon as possible in order to achieve SVR (56).

2.3.2 Prevalence and incidence of HIV-HCV co-infection

HIV and HCV share common routes of transmission (55). While sexual transmission is considered the primary mode of transmission for HIV (8), the sharing of needles during injection drug use is the main mode of transmission for HIV-HCV co-infection (1). Unlike HIV, HCV is rarely transmitted sexually except in among MSM who engage in high risk sexual practices or use drugs during sex also known as Chem Sex (57). Globally, an estimated 2.3 million HIV-positive individuals are co-infected with HCV (58). It is estimated that more than half of those individuals have injected drugs at some point in their lifetime (59). In Canada, there are approximately 75,500 people living with HIV, and 17,000 individuals who are co-infected (59).

The risk factors that are associated with HCV are also the same for the co-infected population in Canada with a disproportionate amount of the infection being in MSM, indigenous communities, and people who inject drugs. Among MSM, the highest risk of sexually acquired HCV infection and re-infection appears to be among HIV positive individuals (60).

2.3.3 Characteristics of co-infected populations

HIV, HCV, and HIV-HCV co-infection individuals are a diverse group with overlap between the HIV and HCV population (58). Given the clinical effects of HIV and HCV and the prevalence of injection drug use among co-infected populations relative to mono-infected populations, studies have compared the characteristics of HIV or HCV mono-infected to HIV-HCV co-infected populations to estimate difference in the vulnerability profiles of those that are co-infected relative to those that are mono-infected (7, 40, 56, 61). Those that are co-infected with HIV and HCV have been found to consistently be of lower social status on average than those that are mono-infected with HIV or HCV. The studies that support this assertion are descriptive observational studies and have been replicated in several places like rural Puerto Rico, Tibet, and 10 European cities with mental health disparities between HIV-HCV co-infected and HIV mono-infected or HCV mono-infected being explained by a baseline difference in socioeconomic factors rather than due to the presence of the other infection (62, 63).

Studies of this type in Canada have found similar results, individuals who were co-infected reported more depressive symptoms, and lower quality of life relative to individuals who were HIV mono-infected (64). Another study with similar findings compared the profiles of social determinants of health for HCV mono-infected and HIV-HCV co-infected individuals. The co-infected participants of this study reported more depressive symptoms; however, they also had less social support, and lower self-esteem than the mono-infected participants (65). However, in all these studies authors have reasoned that the association of HIV-HCV co-infection with the variables of interest were more parsimoniously explained by differences in sociodemographic and behavioral characteristics, specifically poverty and injection drug use, rather than any biological effect of the HCV or HIV infection.

2.3.4 The WHO HCV elimination targets and barriers to reaching them

The WHO in 2016 called for the elimination of HCV as a public health threat by the year 2030 in the global health sector strategy on HCV (2). Elimination of HCV was defined as an 80% reduction in the incidence of HCV and a 65% reduction in HCV related mortality relative to 2015 levels by 2030 (4). In the WHO strategy for the elimination of HCV, individuals who are co-infected with human immunodeficiency virus (HIV) are signaled as a priority group due their increased risk of mortality relative to HCV mono-infected individuals (2). However, one of the issues faced in addressing this pressing matter is that HIV-HCV co-infected individuals are often marginalized, deprived relative to the general population and tend to have reduced access to health care relative to the general population making it harder to reach the WHO goals (5). However, unlike other HCV mono-infected marginalized populations HIV co-infected populations tend to be more engaged in care due to their HIV care. This provides hope that elimination of HCV in the HIV-HCV co-infected population is possible.

One of the major barriers to reaching the WHO goals is retaining precarious individuals in care (66). It is documented that co-infected individuals of lower socioeconomic status and who are more deprived are less likely to stay in care and miss follow up visits and consequently are less likely to access HCV treatment (67). Therefore, it would be useful to identify these individuals at their first visit to potentially engage them in interventions that would improve their retention in care. There are many ways to assess retention in care such as loss to follow up or the proportion of missed visits. In this thesis, we consider non-attendance of a second study visit as a proxy for disengagement from care. It is acknowledged that an individual who misses a second visit may later return and attend a third or fourth visit. Thus, while disengaged in the short term, these individuals may not be permanently lost to follow up. Short term disengagement from care, however, has been associated with non-adherence to HIV treatment, virologic rebound and poor health outcomes and thus is an outcome of interest in itself (68-72). Using such an outcome also offers the advantage of having a fixed amount of time between the first and second visit, allowing us to use logistic regression instead of time to event analysis thereby simplifying our analyses.

2.4 Deprivation and health outcomes

2.4.1 Definition of deprivation

The term "deprivation" in health emerged as a concept in Britain in the 1980s from a long tradition of analyzing social inequalities in relation to health outcomes (73). Peter Townsend defined deprivation as "a state of observable and demonstrable disadvantage relative to the local community or the wider society or nation to which the individual, family or group belongs." Townsend further distinguishes two types of deprivation: material and social (73). The first involves deprivation of the goods and conveniences that are part of modern life like a car, a mobile phone, or access to a local public library. Social deprivation, refers to relationships among individuals in the family, the workplace, and the community. According to Townsend, material deprivation should be distinguished from "poverty", which is more related to lack of the resources, especially financial resources, needed to acquire modern goods and commodities. On the other hand, social deprivation is more closely related to the concept of "social capital", reflecting certain characteristics of social organization, such as isolation or cohesion, individualism or cooperation, mutual assistance, and trust (73).

Deprivation may occur at various levels, for example, with regards to food, clothing, housing, education, or work (74). In fact, a person is considered deprived to the extent that he or she falls below the level attained by the majority of the population or below what is considered socially acceptable in relation to a reference group (75). An important nuance is that deprivation is defined relatively. This means that a group of individuals could be considered deprived relative to the society to which they belong to, but that within the group relative to itself there will be individuals who are more privileged than others (73). This is important when considering HIV-HCV co-infected individuals who by virtue of their infection may be considered deprived relative to the general population, but will also exhibit a great degree of diversity relative to one another. Lastly, studies of deprivation sometimes use other kinds of indices or numerous individual variables, including income, education level, marital status, and residential mobility as well as those already mentioned (76, 77). Variables that distinguish better between co-infected individuals such as incarceration status, and injection drug use history have not been used in previous studies, but could theoretically be used when estimating deprivation indices. The advantage of using these variables is that these variables are closely linked to socioeconomic factors in HIV-HCV co-infected individuals.

In Canada, the most commonly used deprivation index is the Pampalon index (78, 79). The Pampalon index is composed of six indicators: the proportion of unemployed individuals, those with a high school education or less, single parent families, individuals who are separated or widowed or divorced, individuals living alone, and the mean income for the geographic census area of measure (78). This index is calculated at the census level and does not consider variables that are tailored to HIV-HCV co-infected individuals, but rather that are calibrated for the general population.

2.4.2 The health effects of deprivation and HIV-HCV co-infection

Deprivation, in general, and in the two forms as defined by Townsend is closely linked with public health and individual health outcomes. Deprivation has been shown to be related to mortality in the general population and to premature mortality (either all-cause or due specifically to ischemic heart disease or other causes related to tobacco use) (74, 80, 81). Moreover, deprivation has been shown to vary with other forms of morbidity, from cancer to lower physical activity, respiratory diseases, type 2 diabetes, and tooth decay in the general population (74, 80). Material and social deprivation specifically as defined by Townsend have been associated with mental health outcomes such as short-term and long-term use of psychiatric services (73, 82, 83).

HIV monoinfection, HCV monoinfection, and HIV-HCV co-infection tend to be highly prevalent in marginalized populations such as people who inject drugs, people who are homeless, and MSM all who face diverse barriers to healthcare and social stigmatization that exacerbate morbidity and mortality in co-infected populations (40). Deprivation is closely related and overlaps with the idea of social determinants of health (SDoH), which like deprivation play a large role in the health of individuals. SDoH are factors that are social in nature such as an individual's support network, their housing situation, whether they are employed, and various other elements that intersect with their overall health and well-being (84).

These SDoH are a necessary component for several disease states to emerge. For example, people who are HIV-positive are more likely to be infected with HCV than HIV-negative individuals due to common routes of exposure for HIV and HCV such as intravenous drug use (61). In this instance, one of the causes that could eliminate excess HIV-HCV cases is the use of contaminated needles with such needles being a necessary component for the transmission of HIV and HCV. It also logically follows that if you provide clean needles through harm reduction services you will decrease the frequency of situations where an individual would use an unclean needle and thus decrease the overall transmission of both HIV and HCV (85). However, the probability of someone using a shared needle or injecting equipment is strongly influenced by the income, housing situation, and social network of that individual (63). Therefore, instead of providing clean needles to eliminate the use of shared needles during injection drug use one could provide individuals with additional income and housing reducing the likelihood of that individual being in a situation where they would not have resources or shelter that would lead to them using a contaminated needle (67, 86).

2.5 The quantification of deprivation and estimation of deprivation indices

2.5.1 Approaches for developing deprivation indices

In general, there are two ways to combine indicators: the additive approach, and the factor analysis approach, which has been used to develop various socio-economic indices (87). The Pampalon index, the main deprivation index used in Quebec and Canada, is constructed using a factor analysis approach (88). In the additive approach the weights of indicators that are included in the index are determined by a group of experts. However, these weights are subjective in that different experts could reach a different set of conclusions based on the same process. In the factor analysis approach the weight assigned to each indicator is not determined based on the perceptions of the researcher or of a group of professionals, but is determined from the statistical relationships that exist among the selected indicators in the dataset (89). These two approaches are each useful in their own right depending on the type of research question that is being asked. Furthermore, for both approaches it is important to use methods that provide uncertainty about the index. This allows us to have a measure that provides a sense of how uncertain we are in the results from the index. The additive approach is often used to codify expert knowledge into a numerical index whereas, a factor analysis approach uses the observed responses in the data to determine the weights. In our case, we chose to use a factor analysis approach with the goal of using a method that is statistically sound that allows us to estimate the uncertainties around our estimates.

There are several techniques that can be used to generate factor analysis based indices and the appropriate application of what technique to use is largely governed by the type of data that is being analyzed, and if the model is reflective or formative (87). Reflective in this context means that the variables measured arise from the latent construct that you are measuring and that the latent construct does not change based on the values of the items. In this context, formative means that the measured variables are the cause of the latent construct (87). In indices that are formative, methods like principal component analysis or closely related dimension reduction techniques are used to determine the weights (90). In formative indices, it is assumed that all the values of the indicators and their common variance are what makes up an observable quantity that is measured as the index. Contrarily, reflective indices assume that there is a latent trait that gives rise to observed measurable responses (87). In reflective indices, techniques like Rasch models and item response theory (IRT) are used to estimate the hidden latent measure of interest when categorical variables are being analyzed (91). We consider deprivation to be a reflective construct.

2.5.2 The effect of level on the homogeneity of deprivation measures

Regardless if an index is formative or reflective, one must consider if the data collected for the index is measured at an individual or population level (92). There are several trade-offs that one must consider when measuring deprivation at the population vs the individual level (93). For example, it has been shown that when creating area based indices that the size of the social inequalities in health and well-being that will be observed and the accuracy of the observations will depend greatly on the basic geographic unit chosen (94). In Britain, for instance, it has been shown that basing analyses on enumeration districts (mean population of about 500), rather than on wards (mean population of over 5000), reduces errors in classifying individuals, and leads to higher correlations between social inequalities and health outcomes (95).

However, regardless of how small the chosen geographic unit is when using an area based index, there will always be a loss of individual-level information especially amongst the most vulnerable. One of the reasons the most vulnerable tend to be viewed homogenously in area based indices is that these populations are often ghettoized within the same census region. For example, everyone who has an address in the downtown east side of Vancouver have the same value of the Pampalon index (40). Even though it is documented empirically that the level of deprivation varies considerably within the downtown east side (76).

2.5.3 Item construct of indices

Finally, traditional indices like the Pampalon index are created with data that is representative of the general population and tend to not generalize well to marginalized populations (79, 80). For example, the EPICE index in France is an individual level index, but was calibrated and designed to triage all patients in the population of France, a much less marginalized population on average than HIV-HCV co-infected individuals in Canada (96). The EPICE index originally considered a list of 42 candidate variables and used surveys to generate a consensus amongst a random sample of French citizens of which variables they rank as the most important, ultimately including 12 variables in the final index (83, 97). However, many questions in this survey would not be relevant to a large proportion of HIV-HCV co-infected individuals. For example, questions such as “have you traveled in the last year” or “have you been to a show in the last 6 months”. Furthermore, variables like injection drug use in the last 6 months could be useful in distinguishing deprivation in HIV-HCV co-infected individuals and may not be as useful in distinguishing individuals in the general French population (5).

2.5.4 Item response theory and item characteristic curves

In IRT, a continuous numerical index is estimated for individuals based on their response to questions with a binary outcome (91, 98). Every individual is assumed to have a certain numerical value that places each individual along a continuum relative to all of the other individuals based on their response given all the other responses from the other individuals (99). For each value of the individual parameter, there is a certain corresponding probability of answering yes to a question in the analysis. If this function for each item is plotted as a function of the individual parameter we would ideally get a smooth S-shaped curve with the probability of a yes response near zero for the lowest individual's index value and as the individual's index value increases so does the probability of a yes response (91). In IRT this curve is called the item characteristic curve (ICC).

An ICC exists for each item in a model and is used to describe the relation between a positive response to an item and the individual parameter. For every ICC, there are two important hallmarks. First, is the difficulty of the item. This can be thought of as where the item functions along the individual index values. For example, in a classroom setting an easy question will function among the low-ability examinees while a hard question would help to differentiate between high-ability examinees. Therefore, the item difficulty can be thought of as a location index. The second property is the discrimination of an item, which can be thought of as how well an item can differentiate between individuals with an index below the item location and those individuals with an index value above the item location. This manifests as the steepness of the ICC in the middle section with steeper curves indicating items that are better at differentiating between individuals. In the opposite direction, the flatter the middle section and the curve in general the less the item can differentiate since the probability of a yes response and a low index value will be nearly the same, independent of the index value (91, 98). These descriptors are also used to discuss the technical properties of an item. It should be noted that the shape of the ICC curve whether it is close to S shaped or not does not say anything about whether the item really measures some facet of the underlying individual parameter of interest or not. These two properties simply describe the form of the ICC. Whether an item's ICC is an accurate reflection of reality is a question of domain knowledge expertise (100). The Rasch model is a special case of the IRT model where the discrimination parameter is fixed to an equal constant value for all the items and the item difficulty parameters are estimated (91).

IRT is a very powerful tool to obtain a model based individual estimate for a latent construct for a group of individuals. In this thesis, the latent construct of interest is deprivation, which we want to measure for each member of a generalizable cohort of co-infected Canadians. We will use the data from the cohort and apply an IRT model to obtain individual level deprivation estimates that can then be used as a proxy for deprivation in future studies.

3. Study Methodology

3.1 Study design and setting

Data were obtained from the Canadian Co-infection Cohort (CCC), a multi-site prospective cohort of HIV-infected patients with chronic HCV infection or evidence of HCV exposure. Recruitment began in 2003 and as of December 30th, 2018, 1842 patients were enrolled from 18 sites across Canada (41). To accurately reflect the Canadian epidemic, participants were recruited from a variety of HIV centers across the country including those that serve individuals who may be extremely marginalized, access various models of care and have diverse risk profiles.

3.2 Study population

A detailed description of the CCC has been published elsewhere (41). In brief, patients were identified to participate in the CCC study from existing clinic populations at participating centers across Canada. These centers routinely screen all HIV infected patients for HCV infection. Eligible patients were adults over 16 years old with documented HIV infection (HIV-seropositive by enzyme-linked immunosorbent assay with western blot confirmation) and with chronic HCV infection or evidence of HCV exposure (HCV-seropositive by enzyme-linked immunosorbent assay with recombinant immunoblot assay II or enzyme immunoassay confirmation, or if serologically false negative, HCV RNA positive) (41). All such patients were invited to participate in the CCC. Diversity of the participants in the CCC can be found below in Table 3.2.1.

Table 3.2.1: Characteristics of the key variables in the Canadian Co-infection Cohort stratified by province

Province	British Columbia	Ontario	Quebec	Saskatchewan
Sample size	563	409	613	197
Age (mean (SD))	54 (9)	55 (9)	55 (9)	44 (10)
Education (%)				
High school or less	400 (71)	255 (62)	461 (75)	179 (91)
More than high school	152 (27)	153 (37)	149 (24)	17 (9)
Missing	11 (2)	1 (0)	3 (1)	1 (1)
Housing status (%)				
Housed	498 (89)	391 (97)	493 (80)	180 (91)
Vulnerably housed	59 (11)	18 (4)	107 (18)	17 (9)
Missing	6 (1)	0 (0)	13 (2)	0 (0)
Living situation (%)				
Not living alone	221 (39)	209 (51)	241 (39)	128 (65)
Living alone	336 (60)	200 (49)	359 (59)	69 (35)
Missing	6 (1)	0 (0)	13 (2)	0 (0)
Income level (%)				
Less than/equal 1500 CAD/month	426 (76)	265 (65)	508 (83)	158 (80)
Greater than 1500 CAD/month	129 (23)	139 (34)	99 (16)	29 (15)
Missing	8 (1)	5 (1)	6 (1)	10 (5)
Marital status (%)				
Married	113 (20)	98 (24)	76 (12)	52 (26)
Not married/divorced	439 (78)	311 (76)	520 (85)	145 (74)
Missing	11 (2)	0 (0)	17 (3)	0 (0)
Employment (%)				
Unemployed	444 (79)	319 (78)	486 (79)	162 (82)
Employed	111 (20)	89 (22)	126 (21)	34 (17)
Missing	8 (1)	1 (0)	1 (0)	1 (1)
Sexual orientation (%)				
Identify as gay/bisexual men who have sex with men	103 (18)	154 (38)	151 (25)	7 (4)
Do not identify as GBMSM	445 (79)	254 (62)	456 (74)	190 (96)
Missing	15 (3)	1 (0)	6 (1)	0 (0)

Indigenous status (%)				
Non-Indigenous	370 (66)	347 (85)	585 (95)	36 (18)
Indigenous	188 (33)	61 (15)	17 (3)	160 (81)
Missing	5 (0.9)	1 (0)	11 (2)	1 (1)
Incarceration history (%)				
Never incarcerated	139 (25)	171 (42)	199 (33)	33 (17)
Ever incarcerated	350 (62)	205 (50)	395 (64)	158 (80)
Missing	74 (13)	33 (8)	19 (3)	6 (3)
Injection drug use (%)				
Never injected drugs	73 (13)	130 (32)	109 (18)	15 (8)
Ever Injected drugs	484 (86)	279 (68)	502 (82)	182 (92)
Missing	6 (1)	0 (0)	2 (0)	0 (0)
Injection drug use last 6 months (%)				
No	319 (57)	312 (76)	385 (63)	90 (46)
Yes	237 (42)	97 (24)	223 (36)	107 (54)
Missing	7 (1)	0 (0)	5 (1)	0 (0)
Self-reported depression (%)				
No	224 (40)	170 (42)	419 (68)	88 (45)
yes	337 (60)	239 (58)	193 (32)	109 (55)
Missing	2 (0)	0 (0)	1 (0)	0 (0)
Psychiatric hospitalization (%)				
No	406 (72)	310 (76)	466 (76)	154 (78)
Yes	149 (27)	99 (24)	127 (21)	43 (22)
Missing	8 (1)	0 (0)	20 (3)	0 (0)

Data for the CCC is collected bi-annually. Socio-demographic information like education and income and behavioral characteristics such as injection drug use are self-reported in categorical format while clinical characteristics such as previous infection with a sexually transmitted disease and laboratory tests such as HIV viral load are collected by research personnel (41). Details on HCV treatments/responses, end stage liver disease diagnoses and deaths are collected using standardized case report forms.

3.3 Analysis

3.3.1 Objective 1: The estimation of an individual-level deprivation index

There exists no standard way to model deprivation in a statistical context. One of the favored methods in Canada to model deprivation is the Pampalon index, which is an area-based measure (78, 79). One of the issues with area based indices is that they fail to account for individual level heterogeneity that is important to control for in observational studies (101). Additionally, the Pampalon index is designed to account for deprivation in the general population and may have elements that do not generalize well to HIV-HCV co-infected populations. Therefore, we decided to apply an IRT model to estimate a model based individual-level index and include additional covariates based on exploratory data analyses and expert opinion that may be more relevant to HIV-HCV co-infected populations. We decided *a priori* not to include variables which we might wish to evaluate independently in analyses such as age, sex, and gender as these are known to be associated with surrogate measures of deprivation in other analyses (5).

We started by creating a list of candidate variables for inclusion in the final IRT model. We decided *a priori* that we would consider the Pampalon variables for inclusion as well as social and behavioral variables derived from the literature that could be relevant in HIV-HCV co-infected populations (40, 61-63, 78, 102-104). The Pampalon and literature variables were treated as two independent groups for the variable selection process. The variable selection process was defined *a priori* and was applied independently to both groups of variables. The selection process was to compare all possible combinations of two-way chi-squared significant tests (set an at alpha of 0.05), and the grouping between the variables in the output from a multiple correspondence analysis (MCA) (105, 106). Variables that were related to each other at the pre-specified alpha in the chi-squared tests and that also grouped closely together in the

MCA were included in the final lists of variables. From this pre-defined selection process, we chose 9 variables for inclusion into the final model from a total of 19 candidate variables.

We fit an IRT model with the complete cases of the final list of variables (107). The use of the IRT model allowed us to estimate an individual-level deprivation index for every member of our cohort and, evaluate the relative importance of every item in determining an individual's index value in a model based framework (91, 99). We fit two models: one that ignored groupings and another that grouped observations hierarchically based on an individual's province of recruitment through a hierarchical prior specification. The purpose of allowing the items of the model to vary by province is that there are known differences in the prevalence of indigenous populations, income, drug use, and other factors amongst the provinces that could be important to account for when determining an individual's level of deprivation (5, 108-110).

Our proposed model follows notation from Quinn 2004 (107). For our notation, we use *I* as the index for the individual, *j* as the index for the different items (variables), and *k* for the province in which the participant was recruited. Specifically, for the parameterization of the hierarchical model, we let x_{ijk} be the response to the j-th item for person *i* from province *k*. The IRT model assumes there is a latent continuous variable such that if $x_{ijk} = 0 \ then \ x^{*}_{ijk} \in (-\infty, 0]$ and if $x_{ijk} = 1$ then $x^{*}_{ijk} \in (0, \infty)$, with $x^{*}_{ijk} = \alpha_{jk} + \beta_{jk}\theta_{ik} + \epsilon_{ijk}$, with $\epsilon_{ijk} \sim N(0,1)$. The parameter α_{jk} is the response parameter and the parameter β_{jk} is the discrimination parameter. The parameter θ_{ik} is the index associated with subject *i*, and is what we are considering as our individual-level deprivation index.

We compared the simple and hierarchical models by calculating the widely-applicable information criteria (WAIC) for each model to see, which model best fit the data. The individual parameter from the model with the lowest WAIC was selected to be used as the index for the next part of the analysis (111). For WAIC the comparison is relative, references suggest that an absolute difference of 5 between models is substantial and 10 is definitive. The same references warn that it is difficult to establish statistical significance using these criteria and a hard cutoff would not be practical (112).

3.3.2 Objective 2: The validation of an individual-level deprivation index

The next part of the analysis was to examine the association between the index and not attending a second study visit. We fit simple logistic regressions of the index against not having attended a second visit. Additionally, we fit simple logistic regressions with each of the 9 variables that made up the index values. We also fit a multiple logistic model with same outcome and all the components of the index as covariates. We then compared the WAIC of the simple logistic regression with the index values versus the multiple regression model with all the components of the index as covariates to determine which of the two models best fit the data according to WAIC (111).

3.4 Ethics

The CCC is approved by the community advisory committee of the Canadian Institutes of Health Research Canadian HIV Trials Network and by all institutional ethics boards of participating centers (41). The main study was approved by the research ethics boards of all participating institutions. The secondary data analyses presented in this thesis were approved by the Research

Ethics board of the Research Institute of the McGill University Health Centre (REB #2020-6242).

3.5 Reproducibility statement

The code to reproduce the analyses in this thesis is available in a public repository at osf.io/7fp5x/. A fictitious sample generated based on the posterior summaries of the parameters is also available, but the original data is not publicly available as it requires approval from the Canadian Co-infection Cohort to be shared.

4. Study Results

4.1 Preface

The results of this thesis are presented in one manuscript. The manuscript included:

Adam Palayew, Alexandra M. Schmidt, Sahar Saeed, Curtis L Cooper, Alexandre Wong, Valérie Martel-Laferrière, Sharon Walmsley, Joseph Cox, and Marina B Klein. The estimation of an individual-level deprivation index for HIV-HCV co-infected persons in Canada and four Canadian provinces.

The manuscript is targeted at an audience who are involved in HIV-HCV observational research who may wish to account for deprivation in their analyses. It addresses the objectives of this thesis of estimating an individual level deprivation index for co-infected individuals. This manuscript is currently under review at BMC Public Health.

4.2 Manuscript: The estimation of an individual-level deprivation index for HIV-HCV co-infected persons in Canada

Title page

Title: Estimating an individual-level deprivation index for HIV/HCV co-infected persons in Canada

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Abstract: Words (350/350)

Background: HIV-HCV co-infected individuals are often more deprived than the general population. Deprivation may lead to disengagement from care. However, deprivation is difficult to measure, often relying on aggregate data which don't capture individual heterogeneity. We developed an individual-level deprivation index for HIV-HCV co-infected persons that encapsulated social, material, and lifestyle factors.

Methods: We estimated an individual-level deprivation index with data from the Canadian Co-infection Cohort, a national prospective cohort study. We used multiple correspondence analyses and exploratory data analyses to select 9 dichotomous variables at baseline visit: income >$1500/month; education >high school; employment; identifying as gay or bisexual; Indigenous status; injection drug use in last 6 months; injection drug use ever; past incarceration, and past psychiatric hospitalization. We fitted an item response theory model with: severity parameters (how likely an item was reported), discriminatory parameters, (how well a variable distinguished index levels), and an individual parameter (the index). We considered two models: a simple one with no provincial variation and a hierarchical model by province. The Widely Applicable Information Criterion was used to compare the fitted models. Finally, we evaluated the association of the index with non-attendance to a second clinic visit (as a proxy for disengagement) using logistic regression.

Results: We analyzed 1547 complete cases of 1842 enrolled participants; 457 (30%) failed to attend a second visit. The hierarchical model was found to have the best fit. Values of the index were similarly distributed across the provinces. Overall, past incarceration, education, and unemployment had the highest discriminatory parameters. However, in each province different components of the index were associated with being deprived reflecting local epidemiology. For example, Saskatchewan had the highest severity parameter for Indigenous status while Quebec the lowest. A one-unit increase in the index was associated with 17% odds (95% credible interval, 2% to 34%) of not attending a second visit.

Conclusion: We estimated an individual-level deprivation index. The index performed well across diverse provinces and was associated with disengagement from care. This index and the methodology used may be useful in studying health and treatment outcomes that are influenced by social disparities in co-infected Canadians.

Keywords: HIV/HCV co-infection, deprivation, measurement, item response theory

BACKGROUND

HIV/HCV co-infected individuals are often marginalized and of lower socio-economic status (1). Routes of HIV and HCV transmission overlap and are exacerbated by up-stream social determinants of health such as injection drug use (2). The concept of deprivation was defined by Townsend in 1987 as "*a state of observable and demonstrable disadvantage relative to the local community or the wider society or nation to which that individual, family, or group belongs*" (3). Often when evaluating interventions in observational studies one would like to control for deprivation to accurately quantify the impact of an intervention on the desired outcome. The reason deprivation is important to control for is because it is known to lead to bad health outcomes and may confound effects of interest. Not controlling for such differences confounds estimates of interest and can lead to biased analyses. For example, remaining engaged in care is recognized as a critical step towards meeting the World Health Organization targets for HCV elimination (4). Identifying factors associated with disengagement from care therefore is important for tailoring programs to co-infected people. Deprivation may contribute to missed visits directly or indirectly through increasing other risk factors for disengagement (such as substance use) (5).

However, deprivation is a latent construct and cannot be directly measured nor estimated using a single variable. Therefore, we must use several variables but these variables may be highly collinear. To measure deprivation, studies aim to isolate the common variation inherent to several variables and summarize it with numerical scores. The most common measure of deprivation in Canada is the Pampalon Index which was developed in Quebec (6). The Pampalon index is a 6-item index based on an aggregate of a census area, described by the proportion of the population that are: employed, with high school education or more, separated or widowed or divorced, single parent families, live alone, and the average household income (7). The Pampalon index has been used to measure deprivation in other provinces in Canada, in HIV mono-infected, HCV mono-infected, and HIV-HCV co-infected individuals in British Columbia with administrative data (7-9).

While the Pampalon index is useful in describing the deprivation of a census area, it is limited in its ability to describe deprivation among individuals in observational studies. First, it is an area-based index. Area-based indices assume that deprivation is homogeneous across the entire geographic area of measurement, which can lead to a loss of individual-level information by grouping people together who have different individual needs (10, 11). Second, the Pampalon index was primarily designed and validated to measure deprivation in the general population, which may not be applicable to more marginalized populations such as people living with HIV and HCV (12). Variables that help provide good differentiation in the Pampalon index such as the proportion of people who are widowed, separated or divorced may be useful to distinguish between members of the general population, but may not differentiate well for more marginalized populations where marriage is less common. On the other hand, characteristics such as injection drug use and incarceration history may be more useful in distinguishing levels of deprivation within HIV-HCV co-infected populations.

We aimed to develop an individual-level model-based deprivation index that considers social, material, and lifestyle variables for members of the Canadian co-infection cohort (CCC). The purpose of such an individual-level deprivation index is to be able to capture, monitor and account for deprivation in co-infected people. Additionally, we explored the differences in the index among four regions in Canada, and assessed the association between the index and an important health outcome potentially impacted by deprivation, disengagement from care.

METHODS

Study setting and participants:

The CCC is a publicly funded open prospective cohort of approximately 2000 HIV/HCV co-infected individuals recruited from 18 centers across Canada. Since 2003, HIV+ adults with evidence of HCV infection (antibody positive) have been eligible to participate. Data on socio-demographic, behavioral, and clinical characteristics and laboratory data are collected bi-annually. Details on HIV and HCV treatments/responses, clinical diagnoses, and deaths are collected using standardized case report forms (13).

Development of index

Variable pool development: We considered 19 variables potentially associated with material and social deprivation for inclusion in the model. For all analyses, all the variables were dichotomized. For our model, it was important that all the variables had a clear hierarchy, since the model assumes that all levels of every variable are monotonically increasing (14). The variables considered for inclusion fell into two categories: 1) the 6 Pampalon variables and 2) social and behavioral variables associated with deprivation in the literature. We decided *a priori* not to include variables which we might wish to evaluate independently in analyses such as age, sex, and gender as these are known to be associated with deprivation in other analyses (15-17).

Pampalon variables*:*

We adapted five out of six variables used to estimate the Pampalon index. The variables were: high school education or less, living alone (yes/no), relationship status (single/married), employed (yes/no), and income dichotomized into equal to or more than $1500 a month and less than $1500 (based on low income threshold for a single person in Canada in 2008, which was the last year an income poverty line was used in Canada) (18). The proportion of single parent homes was the one variable from the Pampalon index that did not have corresponding individual level data collected by the CCC.

Variables selected from the literature*:*

These variables were selected after performing a literature search in Medline, EMBASE, and PsychInfo focusing on articles reporting on social/behavioral factors associated with HIV/HCV co-infection. Variables identified from the literature were then matched to individual level variables available in our cohort, the reference group for these studies were either HIV or HCV mono-infected (9, 19-24). We considered 14 dichotomous (yes/no) variables, which included: identifying as gay or bisexual, people who are vulnerably housed (defined as experiencing homelessness or living in a shelter), snorted drugs in the last 6 months, injected drugs ever, injected drugs in last 6 months, ever incarcerated, sex client in the last 6 months, sex work in the last 6 months, sex client ever, sex work ever, sexually transmitted infection in the last 6 months, depression, hospitalized at a psychiatric institution, and diagnosed with schizophrenia.

Variables selection process:

Variables were selected for inclusion into the final model using a pre-defined variable selection process. For each group of variables, all possible combinations of two-way χ^2 significance tests (set at an α of 0.05), and the grouping between variables in output from multiple correspondence analysis (MCA) was evaluated (25).

Proposed model:

We fit an item response theory (IRT) model with all complete cases of the final selected variables (26). We used an IRT model because it allowed us to estimate an individual-level deprivation index for every member of our cohort and evaluate the relative importance of every item in determining an individual's score. We fit two models: one that ignored groupings and another that grouped observations hierarchically based on an individual's province of recruitment. The purpose of allowing the items of the model to vary by province is that there are known differences in sociodemographic factors in participants residing from different provinces (such as the prevalence of Indigenous populations, income, drug use) that could influence an individual's level of deprivation (27).

Our proposed model follows Quinn 2004 (28). For our notation, we use *i* as the index for the individual, *j* as the index for the different items (variables), and *k* for the province in which the individual was recruited in. Specifically, for the parameterization of the hierarchical model, we let x_{ijk} be the response to the j-th item for person *I* from province *k*. The IRT model assumes there is a latent continuous variable such that if $x_{ijk} = 0\ then\ x^*_{ijk} \in (-\infty, 0)$ and if $x_{ijk} = 1$ then $x^*_{ijk} \in [0, \infty)$, with $x^*_{ijk} = \alpha_{jk} + \beta_{jk}\theta_{ik} + \epsilon_{ijk}$, with $\epsilon_{ijk} \sim N(0,1)$. The parameter α_{jk} is the response parameter and the parameter β_{jk} is the discrimination parameter. The parameter θ_{ik} is the index associated with subject *i*, and is what we are considering as our individual-level deprivation index.

Item characteristic curves:

An item characteristic curve (ICC) is used to evaluate the probability of responding yes to a given item based on an individual's latent score (14). The ICC is defined for the two-parameter IRT model as $P(\theta_{ik}) = \frac{1}{1+e^{-\beta_{jk}(\theta_{ik}-\alpha_{jk})}}$. The response parameter (α_{jk}) is the location of the inflection point of an ICC, and the discriminatory parameter (β_{jk}) is the slope of an ICC around its point of inflection (29). This allowed us to examine how the different items discriminate as a function of the subject parameter (θ_{ik}), which is our index.

Model selection:

We compared the model that considered provincial grouping to the one that did not. We calculated the widely-applicable information criteria (WAIC) to evaluate which model best fits the data (30). The model with the lowest WAIC was chosen as the index.

Association between the index and not attending a second visit:

We examined the association of our deprivation index at baseline and not attending a second cohort visit (scheduled every 6 months)—as a proxy for disengagement in care. We compared the results of our index in univariate and multiple regression models. All models were fit using a logistic regression. The WAIC was used to determine the model that best fit the data. We chose to use logistic regression because the time between the baseline and when the outcome is assessed is fixed for all individuals obviating the need for time to event analysis.

Statistical analyses:

All analyses, graphics, and proposed model fits were done using the software R (31) and the Stan programming language (32). Functions from the package rstan, provide samples from the posterior distribution of the parameters in the model via Hamiltonian Monte Carlo with a No U-Turn Sampler (33). The 95% posterior credible intervals for each parameter are presented after 5000 iterations with a thinning interval of 1 and 2500 burn-in iterations for 4 chains. The WAIC for each model was calculated using the WAIC function from the loo Package (34). The code to reproduce this analysis is available in a public repository at osf.io/7fp5x/. A fictitious sample generated based on the posterior summaries of the parameters is also available, but the original data is not publicly available as it requires approval from the CCC to be shared.

RESULTS

Overall, 1842 individuals enrolled in the CCC. At cohort entry, the median age was 54 years, 28% were female, 24% Indigenous and 82% reported ever using injection drugs. The median CD4 count was 410 cells/µL, 31 individuals had HIV RNA greater than or equal to 50 copies/mL, and 91% were receiving antiretroviral therapy; 46% had ever received HCV treatment.

Variable selection:

We initially considered 19 variables (Table 1), 5 from the Pampalon group and 14 from the literature group. After applying the selection process, 9 variables, which are starred in Table 1, were selected and used to fit the final model. The output for the χ^2 tests and the MCA for both groups of variables are presented in Additional file 1 along with the final list of candidate variables that were considered for inclusion into the index. We analyzed 1574 complete cases of a possible 1842 enrolled participants for the 9 variables included into the model. Participants from Nova Scotia (n = 13) and Alberta (n = 47) were excluded since there were not enough individuals to evaluate the group level parameters in the hierarchical model.

Table 4.2.1: Characteristics of the participants at baseline according to variables that were considered for inclusion into the model stratified by province. Variables having an asterisk (*) were included in the final model following the variable selection process.

	Quebec	Ontario	British Columbia	Saskatchewan
n	613	409	563	197
Education level (%)*				
High school diploma or less	461 (75)	255 (62)	400 (71)	179 (90)
More than high school	149 (24)	153 (37)	152 (27)	17 (8)
Missing	3 (0.5)	1 (0.2)	11 (2)	1 (1)
Vulnerably housed (%)				
Housed	493 (80)	391 (96)	498 (89)	180 (91)
Vulnerably housed	107 (18)	18 (4)	59 (11)	17 (9)
Missing	13 (2)	0 (0)	6 (1)	0 (0)
Living alone (%)				
Not alone	241 (39)	209 (51)	221 (39)	128 (65)
Alone	359 (59)	200 (49)	336 (60)	69 (35)
Missing	13 (2)	0 (0)	6 (1)	0 (0)
Income (%)*				
<= $1500 CAD/month	508 (83)	265 (65)	426 (76)	158 (80)
> $1500 CAD/month	99 (16)	139 (34)	129 (23)	29 (15)
Missing	6 (1)	5 (1)	8 (1)	10 (5)
Marital Status (%)				
Married	76 (12)	98 (24)	113 (20)	52 (26)
Not Married	520 (85)	311 (76)	439 (78)	145 (74)
Missing	17 (3)	0 (0)	11 (2)	0 (0)
Employment (%)*				
Unemployed	486 (79)	319 (78)	444 (79)	162 (82)
Employed	126 (21)	89 (22)	111 (20)	34 (17)
Missing	1 (0)	1 (0)	8 (1)	1 (1)
Non-GBMSM (%)*				
Identifying as gay or/ bisexual	151 (25)	154 (38)	103 (18)	7 (4)
Identifying as heterosexual	456 (74)	254 (62)	445 (79)	190 (96)
Missing	6 (1)	1 (0)	15 (3)	0 (0)
Indigenous (%)*				
Non-Indigenous	585 (95)	347 (85)	370 (66)	36 (18)
Indigenous	17 (3)	61 (15)	188 (33)	160 (81)

Missing	11 (2)	1 (0)	5 (1)	1 (1)
History of incarceration (%)*				
No history of incarceration	199 (33)	171 (42)	139 (25)	33 (17)
Yes history of incarceration	395 (64)	205 (50)	350 (62)	158 (80)
Missing	19 (3)	33 (8)	74 (13)	6 (3)
Injected drugs ever (%)*				
No injection drug use	109 (18)	130 (32)	73 (13)	15 (8)
Yes injection drug use	502 (82)	279 (68)	484 (86)	182 (92)
Missing	2 (0)	0 (0)	6 (1)	0 (0)
Injected drugs in the previous 6 months (%)*				
No injection drug use in last 6 months	385 (63)	312 (76)	319 (57)	90 (46)
Yes injection drug use in last 6 months	223 (36)	97 (24)	237 (42)	107 (54)
Missing	5 (1)	0 (0)	7 (1)	0 (0)
Snorted drugs in the previous 6 months (%)				
No snort drugs last 6 months	446 (73)	323 (79)	427 (76)	158 (80)
Yes snort drugs last 6 months	144 (24)	71 (17)	104 (19)	35 (18)
Missing	23 (4)	15 (4)	32 (6)	4 (2)
Sex client ever (%)				
Never sex client	421 (69)	311 (76)	413 (73)	174 (88)
Yes sex client ever	183 (30)	94 (23)	136 (24)	23 (12)
Missing	9 (2)	4 (1)	14 (3)	0 (0)
Sex work ever (%)				
No sex work	417 (68)	328 (80)	340 (60)	151 (77)
Yes sex work	188 (31)	80 (20)	213 (38)	46 (23)
Missing	8 (1)	1 (0)	10 (2)	0 (0)
Sex work in the previous 6 months (%)				
No sex work last 6 months	561 (92)	395 (97)	501 (89)	130 (66)
Yes sex work last 6 months	41 (7)	9 (2)	39 (7)	11 (6)
Missing	11 (2)	5 (1)	23 (4)	56 (28)
Depression (%)				
No depression	419 (68)	170 (42)	224 (40)	88 (45)
Depression	193 (32)	239 (58)	337 (60)	109 (55)
Missing	1 (0)	0 (0)	2 (0)	0 (0)
Psychiatric hospital (%)*				
No psych hospital	466 (76)	310 (76)	406 (72)	154 (78)
Yes psych hospital	127 (21)	99 (24)	149 (27)	43 (22)
Missing	20 (3)	0 (0)	8 (1)	0 (0)
Schizophrenia (%)				

No Schizophrenia	510 (83)	399 (98)	537 (95)	183 (93)
Yes Schizophrenia	22 (4)	7 (2)	14 (3)	13 (7)
Missing	81 (13)	3 (0)	12 (2)	1 (0)
Sexually transmitted disease in the previous 6 months (%)				
No sexually transmitted disease last 6 months	568 (93)	369 (90)	502 (89)	185 (94)
Yes sexually transmitted disease last 6 months	34 (6)	35 (9)	43 (8)	5 (3)
Missing	11 (2)	5 (1)	18 (3)	7 (4)

Model based index results:

The simple model yielded a WAIC value of 12413.7 (standard error, 116.0) compared to a WAIC of 11960.6 (standard error, 117.0) for the hierarchical model. Since the model that allowed parameters to differ across the provinces fit the data better, we only present the results from that model. Boxplots for the individual-level parameters had similar values (figure 1) suggesting our index has a similar distribution across the four provinces.

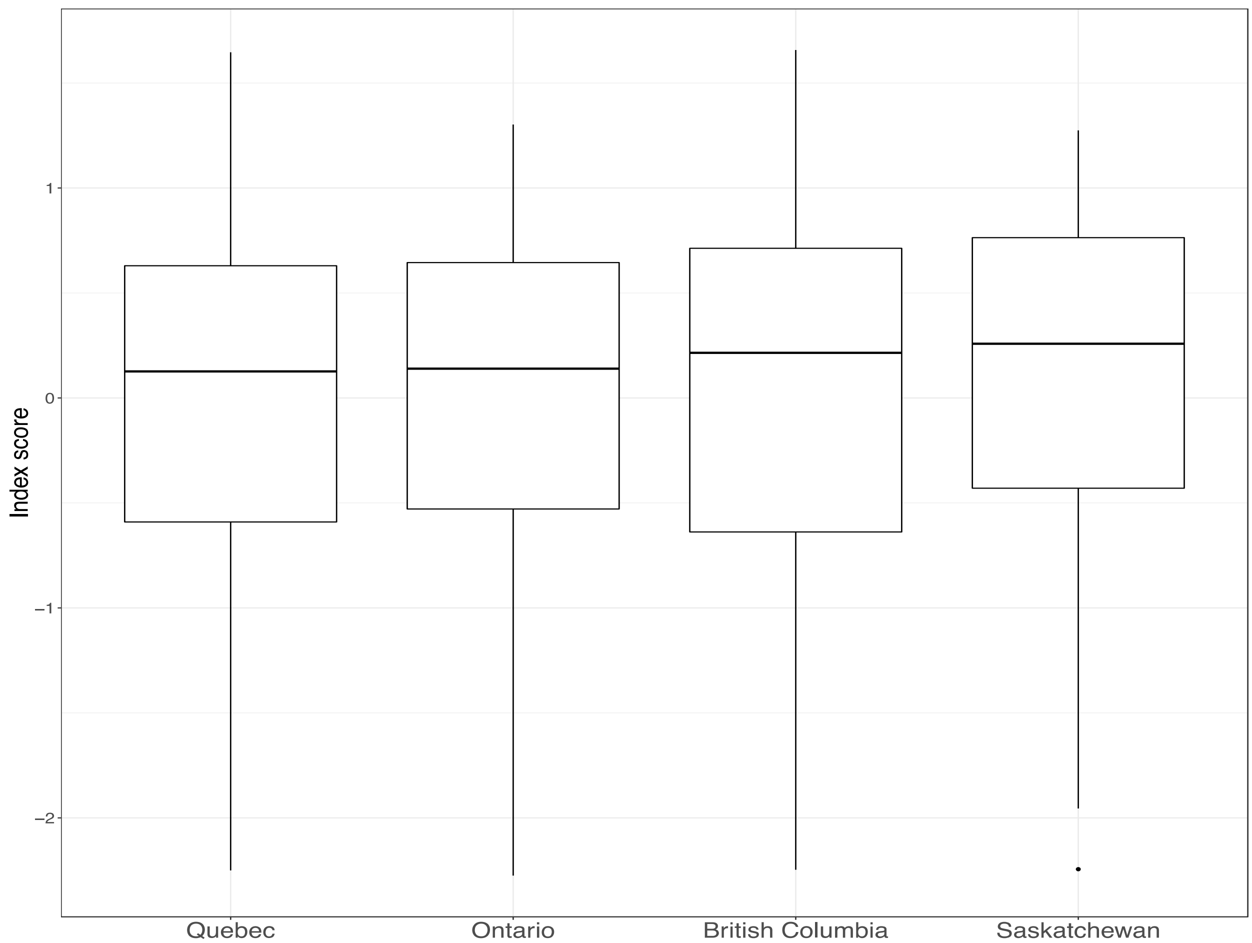

Figure 4.2.1 Boxplot of index score by province: *Posterior summaries of the individual scores for each participant presented as boxplots.*

However, we found differences in how the response and discriminatory parameters varied by province (ICC curves; figure 2). The ICC curves show the probability of responding positively to the question (y-axis) based on the value of the deprivation index (x-axis) and the different colored lines show the variation in response by province (figure 2).

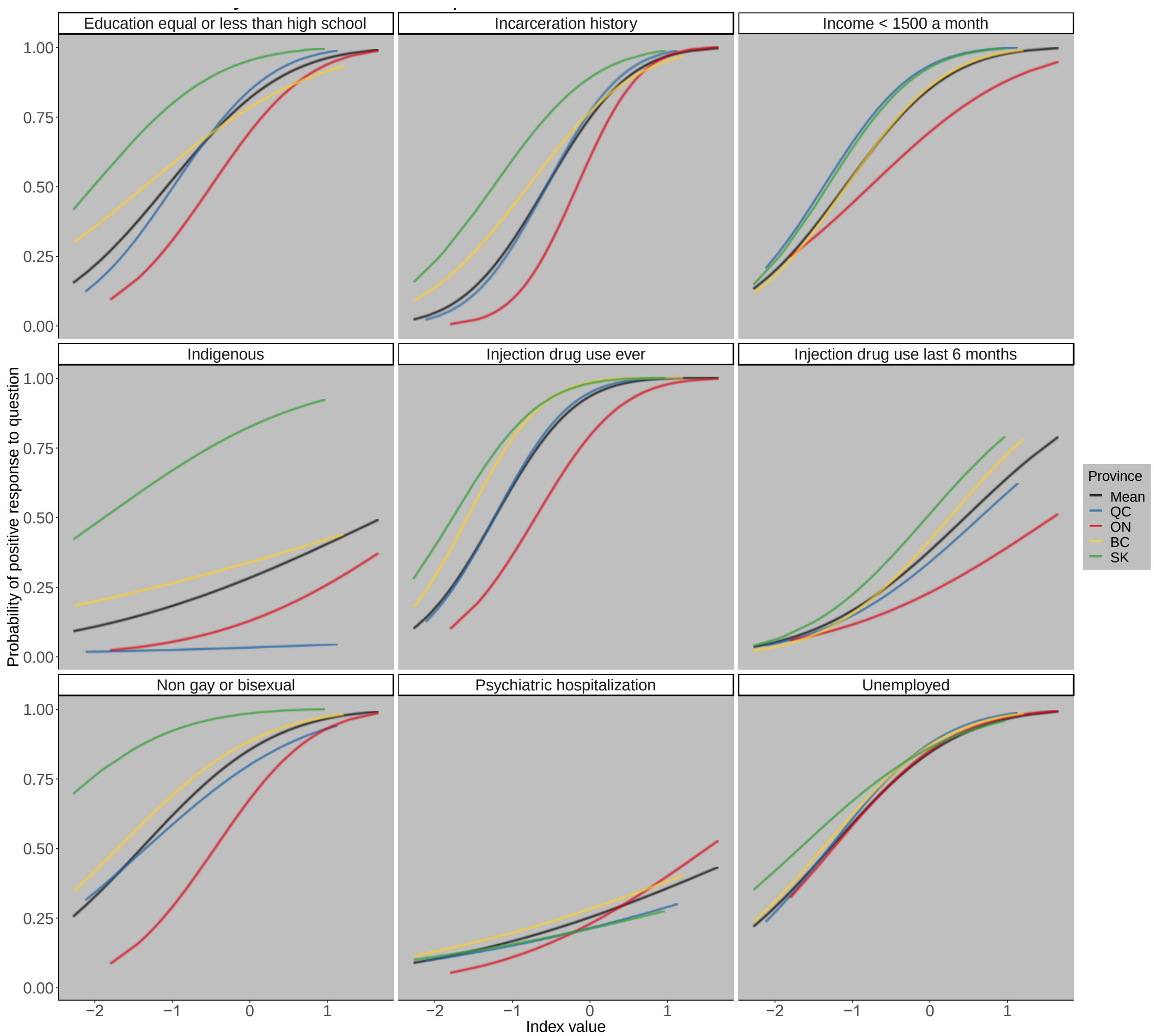

Figure 4.2.2 Variation of IRT by variables for the four provinces: *Variation of the item characteristic curves for each province by variable. The black line represents the mean value for all the indices, the blue line for Quebec, red line for Ontario, yellow line for British Columbia, and the green line for Saskatchewan. The x-axis shows the value of the estimated deprivation index and the y-axis the probability of responding positively to the question.*

For example, we found that history of incarceration and whether someone identified as gay or bisexual were more important in distinguishing between individuals in the province of Ontario than in the other three provinces. However, there were also some variables that showed little regional variation in the discriminatory parameter like unemployment, which had similar ICCs across the four provinces (figure 2). The province that differed most from the others was Saskatchewan which had the highest response parameters for people who were Indigenous, do not identify as gay or bisexual, and for education high school or less due to a higher prevalence of those subgroups relative to the other provinces. This reflects that the population of co-infected participants from Saskatchewan differs demographically from other provinces, having more Indigenous people, fewer gay and bisexual males, and a lower proportion of individuals with post-secondary education compared to the rest of the provinces.

Association of the index and non-attendance at a second visit:

Of 1537 eligible participants, 457 (30%) failed to attend a second visit. In the univariable logistic regression, a one-unit increase in the index score was associated with a 17% increase in the odds (95% posterior credible interval: 2%, 34%), of not attending a second visit. Many of the covariates that make up the index (e.g. non-gay bisexual men who have sex with men (non-GBMSM), and unemployed) were also associated with not attending a visit in univariable analyses, but these estimates were not very precise (Table 2). The multiple regression analysis demonstrates that there is potential for individual components contained in the index to be confounded by, or correlated with, each other if they are included as independent covariates to adjust for deprivation. Furthermore, as expected, including all the covariates in a single multiple regression model reduced precision of individual estimates as the variables are all highly correlated to one another.

Table 4.2.2: *Univariable and multivariable regressions odds ratios. The point estimates are the mean of the posterior summary and the 95% credible interval of the exponentiated odds ratios.*

Variables	Univariable analyses	Multivariable analysis
Index score (per unit)	1.17 [1.02, 1.34]	NA
Education > high school	0.87 [0.68, 1.11]	0.83 [0.62, 1.11]
Incarceration history	0.89 [0.71, 1.13]	0.83 [0.63, 1.10]
Injection drug use ever	0.87 [0.66, 1.17]	0.87 [0.62, 1.24]
Injection drug use in the last 6 month	1.08 [0.86, 1.35]	1.12 [0.88, 1.44]
Non-GBMSM	1.28 [0.98, 1.69]	1.51 [1.11, 2.05]
Unemployed	1.22 [0.92, 1.63]	1.35 [0.98, 1.86]
Income less than $1500 a month	0.91 [0.70, 1.18]	0.84 [0.62, 1.14]
Psychiatric hospitalization	0.96 [0.74, 1.23]	0.98 [0.75, 1.27]
Indigenous	0.95 [0.73, 1.22]	0.96 [0.74, 1.25]

WAIC for the model with the index alone was 1900.7 whereas the WAIC for the multivariable model with all the indicators was 1907.5 indicating that the model using the index alone also had a better goodness of fit.

DISCUSSION

We developed an individual-level index incorporating social, material, and lifestyle components for Canadians who are co-infected with HIV/HCV. High values of this index identify participants with more vulnerable profiles. While individual components of the model varied by province – reflecting local HIV-HCV epidemiology – the index itself performed similarly across the country.

We illustrated how the index could be used to evaluate an outcome that should be affected by deprivation – higher values of the index were strongly associated with lack of attendance at a second cohort visit.

The index has several advantages over the most commonly used deprivation index, the Pampalon index (6). Unlike the Pampalon index, an area based index, our index represents a more individualized measure of deprivation compared with assigning everyone in the same census area the same value of deprivation (35). This allows for more confidence that the deprivation value assigned to an individual is reflective of their true situation than when using an area based index (36). Additionally, our index included variables which are particularly relevant for deprivation in HIV-HCV co-infected individuals and have not been used in any previous deprivation indices to our knowledge (3, 6, 12, 37-42).

As a single summary measure of deprivation, the index offers value in that it captures the effects of multiple variables that contribute to deprivation simultaneously, preserving degrees of freedom and thus offering improved precision. As a tool for adjusting for deprivation in future studies, our score summarizes the shared variation among the variables eliminating the need for including multiple covariates to control for deprivation and therefore is more parsimonious, which is beneficial. We illustrate this when evaluating a relevant outcome, disengagement from care. The model with the index alone provided a much lower WAIC compared to the multivariable model with all variables contained in the index. Additionally, the individual estimates from the model that contained all the covariates led to wider ranges of the 95% posterior credible intervals, indicating that the posterior variances of the coefficients were greater when compared to the coefficients from the univariate model counterparts. This is probably because these covariates are correlated (Table 2). Our index naturally accounts for this correlation among these covariates, summarizing the characteristics of an individual into a single number. Furthermore, controlling for multiple variables can particularly be an issue if the variables are each highly associated with exposures of interest. For example, if one were to study the effect of being released from jail on the rate of overdose and needed to control for deprivation, our index would be better than including covariates that comprise the index such as injection drug use in the last 6 months, injection drug use ever, and history of incarceration. These controlling variables would be highly associated with the exposure (being released from jail) and thus may produce unstable estimates of the parameter of interest, the effect of release from jail, due to the high collinearity of the included variables. However, by including the joint effect of the combined variables into the model as a single variable we overcome this problem. Additionally, if one tried to control for deprivation in the previous example using some of the other variables in the index such as income and education these variables would not provide as much information about an individual's deprivation as our index.

Limitations:

The main limitation of our study was that the items selected for inclusion in the index were partly subjective. Individuals may differ on what they believe should be included in the model. In our model, we included the 9 variables using a variable selection process, which considered the peer-reviewed literature, statistical associations amongst the candidate variables and *a priori* expert opinion. Another limitation is that the index is based exclusively on the data collected in our cohort, therefore, our score may not generalize well to co-infected individuals in other settings. However, the CCC is a very diverse cohort and is representative of a wide range of individuals across Canada in multiple provinces (13). Since our index performed well across all four provinces, despite their diverse socio-demographics, it is reasonable to assume that if we were to refit this model in another high-income country similar to Canada, like Australia, that it might perform well, provided that the same variables are available and data are robust. Finally, we dichotomized the variables that were included in the model and this could lead to a loss of information. Although there are more levels in many of our variables we decided to dichotomize them due to concerns about sample size in small sub categories. Moreover, a strict monotonically increasing order is required for all variables in the model. When adding more categories, we need to make sure that there is a clear hierarchy among them, which is not possible for some variables such as Indigenous status, or non-GBMSM, which would need to have more than 2 categories. Additionally, the outcome that we used was non-attendance of a second cohort visit, but this may not accurately capture disengagement from care as individuals could attend a subsequently scheduled appointment. Gaps in attendance in care are common in more marginalized populations who have difficulty accessing the healthcare system for a variety of reasons and may only attend erratically.

CONCLUSIONS

We estimated a novel individual-level index that measures deprivation in a national representative cohort of HIV/HCV co-infected Canadians. This score described unique deprivation profiles for co-infected individuals across different provinces and showed how variables that made up the score influenced the individual index in each province. The score was also associated with disengagement from care in the short term. Such an index could be valuable clinically to identify individuals who are more prone to disengage from care and in future analyses when it is important to account for deprivation such as evaluating access to HCV direct acting antiviral treatment. If validated in other settings, it may be a valuable tool for studying health outcomes in HIV-HCV co-infection in observational studies.

LIST OF ABBREVIATIONS

CCC: Canadian Co-infection Cohort

HCV: Hepatitis C Virus

HIV: Human Immunodeficiency Virus

IRT: Item Response Theory

MCA: Multiple Correspondence Analysis

Non-GBMSM: Non-Gay/Bisexual men who have sex with men

WAIC: Widely Applicable Information Criterion

DECLARATIONS:

Ethics approval and consent to participate: The CCC is approved by the community advisory committee of the Canadian Institutes of Health Research Canadian HIV Trials Network. The main study was approved by the Research Ethics Board of the McGill University Health Centre (REB# 2006-1875) and by all institutional ethics boards of participating centers. This secondary data analyses presented in this thesis were approved by the Research Ethics board of the of the McGill University Health Centre (REB #2020-6242). Written informed consent was obtained from all individual participants included in the study.

Availability of data and materials: The code to reproduce this analysis is available in a public repository at osf.io/7fp5x/. A fictitious sample generated based on the posterior summaries of the parameters is also available, but the original data is not publicly available as it requires approval from the CCC to be shared.

Competing interests: AP, AMS, and SS have nothing to disclose. CLC reports grants and personal fees from AbbVie, grants and personal fees from Gilead, personal fees from Merck, all outside the submitted work. AW reports personal fees and other from Merck, personal fees and other from Gilead, personal fees and other from Bristol Myers Squibb, personal fees and other from AbbVie, all outside the submitted work. VML reports grants and personal fees from Merck, grants and personal fees from Gilead, grants and personal fees from AbbVie, all outside the submitted work. SW reports grants, personal fees and non-financial support from Merck, grants, personal fees and non-financial support from ViiV Healthcare, grants, personal fees and non-financial support from GSK, grants, personal fees and non-financial support from Gilead Sciences, outside the submitted work. JC reports grants and personal fees from ViiV Healthcare, grants and personal fees from Merck, grants and personal fees from Gilead, all outside the submitted work. MBK reports grants from Canadian Institutes of Health Research (CIHR), grants from CIHR Canadian HIV Trials Network, grants from Réseau sida/MI du Fonds de recherche Québec-Santé, during the conduct of the study; grants for investigator-initiated trials from Merck, grants from ViiV Healthcare, grants from Gilead, personal fees from AbbVie, personal fees from Merck, personal fees from ViiV Healthcare, personal fees from Gilead, all outside the submitted work.

Funding: This work was supported by Fonds de recherche du Québec –Santé; Réseau sida/maladies infectieuses, the Canadian Institute for Health Research (CIHR; grant number FDN-143270); and the CIHR Canadian HIV Trials Network (grant number CTN222). AP is supported by a MSc award from Fonds de recherche du Québec and the Canadian Network for

Hepatitis C. MBK is supported by a Tier I Canada Research Chair. The funders had no role in the production of this manuscript.

Author Contribution: MBK, SS, AMS, and AP contributed to the study conception and design. Data collection, cohort recruitment, was done by MBK, CLC, AW, VML, SW, and JC. The analyses were performed by AP with support from MBK and AMS. AP, AMS, SS, and MBK interpreted the data. The first draft of the manuscript was written by AP, and was revised by all authors who then approved the final submitted manuscript.

Acknowledgements: We would like to acknowledge the participants of the Canadian Co-Infection Cohort (CTN222), the Co-Investigators, Lisa Barrett, Jeff Cohen, Brian Conway, Curtis Cooper, Pierre Côté, Joseph Cox, M. John Gill, Shariq Haider, David Haase, Mark Hull, Valérie Martel-Laferrière, Julio Montaner, Erica E. M. Moodie, Neora Pick, Danielle Rouleau, Aida Sadr, Steve Sanche, Roger Sandre, Mark Tyndall, Marie-Louise Vachon, Sharon Walmsley, Alexander Wong, and the study coordinators/nurses.

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5. Discussion

5.1 Interpretation of results

The manuscript presented in this thesis detailed the results of the estimation of an individual-level deprivation index for individuals that are co-infected with HIV-HCV. The estimated individual-level deprivation index identified different profiles of deprivation in the four provinces that were examined. We illustrated how the index could be used to evaluate an outcome that would be predicted to be affected by deprivation – higher values of the index were strongly associated with lack of attendance at a second cohort visit.

The level of deprivation as determined by the index was found to have a similar minimum value, maximum value, and range of distribution across the four different provinces. However, how much each variable contributed to an individual's index value varied by province. This is interpreted to mean that even though every province has individuals who are equally deprived, what is meant by deprivation differs between the provinces. For example, it was found the injection drug use ever and injection drug use in the last 6 months was more important in determining the value for a patient from British Columbia than form Ontario (Figure 5.1.1). However, both injection drug use variables were important in determining the index value of individuals for all provinces. Indigenous status provides another example, which is not important in knowing someone's index value for Quebec compared to Saskatchewan, where nearly everyone with a high deprivation index value identifies as Indigenous; however, regardless of the index value, by virtue of being in Saskatchewan there is approximately a 50% probability that a participant would identify as Indigenous (Figure 5.1.1). Additionally, there were two variables that discriminated equally in all the provinces, employment, and injection drug use ever.

Employment was one of the most important variables in determining an individual's index value in every province and varied little between the four provinces analyzed.

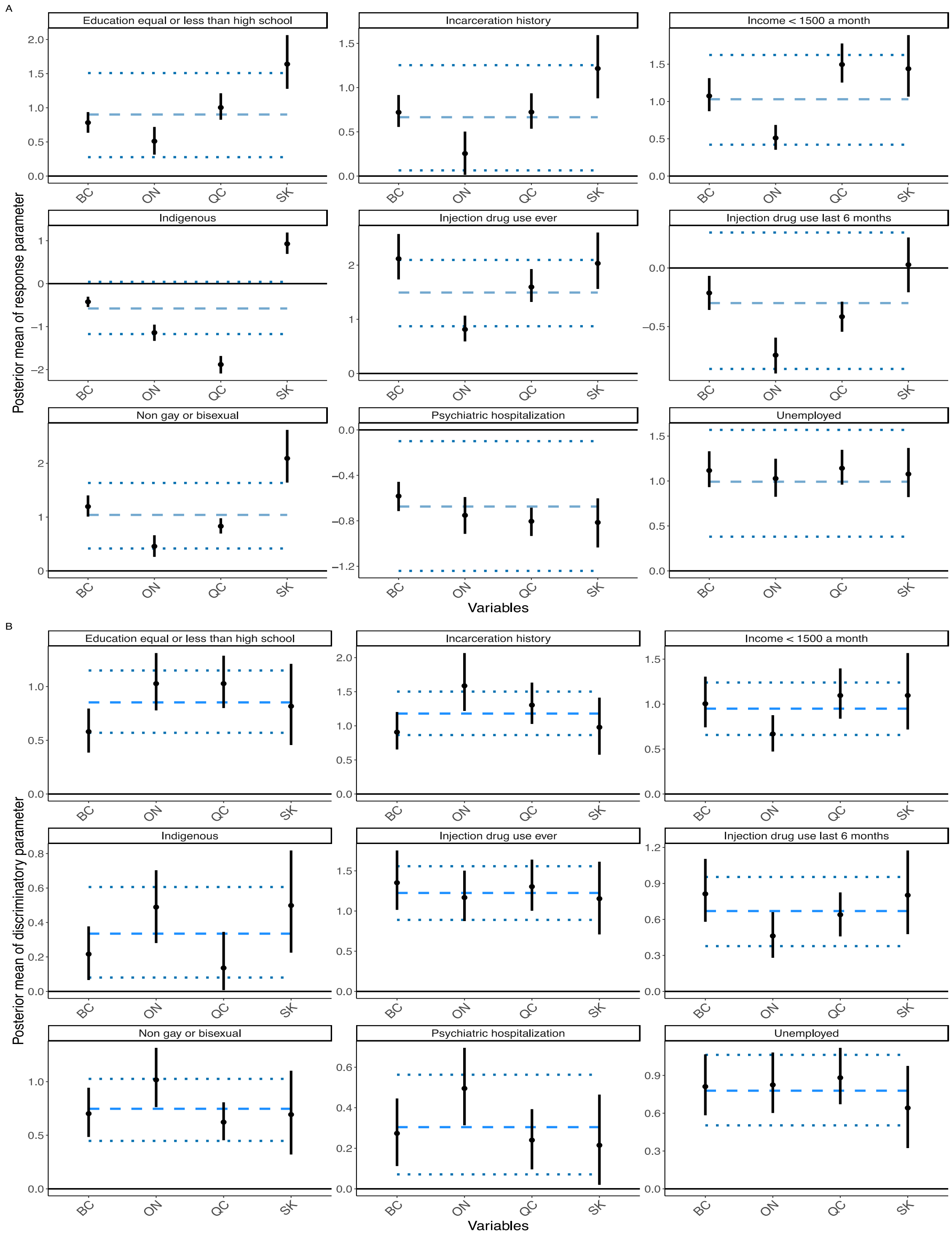

Figure 5.1.1: *Posterior summaries of the alpha (A) and beta (B) parameters for the hierarchical IRT model (mean = solid circle and 95% credible intervals: segments). In each panel the horizontal dashed line represent the posterior mean and the dotted lines are the limits of the 95% posterior credible intervals of the respective global parameter.*

Normally, variables such as injection drug use in the last 6 months and sexual orientation are not used in deprivation measurements for the general population, but were shown in this study to be informative for determining the deprivation index value of an individual co-infected with HIV-HCV. This could mean that tailored interventions are required to address the social necessities of co-infected individuals such as housing first policies or universal basic income. It was important for us to include these variables into the model because while rare in the general population, exposures such as injection drug use in the last 6 months are much more common in the HIV-HCV co-infected population and are often reflective of underlying socioeconomic status and can help distinguish degrees of deprivation amongst more marginalized individuals.

The second objective serves to illustrate how a deprivation index might be useful in assessing health outcomes that are important to further HCV elimination among co-infected patients. Given the importance of retention in care to reaching the WHO elimination targets, we selected non-attendance to a second visit as a reasonable proxy for short term disengagement from care. Individuals who fail to return to visits in the cohort (which are generally paired with routine clinical visits in the study) have less opportunity to undergo medical evaluations and counselling required to initiate HCV treatment and may be considered by health providers as not adherent to treatment and thus too risky to receive expensive therapies. We hypothesized non-attendance would be associated with the level of deprivation experienced by participants. Non-attendance of a second study visit is a good proxy for disengagement from care as it is also associated with negative health outcomes (72).

In the regression analysis, we found that there was an association between the index values and the outcome in both the simple and multiple regression analyses. The point estimate of the odds ratio was 1.17 (95% posterior Credible Interval:1.02, 1.34) suggesting a 17% increase in the odds of not attending a second visit for a one unit increase in the deprivation index. However, it should be considered that we are not trying to predict if a subject will not attend a second visit, but rather examining the association between the level of deprivation as measured by our index and an outcome likely to be associated with deprivation. As a single summary measure of deprivation, the index offers value in that it captures the association among multiple variables that contribute to deprivation simultaneously, preserving degrees of freedom and thus offering improved precision. As a tool for adjusting for deprivation in future studies, by summarizing the shared variation among variables, our index eliminates the need to include multiple covariates to control for deprivation in a single model and therefore is more parsimonious, which from a statistical point of view is beneficial. We illustrate this when evaluating a relevant outcome, disengagement from care. The model with the index alone provided a much lower WAIC compared to the multiple logistic regression model which considers all variables contained in the index. Additionally, the individual estimates from the model that contained all the covariates led to wider ranges of the 95% posterior credible intervals, indicating that the posterior variance of the coefficients were greater when compared to those obtained from the univariate model counterparts. This is probably because these covariates are correlated. Our index naturally accounts for this correlation among these covariates, summarizing the characteristics of an individual into a single number.

5.2 Strengths and limitations

An advantage of the IRT model that was used in this thesis was that it provided a model based estimate with uncertainty intervals around the index values. Additionally, according to the WAIC, the hierarchical model was a better fit for the data than the IRT model without the hierarchical structure accounted for. This allowed us to estimate an individual-level deprivation index for every member of our cohort and, evaluate the relative importance of every item in determining an individual's index value while considering provincial grouping. It is important to account for provincial grouping as there are known provincial differences in the prevalence of Indigenous populations, income levels, drug use and other factors that are important when determining an individual's level of deprivation (5, 113). In addition to the hierarchical structure of the model another distinct advantage is that the estimation procedure followed the Bayesian paradigm. This allowed for the uncertainty about the unknown quantities in the model to be naturally accounted for with no need to resort to large sample theory (114).

Another key strength of the current study was the diversity of the variables that were considered for and included in the final model. This provided us with added resolution by including variables like incarceration history that would not have been possible if we only considered traditional indicators for deprivation such as monthly income. This allowed us to estimate a measure that went beyond the variables that would be used for a deprivation index in the general population. It was important to include these extra variables to model deprivation in HIV-HCV co-infected individuals as the traditional deprivation measures are tailored to the general population and would not distinguish between co-infected individuals as well as the variables that were included in the index as described above. One of the main limitations of our study was that the items selected for inclusion in the index were partly subjective. Individuals could differ in terms of what they believe should be included in the model. In our model, we included the 9 variables using a thorough variable selection process, which considered the peer-reviewed literature, statistical associations amongst the candidate variables and a priori expert opinion. We also dichotomized the variables that were included in the model and this could lead to a loss of information. Although there are more levels in many of our variables we decided to dichotomize them due to concerns about sample size in small sub-categories. Moreover, a strict monotonically increasing order is required for all variables in the model. When adding more categories, we need to make sure that there is a clear hierarchy among them, which is not possible for some variables such as Indigenous status, or non-GBMSM, which would need to have more than 2 categories.

Another limitation is that the index is based exclusively on the data collected in the cohort, which is observational in nature. Common challenges with observational data include selection bias/generalizability; information bias, and other pitfalls. First there is always the concern about selection bias which can lead to a lack of generalizability. We believe that the CCC generalizes well to co-infected individuals in care across Canada and potentially to other countries with similar demographics. The cohort does not reflect co-infected persons who have never been diagnosed or who do not access care at all. However, in Canada this is estimated to be only 20-30% of the total co-infected population (115). The CCC approaches all eligible patients and has recruited actively from a broad range of care models (primary care, tertiary care and street outreach programs) in urban and semi-urban settings in an attempt to capture a diverse cohort reflective of the epidemic. The CCC comprises all key risk groups in the epidemic across Canada throughout multiple provinces as shown in tables earlier in this thesis (Table 3.2.1 and Table 4.2.1) (41). Since our index reflected local epidemiology across all four provinces, despite their diverse socio-demographics, it is not unreasonable to assume that if we were to apply a similar model in another country like Canada (e.g. Australia), that it would be informative about deprivation in a similar way. For example, the index may identify common factors across situations like Canada and Australia and maybe highlight that Indigenous status is important to determining deprivation levels for specific territories. Future work should assess the generalizability of our approach in other settings and in HCV mono-infection cohorts.

There remains a chance that selection bias impacted our results: some people approached to participate refuse to do so (<20%). Also, we excluded those that did not have complete responses for all variables of interest; people who chose not to respond to sensitive questions may differ from those who do. However, since the number of people who did not have complete information was low (15%) compared to the total number of people included in the analysis we believe there to be a low risk of bias in our results. Furthermore, the number of missing variables were not disproportionately represented by any province or by any of the variables. In observational epidemiology, information biases like social desirability bias can impact the quality of the data and the results. Social desirability bias could have impacted our results as people could have underreported certain exposures such as their incarceration history and injection drug use as these variables are self-reported. There is little evidence for this however given that more than 80% of our cohort self-reported a history of injection drug use and over 60% report a history of incarceration.

5.3 Areas for future research

In the future, we would like to further develop the index so that as to model index values of individuals through subsequent visits. This would allow us to better assess time-varying effects as it would allow us to control for deprivation in a time dependent manner. Additionally, this would allow us to see if deprivation as an outcome changes based on specific interventions such as the completion of hepatitis C treatment. We also want to test the relationship between the index and various other health outcomes that require more complicated modelling than logistic regression such as access to second generation DAAs for HCV. Generalizing to other cohorts in Canada and around the world is also an area of interest for future applications of the methods used in the development of the index.

One of the main advantages of following the Bayesian paradigm is that a doctor can update her own belief about, say, a patient attending a second visit. The approach proposed in this work can be used to estimate the vulnerability index of new patients and to predict the probability of a new patient attending a second visit. To this end, a doctor could be provided with a spreadsheet containing the posterior sample of the parameters from the IRT model; then the doctor would enter the values of the variables of the patient and the spreadsheet could provide not only an estimate of the patient’s vulnerability index but also the probability of that patient attending a second visit.

6. Conclusions

We estimate an individual level deprivation index for HIV-HCV co-infected Canadians, which reflected local provincial epidemiology. The index was associated with non-attendance of a second visit in a simple logisitic regression analysis and this model was a better fit to the data than the multiple logistic regression that included all the variables that composed the index. This research demonstrates the utility of IRT in estimating an individual-level deprivation index. Such methods could be used as a new approach to generate composite socioeconomic indices as IRT methods offer several useful advantages over traditional dimension reduction techniques that are routinely used to create composite indicators.

7. References

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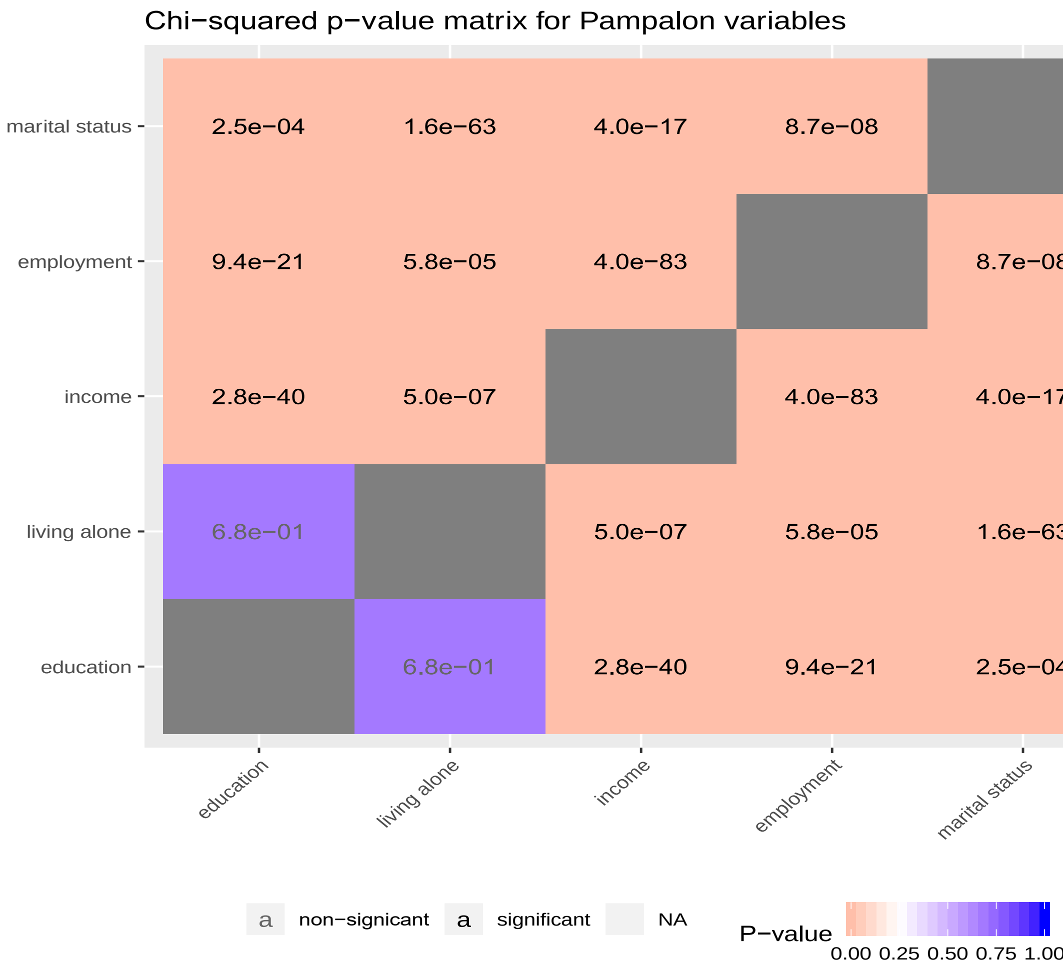
Estimating an individual-level deprivation index for HIV/HCV co-infected persons in Canada: Appendix 1

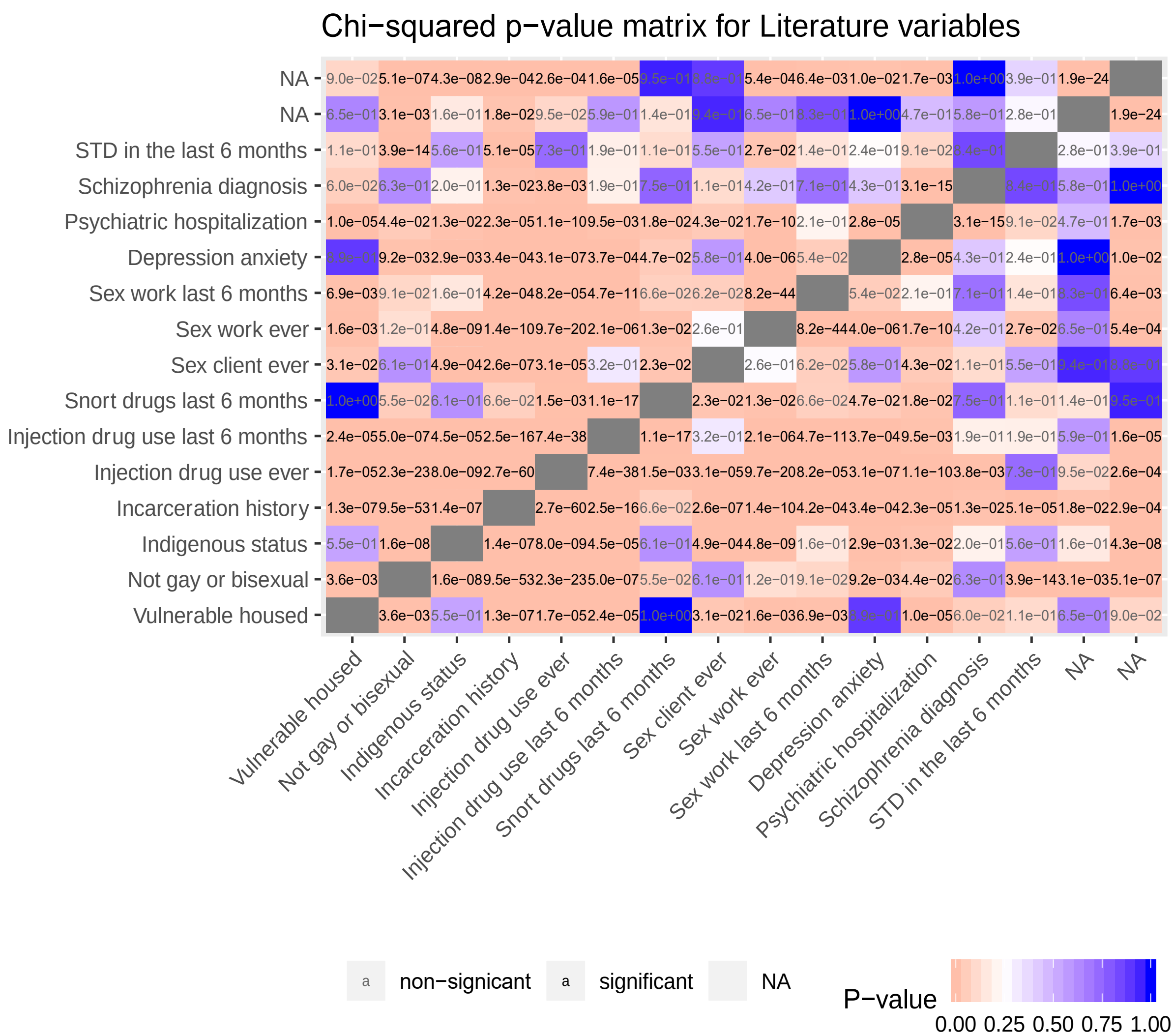
Apendix 1 selection criteria results

This is appendix 1 for the manuscript titled, "Estimating an individual-level deprivation index for HIV/HCV co-infected persons in Canada". In this appendix we present the graphical output of the selectrion criteria that is described in the methods of the article. In this appendix we present two heat-maps of chi-squared p-values to show all pair-wise statistical associations within the two different groups of variables. Additionally, we present the results of multiple correspondance analyses (MCA) for the two groups of variables.

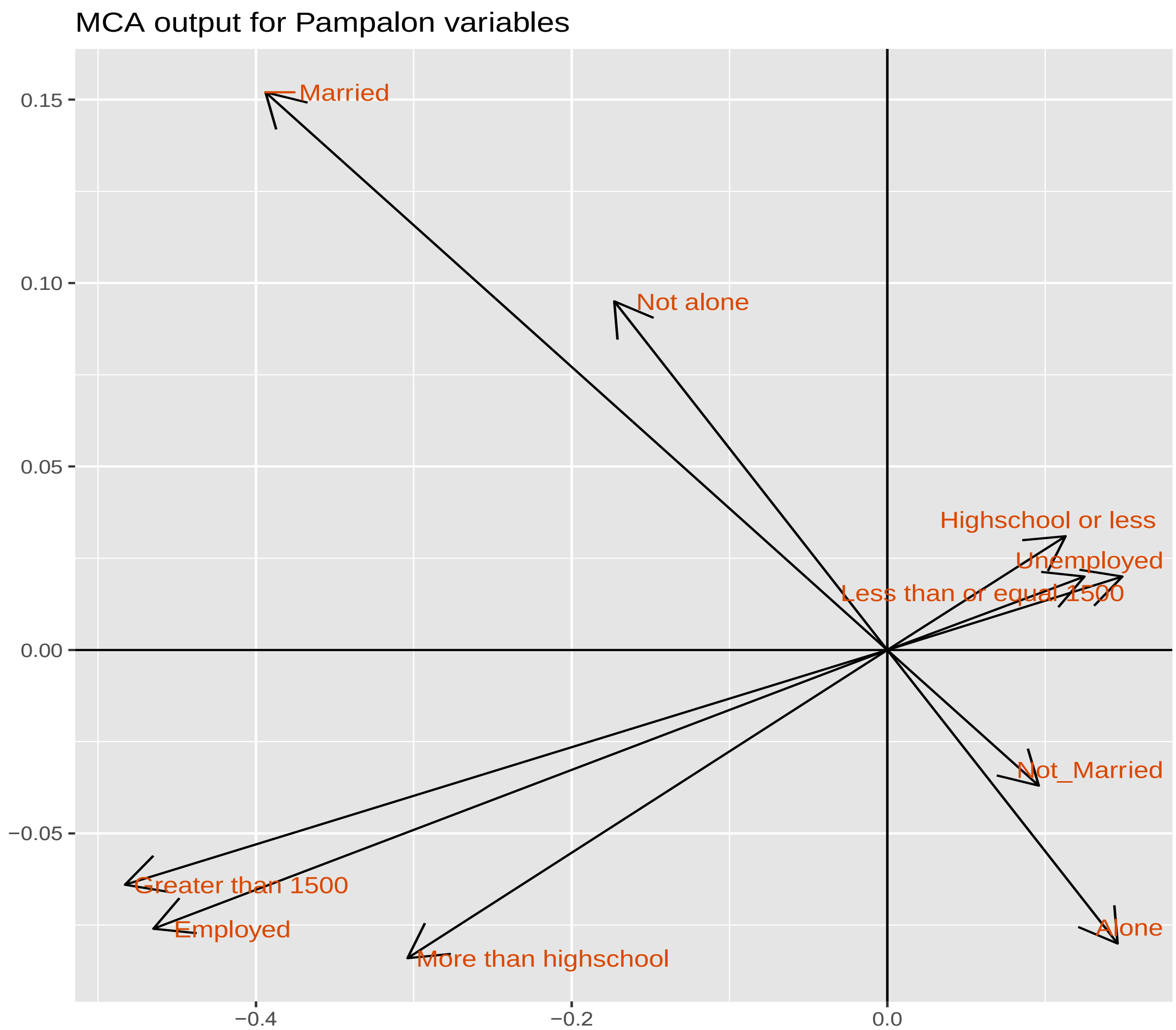
List of figures in appendix 1



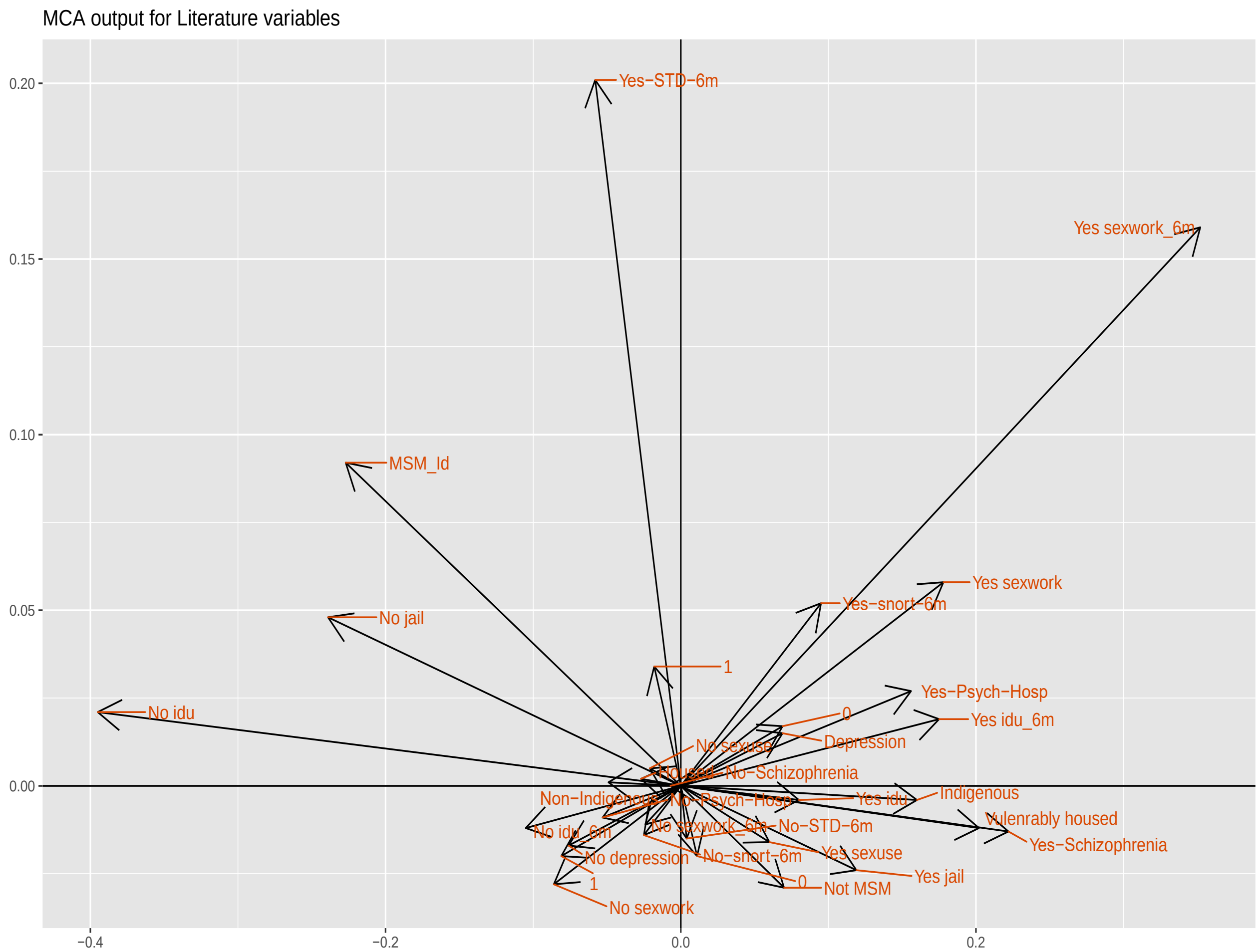
Heatmap of all p-values from pairwise chi-squared tests of the Pampalon variable. Text values in light grey are considered statistically significant at an alpha = 0.05 and values in black text are non-significant at an alpha = 0.05.



Heatmap of all p-values from pairwise chi-squared tests of the literature variable. Text values in light grey are considered statistically significant at an alpha = 0.05 and values in black text are non-significant at an alpha = 0.05.



Multiple correspondence analysis of the Pampalon variables. We can see from the Pampalon variables that there is an association between variables along the major x-axis.



Multiple correspondence analysis of the literature variables. We can see that there is an association of variables of interest like injection drug use, MSM, and psychiatric hospitalization that map well will the major x-axis.