

Pathways From HIV-Related Stigma to Antiretroviral Therapy Measures in the HIV Care Cascade for Women Living With HIV in Canada

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Background: Associations between HIV-related stigma and reduced antiretroviral therapy (ART) adherence are widely established, yet the mechanisms accounting for this relationship are underexplored. There has been less attention to HIV-related stigma and its associations with ART initiation and current ART use. We examined pathways from HIV-related stigma to ART initiation, current ART use, and ART adherence among women living with HIV in Canada.

Methods: We used baseline survey data from a national cohort of women living with HIV in Canada ($n = 1425$). Structural equation modeling using weighted least squares estimation methods was conducted to test the direct effects of HIV-related stigma dimensions (personalized, negative self-image, and public attitudes) on ART initiation, current ART use, and 90% ART adherence, and indirect effects through depression and HIV disclosure concerns, adjusting for sociodemographic factors.

Results: In the final model, the direct paths from personalized stigma to ART initiation ($\beta = -0.104$, $P < 0.05$) and current ART

use ($\beta = -0.142$, $P < 0.01$), and negative self-image to ART initiation ($\beta = -0.113$, $P < 0.01$) were significant, accounting for the mediation effects of depression and HIV disclosure concerns. Depression mediated the pathways from personalized stigma to ART adherence, and negative self-image to current ART use and ART adherence. Final model fit indices suggest that the model fit the data well [$\chi^2(25) = 90.251$, $P < 0.001$; comparative fit index = 0.945; root-mean-square error of approximation = 0.044].

Conclusions: HIV-related stigma is associated with reduced likelihood of ART initiation and current ART use, and suboptimal ART adherence. To optimize the benefit of ART among women living with HIV, interventions should reduce HIV-related stigma and address depression.

Key Words: HIV stigma, women, antiretroviral therapy, adherence, depression, structural equation modeling

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INTRODUCTION

The HIV care cascade encompasses stages between HIV acquisition to virological suppression.¹ Engaging people living with HIV (PLWH) in the HIV care cascade is vital to reaching the UNAIDS 90-90-90 goals, which include 90% of PLWH diagnosed, 90% of persons diagnosed with HIV initiating antiretroviral therapy (ART), and 90% of people taking ART virally suppressed.² Suboptimal adherence may contribute to virological failure—when ART treatment fails to suppress a person's viral load to less than 200 copies per millimeter—and death among PLWH^{3–6} and can contribute to virological resistance.^{7,8} Meta-analytic findings from 102 independent estimations of ART adherence reported over one-third of participants ($n = 33,199$) had less than 90% adherence—suggesting significant ongoing concerns with suboptimal adherence globally.⁹

Women account for one-fifth of PLWH in Canada¹⁰ and over half of PLWH worldwide.¹¹ Sex disparities are well documented in access to HIV care and outcomes, even within contexts of universal access to health care, such as Canada.^{12,13} For example, a Canadian longitudinal study of PLWH who use injection drugs ($n = 545$) reported that female sex was associated with a 30% reduction in the odds of 95% adherence to ART, after adjusting for clinical characteristics

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and drug use patterns.¹² These findings underscore the importance of examining factors that are associated with ART initiation, use, and adherence among women living with HIV (WLWH) in Canada.

HIV-related stigma and discrimination compromise access to the HIV care continuum among WLWH,^{14–17} including reduced access to HIV prevention, early access to treatment, and suboptimal ART outcomes.¹⁸ Stigma processes include labeling, loss of status, and discrimination in contexts of unequal power distribution.¹⁹ Stigma types include: anticipated, expecting or fearing discrimination, stereotyping, and prejudice from others in the future; perceived, perceptions of the existence and severity of stigmatizing attitudes in the community; enacted, experienced acts of violence, poor treatment, and discrimination from others; and internalized, acceptance of negative societal beliefs about PLWH by PLWH themselves.^{20–22}

HIV-Related Stigma and ART Outcomes, Depression, and HIV Disclosure Concerns and Behaviors

There is a well-established negative association between HIV-related stigma and ART adherence.^{23–25} Katz et al's²⁴ systematic review and metasynthesis assessed the relationship between HIV-related stigma and ART adherence. Results from 34 qualitative studies suggest that HIV-related stigma may compromise adherence through intrapersonal (reduced adaptive coping strategies) and interpersonal (disclosure practices, concealment, and reduced social support) processes.²⁴ Quantitative study results (n = 41) assessed whether associations existed between HIV-related stigma and non-adherence. Most cross-sectional—but not longitudinal—studies confirmed associations between stigma and lower adherence. In a more recent review, Sweeney and Venable²³ reviewed quantitative studies (n = 38) to further explore the causal mechanisms accounting for the associations between HIV-related stigma and adherence. This review examined types of HIV-related stigma and adherence; most studies that assessed a single dimension (eg, anticipated) of stigma found associations with lower adherence. All studies that examined more than 1 stigma dimension (eg, anticipated, enacted, and internalized) found an association between at least 1 type of stigma and nonadherence.²³ Scant studies in the review explored more than 1 stigma dimension with adherence. The review identified 2 empirically supported pathways between HIV-related stigma and adherence: the first pathway was from HIV-related stigma to increased depression and worse adherence, and the second was from HIV-related stigma to reduced self-efficacy and subsequently reduced adherence. One pathway emerged in qualitative findings but was not examined in quantitative studies: from HIV-related stigma, to HIV disclosure concerns, to reduced adherence.²³ Although this lack of study may be because HIV disclosure concerns are often considered a manifestation or type of HIV-related stigma, as these authors suggest, further studies are needed to examine specific causal mechanisms, including potential mediators, between HIV-related stigma and reduced adherence. Moreover, a recent conceptual model

described by Turan et al²² that explored causal pathways and potential mediators between different types of HIV-related stigma (enacted, community/perceived, anticipated, and internalized) and ART adherence identified nondisclosure as a potential mediator between HIV-related stigma and poor ART outcomes, and suggested nondisclosure is a manifestation of anticipated or perceived stigma. Another knowledge gap is that stigma dimensions have commonly been assessed in isolation (eg, only anticipated, perceived, enacted, or internalized stigma)²²; the inclusion of multiple forms of stigma in 1 model would allow for estimation of the association between variables without measurement error.

Depression may play a mediating role in the relationship between HIV-related stigma and HIV care cascade outcomes. Depression is a widely established concern among PLWH,²⁶ and is associated with both HIV-related stigma among PLWH^{27–29} and lower odds of retention in care³⁰ and reduced adherence.^{31,32} Three studies have assessed mental health issues (broadly),³³ depressive symptoms,³⁴ and depression diagnoses,³⁵ as a mediator between HIV-related stigma and poor ART adherence. Although Sayles et al³³ found that mental health issues fully mediated the relationship between internalized HIV-related stigma and nonadherence in their multivariate logistic regression analysis, Rao et al³⁴ found that depression partially mediated the association between HIV-related stigma (a composite measure of internalized and enacted stigma dimensions) and lower adherence among PLWH (n = 720) in their structural equation model. Studies by DiIorio et al³⁵ and Sayles et al³³ assessed 1 dimension of HIV-related stigma—internalized—precluding our understanding of the role of other stigma dimensions in this relationship.

Interpersonal factors, such as HIV disclosure concerns and HIV disclosure behavior, may mediate associations between HIV-related stigma and ART adherence.^{22,23} HIV disclosure, the act of a PLWH telling another person about their HIV diagnosis, continues to be feared and stressful,³⁶ particularly if inadvertent.²³ Qualitative studies suggest that a fear of inadvertently disclosing one's HIV-positive serostatus through discovery of ART use may present barriers to ART adherence.^{32,37–39} A qualitative study of pregnant and breastfeeding women who had initiated ART at the time of pregnancy (n = 57) described the mechanisms that women used to protect themselves from disclosure, such as throwing away ART containers.³⁸

Disclosure behaviors may have positive or negative associations with ART outcomes. Some studies have demonstrated that WLWH are less likely to disclose than men⁴⁰; this may be associated with sex inequity.⁴¹ Qualitative studies have shown that HIV disclosure increases a woman's risk of intimate partner violence after diagnosis, this may be particularly challenging for women in serodiscordant or unknown partner status couples.^{38,42} Women may also experience economic loss after disclosure.⁴³ HIV-related stigma may thereby reduce likelihood of disclosure.⁴¹ For example, in a multisite observational cohort study of WLWH in Zambia, Thailand, and Brazil (n = 299), women who reported higher anticipated stigma had a 70%

reduction in the odds of HIV disclosure to sexual partners.⁴¹ A meta-analysis exploring associations between HIV-related stigma, social support, and HIV disclosure found a small but consistent relationship between HIV-related stigma and reduced HIV disclosure.³⁶ The associations between HIV-related stigma and HIV disclosure concerns or behavior, and between HIV disclosure concerns or behavior and adherence, have been cited within the literature, yet no peer-reviewed published studies were located that quantitatively tested HIV disclosure concerns or behavior as a mediator of the relationship between HIV-related stigma and ART adherence.²³

Few studies have explored relationships between HIV-related stigma and HIV care cascade outcomes beyond ART adherence. This is particularly important in the context of test-and-treat approaches to ART initiation that recommend that all PLWH begin treatment on diagnosis.⁴⁴ Patel et al's³⁷ qualitative study with PLWH (n = 33) reported that HIV disclosure concerns presented a barrier to ART initiation. Moreover, participants reported that HIV-related stigma, including both anticipated and enacted stigma, prevented both HIV disclosure and initiation of ART. In another qualitative study,⁴⁵ newly diagnosed WLWH described HIV-related stigma and fear of disclosure as concerns for ART initiation.

Gaps in the Literature, Study Objective, and Hypotheses

To meet the HIV care cascade goals, there needs to be a better understanding of the mechanisms by which HIV-related stigma influences ART initiation, use, and adherence.²² Our study objective was to test a conceptual model exploring associations between a multidimensional HIV-related stigma construct and ART initiation, current ART use, and >90% ART adherence among WLWH

in Canada. We examined direct relationships between HIV-related stigma and these variables, and indirect associations through depression and HIV disclosure concerns as mediators.

METHODS

This analysis draws on baseline cross-sectional survey data collected as part of a national cohort study (Canadian HIV Women's Sexual & Reproductive Health Cohort Study [CHIWOS]) conducted in Ontario, QC, and British Columbia, Canada between August 2013 and May 2015.^{46,47} Data were collected by WLWH and/or women not living with HIV from highly affected communities (eg, transgender women) trained as peer research associates who recruited self-identified WLWH aged 16 years or older using purposive sampling methods (eg, word-of-mouth) and venue-based recruitment (eg, HIV clinics). Community advisory boards were formed to enhance targeted recruitment of women overrepresented in Canada's HIV epidemic, including transgender-specific and Indigenous community advisory boards. The 90–120 minutes of survey included questions about sociodemographic factors, health care access, physical/mental health outcomes, stigma, and discrimination. Surveys were administered by peer research associates using a web-based interface in a confidential location (eg, AIDS service organization, space in or near clinics, and women's home) or by telephone or Skype for some rural residents located in British Columbia's interior, and Northern Ontario and Quebec.⁴⁸ All participants provided informed consent before commencing the interview, consistent with the ethics protocol approved by Women's College Hospital, University of Toronto (Ontario), Simon Fraser University and the University of British Columbia/Providence Health (British Columbia), and McGill University Health Centre (Quebec). Participants received a \$50 Canadian honorarium for their participation.

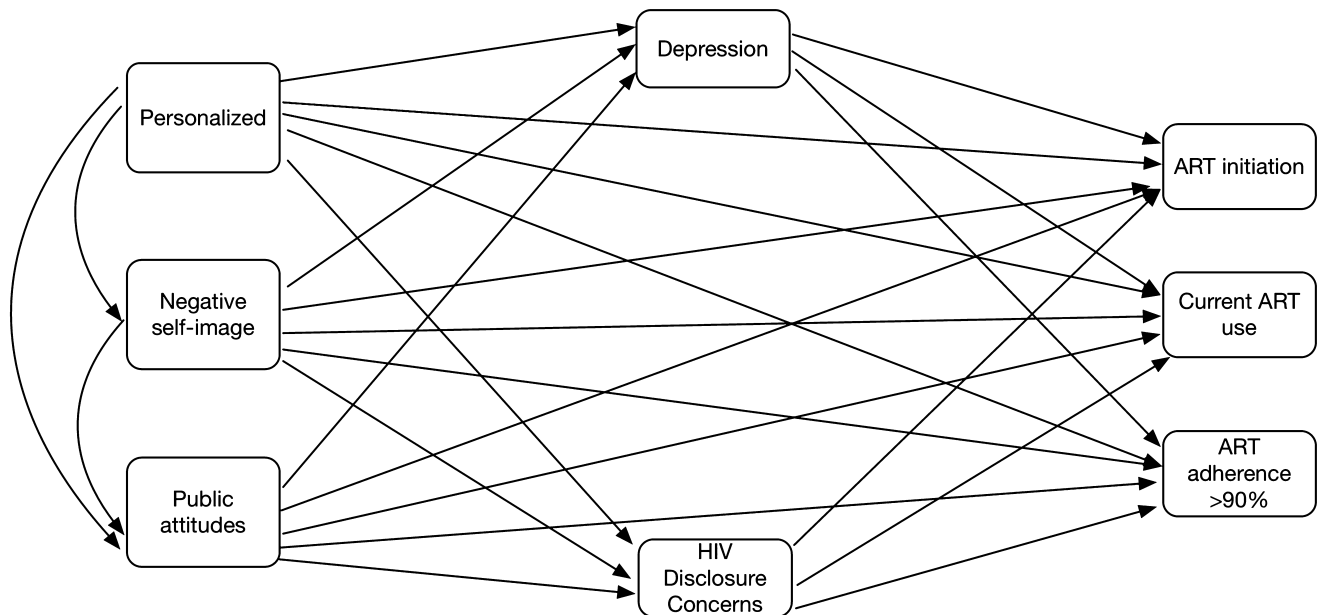


FIGURE 1. Conceptualized pathways from HIV-related stigma to ART initiation, current ART use, and >90% ART adherence.

TABLE 1. Demographic Information Among Women With HIV in Canada (N = 1425)

Variables	Total, Median (IQR)/N (%)	Missing (n)
Age	43 (35–50)	
Immigration status		7
Canadian citizen	1155 (81.45)	
Landed immigrant/permanent resident	168 (11.85)	
Refugee/protected person/refugee claimant/persons in need for protection	63 (4.44)	
Here with temporary work papers/humanitarian and compassionate approval/visitor/student visa/illegal	34 (2.39)	
Ethnicity background		
White	585 (41.05)	
Indigenous	318 (22.32)	
Black	418 (29.33)	
Other	104 (7.30)	
Household gross yearly income		43
Less than \$20,000	1001 (65.41)	
\$20,000–\$40,000	284 (20.55)	
Greater than \$40,000	194 (14.04)	
Marital status		8
Legally married/common-law/in a relationship, not living together	456 (32.18)	
Single	689 (48.62)	
Separated/divorced/widowed	272 (19.20)	
Education less than high school	227 (16.01)	7
No. of dependents	0 (0–1)	5
Sex work involvement	221 (15.51)	
History of injection drug use		27
Never used injection drugs	959 (68.60)	
Previously used injection drugs, not currently	316 (22.60)	
Currently using injection drugs	123 (8.80)	
Years of HIV diagnosis	31 (25–37)	48
Viral load: 200–500 cells/mm ³	387 (33.25)	
Viral load: >500 cells/mm ³	701 (60.22)	
Viral load response: undetectable	1100 (84.36)	121
Access to HIV care	1313 (93.45)	20

IQR, interquartile range.

Measures

Clinical outcomes included ART initiation, currently being on ART, and ART adherence. ART initiation was assessed dichotomously by “Have you ever taken Antiretroviral Medications (ARVs) for your own health” (Yes = 1, No = 0). Currently on ART was measured also dichotomously by “Are you currently on Antiretroviral Medications (ARVs)” (Yes = 1, No = 0). ART adherence was measured continuously by asking participants to provide their best estimate about how much medication they took in the past month from 0% to 100%. For the purpose of this study, we categorized this variable into 2 values: (1) ≥90% adherence; (0) <90% adherence.⁴⁹

HIV-related stigma was measured with Wright’s shortened 10-item version of Berger’s HIV-Stigma Scale (score range: 0–100; Cronbach α = 0.85).⁵⁰ For the purpose of this study, we

included 3 subscales of this HIV-related scale: personalized (“I have been hurt by how people reacted to learning I have HIV”; “I have stopped socializing with some people because of their reactions of my having HIV”; and “I have lost friends by telling them I have HIV”), negative self-image (“Having HIV makes me feel unclean”; “I feel that I am not as good a person as others because I have HIV”; “Having HIV makes me feel that I’m a bad person”), public attitudes (“Most people think that a person with HIV is disgusting”; and “Most people with HIV are rejected when others find out”).⁵⁰ We omitted the HIV disclosure subscale, as we measured this as a separate construct and potential mediator between HIV-stigma and ART outcomes, using a different measure (detailed below). Items of the HIV-related stigma scale were measured using a Likert scale (strongly agree, agree, neither agree nor disagree, disagree, and strongly disagree). For conceptual purposes, the personalized stigma subscale measures enacted HIV-related stigma, the negative self-image subscale measures internalized HIV-related stigma, and the public attitudes subscale measures perceived HIV stigma.

Potential mediators included depression and HIV disclosure concerns. Depression was assessed using the Center for Epidemiologic Studies Depression 10-item Scale (CES-D 10; eg, “How often in the past week were you bothered by things that don’t usually bother you”)^{51,52} (score range: 0–30; Cronbach α = 0.87). Higher scores in the CES-D 10 indicate higher level of depression. Depression scale items were measured using a Likert scale (most or all the time, occasionally or a moderate amount of time, same or a little of the time, and rarely or none of the time). HIV disclosure concerns were measured with a HIV/AIDS quality of life (HAT-QOL) sub-scale, which contains 6 questions regarding disclosure practices among HIV-positive people (“I’ve limited what I tell others about myself”; “I have been afraid to tell other people that I have HIV”; “I have been worried about my family members finding out that I have HIV”; “I have been worried about people at my job/routine daily activities finding out that I have HIV”; “I have been worried that I will lose my source of income if other people find out that I have HIV”; and “I have been worried that I will lose access to health services or care if people find out that I have HIV”).^{53,54} Scores range from 0 to 24. Cronbach α for the HIV disclosure scale was 0.95. Items of disclosure concerns were measured using a Likert scale as well (strongly agree, agree, neutral, disagree, or strongly disagree). Items were reverse coded and summed so that a higher score indicated more disclosure concerns. For all scales, ambiguous responses (ie, prefer not to say/don’t know) and missing values were excluded from analyses.

We included several sociodemographic factors in this study as covariates, including age (continuous), legal relationship status (single vs. married/common laws), immigration status (Canadian citizen, landed immigrant/permanent resident, refugee, and other), ethnicity (Indigenous, Black, white, and other), education (less than high school vs. high school or higher), injection drug use history (never used injection drugs, previous injection drug use but not current, and current injection drug use), and years of HIV diagnosis (continuous). Viral load was assessed with a self-reported measure that was validated among a subsample of participants from the CHIWOS study (n = 356) whose data could be linked with clinical data; 94% of women correctly self-reported an undetectable viral.⁵⁵

TABLE 2. Unadjusted and Adjusted Logistic Regression of ART Initiation, Current ART Use, and >90% ART Adherence on HIV-Related Stigma Among Women With HIV in Canada (N = 1418)

Variables	ART Initiation		Current ART Use		>90% ART Adherence	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*	Unadjusted OR (95% CI)	Adjusted OR (95% CI)*
HIV-related stigma (personalized)	0.97 (0.95–0.98)***	0.97 (0.94–0.99)*	0.96 (0.95–0.98)***	0.96 (0.94–0.98)**	0.98 (0.96–0.99)*	1.00 (0.98–1.02)
HIV-related stigma (negative self-image)	0.96 (0.94–0.97)***	0.97 (0.95–0.99)*	0.97 (0.95–0.98)***	0.99 (0.97–1.01)	0.97 (0.96–0.99)**	0.99 (0.97–1.01)
HIV-related stigma (public attitude)	0.95 (0.92–0.99)**	1.00 (0.95–1.06)	0.96 (0.94–0.99)*	1.01 (0.97–1.06)	0.97 (0.94–0.99)*	0.98 (0.94–1.02)
HIV disclosure concerns	0.98 (0.95–1.01)	0.98 (0.94–1.03)	1.01 (0.98–1.05)	0.98 (0.94–1.01)	1.01 (0.98–1.05)	1.03 (0.99–1.07)
Depression	1.05 (1.03–1.08)***	1.05 (1.02–1.09)**	1.03 (1.01–1.05)**	1.06 (1.01–1.06)**	0.95 (0.93–0.97)***	0.96 (0.94–0.98)**

Covariates include: age, ethnicity background, immigrant status, relationship status, education level, history of injection drug use, and years with HIV.

* $P < 0.05$, ** $P < 0.01$, and *** $P < 0.001$.

Statistical Analyses

We first conducted descriptive analyses of all variables for the full sample. Unadjusted and adjusted logistic regression models were used to estimate the odds ratio (OR) of clinical outcomes (ART initiation, current ART use, and 90% ART adherence).

Structural equation modeling was conducted using weighted least square estimation methods to test the direct effects of HIV-related stigma dimensions (personalized, negative self-image, and public attitude) on HIV care cascade outcomes (ART initiation, current ART use, and 90% ART adherence), and the indirect effects through depression and HIV disclosure concerns, adjusting for sociodemographic factors. Model fit was assessed using: χ^2 , root-mean-square error of approximation (RMSEA), and comparative fit index (CFI). A score of <0.05 for RMSEA and a score greater than 0.90 for CFI indicate an acceptable fit.⁵⁶ Figure 1 illustrates all the tested path models.

Statistical significance was set at the $P < 0.05$ level. Missing responses were excluded from the analyses. All statistical analyses were performed using STATA (version 14.0) and Mplus (version 1.40).

RESULTS

Participant Characteristics

Table 1 reports sociodemographic characteristics for the whole sample (N = 1425). Participants were a median age of 43 years old (interquartile range = 35–50). Most of the sample (81.5%) reported being Canadian citizens. Approximately two-thirds (65.3%) of the participants received less than Canadian \$20,000 annual household income. One-third (32.2%) of the participants were legally married/in a relationship/common law. Most participants (87.4%) had initiated ART treatment. Most participants reported currently taking ART (83.07%). More than four-fifths of participants (82.68%) reported >90% adherence.

Multivariate Logistic Regressions on Correlates of ART Initiation, Currently on ART and Medication Adherence

Table 2 illustrates the unadjusted and adjusted (A) OR for ART initiation, current ART use, and >90% ART adherence. All results were adjusted for age, ethnicity background, immigration status, relationship status, and education level. The odds of ART initiation were negatively associated with personalized HIV-related stigma [AOR: 0.97, 95% confidence interval (CI): 0.95 to 0.99], negative self-image (AOR: 0.97, 95% CI: 0.95 to 0.99), and positively associated with depression (AOR: 1.05, 95% CI: 1.02 to 1.09). The odds of currently taking ART were lower for participants with higher personalized HIV-related stigma (AOR: 0.96, 95% CI: 0.94 to 0.98), and higher for participants reporting depression (AOR: 1.06, 95% CI: 1.01 to 1.06). The likelihood of reporting >90% ART adherence was lower for participants reporting depression (AOR: 0.96, 95% CI: 0.94 to 0.98).

Structural Equation Modeling

Structural equation modeling was conducted to examine the direct and indirect effects of HIV-related stigma dimensions (personalized, negative self-image, public attitudes) on HIV care cascade outcomes: ART initiation, currently on ART, and >90% ART adherence. Final model fit indices suggested that the model fit the data well [$\chi^2(25) = 90.251$, $P < 0.001$; CFI = 0.945; RMSEA = 0.044; weighted root-mean-square residual = 1.026]. Table 3 displays the results of the final model.

Figure 2 illustrates the model with standard coefficients and their significance levels of each pathway. The standardized coefficient indicated that with a SD increase of the independent variable, the dependent variable would increase by x SD, holding all other variables constant.⁵⁷ Standard errors were included in parenthesis. In the final model, the direct paths from personalized HIV-related stigma to ART initiation ($\beta = -0.104$, $P < 0.05$: direct effect, $\beta = 0.014$,

TABLE 3. Final Path Model Parameter Estimates of ART Initiation, Current ART Use, and >90% ART Adherence Among Women With HIV in Canada (N = 1418)*

Parameter	Coefficient (SE)	Critical Ratio	P	Standardized Estimate
ART initiation				
HIV-related stigma (personalized)	-0.015 (0.006)	-2.409	<0.05	-0.096
HIV-related stigma (negative self-image)	-0.017 (0.006)	-2.639	<0.01	-0.153
HIV-related stigma (public attitude)	0.003 (0.009)	0.339	0.734	-0.036
HIV disclosure concerns	-0.005 (0.010)	-0.488	0.625	0.005
Depression	0.030 (0.007)	4.141	<0.001	0.206
Current ART use				
HIV-related stigma (personalized)	-0.019 (0.006)	-3.480	<0.01	-0.142
HIV-related stigma (negative self-image)	-0.019 (0.006)	-1.320	0.187	-0.055
HIV-related stigma (public attitude)	0.005 (0.010)	0.499	0.618	-0.020
HIV disclosure concerns	-0.008 (0.009)	-0.845	0.398	-0.031
Depression	0.021 (0.007)	3.211	<0.001	0.136
>90% ART adherence				
HIV-related stigma (personalized)	-0.002 (0.006)	-0.308	0.758	-0.015
HIV-related stigma (negative self-image)	-0.003 (0.006)	-0.543	0.587	-0.026
HIV-related stigma (public attitude)	-0.014 (0.011)	-1.317	0.188	-0.066
HIV disclosure concerns	0.011 (0.010)	1.098	0.272	0.052
Depression	-0.023 (0.006)	-3.926	<0.001	-0.169
HIV disclosure concerns				
HIV-related stigma (personalized)	0.024 (0.014)	1.683	0.092	0.043
HIV-related stigma (negative self-image)	0.111 (0.014)	8.119	<0.001	0.193
HIV-related stigma (public attitude)	0.165 (0.023)	7.050	<0.001	0.169
Depression				
HIV-related stigma (personalized)	0.074 (0.025)	3.035	<0.01	0.085
HIV-related stigma (negative self-image)	0.238 (0.023)	10.215	<0.001	0.266
HIV-related stigma (public attitude)	0.102 (0.046)	2.196	<0.05	0.067

*All results were adjusted by age, relationship status, ethnicity background, immigration status, education level, history of injection drug use, and years with HIV. SE, standard error.

$P < 0.05$: indirect effect) and current ART use ($\beta = -0.142$, $P < 0.01$: direct effect, $\beta = 0.010$, $P < 0.05$: indirect effect), negative self-image to ART initiation ($\beta = -0.113$, $P < 0.01$: direct effect, $\beta = 0.043$, $P < 0.01$: indirect effect) were significant, accounting for the mediation effects of depression and HIV disclosure concerns. Depression fully mediated the pathway from personalized HIV-related stigma to >90% ART adherence ($\beta = -0.014$, $P < 0.05$), and the pathway

from negative self-image HIV stigma to current ART use ($\beta = 0.036$, $P < 0.01$) and >90% ART adherence ($\beta = -0.045$, $P < 0.001$). Depression partially mediated the relationship between negative self-image and ART initiation ($\beta = 0.047$, $P < 0.001$), current ART use ($\beta = 0.037$, $P < 0.01$), and personalized HIV-related stigma and ART initiation ($\beta = 0.015$, $P < 0.05$), current ART use ($\beta = 0.012$, $P < 0.05$).

DISCUSSION

HIV-related stigma was associated with less engagement across the HIV care cascade in the form of reduced ART initiation, ART adherence, and ART use among this large cohort of WLWH. An intrapersonal (depression) level factor partially mediated these associations. Our findings offer insight into the role HIV-related stigma may play in limiting engagement in HIV care.

First, our findings corroborate studies that report negative associations between HIV-related stigma and ART outcomes such as adherence.²³⁻²⁵ We build on qualitative studies to provide quantitative evidence demonstrating that HIV-related stigma, and in particular, negative self-image, a measure of internalized HIV-related stigma, and personalized HIV-related stigma, a measure of enacted HIV-related stigma, are barriers to ART initiation.^{37,45} We contribute to the literature by examining these different dimensions of HIV-related stigma, in addition to negative public attitudes (a measure of perceived HIV-related stigma) in relation to multiple ART outcomes. Specifically, we found that enacted HIV-related stigma influenced both ART initiation and current ART use, and internalized HIV-related stigma influenced ART initiation, accounting for the mediation effects of depression. Interestingly, perceived HIV-related stigma was not associated with any ART outcome. These findings corroborate theorizing by Turan et al²² who suggest that different types of HIV-related stigma may be differentially associated with ART adherence and indicate a need for multilevel interventions. Structural interventions could focus on reducing enacted HIV-related stigma, and intrapersonal interventions could address internalized HIV-related stigma.

These findings also suggest that depression is a particularly important underlying mechanism of suboptimal ART outcomes for WLWH. First, consistent with much research studies, depression was significantly and positively associated with all HIV-related stigma dimensions²⁷ and negatively associated with ART adherence.^{31,32} Moreover, depression mediated the pathways between enacted and internalized stigma dimensions and ART adherence. These findings underscore the importance of addressing intrapersonal (internalized HIV-related stigma and resultant depression) and structural (enacted HIV-related stigma) factors to improve ART adherence for WLWH. However, depression only partially mediated the relationship between enacted and internalized HIV-related stigma and ART initiation and current ART use, underscoring the important role of HIV-related stigma as a driver of health.²²

Interestingly, we also found that depression was positively associated with ART initiation and current use. This finding is consistent with emerging research; for

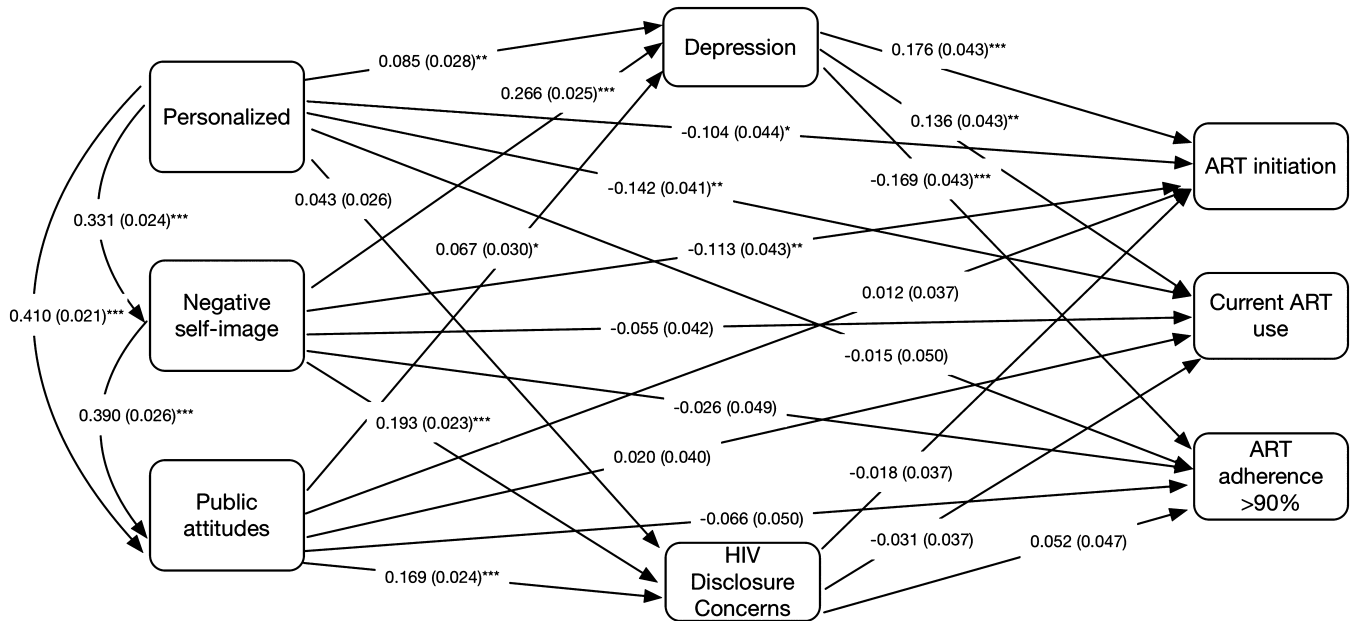


FIGURE 2. Final path analysis results for HIV-related stigma on ART initiation, current ART use, and ART adherence >90%. Standard coefficients are reported with the standard errors in parentheses. Statistical significance is noted with the following notations; **P* < 0.05, ***P* < 0.01, ****P* < 0.001. Covariates include age, ethnicity, immigration status, relationship status, education level, and years with HIV.

example, a longitudinal study conducted in Kenya (n = 162) similarly found that depressive symptom severity was associated with greater odds of ART initiation.⁵⁸ It is plausible that WLWH may seek health care because of depression, promoting ART initiation and maintenance, even while acting as a barrier to optimal ART adherence. Depression is common among people newly diagnosed with HIV⁵⁹ and may persist over time due in part to HIV-related stigma. Depression interventions may have limited or brief impacts on adherence^{60,61} if not coupled with evidence-based HIV-stigma reduction interventions that address both depression and social contexts (eg, stigma) that contribute to depression.^{62,63}

We found that all HIV-related stigma dimensions were associated with higher HIV disclosure concerns, although disclosure concerns were not associated with ART outcomes and did not mediate the association between HIV-related stigma and ART outcomes. Future studies should seek to measure disclosure behaviors, the context under which disclosure occurs (eg, purposely, inadvertently; by self, by others),²² and disclosure outcomes, which still constitute a gap in the literature.²³ Studies focused on understanding HIV disclosure must take into account the legal and sexed contexts within which disclosure occurs for WLWH, and the particular concerns related to violence and economic insecurity for women after disclosure.^{41,42} Most research studies on disclosure among WLWH has emerged from low- and middle-income contexts. More research studies are necessary about HIV disclosure practices among WLWH in Canada, a country with one of the strictest laws of criminalization of HIV nondisclosure globally.⁶⁴ A systematic review of studies assessing the impact of the criminalization of HIV nondisclosure on HIV testing and diagnosis, linkage and retention

in care, and ART adherence⁶⁵ found only 2 studies focused on women.

Our study has limitations. The cross-sectional design limits the ability to assess causation, and reverse causation is possible. For example, some studies have found an increase in HIV-related stigma and depression after ART initiation.⁶⁶ This could be better understood using a longitudinal design. The use of a purposive, nonrandom sampling strategy may have resulted in oversampling WLWH already engaged in care. Women engaged in HIV care may differ from those not engaged in care across key sociodemographics, in addition to levels of marginalization. However, we oversampled WLWH experiencing intersecting forms of marginalization including substance use and sex work to reduce this sampling bias.⁴⁶ Data were self-reported, and therefore subject to recall and social desirability bias, including the ART outcome variables. Other indicators, such as unannounced pill counts or viral load, may be more robust. Similarly, a systematic review of studies (n = 77) that used self-report measures of ART adherence found that self-reported adherence was significantly related to adherence as assessed by other measures, such as electronic drug measure and pill count in 79% of studies comparing measurement approaches.⁶⁷ Because of the differing national roll out of test and treat,⁶⁸ a proportion of those who have not initiated or are not currently using ART may have not initiated because of lack of provider recommendation. However, regardless of ART recommendation practices, HIV-related stigma is important to consider across the cascade and is associated with the range of ART outcomes.

Despite these limitations, our study has several strengths. First, we enhance understanding of pathways

between HIV-related stigma dimensions and ART adherence, and this can inform tailored adherence strategies. Previous qualitative^{37,45} and conceptual²³ work have theorized a pathway between HIV-related stigma and ART adherence mediated by HIV disclosure concerns and behaviors, and we contribute to this evidence base by testing this pathway using a large sample size and robust structural equation model analyses. Second, our use of a multidimensional measure of HIV-related stigma including personalized stigma, negative self-image, and negative public attitudes, provides a comprehensive measure of multiple stigma dimensions that may shape health behaviors. Finally, we broaden the focus from HIV-related stigma and ART adherence to other components that are critical to the HIV care cascade: ART initiation and currently taking ART. To the best of our knowledge, we are among the first quantitative studies to examine these relationships—this can inform interventions and programs that span the cascade.

Antiretroviral uptake and adherence remain suboptimal globally⁹ and among WLWH in our sample. Future research should draw on evidence-based HIV-stigma reduction strategies^{62,63} and expand on these interventions to target multiple stigma dimensions, as these are likely to contribute to the UNAIDS 90-90-90 goals. Until a concerted effort is made to address the drivers of HIV-related stigma at individual, interpersonal, and structural levels, WLWH will experience barriers to engaging across the HIV care cascade that will compromise their health and well-being.

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