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## ART Adherence among Men Who Have Sex with Men Living with HIV: Key Challenges and Opportunities

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## ART adherence among men who have sex with men living with HIV: key challenges and opportunities

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### Abstract

**Purpose of review**—In the United States, gay, bisexual, and other men who have sex with men (MSM) are disproportionately affected by HIV. High levels of adherence to antiretroviral therapy (ART) can dramatically improve outcomes for persons living with HIV and reduce the risk of HIV transmission to others. Yet, there are numerous individual, social, and structural barriers to optimal ART adherence. Many of these factors disproportionately impact Black MSM and may contribute to their poorer rates of ART adherence. This review synthesizes the key challenges and intervention opportunities to improve ART adherence among MSM in the United States.

**Recent findings**—Key challenges to ART adherence including stigma, violence, depression, and substance use. Black MSM are significantly disadvantaged by several of these factors. There are several promising interventions to improve ART adherence among MSM, and there remains an opportunity to culturally-tailor these to the needs of Black MSM populations to enhance adherence.

**Summary**—Despite high rates of HIV among MSM, there continues to be a paucity of research on the various contributors to poor ART adherence among this population. Similarly, few interventions have been tested that lead to increased and sustained ART adherence among Black MSM.

### Keywords

Antiretroviral therapy (ART) adherence; Men who have sex with men; stigma; violence; depression

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This article does not contain any studies with human or animal subjects performed by any of the authors

## Introduction

In the United States (US), although the overall rates of HIV have remained relatively stable over the past decade, the incidence of new infections have increased among men who have sex with men (MSM), with those who are young and Black bearing the highest burden. Almost 70% of new infections among adolescents and adults in 2018 were attributable to male-to-male sexual contact.<sup>1</sup> Black and Latinx MSM face the greatest burden of HIV; 1 in 2 Black MSM and 1 in 5 Latinx MSM are projected to acquire HIV in their lifetime, compared to 1 in 11 white MSM.<sup>2</sup> These disparate rates highlight the fact that there are several distinct HIV epidemics.

Adherence to antiretroviral therapy (ART), a core tenet of the United States National HIV/AIDS strategy,<sup>3</sup> and a critical step in the HIV care continuum,<sup>4,5</sup> can improve health outcomes for people living with HIV (PLH) and reduce HIV transmission.<sup>6</sup> Since 2012, all US adults living with HIV have been recommended to initiate ART.<sup>7,8</sup> For patients who maintain adequate levels of ART adherence, HIV can be a manageable chronic condition and reduce risk for opportunistic infections.<sup>9,10</sup> Consequently, adherence is essential in suppressing viral load, maintaining high CD4 cell counts, prolonging survival, and reducing risk of transmitting HIV to others.<sup>6,11,12</sup> Viral suppression is the basis for the global public health initiative, Treatment as Prevention (TaP).<sup>13</sup> As such, optimal ART adherence is essential not only in improving individual health outcomes but also in the eradication of new infections. Additionally, ART adherence is associated with reductions in hospitalizations<sup>14</sup> and mortality,<sup>15–17</sup> slowed HIV disease progression,<sup>18,19</sup> and improved quality of life.<sup>20</sup> Yet, estimates suggest that approximately 63% of patients living with HIV have optimal ART adherence,<sup>12</sup> far lower than the goal of 90% set forth by UNAIDS.<sup>21</sup> In the US, only 60% of all MSM diagnosed with HIV are estimated to achieve viral suppression,<sup>22</sup> with significantly lower rates documented among young MSM.<sup>23</sup> Black and Latinx MSM have poorer viral suppression rates relative to their White MSM counterparts, even after adjusting for insurance type, duration of ART use, and CD4<sup>+</sup> cell count.<sup>24</sup> Moreover, although ART prescription and viral suppression rates increased among all racial and ethnic groups of MSM between 2009 and 2013, racial and ethnic disparities remain, particularly between Black and White MSM.<sup>25</sup> Black PLH are less likely to be engaged in HIV care, receive ART, and adhere to ART long enough to be virally suppressed compared to individuals of other races or ethnicities.<sup>26–28</sup> Racial and ethnic minority youth are at particularly high risk of poor ART adherence and thus, having a detectable viral load.<sup>27,29</sup>

The purpose of this review article is to identify key challenges to ART adherence faced by MSM in the United States and posit some of the mechanisms by which they may compromise ART adherence. In doing so, we highlight how factors such as stigma, substance use, depression, anxiety, and violence are structural factors that have been linked to suboptimal ART adherence and disproportionately impact Black and Latinx MSM. We conclude with highlighting several promising interventions to improve adherence rates.

## Challenges to achieving optimal ART adherence among MSM living with HIV

### Stigma

There is strong evidence that various domains of stigma contribute to poor ART adherence.<sup>30,31</sup> Stigma domains include: enacted stigma, or prior experiences with discrimination, prejudice, and stereotyping associated with one's HIV status; anticipated stigma, or the expectation of discrimination or prejudice from others due to one's serostatus; and internalized stigma, or the self-endorsing negative feelings and beliefs about living with HIV.<sup>32-34</sup> Stigma is particularly important to consider for MSM and MSM of color, for whom HIV stigma may intersect with stigmas associated with their sexual and racial identities.<sup>35</sup> The stigmatization and marginalization of racial and ethnic minorities in the United States can include overt discrimination and mistreatment as well as brief, commonplace microaggressions.<sup>36</sup>

The literature on the mechanisms linking stigma to ART adherence and other poor HIV health outcomes remain limited, yet there are several proposed causal mechanisms including vulnerability to mental health challenges<sup>37,38</sup> and reduction in self-efficacy for medication taking,<sup>39</sup> although such mechanisms remain understudied, particularly among Black and Latinx MSM. A 2016 systematic review by Sweeney and Venable found mounting evidence that numerous HIV stigma indicators interfere with ART adherence among PLH by reducing self-efficacy for adherence and self-care and raising concerns about inadvertent disclosure of HIV status.<sup>30</sup> Yet, studies that have examined multiple domains of stigma have revealed variation in the ways in which stigma influences ART adherence.

Enacted stigma includes experiences of discrimination and prejudice associated with living with HIV or having other stigmatized identities, including sexual, gender, and racial identity. Perceived discrimination is associated with suboptimal ART adherence.<sup>40</sup> This is evidenced by research by Galvan and colleagues (2017), that found that among Latino PLH, perceived discrimination associated with being Latino and living with HIV were associated with lower ART adherence, mediated by medical mistrust.<sup>41</sup> Similarly, Eaton and colleagues (2015) found that perceived stigma or mistreatment due to sexual identity or race from health care providers was associated with longer elapsed time since last appointment with an HIV provider among Black MSM, which may interfere with ART adherence.<sup>42,43</sup> Experiences of discrimination may negatively impact patient-provider relationships and make it difficult for racial and ethnic minority patients to trust providers, subsequently affecting ART adherence. Although not specific to MSM, data from the Women's Interagency HIV Study (WIHS) found that perceived discrimination in healthcare settings may contribute to internalized HIV stigma, with downstream adverse effects on ART adherence.<sup>44</sup> Future longitudinal studies among MSM PLH are needed to better understand how health care institutions and practices influence patient experiences and perceptions of discrimination and stigma and contribute to suboptimal HIV outcomes.

Research suggests the relationship between discrimination and ART adherence may be mediated by medical system mistrust.<sup>41</sup> Institutionally-sanctioned discrimination and

medical mistreatment have contributed to medical mistrust among Black Americans.<sup>42,45,46</sup> Furthermore, beliefs implicating the government in the origins of HIV and withholding of a cure, may be rooted in historical mistreatment of Black Americans including medical experimentation on Black slaves, involuntary sterilization, and the Tuskegee Syphilis Study.<sup>47</sup> Medical mistrust may be related to historical and contemporary stigma and discrimination against Black Americans,<sup>47-49</sup> particularly in healthcare settings.<sup>35,42</sup> Medical mistrust is associated with lower rates of ART adherence and higher viral load among Black MSM,<sup>46,50,51</sup> and associations between medical mistrust and non-adherence to ART are stronger among older Black MSM, as compared to their younger, white counterparts.<sup>52</sup>

Research on the relationship between anticipated HIV stigma, or the expectation that one will experience prejudice and discrimination as a result of others learning of their HIV status, and ART adherence has had mixed conclusions.<sup>53-56</sup> Recent cross-sectional research with a sample of primarily Black PLH found anticipated stigma to be positively associated with increased medication concerns and treatment non-adherence.<sup>57</sup> However, in our prior research, greater concerns about public attitudes toward HIV (anticipated stigma) were positively associated with medication adherence, such that individuals who were more concerned about how the public perceived PLH had greater ART adherence than those who were less concerned about public perceptions.<sup>58</sup> Greater research is needed to understand anticipated stigma experienced by PLH and its effects on ART adherence.

Extant, albeit limited, research suggests that internalized stigma has a stronger association with suboptimal ART adherence<sup>53,59</sup> than anticipated or enacted stigma.<sup>53,60</sup> Researchers have found that PLH who internalize HIV-related stigma may have lower medication self-efficacy or confidence in their ability to adhere to ART, particularly during difficult times, which can decrease adherence.<sup>61</sup> PLH with internalized HIV stigma may also face concerns about being seen taking HIV medications, subsequently reducing adherence.<sup>61</sup> Drawing on recent research from other PLH populations, data suggest that internalized stigma may negatively influence medication adherence via decrease adherence self-efficacy or avoidant coping.<sup>61,62</sup> However, more research is needed on how internalized stigma affects ART adherence among MSM, particularly racial and ethnic minority MSM, who often face compounded stigma and discrimination related to the intersection of race, sexual identity and HIV status.<sup>63,64</sup>

## Violence and trauma

Trauma and violence disproportionately affect MSM living with HIV<sup>65</sup> and influence HIV care outcomes via a variety of psychological (e.g. post-traumatic stress disorder, depression, anxiety) and behavioral (e.g. substance use) sequelae.<sup>66,67</sup> In our previous research with young Black MSM, we found high levels of exposure to community violence; 40% of participants had a close friend or relative die due to community violence, 52% had been a victim of violence, and 42% had witnessed a gun-related incident in their community. Furthermore, high levels of community violence were associated with significantly lower odds of ART adherence.<sup>68</sup> Similar results have been found among PLH who have experienced extreme violence or death-related trauma; in a recent study by Brown and colleagues (2019), men who reported exposure to any trauma were 58% less likely to be

adherent to ART; those who experienced extreme violence or death-related trauma were 63% less likely to be adherent to ART.<sup>69</sup>

Research has examined HIV-related health outcomes among PLH who have experienced Intimate partner violence (IPV), although research among IPV among MSM PLH is lacking. Most commonly IPV literature among PLH focuses on women in opposite-sex relationships.<sup>70–72</sup> Yet, rates of IPV among MSM are comparable or higher to those seen among heterosexual women,<sup>73</sup> with estimated prevalence range from 12%<sup>74</sup> to 45%.<sup>75</sup> Yet little recent research has examined the effects of IPV on ART adherence among MSM. Finally, childhood sexual abuse (CSA) is another form of violence that disproportionately affects MSM<sup>76,77</sup> and PLH.<sup>78–82</sup> Research has shown a strong and positive relationship between CSA and HIV risk behaviors and infections<sup>83</sup> and poorer HIV continuum of care outcomes<sup>84</sup> among MSM. Although extant research is mixed, recent literature suggests trauma and violence might negatively impact ART adherence through a variety of mechanisms. For example, trauma may induce substance misuse which is negatively correlated with ART adherence.<sup>85</sup> Persons who engage in heavy substance use might forget to take their medications, may have more missed medical appointments and/or forget to fill prescriptions. Additionally, trauma may also induce depression, feelings of low self-efficacy and self-worth, mood dysregulation all of which in some studies are associated with lower rates of self-care and compliance with positive health seeking behaviors and medical adherence.<sup>86,87</sup>

### Substance use

Alcohol and substance misuse are among the most common barriers to ART adherence among adults and adolescents living with HIV.<sup>68,88–91</sup> Substance use is a well-documented risk factor for HIV infection among MSM and may exist prior to one's HIV infection.<sup>92,93</sup> MSM may use substances to cope with experiences of shame, stigma, and inhibition when exploring sexual desires and identities, increasing risk for HIV.<sup>94</sup> Additionally, PLH may also use substances as a coping mechanism for dealing with an HIV diagnosis.<sup>95</sup> A qualitative study with Black and Latinx PLH (60% of whom were MSM) found that heavy substance use, as compared to social or casual use, impeded ART initiation by undermining medication management abilities and contributing to depressive symptoms.<sup>96</sup>

In a longitudinal examination of ART adherence among young Black MSM, our prior research found that higher levels of alcohol and marijuana use were among the strongest predictors of suboptimal ART adherence.<sup>91</sup> Alcohol use can impede ART adherence through multiple mechanisms, including impaired memory, cognitive distortions, hangover effects, and other factors leading to treatment lapses.<sup>97,98</sup> Furthermore, as many as half of people on ART who drink alcohol intentionally delay or forgo taking their ART when drinking,<sup>99–101</sup> partially due to toxicity concerns about mixing alcohol and certain HIV antiretrovirals. Although mixing ART with alcohol is not completely benign, it does not present toxicity concerns and there are no major health concerns resulting from mixing ART medications and antiretrovirals.<sup>100</sup> In other research with young Black MSM, researchers demonstrated a relationship between anxiety and alcohol and marijuana use, which contributed to poor ART adherence.<sup>102</sup> Similar research found that among a sample of Black youth living with HIV,

poor ART adherence was positively associated with higher psychological distress and weekly marijuana use.<sup>103</sup>

A large body of research has examined the use of methamphetamine among MSM.<sup>104–106</sup> Research by Feldman and colleagues (2015) found that among a sample of MSM living with HIV in New York, crystal meth use was associated with unsuppressed viral load.<sup>106</sup> Similarly, researchers have found that among MSM living with HIV with recent methamphetamine use, only 25% reported taking at least 90% of their ART medications.<sup>105</sup> However, they also found that substance use disorder treatment was also associated with significantly greater odds of ART adherence.<sup>105</sup> This has been supported by other research, which has found substance use treatment to help facilitate ART initiation and adherence. For example, medications for opioid use disorder, such as methadone maintenance treatment, can positively benefit ART adherence. A systematic review and meta-analysis on opioid substitution programs on HIV treatment outcomes found that opioid treatment programs were associated with a 69% increase into ART initiation, a two-fold increase in ART adherence, and a 45% increased odds of viral suppression.<sup>107</sup> More recent research, however, has shown that among opioid-dependent individuals maintained in a methadone treatment program, one in five were not able to achieve viral suppression.<sup>108</sup> A systematic review of HIV treatment adherence among people who inject drugs found that substance use treatment, specifically methadone maintenance therapy, facilitates ART adherence.<sup>109</sup> Individuals who use drugs and are newly diagnosed with HIV have faster entry into HIV care when they participate in substance use treatment compared to those who do not participate in substance use treatment.<sup>110</sup>

### Depressive symptoms

Depression is one of the most commonly-reported mental health challenges experienced by MSM living with HIV.<sup>111</sup> Prevalence of major depressive disorder among PLH have been reported to be as high as 37%, three times the rate found in general populations.<sup>112,113</sup> Depression is associated with feelings of worthlessness, hopelessness, low self-efficacy, and loss of interest, which can act as barriers to self-care behaviors needed for disease management and ART adherence.<sup>114,115</sup> MSM living with HIV may also use avoidant coping strategies to minimize the stress associated with their HIV status, including evading activities related to managing their HIV such as engagement in care and ART adherence.<sup>116</sup>

Numerous studies have examined the relationship between depression and sexual risk behaviors among MSM,<sup>111,117,118</sup> yet fewer have explored the effects of depression on ART nonadherence.<sup>119–121</sup> A systemic review of the literature found that the odds of achieving optimal ART adherence were lower among persons reporting depression when compared with those reporting no depression.<sup>122</sup> However, a recent study among MSM in San Francisco found no evidence that depressive symptoms lead to an increase in ART nonadherence among men living with HIV, although they did find an association between depressive symptoms and concurrence of ART nonadherence and condomless sex.<sup>121</sup>



## Syndemics

Although we briefly reviewed the literature on the independent contributions of stigma, violence, substance use, and depressive symptoms on ART adherence, there is evidence to suggest that for some MSM, many of these psychosocial conditions are co-occurring and mutually-reinforcing, operating as part of a syndemic.<sup>31,123–125</sup> Syndemics refers to the co-occurrence and interaction of multiple psychosocial and health conditions at the individual- and population-level that synergistically contribute to an excess burden of disease, including HIV.<sup>126</sup> Partly due to racism, structural inequality, residential segregation, a higher proportion of poverty, and policing, Blacks and Latinx populations face greater syndemic conditions.<sup>127</sup> Research has demonstrated how various co-occurring psychosocial conditions, including depression, childhood sexual abuse, intimate partner violence, and polysubstance use, increase risk for HIV and poor HIV outcomes.<sup>125,128,129</sup> The exact mechanisms by which syndemics influence ART adherence have yet to be untangled. For example, greater syndemic conditions may contribute to higher levels of stress, decreasing ability to plan and engage in daily health care behaviors.<sup>130</sup> Alternatively, syndemic conditions may impede self-efficacy around medication adherence and other self-care behaviors.<sup>130</sup> Additional research is needed to understand the pathways by which syndemics influence ART adherence, particularly for Black MSM.

Research by Friedman and colleagues (2016) found that among a racially diverse sample of MSM living with HIV, ART non-adherence was positively associated with increased syndemic conditions including depressive symptoms, polysubstance use, and sexual risk behaviors.<sup>127</sup> These findings were supported by more recent research by Harkness and colleagues (2018); in a longitudinal analysis of MSM living with HIV, they found that syndemic conditions were additively and longitudinally associated with greater non-adherence to ART.<sup>130</sup> Research with youth living with HIV has found that multiple conditions, including depression, anxiety, substance use, and HIV stigma, have an additive effect on ART adherence, with increasing numbers of conditions decreasing the likelihood of adherence and reducing the odds of viral suppression.<sup>102</sup> Similarly, among adults, greater number of syndemic conditions, including childhood abuse, current violence exposure, alcohol or substance dependence, post-traumatic stress disorder, anxiety, and other mood disorders) were associated with increased odds of reporting suboptimal ART adherence.<sup>131</sup>

## Promising interventions to improve ART adherence among MSM

Given suboptimal rates of ART adherence among MSM, and especially those who are Black and Latinx, researchers and healthcare providers have been working to identify and intervene on the key barriers to adherence. However, despite the clear need, few ART adherence interventions have explicitly focused on MSM.<sup>10,132,133</sup> In a 2017 systematic review of United States-based ART adherence interventions published between 2007 and 2015, only two focused on MSM.<sup>132</sup> A 2018 review of more recently published studies identified an additional six mHealth ART adherence interventions for MSM living with HIV.<sup>133</sup> A 2015 systematic review of interventions to enhance ART adherence among diverse samples of PLH found a paucity of high-quality that were effective at improve ART adherence and clinical outcomes.<sup>134</sup> Despite the paucity of research, collectively, these



findings have implications for future adherence research and intervention development to address poor adherence among PLH.

In general, adherence randomized trials have only demonstrated a modest effect in improving adherence, which may be due to the multiple individual and structural challenges facing many PLH,<sup>88</sup> and the multiple syndemic conditions faced by MSM as described above. There is a need for multi-level interventions that address the structural and social barriers to ART adherence. For example, stigma and resilience theories suggest that neighborhoods with lower levels of HIV stigma and homonegativity may be more supportive of ART adherence, facilitating supportive social networks and positive behavioral and attitudinal norms.<sup>135–137</sup> Interventions are needed that address mistrust of the health care system, racism and homonegativity, and other social inequities facing Black MSM. Rather than focusing on modifying patient behaviors, efforts are needed to improve systems and communities in which Black MSM live and develop services tailored to meet the needs of Black MSM.

For youth, specifically, there are relatively few tested interventions to improve ART adherence, most with only modest effects.<sup>138–145</sup> A systematic review by Shaw and Amico (2016) of effective ART adherence intervention strategies for youth found evidence of promising results among several pilot studies, but highlighted the need for more adherence-related trials with youth with larger sample size, longer follow-up periods, and tailoring to specific populations (e.g. sexual and gender minorities or racial minorities).<sup>146</sup> Interventions that focus on primary drivers of poor adherence such as reminders<sup>140,142</sup> or motivation to take medication,<sup>139</sup> engagement with the healthcare system,<sup>147</sup> or providing social support for medication adherence<sup>141,145</sup> may be appropriate for some PLH, yet individuals experiencing multiple psychosocial and syndemic barriers to adherence would likely benefit from more intensive multi-level interventions.<sup>148</sup>

Interventions utilizing social networks may also hold promise. A recent study among a diverse sample of MSM living with HIV utilized existing social network support to enhance ART adherence. Results indicate that reminders from a social network member to take ART medications ameliorated the negative association between depression and ART adherence. Similar peer-to-peer support interventions among existing social networks may be a cost-effective way of improving ART adherence, particularly among PLH with depression.<sup>149</sup>

Social network interventions, when combined with mhealth or electronic tools, may be particularly beneficial, as there is compelling evidence for technology-based interventions that improve ART adherence. mHealth interventions to support ART adherence including text messages, apps, and social media interventions, have demonstrated acceptability, feasibility, and preliminary efficacy.<sup>133,150</sup> For example, *Thrive with Me* is a technology-delivered peer-support ART adherence intervention for MSM that includes electronic peer communication, tailored adherence information, text message reminders, and text-based mood, adherence, and substance use-self-monitoring. Pilot results demonstrated high feasibility, acceptability, and significant improvement in self-reported ART adherence.<sup>151</sup> A larger, RCT is currently underway.<sup>152</sup> LeGrand and colleagues (2016) recently demonstrated high feasibility and acceptability of a gaming app to improve adherence among young PLH.

<sup>150</sup> Similarly Horvath and colleagues (2016) found support for a mobile phone app to optimize ART adherence among MSM living with HIV who use stimulants.<sup>153</sup> These studies demonstrate the promise of such novel interventions, yet more research is needed to test the effectiveness of apps in improving ART adherence.

Given the strong relationship between substance use, depression, and suboptimal ART adherence, interventions are needed that treat substance use disorders and mental health to help individuals better manage their healthcare.<sup>89</sup> However, a recent meta-analysis of psychological interventions to improve ART adherence found that although individual-level psychological interventions, including cognitive behavioral therapy or other discussions of cognitions, motivations, and expectations are effective strategies to improve ART adherence in the short-term, there is a lack of evidence demonstrating long-term improvements in ART adherence and clinical outcomes.<sup>154</sup> Yet, despite a growing literature base, more intervention trials are needed with longer follow-up periods, dose monitoring adherence measurement strategies, and greater attention to the specific components of technology that impact ART adherence and the individuals most likely to benefit from such approaches.<sup>155</sup> While all the above-mentioned interventions are promising there is an opportunity include more racialized populations into these clinical trials, so that findings and evidence are based on and relevant to diverse populations. In addition, the expertise of Black and Latinx communities must be better harnessed and incorporated by developing more authentic and reciprocal relationships with university and communities in order to better understand and address the barriers to ART adherence among these populations.

## Conclusions

The barriers to optimal ART adherence among MSM are multifaceted and likely require similarly multifaceted interventions that adequately account for complex and indirect barriers to adherence (e.g. stigma and community violence). The vast majority of ART adherence interventions focus on the individual-level behavioral and psychosocial interventions.<sup>156</sup> While such interventions have been implemented with varying levels of success, a review of the literature also highlights the importance of intervening in more distal factors including stigma and violence. As MacDonell and colleagues (2010) have previously noted, successful ART adherence interventions must target the broad range of factors that influence ART adherence decisions, including cultural, developmental, psychosocial, and societal factors.<sup>157</sup> Thus, while screening for and intervening on behavioral barriers to ART adherence (e.g. depressive symptoms, substance use), more research is needed to understand and intervene on social and structural barriers to adherence.

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