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Association between Perceived Discrimination in Healthcare Settings and HIV Medication Adherence: Mediating Psychosocial Mechanisms

Bulent Turan¹ · Anna Joy Rogers² · Whitney S. Rice¹ · Ghislaine C. Atkins¹ · Mardge H. Cohen³ · Tracey E. Wilson⁴ · Adaora A. Adimora⁵ · Daniel Merenstein⁶ · Adebola Adedimeji⁷ · Eryka L. Wentz⁸ · Igho Ofotokun⁹ · Lisa Metsch¹⁰ · Phyllis C. Tien¹¹ · Mallory O. Johnson¹² · Janet M. Turan² · Sheri D. Weiser¹³

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Abstract There is insufficient research on the impact of perceived discrimination in healthcare settings on adherence to antiretroviral therapy (ART), particularly among women living with HIV, and even less is known about psychosocial mechanisms that may mediate this association. Cross-sectional analyses were conducted in a sample of 1356 diverse women living with HIV enrolled in the Women's Interagency HIV Study (WIHS), a multi-center cohort study. Indirect effects analysis with bootstrapping was used to examine the potential mediating roles of internalized stigma and depressive symptoms in the association between perceived discrimination in healthcare settings and ART adherence. Perceived discrimination in healthcare settings was negatively associated with optimal (95% or better) ART adherence (adjusted odds ratio (AOR) = 0.81, p = 0.02, 95% confidence interval (CI) [0.68, 0.97]). Furthermore, internalization of stigma and depressive symptoms mediated

Bulent Turan bturanb@uab.edu; bturanb@gmail.com

- ¹ Department of Psychology, University of Alabama at Birmingham, 415 Campbell Hall, 1530 3rd Avenue South, Birmingham, AL 35294-1170, USA
- ² Department of Health Care Organization and Policy, School of Public Health, University of Alabama at Birmingham, Birmingham, AL, USA
- ³ Department of Medicine, Stroger Hospital, Chicago, IL, USA
- ⁴ Department of Community Health Sciences, School of Public Health, State University of New York Downstate Medical Center, Brooklyn, NY, USA
- ⁵ School of Medicine and UNC Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
- ⁶ Department of Family Medicine, Georgetown University Medical Center, Washington, DC, USA

the perceived discrimination-adherence association: Serial mediation analyses revealed a significant indirect effect of perceived discrimination in healthcare settings on ART adherence, first through internalized HIV stigma, and then through depressive symptoms (B = -0.08, SE = 0.02, 95% CI [-0.12, -0.04]). Perceiving discrimination in healthcare settings may contribute to internalization of HIV-related stigma, which in turn may lead to depressive symptoms, with downstream adverse effects on ART adherence among women. These findings can guide the design of interventions to reduce discrimination in healthcare settings, as well as interventions targeting psychosocial mechanisms that may impact the ability of women living with HIV to adhere to ART regimens.

- ⁷ Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY 10461, USA
- ⁸ Department of Epidemiology, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, USA
- ⁹ School of Medicine, Emory University, Atlanta, GA, USA
- ¹⁰ Department of Sociomedical Sciences, Mailman School of Public Health, Columbia University, New York, NY, USA
- ¹¹ Department of Medicine, Department of Veteran Affairs Medical Center, University of California, San Francisco and Medical Service, San Francisco, CA 94121, USA
- ¹² Department of Medicine, University of California, San Francisco, San Francisco, CA 94121, USA
- ¹³ Division of HIV, ID and Global Medicine, Department of Medicine, University of California, San Francisco, San Francisco, CA 94121, USA

Introduction

HIV-related stigma may be experienced by people living with HIV (PLWH) in various settings, but stigma and discrimination experienced (or perceived) in healthcare settings may be particularly detrimental to health outcomes for PLWH [1]. Studies suggest that HIV-related discrimination is still prevalent in healthcare settings [2] and between 26 and 40% of PLWH report discrimination by a healthcare worker since becoming infected with HIV [3–5]. Stigma in this context may affect the quality of healthcare services by providers, utilization of services by individuals living with or at high risk for HIV infection, as well as have damaging psychosocial effects for PLWH [6].

Quality of care may be compromised when providers express stigmatizing attitudes through nonverbal behaviors such as avoidance of physical proximity and eye contact [7], lack of touch [8], expression of discomfort [4], or differential treatment, such as the use of excessive precautions or isolation measures [9], or deferring prescribing antiretroviral therapy for active injection drug users [10]. In more overt cases, PLWH have been gossiped about or verbally abused by health workers [9], had their confidentiality breached [11], or were even denied care [3, 12].

If PLWH perceive stigma and discrimination from healthcare providers, this can also impact their care utilization behaviors, such as adherence to scheduled appointments [13] and timing of presentation to healthcare facilities for testing and treatment, which are often delayed beyond the stage of optimal therapy initiation [14]. Evidence suggests that actual discrimination is associated with perceived discrimination [15, 16], but the strength of the association may be attenuated due to the difficulty associated with directly observing acts of discrimination [16]. The magnitude of this association may also depend on how the person living with HIV appraises the interaction [17]. Perceived discrimination due to one's HIV status may be an important construct to assess when examining certain outcomes, including health behaviors of PLWH. Perceived social support has been shown to be a better predictor of improvements in the mental health of PLWH [18] (and of individuals with social anxiety [19]) than actual social support, and subjective socioeconomic status is a better predictor of positive health outcomes than objective socioeconomic status [20, 21]. As has been argued in the literature on perceived socioeconomic status [22], the theoretical importance of examining perceived discrimination in healthcare settings may be even more important when it is hypothesized that the effect of discrimination on outcomes is mediated by psychological/emotional processes (e.g., internalized stigma or depressive symptoms).

Perceiving HIV-related stigma and discrimination from various sources may compromise psychological resources

of PLWH such as adaptive coping and social support, thus reducing their ability to successfully adhere to antiretroviral therapy (ART) [23, 24]. Research suggests that perceived strength of the provider-patient relationship is associated with ART adherence [25, 26]. However, there are few studies from the United States (US) investigating the impact of perceived HIV-related stigma and discrimination from healthcare providers on ART adherence. A 2013 review of the literature on stigma and discrimination in healthcare settings in the US or other industrialized nations [1] discussed numerous studies on the types of discrimination experienced within treatment settings. However, it reported only a few studies that examined the effects of stigma in healthcare settings on health outcomes such as appointment adherence [13] and engagement in care [4]. In particular, the review included only one study on ART adherence [5], with results indicating that discriminatory healthcare experiences were not associated with poorer ART adherence in that study population. However, this study by Thrasher et al. was based on data collected in the mid-1990s when ART first became widely available and optimism over the drugs was high. In addition, the study did not have a large proportion of minority women and thus may not be representative of the populations currently living with and at high risk of acquiring HIV. Minority women in the US are disproportionately affected by HIV [27], have distinct historical bases for medical distrust [28], and may experience effects of HIV-related stigma in greater magnitude [29], compared to non-minority groups. Thus, studies addressing this gap in the literature on the association between perceived discrimination in healthcare settings and ART adherence should include samples with a large proportion of minority women.

If an association between the perception of discrimination in healthcare settings and ART adherence exists, it is important to understand potential mediating mechanisms. Given the importance of consistent ART adherence for maintaining viral suppression, preventing the development of treatment-resistant HIV strains, and reducing risk of transmission, interventions to reduce risk factors for sub-optimal adherence are crucial [24]. However, interventions to reduce HIV stigma and discrimination from different sources have had mixed success [30, 31]. This may be due in part to our lack of understanding about the role of psychosocial factors as mediating mechanisms for the impact of HIV-related stigma and discrimination on health behaviors. To design effective interventions, it is crucial to base the design on a conceptual model that accurately reflects how perceptions of discrimination, an interpersonal experience, impacts intrapersonal processes that determine the health behaviors of a person living with HIV at an individual level.

Proposed Conceptual Model

We hypothesized that depressive symptoms may be a mediating mechanism in the association between the perception of HIV-related discrimination in healthcare settings and ART adherence. Symptoms of depression have consistently been shown to impact HIV medication (ART) adherence across populations [29, 32]. According to our conceptual model, perceiving discrimination in healthcare settings may contribute to symptoms of depression—including fatigue, diminished ability to concentrate, and feelings of worthlessness—ultimately impacting the ability of individuals perceiving discrimination to adhere to complex medication regimens.

We hypothesized that internalization of stigma may be an additional mediating mechanism. The concept of internalized stigma is based on the assumption that some PLWH may convert a negative external stimulus (e.g., discrimination)—whether actual or perceived—into an internal reality whereby they accept and endorse presumed negative connotations by others about having HIV [33]. Supporting this hypothesis, a recent experience sampling study found that perceived acts of discrimination during daily life are associated with increased feelings of internalized stigma in within-person analyses [34]. We hypothesize that internalized stigma may in turn lead to emotional, cognitive, and affective changes such as depressive symptoms, which may subsequently impact health behaviors.

Based on the above model, we used cross-sectional data to examine a serial mediation hypothesis: Perceived discrimination related to women's HIV status in healthcare settings is associated with internalized stigma, which in turn contributes to depressive symptoms, which in turn results in sub-optimal ART adherence. The current analysis provides a critical first step in testing the hypothesized conceptual model. Our findings may provide justification for the conduct of a future longitudinal analysis to confirm the hypothesized mediation pathway. If confirmed, intervention development to prevent the specific effects of perceived discrimination in healthcare settings may become an important focus.

Methods

Study Participants

Our analyses used data from the Women's Interagency HIV Study (WIHS), a multi-site cohort study that has enrolled women living with HIV in nine WIHS sites across various regions of the US (Birmingham, AL/Jackson, MS; San Francisco/Bay Area, CA; Washington, DC; Miami, FL; Atlanta, GA; Chicago, IL; Chapel Hill, NC; Bronx/Manhattan, NY; Brooklyn, NY), as previously described [35, 36]. WIHS study participants were recruited from a range of different settings including HIV primary care clinics, HIV testing sites, hospital-based programs, drug rehabilitation programs, women's support groups, and referrals from enrolled participants. Participants complete a semiannual physical examination, provide biological specimens, and complete an interviewer-administered questionnaire in either English or Spanish. Measures of discrimination in healthcare settings and internalized stigma were recently added to the battery of measures. Cross-sectional analyses for the current article included 1356 women currently on ART for whom data on medication adherence, internalized stigma, and healthcare discrimination were available from their last study visit between April 2014 and March 2015 (excluding 176 participants from the analyses). The protocol was approved by the Institutional Review Board at each site's institution and by the WIHS Executive Committee and participants provided written informed consent.

Measures

HIV-Related Discrimination in Healthcare Settings

In the WIHS questionnaire, participants responded to a single item, "I feel discriminated against in healthcare settings because of my HIV status" in order to assess the level of discrimination that they perceived from their collective healthcare team. This item was adapted from a survey measuring stigma and discrimination experienced by people living with HIV/AIDS in South Africa [37] and from the widely used Experiences of Discrimination Scale [38], which has been successful in predicting health outcomes using global perceptions of discrimination in different settings. Responses were given using a four-point scale (strongly disagree to strongly agree).

Internalized HIV-Related Stigma

We used the negative self-image subscale of the revised HIV stigma scale [39] adapted from Berger et al. [33] to assess current internalized HIV-related stigma. This subscale is composed of seven items (for example, "I feel I'm not as good as others because I have HIV/AIDS."), rated on a fourpoint scale (strongly disagree to strongly agree), and showed high internal consistency and test–retest reliability in previous studies [40, 41]. Cronbach's alpha reliability coefficient for the subscale was 0.88 in the current sample.

Depressive Symptoms

WIHS uses the 20-item Center for Epidemiological Studies Depression (CES-D) scale, which has response options ranging from 0 (rarely or none of the time) to 3 (most or almost all of the time), to assess depressive symptoms. This scale has been shown to predict antiretroviral therapy adherence in various populations [32].

Adherence

ART adherence is assessed in WIHS by asking participants to self-report how often they took their medications as prescribed over the past 6 months, with response options ranging from 1 (100% of the time) to 5 (I haven't taken any of my prescribed medications). This measure has been shown to be a valid measure of adherence [42, 43]. As in previous studies [29, 44], we used the cutoff for optimal versus sub-optimal adherence to be at 95%, resulting in a dichotomized variable.

Data Analyses

In preliminary analyses, a multiple linear regression model was used to examine the association between demographic variables (covariates used in main analyses) and perceived discrimination in healthcare settings. To test our main hypothesis, logistic regression analysis was conducted using ART adherence as the dependent variable and perceived discrimination in healthcare settings as the independent variable. Next, depression scores were added to the model. In all analyses, we adjusted for covariates that previous research identified as important when examining stigma-adherence associations: race, age, time on ART, illicit drug use, income, and education. As an additional sensitivity analysis, we re-ran models on women of color only to determine if the associations were similar in this subpopulation.

Mediation analysis was used to test whether the association between perceived discrimination in healthcare settings and sub-optimal HIV medication adherence is mediated by depression scores, utilizing the indirect effects analysis with bootstrapping for dichotomous outcomes developed by Hayes [45]. In this method, a significant indirect effect (indicated by a confidence interval that does not include zero) suggests mediation. Finally, we used a serial mediation analysis to examine the hypothesis that perceived discrimination in healthcare settings leads to internalized HIV stigma, which in turn leads to higher depression scores, which in turn leads to sub-optimal adherence. In all mediation analyses 1000 bootstrap samples were used. The covariates race, age, time on ART, illicit drug use, income, and education were entered as control variables in all mediation analyses as well. All analyses were performed using SPSS (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.).

Results

Demographic and patient characteristics of the sample can be found in Table 1. When entered simultaneously into a multiple linear regression, none of the demographic variables (covariates used in main analyses), except for illicit drug use, were significantly associated with perceived discrimination in healthcare settings. Illicit drug use was associated with higher perceived discrimination in healthcare settings (B = 0.11, t = 1.98, p = 0.048). In a logistic regression analysis, perceived discrimination in healthcare settings was significantly associated with sub-optimal medication adherence (adjusted odds ratio (AOR) = 0.81, p = 0.02, 95% confidence interval (CI) [0.68, 0.97]). In this analysis, the covariates younger age, more time on ART, using illicit drugs, and not being white of non-Hispanic origin were also significantly associated with sub-optimal adherence (all p values < 0.02), whereas the remaining covariates, income and education, were not significantly associated with adherence (both p values > 0.80). When depression scores were added to the model, perceived discrimination in healthcare settings was no longer significantly associated with adherence (AOR = 0.91, p = 0.35, CI [0.76, 1.10]), whereas depression scores were significantly associated with sub-optimal adherence (AOR = 0.97, p < 0.001, CI [0.96, 0.99]).

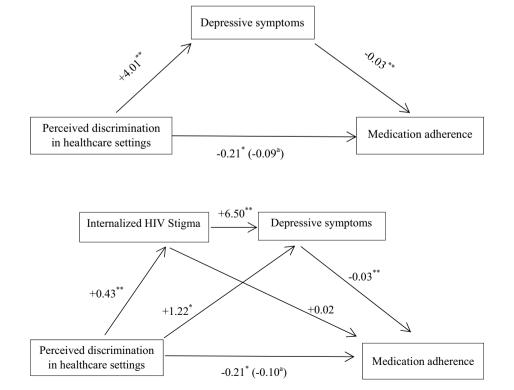
A mediation analysis (see Fig. 1) suggested that the association between perceived discrimination in healthcare settings and HIV medication adherence is mediated by depressive symptoms. The indirect effect of discrimination in healthcare settings on HIV medication adherence through depression scores (the product of the paths + 4.01and -0.03) was significant (B = -0.11, SE = 0.03, 95% CI [-0.18, -0.06]). This result suggests that depressive symptoms account for the association between perceived discrimination in healthcare settings and medication adherence. In this analysis controlling for depressive symptoms, the direct effect of discrimination in healthcare settings on HIV medication adherence was not significant (B = -0.09, SE = 0.10, 95% CI [-0.28, 0.10]), which suggests that when the mediating effect of depressive symptoms is controlled, the remaining effect of discrimination in healthcare settings on HIV medication adherence is no longer significant.

In our serial mediation analysis (see Fig. 2), the indirect effect of discrimination in healthcare settings on sub-optimal HIV medication adherence, first through internalized HIV stigma and then through depressive symptoms (the product of the paths + 0.43, + 6.50, and - 0.03) was significant (B = -0.08, SE = 0.02, CI [-0.12, -0.04]). This result supports the serial mediation hypothesis: discrimination in healthcare settings predicts internalized HIV stigma, which in turn predicts depressive symptoms, which in turn predicts sub-optimal HIV medication adherence. In this model, the indirect effect of discrimination in healthcare settings on

Variable		N (%)
Race		
Non-Hispanic white		149 (11.0)
Hispanic-white		67 (4.9)
Non-Hispanic black		951 (70.1)
Hispanic-black		27 (2.0)
Hispanic-other		118 (8.7)
Other		44 (3.3)
Illicit drug use		
Yes		297 (22.0)
No		1056 (78.0)
Language preference		
English		1299 (96.0)
Spanish		54 (4.0)
Adherence		
< 95%		236 (17.4)
$\geq 95\%$		1120 (82.6)
Variable	Mean (SD)	Range
Age (years)	48.75 (9.05)	25-80
Education	4.10 (1.05)	1–7
Income	3.29 (2.06)	1-8
Days on ART	3832 (2466)	1-8086
Internalized HIV-related stigma	1.80 (0.67)	1–4
Depressive symptoms	12.15 (11.30)	0–56
Perceived healthcare discrimination	1.72 (0.79)	1–4

Fig. 1 Depressive symptoms mediate the effect of perceived discrimination in healthcare settings on medication (ART) adherence. *Note* Associations are presented as path coefficients (unstandardized). ^aWhen depressive symptoms are in the model. *p < 0.05; **p < 0.01

Fig. 2 Serial mediation model in the association between perceived discrimination in healthcare settings and sub-optimal medication (ART) adherence. *Note* Associations are presented as path coefficients (unstandardized). ^aWhen internalized HIV stigma and depressive symptoms are in the model. *p < 0.05; **p < 0.01



HIV medication adherence through only depressive symptoms (the product of the paths + 1.22 and -0.03 in Fig. 2) was significant: B = -0.04, SE = 0.02, CI [-0.08, -0.01]). However, the effect of perceived discrimination in healthcare settings on HIV medication adherence through only internalized HIV stigma (the product of the paths 0.43 and 0.02 in Fig. 2) was not significant (B = 0.01, SE = 0.07, CI [-0.11, 0.15]). Furthermore, in this model that includes depressive symptoms, the path from internalized stigma to HIV medication adherence (B = 0.02) was not significant, which suggests that the effect of internalized HIV-related stigma on HIV medication adherence is mostly mediated by depressive symptoms. In the serial mediation analysis, the direct effect of discrimination in healthcare settings on HIV medication adherence was not significant (B = -0.10, SE = 0.11, 95% CI [- 0.31, 0.11]), suggesting that when the mediating effects of both mediators are controlled, the remaining effect of discrimination in healthcare settings on HIV medication adherence is no longer significant. We reran all models excluding non-Hispanic white women, and all main effects and mediators were similar.

To evaluate possible reverse causality (i.e., internalized HIV stigma and/or depression leads to interpreting neutral interactions in healthcare settings as discrimination, which leads to suboptimal adherence) we examined the mediating role of perceived discrimination in healthcare settings in the association that internalized stigma (or depression) has with sub-optimal adherence. Neither the indirect effect of internalized stigma (B = -0.09, SE = 0.07, CI [-0.23, 0.06]) nor the indirect effect of depression (B = -0.002, SE = 0.002, CI [-0.006, 0.002]) on sub-optimal adherence through perceived discrimination in healthcare settings was significant.

Discussion

Previous literature has suggested a negative impact of discrimination in a healthcare setting on the delivery and utilization of HIV services by PLWH, but less is known about the impact of perceived stigma and discrimination in a healthcare setting on ART adherence by PLWH, which is closely linked to HIV-related health outcomes. The current study helps fill this gap in knowledge by examining the association between perceived discrimination in healthcare settings and sub-optimal HIV medication adherence among women. We also examined the mediating roles of internalized HIV-related stigma, and subsequently depressive symptoms, in this association. We found that perceived discrimination in a healthcare setting was significantly associated with sub-optimal ART adherence. Furthermore, this association was mediated in a serial fashion by internalized stigma and by depressive symptoms: perceived discrimination in healthcare settings was associated with internalized HIV stigma, which in turn was associated with depressive symptoms, which in turn was associated with sub-optimal adherence. Although our results suggest that depression operates as a mediator of the perceived discrimination-adherence association independently of the process of internalization (i.e., women living with HIV may perceive discrimination and experience resultant depressive symptoms, which leads to sub-optimal ART adherence), the internalization of stigma also appears to impact ART adherence through depressive symptoms.

Our results are in line with the finding that depressive symptoms are associated with internalized stigma [46, 47], and may mediate the association between internalized stigma and poorer ART adherence [29, 48], based upon longitudinal and cross-sectional findings, respectively. We believe that this study adds to growing evidence that actual or perceived discrimination from various sources-including healthcare workers, community members, and close interpersonal relationships-can contribute to feelings of worthlessness and self-blame, ultimately disrupting adherence to ART regimens [34]. Building on the HIV stigma framework by Earnshaw and Chaudoir [49], theoretical work has suggested that identifying the source of stigma (friends, family, strangers, health providers, etc.) is important in predicting different health behaviors that PLWH adopt in response to stigma [24, 50]. Perceived stigma and discrimination in healthcare settings may impact health behaviors and outcomes differently than community stigma or stigma from family and friends. Stigma in a healthcare setting has been associated with reduced physician trust and non-suppressed viral load [51], and the quality of a patients' relationship with their HIV care provider seems to play an important role in ART adherence [52].

Although minority women in the US are disproportionately affected by HIV [27], have distinct historical bases for medical distrust [28], and may experience effects of HIV-related stigma in greater magnitude [29] compared to non-minority groups, there is a paucity of research on the perception of HIV-related discrimination in healthcare settings in this population. Thus, minority women represent a key population within which to address this gap in the literature on the association between discrimination in healthcare settings and ART adherence. Our sample, which comprises 89% minority-identifying participants, adds to the literature, which has otherwise assessed healthcare discrimination and its impact on ART adherence in populations with fewer women of color [5].

Future longitudinal studies are required to warrant intervention development to address these potential downstream effects of perceived HIV discrimination in healthcare settings. Nevertheless, these findings may suggest practical considerations for institutions that provide healthcare to

women living with HIV and for people living with other chronic stigmatized conditions. First, clinical organizations with an interest in evidence-based practice may want to keep providers informed as to current perceived experiences of discrimination in healthcare settings by women living with HIV from various U.S. regions, particularly considering that these perceived experiences are associated with downstream outcomes (i.e., depression and suboptimal adherence) that place greater burden on the healthcare system [53, 54]. Additionally, healthcare organizations interested in clinic quality may consider assessment of providers' baseline knowledge of HIV discrimination in healthcare settings and its potential negative impacts, in order to determine whether healthcare provider education would be beneficial. Some healthcare institutions may further consider actual evaluation of implicit and explicit HIV-related biases in healthcare settings. A recent assessment of healthcare setting stigma among providers in Alabama [2] informed the adaptation and implementation of an intervention in which healthcare professionals and PLWH learned about HIV-related stigma and were equipped with the skills to address HIV-related stigma in the community and in the healthcare setting, which has shown promise in pilot assessments [55].

Theoretical formulations distinguish different dimensions of HIV-related stigma, such as enacted stigma (actual experiences of discrimination), perceived community stigma (perceived severity of stigmatizing attitudes in the community against PLWH in general), internalized stigma, and anticipated stigma (expectation of negative attitudes due to one's HIV positive status) [24, 49]. In this article, we focused on perceptions of enacted stigma in healthcare settings, which may be a better predictor of health outcomes than actual experiences, and this association may be mediated by internalized stigma. A recently proposed theoretical framework suggests that different dimensions of HIV-related stigma may mediate the effect of other stigma dimensions [24]. Future studies can examine the complex mechanisms through which different dimensions of stigma affect health outcomes for PLWH.

A deeper understanding of the process of stigma internalization and depression may allow providers to identify and challenge manifestations of stigma and discrimination in their own practices. This understanding may also prompt strategies to hamper the development of internalized stigma or depressive symptoms among women living with HIV, and potential downstream effects. Strategies for the reduction of internalized stigma are suggested by the extant literature. A recent intervention to reduce internalized HIV stigma among African American women is on the horizon, consisting of group exercises in which women share stigma experiences and engage in role play scenarios designed to develop coping mechanisms and increase social support [56]. Future research may consider the feasibility of incorporating an internalized stigma reduction component into an existing and efficacious behavioral intervention for depression and adherence [57], or in combination with a medical intervention for depression, which have achieved clinically significant improvements in symptoms of depression but have had limited effects on ART adherence [58].

One of the strengths of this study was the geographically and racially diverse and large sample of women living with HIV from across the US, contributing to the generalizability of our results. We also used valid and reliable measures of assessment, such as the multi-item measure of internalized HIV-related stigma, which has incorporated relevant constructs and demonstrated discriminant validity [39]. In terms of analysis, we used mediation modeling with bootstrapping to examine the interconnected relationships, thus enabling us to examine how perceptions of interpersonal relationships could impact intrapersonal factors and behaviors.

This study has several limitations. First, since this study is based on cross-sectional data, we are unable to infer that the serial mediation relationship between perceived discrimination in healthcare settings and non-optimal adherence is causal. Second, our measure of perceived discrimination in healthcare settings was based on a single item. Our findings need to be replicated in future studies using multi-item discrimination scales. Third, self-reported measures of ART adherence have been criticized for their susceptibility to recall and social desirability biases. On the other hand, since self-report may overestimate actual adherence behavior, the report of any sub-optimal adherence is of clinical relevance and any significant associations with it warrant further exploration as endorsed by adherence guidelines [59].

In conclusion, much is at stake when people living with HIV perceive discrimination in a healthcare setting. The present findings suggest that perceived discrimination in healthcare settings contributes to internalization of HIVrelated stigma by women living with HIV, which in turn leads to depressive symptoms, with adverse effects on ART adherence. Future research should assess whether the serial mediation relationship described in this study holds true in longitudinal studies and also among men living with HIV. Interventions that aim to reduce HIV-related stigma and discrimination in healthcare settings may not only seek to document the impact on patient-reported perceptions of discrimination, but also on potential reductions in internalized stigma and depression, with the ultimate goal of improving health behaviors and outcomes.

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WIHS (Principal Investigators): UAB-MS WIHS (Michael Saag, Mirjam-Colette Kempf, and Deborah Konkle-Parker), U01-AI-103401; Atlanta WIHS (Ighovwerha Ofotokun and Gina Wingood), U01-AI-103408; Bronx WIHS (Kathryn Anastos), U01-AI-035004; Brooklyn WIHS (Howard Minkoff and Deborah Gustafson), U01-AI-031834; Chicago WIHS (Mardge Cohen, Audrey French), U01-AI-034993; Metropolitan Washington WIHS (Mary Young), U01-AI-034994; Miami WIHS (Margaret Fischl and Lisa Metsch), U01-AI-103397; UNC WIHS (Adaora Adimora), U01-AI-103390; Connie Wofsy Women's HIV Study, Northern California (Ruth Greenblatt, Bradley Aouizerat, and Phyllis Tien), U01-AI-034989; WIHS Data Management and Analysis Center (Stephen Gange and Elizabeth Golub), U01-AI-042590; Southern California WIHS (Alexandra Levine and Marek Nowicki), U01-HD-032632 (WIHS I-WIHS IV). The WIHS is funded primarily by the National Institute of Allergy and Infectious Diseases (NIAID), with additional co-funding from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), the National Cancer Institute (NCI), the National Institute on Drug Abuse (NIDA), and the National Institute on Mental Health (NIMH). Targeted supplemental funding for specific projects is also provided by the National Institute of Dental and Craniofacial Research (NIDCR), the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Deafness and other Communication Disorders (NIDCD), and the NIH Office of Research on Women's Health. WIHS data collection is also supported by UL1-TR000004 (UCSF CTSA) and UL1-TR000454 (Atlanta CTSA). This research was also supported by the University of Alabama at Birmingham (UAB) Center for AIDS Research CFAR, an NIH funded program (P30 AI027767) that was made possible by the following institutes: NIAID, NCI, NICHD, NHLBI, NIDA, NIA, NIDDK, NIGMS, and OAR. Trainee support was provided by the Agency for Healthcare Research and Quality (Grant No. T32HS013852).

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