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Impact of HIV-related stigma on medication adherence among persons living with HIV

Shannon M Sweeney, Luke D Mitzel and Peter A Vanable

This paper reviews recent studies on HIV-related stigma and medication adherence, including: (1) summary of the empirical evidence linking stigma to adherence, (2) discussion of proposed causal mechanisms of the stigma and adherence relationship, (3) examination of studies that have empirically tested causal mechanisms, and (4) methodological critique and directions for future research. Although there is substantial empirical evidence linking stigma to adherence difficulties, few studies provide data on psychosocial mechanisms that may account for this relationship. Two proposed causal mechanisms include (a) concerns about inadvertent disclosure of HIV status and (b) depressive symptoms. Future research should assess the multiple domains of stigma, address the multidimensionality of adherence, and include prospective analyses to test mediating variables.

Address
College of Arts & Sciences, Department of Psychology, Syracuse University, Syracuse, NY 13244, USA

Corresponding author: Vanable, Peter A (pvanable@syr.edu)

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Introduction

People living with HIV (PLWH) continue to encounter powerful stressors, one of which is the widespread social stigma associated with having HIV. Current research indicates that HIV-related stigma negatively impacts both the mental and physical health of PLWH [1,2]. Importantly, stigma has the potential to interfere with adherence to HIV medication regimens by virtue of its impact on coping and mental health functioning. Research also indicates that fear or anxiety over inadvertent disclosure of HIV status may result in poor adherence. For PLWH, strict adherence to antiretroviral medication regimens is necessary to prevent treatment failure and development of resistant virus [3–5]. Thus, clarifying the relationship between stigma and medication adherence has the potential to inform our understanding of barriers to optimal adherence and, subsequently, contribute to the development of interventions to improve HIV medication adherence.

The current article reviews quantitative and qualitative research that examines the relationship between HIV-related stigma and medication adherence in PLWH, with an emphasis on the most recent studies (2012–2014). First, we provide an overview of different types of HIV-related stigma. Following this overview, the article focuses on: (1) quantitative associations linking stigma to adherence and (2) proposed causal mechanisms of the relationship between stigma and adherence. Although only one of these mechanisms has been empirically tested, both mechanisms have the potential to advance scientific research and clinical practice. Finally, future directions and clinical implications are discussed.

Overview of HIV-related stigma

Stigma is a discrediting attribute that reduces a whole or usual person to a discounted person [6]. HIV-related stigma is considered a particularly complex phenomenon, given its associations with already marginalized behaviors, including injection drug use, sexual promiscuity, and homosexual behavior [7,8]. One recent framework hypothesizes that there are three different types of HIV-related stigma presumed to impact PLWH, and that these different types operate distinctly [9••]. First, *anticipated stigma* involves expectations of discrimination, stereotyping, and/or prejudice from others in the future due to one's serostatus. Similarly, *enacted stigma* involves experiences of discrimination, stereotyping, and/or prejudice from others that have already occurred. Finally, *internalized stigma* refers to self-endorsing negative feelings and beliefs about having HIV. These three stigma domains are conceptually related but distinct constructs [9••].

Quantitative associations between stigma and adherence

Single measures of stigma

Stigma measurement plays a vital role in understanding the relationship between stigma and medication adherence. Some of the earliest work addressing the relationship between stigma and adherence assessed a single domain of stigma, such as enacted or anticipated stigma [10–12]. In one of the first studies, Vanable and colleagues [12] reported a significant relationship between negative behaviors and mistreatment due to one's HIV status (i.e.,

enacted stigma) and poor medication adherence. A more common approach for studies published in recent years has been to use a single measure that includes items assessing multiple domains of stigma (i.e., anticipated, enacted, and internalized stigmas). The popularity of this approach is likely related to research indicating that stigma is a multidimensional construct [13], and thus reflects efforts by researchers to capture the full range of stigma domains.

Many of these studies have found that stigma is significantly associated with self-reported adherence difficulties at the multivariate level, after adjusting for factors such as demographics, perceived health, and alcohol and drug use [14–17]. However, additional studies have identified distinctions between univariate and multivariate analyses, particularly when depressive symptoms are considered alongside stigma [18,19•,20]. Of particular interest is a study by Levi-Minzi *et al.* [18], in which a stigma measure composed of four subscales was associated with adherence in univariate analyses, but adherence failed to predict any of the individual stigma subscales at the multivariate level. Instead, depression and social support emerged as significant predictors of these stigma subscales. Findings such as these suggest a more complex relationship between stigma and adherence, with depressive symptoms potentially playing a mediational role. With only two recent exceptions [21,22], studies examining a single measure of stigma have found a link to adherence difficulties.

Multiple measures of stigma

Compared to studies using single measures, assessment of multiple domains has been less explored in studies examining the impact of stigma on adherence. This approach includes measuring multiple domains of stigma (i.e., anticipated, enacted, and internalized stigmas) and examining their independent effects in multivariate analyses. The utility of this approach is that it may illuminate unique associations between different stigma domains and adherence difficulties.

Because researchers vary in the number and types of stigma domains they assess, the results can be difficult to compare across studies. Nonetheless, measures of internalized and anticipated stigmas have been found to be more consistently associated with adherence difficulties in multivariate analyses than enacted stigma measures [23••,24–27]. Of particular interest are two studies that simultaneously assessed internalized, anticipated, and enacted stigmas in multivariate analyses. Whereas Tilahun *et al.* [26] found a signification association between both internalized and anticipated stigmas and self-reported adherence difficulties, Earnshaw *et al.* [23••] found a marginal association between only internalized stigma and self-reported adherence difficulties. These findings suggest that anticipated and internalized stigmas may exert a more proximal influence on adherence behavior than enacted stigma.

Proposed causal mechanisms linking stigma to poor adherence

Disclosure concerns

Concerns regarding disclosure of HIV status may help to explain the association of stigma to adherence difficulties. PLWH's past experiences of stigma can intensify the desire to hide their illness in order to avoid further stigma. In turn, efforts to avoid illness disclosure may then interfere with medication adherence. Evidence that disclosure concerns play a role in the association of stigma to adherence emerges from qualitative studies. PLWH report not taking pills in public places or skipping doses if privacy is compromised [28,29]. In such situations, fear of inadvertently disclosing HIV status is frequently cited as the primary reason for missing doses [30]. Thus, by their own report, PLWH often choose to limit pill-taking behaviors to times and places in which there is little danger of revealing one's HIV status.

The threat of revealing one's HIV status is often pervasive across family and work contexts. PLWH cite concern about potential stigma and negativity from family members and intimate partners as reasons to avoid disclosing their HIV status [31,32]. Additionally, PLWH express a strong desire to conceal their medications in the workplace to avoid coworker questions about their health or inadvertent discovery of HIV medications. Coworker discovery of HIV status can lead to humiliation, alienation, or even possible termination [31–33]. Secretive measures, such as only taking pills on the way to work or hiding medication containers in bags once at work, can disrupt an already complicated medication regimen, increase the likelihood of delayed or skipped doses, and ultimately result in suboptimal medication adherence.

While qualitative work illustrates how stigma may interfere with adherence, quantitative research has not yet examined disclosure concerns as a mechanism that helps to explain the stigma-adherence relationship. There is, however, some evidence from quantitative work that disclosure concerns are relevant to this relationship. Studies show that PLWH are more likely to be concerned about disclosing their HIV status if they have experienced past stigma [34,35]. Additional research is needed to clarify the connection between stigma, disclosure concerns, and adherence.

Depression

Depressive symptoms may help to explain the association of stigma to adherence difficulties. PLWH may have internalized negative beliefs or feelings about having HIV. This internalized stigma may enhance vulnerability to depressive symptoms, such as increased fatigue, diminished concentration, and feelings of worthlessness,

which may cause lapses in adherence. Several recent studies empirically tested depressive symptoms as a mediator between stigma and adherence. These studies used measures combining multiple domains of stigma and self-reported measures of adherence. In one recent study, we found that depression, as assessed by the Center for Epidemiological Studies Depression Scale (CES-D), fully mediated the relationship between stigma and adherence difficulties [36•]. Consistent with these findings, Rao *et al.* [19•] found that depression, as assessed by the Patient Health Questionnaire (PHQ-9), partially mediated the relationship between stigma and adherence difficulties. In contrast, a study by DiIorio *et al.* [37•] using structural equation modeling found that self-efficacy mediated the relationship between stigma and adherence. Depressive symptoms, as assessed by four items from the CES-D, were instead found to mediate the relationship between social support and adherence.

The studies by Rao *et al.* [19•] and Mitzel *et al.* [36•] are the first to provide evidence that stigma may enhance vulnerability to depressive symptoms, which in turn may interfere with self-care related activities such as adherence. However, neither study controlled for important covariates, including social support and self-efficacy. Controlling for self-efficacy may be particularly important, as the perception of increased barriers to adherence that results from mental illness may be the proximal determinant of adherence difficulties [37•]. Understanding the specific types of depressive symptoms associated with stigma may also be essential, as one study reports that cognitive symptoms affect adherence more than vegetative symptoms [38]. Internalized stigma may have a stronger link to cognitive depressive symptoms, such as depressed mood, loss of interest, worthlessness, and poor concentration. In contrast, vegetative depressive symptoms, such as fatigue, loss of appetite, sleep disturbance, and psychomotor agitation, may overlap with HIV-related symptoms and inaccurately represent depressive symptomatology [39].

Conclusions and directions for future research

The present review summarizes recent research suggesting that first, stigma interferes with medication adherence among PLWH and second, disclosure concerns and depressive symptoms are two possible mediators of this relationship. We believe several directions for future research are especially promising.

First, research is characterized by the widespread use of global measures of stigma, which combine multiple domains of stigma into a unidimensional scale. A subset of studies have examined multiple domains of stigma simultaneously, an approach that can help to identify unique associations between stigma domains and adherence. Continued assessment of multiple domains of stigma, such as those delineated by Earnshaw *et al.* [9••], will allow for better comparisons across studies and provide more firm conclusions about these unique associations.

Second, despite frequent discussion of stigma as a multidimensional construct within this literature, it is striking that recent research has not also considered adherence as a multidimensional construct. Importantly, our recent work confirms the relevance of two types of nonadherence [40]. Intentional nonadherence includes an active decision-making process to disregard professional advice, whereas nonadherence that occurs inadvertently involves a passive process which is less strongly associated with beliefs and cognitions [41–43]. Our ongoing work is testing the hypothesis that stigma may be associated with intentional nonadherence.

Third, much of the available research has focused on direct associations between stigma and medication adherence. It will be important to expand this research by investigating the causal mechanisms accounting for this association. Recent studies have identified depressive symptoms as a possible mechanism. Another possible mechanism, concerns about inadvertent disclosure of HIV status, has been hypothesized but not tested using quantitative methodologies. Future studies should also test causal mechanisms between multiple domains of stigma and adherence in prospective analyses.

Finally, enhancing our understanding of these mediators may lead to subsequent improvements in interventions for adherence. Intervention effectiveness may be enhanced by including modules to strengthen PLWH's capacity to cope with stigma [44]. For example, treatment could involve educating patients about the interconnected nature of stigma, depressive symptoms, and adherence difficulties. Furthermore, we hypothesize that problem-solving focused on concerns regarding disclosure of HIV status may help PLWH to navigate the complex challenge of maintaining optimal adherence rates even if not open about one's HIV status. As future research continues to elucidate barriers and facilitators to optimal medication adherence, interventions must incorporate research advances in order to maximize the health and prevention benefits from antiretroviral medications for PLWH.

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