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Authors

Sauceda, John A

Neilands, Torsten B

Johnson, Mallory O

et al.

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An update on the barriers to adherence and a definition of self-report non-adherence given advancements in antiretroviral therapy (ART)

John A. Sauceda[1], **Torsten B. Neilands**[1], **Mallory O. Johnson**[1], and **Parya Saberi**[1]

[1]Center for AIDS Prevention Studies, Department of Medicine, University of California - San Francisco, San Francisco, CA, United States

Abstract

Relying on the most frequently reported barriers to adherence and convenient definitions of non-adherence may lead to less valid results. We used a dominance analysis (a regression-based approach) to identify the most important barriers to adherence based on effect size using data collected through an online survey. The survey included the Adherence Barrier Questionnaire, self-reported non-adherence defined as a 4-day treatment interruption, and HIV clinical outcomes. The sample (N = 1, 217) was largely male, gay identified, and White. Nearly 1 in 3 participants reported “simply forgot” as a barrier; however, in a dominance analysis, it yielded a small effect size it its association with a 4-day treatment interruption. Further, dominance analyses stratified by race/ethnicity and age suggested that not all barriers impact all groups equally. The most frequently reported barriers to adherence were not the most important, and interventions should focus on barriers more strongly linked to clinical outcomes.

Keywords

Antiretroviral Therapy; Adherence Barriers; Adherence; Dominance Analysis; Relative Importance

INTRODUCTION

Current preferred antiretroviral therapy (ART) regimens are simpler, better tolerated, and more potent but less toxic [1, 2]. These features of ART have major implications for adherence research. For example, currently preferred ART regimens are forgiving of minor lapses in adherence given their potency, which challenges the validity of defining non-adherence as “imperfect” or “sub-optimal” without recognizing the pattern of missed doses

Corresponding Author: John A. Sauceda, Ph.D., M.Sc., Center for AIDS Prevention Studies, University of California, San Francisco, 550 16th Street 3rd Floor, San Francisco, CA, United States, john.sauceda@ucsf.edu.

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards; as approved by the University of California, San Francisco’s Institutional Review Board.

Informed consent: Informed consent was obtained from all individual participants included in the study.

[3–5]. And given the simplicity and tolerability of current preferred ART, many "traditional" barriers to adherence (e.g., regimen complexity, feeling sick) are obviated [6].

Although the literature on the barriers to adherence is vast, there is limited empirical data to show which barriers have the biggest impact on adherence (i.e., beyond those most frequently reported by patients or cited in studies) [6, 7]. For example, in one Danish cohort study, "simply forgot" was the most frequently reported barrier to adherence regardless of the level of adherence or viral load (VL) [8], while another study of 11 AIDS Clinic Trials Group datasets found that the most frequently reported barriers by participants were not the barriers most associated with a detectable VL [9].

In research and clinical settings, self-report measures are and will continue to be the most convenient tool for assessing adherence and the barriers to adherence [10]. However, the potency of ART challenges the ecological validity of popular and convenient definitions of self-reported non-adherence that continue to be used (e.g., a number of doses missed in past 7 days, less than 100% of doses taken in the past 30 days, or adherence above/below an arbitrary threshold of 80%) [4, 6, 11, 12]. To better approximate treatment failure risk, non-adherence as a treatment interruption could be used [13]. A treatment interruption is conceptually more valid because it measures the number of days that ART was not taken (i.e., the therapeutic coverage was low or zero) [12, 13].

To address the aforementioned gaps in the literature, this study re-examines the "traditional" barriers to adherence by empirically evaluating how "important" they are to a 4-day ART treatment interruption (i.e., "importance" is determined by effect size in a dominance analysis). First, the most-to-least frequently reported barriers to adherence were ranked by the percentage of participants reporting a particular barrier. Second, using a regression-based dominance analysis, the same barriers were ranked from most-to-least important by effect size. Our *primary hypothesis* was that ranking barriers to adherence by frequency yields a different order than ranking by effect size (i.e., the empirical approach). Our *exploratory analysis* tested if the rankings of barriers by effect size were invariant across race/ethnicity and age subgroups.

METHODS

Data come from a survey study that recruited people living with HIV (PLWH) in the U.S from online social media platforms. The objective of the study was to harness mobile technologies and social media to more effectively recruit PLWH in research, which can help avoid selection biases associated with some structural barriers to research (e.g., ability to take time off work, travel to research site). The survey questions focused on factors that affect ART adherence [14]. To facilitate enrollment and eliminate barriers to participation, advertisements for the study survey were placed on Facebook, Twitter, Craigslist, etc., which could be accessed at any time from May to August of 2013. Each social media advertisement contained a web link to an online Qualtrics research survey. Each web-link directed individuals to the eligibility screener and online consent form [14].

Participants

Participants were 1) 18 years or older, 2) HIV-positive, 3) and currently living in the U.S. To eliminate repeat and fraudulent surveys, the survey program only allowed for one Internet Protocol (IP) address to be used (which was not collected or known to the authors for privacy protection), and no monetary incentives were provided. Motivation to complete the survey was enhanced by placing relevant HIV medical facts throughout the survey and embedding a video link that described the development of a new HIV treatment. No identifying information was collected to enhance privacy, and data were stored on encrypted university servers. The survey had 112 questions and nearly 87% of individuals who answered the first question completed all questions [14]. The [Redacted for blind review] Institutional Review Board approved this study.

Measures

Demographics—Study demographics included age, sex at birth (male or female), education income, and race and ethnicity (non-Latino White, African American, Latino and other).

ART and HIV Clinical Data—Participants reported the daily dosing frequency of their ART regimen, which was coded as: 1) once daily, 2) twice daily, and 3) three-times a day or greater, and their CD4+ cell count (range 0 to 3,000 cells/mm^3) and HIV viral load (VL) laboratory test result from their most recent clinic visit ("undetectable" = 0, "detectable" = 1) [15].

AIDS Clinical Trials Group Adherence Barrier Questionnaire (ABQ)—The ABQ assesses 14 reasons (i.e., barriers) for missing a dose of ART [16]. The items read as "in the past when you have missed your [ART], have you missed taking your medications because…e.g., you were away from home, or simply forgot (Table 2 list all items). Participants responded "yes" or "no" to each barrier as it applied to them. Additionally, to better capture the breadth of possible barriers to adherence (those not included in the ABQ measure), six additional barriers were used in this study that were derived from qualitative interviews for the purposes of developing a modern, telehealth adherence intervention: "had problems with your pharmacy"; "had problems with your insurance company"; "were drinking alcohol"; "were using illicit drugs"; "were reminded of having HIV" and "other reasons" [17].

Preliminarily, there were a total of 20 barriers but seven barriers were rarely reported. Any barrier with less than a 2% response was eliminated from the study *a priori* (e.g., <1% or 7 of 1217 participants reported "felt good" or "had too many pills to take" as a reason for a missed dose). The 13 remaining barriers were collapsed into 9 distinctly "intervenable" categories of barriers upon review by a clinical pharmacist/researcher, two psychologists, and a statistician. Consensus was achieved before any statistical tests were run. The collapsed barriers were the alcohol and drug barrier (i.e., yes to "drinking alcohol or using illicit drugs"), the pharmacy and insurance barrier (i.e., yes to "problems with pharmacy" or "problems with insurance"); and the "away from home", "busy with other things", and "routine change" barriers into one item titled the "day-to-day life" barrier. The final list is in

Table 2 (7 of 9 were original ABQ items). Total scores are the summation of the number of barriers reported.

ART Non-adherence—Non-adherence was defined as self-reporting *at least one 4-day period where zero ART doses were taken in the past three months* (0 = no interruption, 1 = at least one interruption) [18]. For descriptive purposes, we also assessed adherence as the percent of ART taken (on a scale from 0% to 100%) and ART ability ratings (i.e., rate your ability to take all your medications as prescribed from 0-*very poor* to 6–*excellent*) in the past 30 days [19].

Statistical Analysis

Descriptive statistics were used to characterize the sample and bivariate correlations were used to test associations among adherence variables. We compared the most-to-least frequently reported barriers to adherence (from the largest to smallest percentages of responses) against the most-to-least important barriers to adherence based on effect sizes (described below) to examine whether perceptions about the barriers to adherence are ranked in the same order as the barriers most strongly associated with a 4-day treatment interruption.

Overview of Dominance Analysis and Predictor "Importance"—Dominance analysis is a pairwise regression approach that tests *all possible* barriers against one another as a measure of predictor "importance." In dominance analysis, "importance" refers to size of the effect rather than the adjective to mean "of great significance". Thus, this analysis is suited to answer *what is the most important barrier to adherence?* (e.g., is the "simply forgot" barrier is more important than the "feeling depressed/overwhelmed" barrier?) [20–22]. In dominance analysis, each barrier (i.e., predictor) competes against every other barrier in its ability to predict ART non-adherence. For reasons beyond the scope of this study, [20, 21] traditional multiple regression is not appropriate for assessing "importance," especially when multi-collinearity is an issue (i.e., when predictors are all correlated). The effect size is called a dominance weight and is the *average squared semi-partial correlation* (i.e., corrects for multicollinearity) between each barrier and a treatment interruption (larger weight = more importance). We performed a dominance analysis in the total sample and then conducted exploratory stratified analyses to investigate how the importance of each barriers may vary by race/ethnicity: a) non-Latino Whites, b) Latinos, and c) African Americans, and by age: a) young adults (18–29 yrs.), b) middle-aged adults (30–49 yrs.), and c) older adults (>50 yrs).

Interpreting Dominance Weights and Patterns—Dominance weights reveal the strength of association between each barrier and a 4-day treatment interruption, while dominance patterns characterize the consistency of importance (i.e., *does one barrier consistently outperform other barriers in predicting ART non-adherence?*) [20]. Dominance patterns are qualified as *general* (least dominant), *conditional* (somewhat dominant) or *complete* dominance (most dominant) [21]. These patterns describe the size of each barrier's dominance weight relative to its consistency in being less, equal, or more important than every other barrier [20].

Odds Ratios

After the dominance analysis was conducted, we used M*plus* software to conduct a path model and set the five barriers with the largest dominance weights to predict the odds of a treatment interruption (scores of 0 or 1), which in turn was postulated to predict odds of a detectable VL (scores of 0 or 1), after adjusting for age and sex at birth (covariates that evidenced preliminary bivariate associations with adherence). We chose the five barriers with the largest weights for ease of interpretation (however, all barriers are listed in the tables throughout the paper). The path analysis is complementary to the dominance analysis in that it provides estimates of each barrier in the familiar odds ratio metric and enables examination of barriers' effects on non-adherence and VL simultaneously.

RESULTS

The total sample (N = 1, 217) was largely male (94.7%), gay identified (87.1%) and non-Latino White (76.3%), with an average age of 46.7 years (SD = 10.9). A majority of participants reported a once-daily dosed ART regimen (~70%) and 13% reported a detectable VL. Table 1 list the full set of descriptive statistics.

Participant Rankings

Overall, 39.2% of the total sample reported no barriers to adherence, 30.2% reported one, 16.1% reported two, and 14.4% reported three or more (range 0 to 7; M = 1.16, SD = 1.33). Five of the nine most frequently reported barriers in the total sample were "simply forgot" (33.7%), "day-to-day life" (27.6%), "drinking alcohol or using illicit drugs" (10.5%), "felt depressed/overwhelmed" (9.5%) and "ran out of pills" (6.6%). Table 2 lists all nine barriers. Greater total barrier count scores were negatively associated with adherence ability ratings (r = −0.38, p<.001) and the percent of ART doses taken in the past 30 days (r = −0.24, p < 0.001), positively associated with a treatment interruption (r = 0.24, p < 0.001), and not directly associated with VL (r = .01, p = 0.73). A treatment interruption was negatively associated with adherence as past 30-day adherence ratings (rs = −0.45 and −0.36, p < 0.001; See Table 1).

Dominance Analysis for the Total Sample

The gray scale in Table 2 shows how the participant rankings of each of the nine barriers differed from the results of a dominance analysis. In terms of importance and parsimony, we focused on five of the nine barriers with the largest dominance weights (standardized average squared semi-partial correlations), which were: "fell asleep/slept through dose time" (0.329), "felt depressed/overwhelmed" (0.313), "day-to-day life" (0.116), "wanted to avoid side-effects" (0.110), and "drinking alcohol or using drugs" (0.040). All rankings are listed in Table 2.

In support of the *primary hypothesis*, differences were observed between participants' perceptions about the barriers to adherence and empirical results from a dominance analysis. First, the "fell asleep/slept through dose" barrier was the single most important barrier to adherence (0.329; ranked #1 in the dominance analysis), although it was the sixth most frequently reported barrier (6.2% of the total sample). Second, the "felt depressed/

overwhelmed" barrier was the second most important barrier (0.313) although it was the fourth most frequently reported barrier (9.5%). Lastly, a large difference occurred with the "wanted to avoid side-effects" barrier, which was the fourth most important barrier (0.110) but second to last (4.1%) in terms of frequency reported. Table 2 displays all comparisons. Notably, the "simply forgot" barrier was overwhelmingly the most frequently reported barrier to adherence (33.7%), yet yielded a small dominance weight (0.035). Table 2 shows all patterns and weights.

Dominance Analysis Patterns for the Total Sample

The three barriers with the largest dominance weights ("fell asleep/slept through dose," "felt depressed/overwhelmed," and "day-to-day life" barrier; Table 2) were shown to be more important than other barriers based the dominance pattern conditions. The conditions describe the size of each of the three barrier dominance weights as being consistently more important than other barriers in predicting ART non-adherence.

The #1 ranked "fell asleep/slept through dose" barrier and #2 ranked "felt depressed/overwhelmed" barrier *completely* dominated all others barriers (but not each other). The interpretation of this pattern is that the "fell asleep/slept through dose" and "felt depressed/overwhelmed" barriers singularly contributed the most variance to the outcome of ART non-adherence when compared to any other barrier in any other model tested. Similarly, the #2 ranked "felt depressed/overwhelmed" barrier c*onditionally* dominated the #3 ranked "day-today life" barrier (i.e., the *average* variance contributed by the "felt depressed/overwhelmed" barrier across all possible regression models was greater than the size of any contribution made by the "day-to-day" life barrier).

Exploratory Dominance Analysis by Race and Ethnicity

The results of dominance analyses conducted for each subgroup are displayed in Table 3 (the gray scale is used to show the how the three most importance barriers varied across these stratified subgroups). No race/ethnicity subgroups ranked all nine barriers to adherence exactly the same, although some similar patterns emerged. Again, the "simply forgot" barrier was not shown to be the most important barrier for any one subgroup in each analysis.

Non-Latino Whites and Latinos were most similar in their ranking of barriers (Table 3). A noticeable difference was that the "ran out of pills" barrier yielded a larger dominance weight among Latinos (0.151 vs. 0.004), while the "felt depressed/overwhelmed" barrier yielded a larger dominance weight for the non-Latino Whites (0.152 vs. 0.020). For African Americans, the "drinking alcohol or using illicit drugs" barrier yielded the largest dominance weight (0.521), while the importance of the "day-to-day life" and "fell asleep/slept through dose" was less when compared to non-Latino Whites and Latinos.

Exploratory Dominance Analysis by Age

For the young adults, the "drinking alcohol or using illicit drugs" yielded the largest dominance weight (0.521; i.e., #1 rank; Table 3). For the middle-aged adults, the "felt depressed/overwhelmed" barrier yielded the largest dominance weight (0.454). For the older

adults, as with the total sample, the "fell asleep/slept through dose" barrier yielded the largest dominance weight (0.580; Table 3). Each age subgroup had a varied pattern of barrier rankings, although the "alcohol and/or illicit drugs" and "wanted to avoid side-effects" barriers was the most similar in terms of effect size and ranking across each subgroup (Table 3).

Odds Ratios for Empirically-derived Barriers

The "felt depressed/overwhelmed" barrier yielded the largest odds ratio; which was associated with 2.6 times greater odds of reporting a treatment interruption ($OR = 2.6$, $p < 0.01$). The "drank alcohol or used illicit drugs" barrier, "fell asleep/slept through dose" barrier, and "day-to-day life" barrier were all associated with greater odds for reporting a treatment interruption of similar size (*OR*s range 1.34 to 1.46; Table 4), respectively. The "wanted to avoid side-effects" barrier was not associated with a treatment interruption ($p = 0.36$). For the covariates, only age was associated with a treatment interruption ($OR = 0.74$, $p < 0.05$; Table 4). Reporting a treatment interruption was associated with greater odds of a detectable VL ($OR = 1.16$, $p < 0.05$).

DISCUSSION

Advancements in ART compelled us to reconsider the definition of ART non-adherence, the barriers to adherence, and the ecological validity of these constructs [1]. We chose a 4-day treatment interruption because four days was generally considered (across multiple drug classes) to be the maximum number of days where no ART could be taken but therapeutic coverage could be present [5, 13, 23, 24]. A major finding that we replicated was that "simply forgot" was overwhelmingly the most frequently reported reason for missing a dose of ART (in approximately 1 in 3 participants), yet a barrier shown in our study to have limited empirical evidence of a relationship to a 4-day treatment interruption [8, 9]. In contrast, the "fell asleep/slept through dose" barrier was most strongly associated with ART non-adherence. Our primary hypothesis was supported by data showing that the most frequently reported barriers to adherence were not the barriers most important to ART non-adherence, generally, and that the "feeling depressed" was the second most important predictor of ART non-adherence.

Our exploratory analysis showed that no one barrier to adherence was most important to all race/ethnic or age subgroups. However, similar barriers to adherence patterns did emerge, as has been evidenced in both domestic and international studies on the barriers to adherence [7]. The results generally showed that mental health and substance use (as barriers) continue to be central targets for adherence interventions for different groups of PLWH.

Implications for Interventions and HIV Clinical Care

Patients reports of "simply forgetting" to take doses of ART may be a proxy for disclosing other, more sensitive reasons for missed doses. Given the infrequency of reporting sleep problems, [25] or stigma surrounding pervasive mental illness and drug use, [26] PLWH may not recognize or be less inclined to report sleep difficulties or psychological distress as a reason for non-adherence, which may lead them to default to reporting "simply

forgetting." In the absence of a long-acting injectable ART, HIV care providers may need to probe beyond "simply forgetting" as a reason for non-adherence, or delve into causes of forgetfulness. And given the high prevalence of sleep problems documented in PLWH, recognition and treatment for sleep problems can be a short-term solution [25].

These data make clear that simpler ART regimens do not overcome the psychosocial barriers to adherence, which must be addressed to make strides in furthering the "Treatment as Prevention" strategy. Relying on self-reported reasons for non-adherence may lead toward intervention targets that do not thoroughly capture the root causes of non-adherence, [6] while use of arbitrary thresholds of adherence measures that do not recognize patterns of non-adherence with more current ART regimens may lead to results that are less clinically useful and less valid [11].

Finally, in our sample, nearly 70% and 29% of participants were on a single-dose or twice-daily dose ART regimen; thus, the pill burden and regimen complexity barriers were rarely reported. We should note that we included data from all participants because meta-analytic evidence suggests persons on once-daily, versus twice-daily, dosed ART are not more likely to achieve viral suppression [27]. However, these simpler regimens were not immune to extended gaps in ART coverage of at least four days [18]. Thus, simpler ART does not obviate the behavioral problems associated with non-adherence.

Limitations

First, all data were anonymously self-reported, including adherence, barriers to adherence, and HIV clinical outcomes [15]. We also only analyzed the barriers to adherence in a binary form ("yes" or "no"), rather than on a frequency interval scale ("often" to "rarely). However, no incentives to participate were provided and the direction of the effect was non-adherence (negative outcome), as opposed to adherence (positive outcome), which is more prone to social desirability effects. Second, a replication study is needed to support the stability of the dominance weights. Dominance analysis is not an inferential test, per se (i.e., it lacks a null hypothesis significance test), but rather estimates effect sizes only. However, like inferential tests, the stability of the effect sizes may vary based on sampling error, sample size and the population of study. And given the sample sizes for each stratified analysis, all stratified dominance weights should be interpreted cautiously. However, given prior evidence to support our findings, this is a first step toward empirically testing the importance of barriers to adherence. Third, although we included participants who were on twice-daily dosed ART, there is no evidence to suggest a systematic difference between these participants and those on single-dose ART with respect to their ability to achieve viral suppression [27]. Fourth, this sample consisted of mostly college educated and gay-identified men who use online social media and completed the survey with no external incentives, which may not represent the diverse population of PLWH in the U.S. We also attempted to collect partial zip code numbers to identify regions in the U.S. where surveys were being taken, but this information was inconclusive and could not be analyzed. Lastly, because data were anonymous, we did not collect our own assays and could not determine definitively the effect of a treatment interruption on the VL outcome.

Conclusions

Advancements in ART have major implications for what we consider the primary barriers to adherence, the utility of self-reported measures of non-adherence, and their impact on clinical outcomes. We stress the importance of the continued pursuit of solutions for mental health problems and substance use that so many patients living with HIV deal with. It is critical for adherence interventions to target barriers that are important in explaining treatment interruption and virologic response.

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Table 1

Participant characteristics

	Total Sample *N* = 1,217
Age, Mean (SD)	46.7 (10.9)
Sex at Birth, Male %	94.7%
Education (%)	
< HS diploma	3.0%
HS diploma or GED	26.2%
Some College	26.3%
College or higher	44.5%
Income (%)	
< $20,000	31.9%
$20,000 to $39,999	25%
$40,000 to $59,999	14.9%
> $60,000	28.2%
Race/Ethnicity (%)	
Non-Latino White	76.3%
Latino	12.2%
African American	9.1%
Other	2.4%
CD4+ Cell Count, Mean (SD)	637 (311)
Percent with a detectable HIV Viral Load (%)	13%
Daily Dosing Frequency of Antiretroviral Therapy (%)	
Once-daily	69.8%
Twice-daily	28.8%
Three times a day or greater	1.4%
Self-reported Adherence (%)	
Past 30-day Visual Analog Scale, Mean (SD)	95.5 (12.47)
Four-day treatment interruption in past 3 months	14%
Adherence ability mean (1 = very poor to 6 = excellent)	5.5

Table 2

Most-to-least important barriers to adherence based on participant responses and a dominance analysis

Standardized Dominance Weights	Dominance Analysis Rankings of Adherence Barriers	Participant Rankings of Adherence Barriers	Total Sample %(*n*)
0.329	#1 Fell asleep/slept through dose time †	#1 Simply forgot	33.7% (*n* = 410)
0.313	#2 Felt depressed/overwhelmed †	#2 Day-to-day life	27.6% (*n* = 336)
0.116	#3 Day-to-day life	#3 Drinking alcohol or using illicit drugs	10.5% (*n* = 128)
0.110	#4 Wanted to avoid side-effects †	#4 Felt depressed/overwhelmed	9.5% (*n* = 116)
0.040	#5 Drinking alcohol or using illicit drugs	#5 Ran out of pills	6.6% (*n* = 80)
0.035	#6 Simply forgot	#6 Fell asleep/slept through dose time	6.2% (*n* = 75)
0.028	#7 Ran out of pills	#7 Problems with pharmacy and insurance	4.5% (*n* = 55)
0.026	#8 Felt sick or ill †	#8 Wanted to avoid side-effects	4.1% (*n* = 50)
0.003	#9 Problems with pharmacy and insurance	#9 Felt sick or ill	3.0% (*n* = 36)

Note. The gray scale is used to visualize the barrier rankings, and how the rankings differed between participant rankings and dominance analysis rankings. Standardized dominance weights show how important each barrier was to predicting a 4-day treatment interruption.

† = Barriers most important in a dominance analysis.

Table 3

Dominance analysis rankings stratified by race/ethnicity and age

Non-Latino White (*n* = 929)		**Latinos (*n* = 148)**		**African Americans (*n* = 110)**	
Adherence Barrier	**Dominance Weights**	**Adherence Barrier**	**Dominance Weights**	**Adherence Barrier**	**Dominance Weights**
#1 Day-to-day life	0.290	#1 Asleep/slept through dose time	0.288	#1 Alcohol or using illicit drugs	0.521
#2 Asleep/slept through dose time	0.178	#2 Day-to-day life	0.237	#2 Felt sick or ill	0.183
#3 Problems with pharmacy/insurance	0.163	#3 Ran out of pills	0.151	#3 Simply forgot	0.081
#4 Simply forgot	0.157	#4 Simply forgot	0.142	#4 Wanted to avoid side-effects	0.066
#5 Felt depressed/overwhelmed	0.152	#5 Alcohol or using illicit drugs	0.067	#5 Felt depressed/overwhelmed	0.051
# 6 Alcohol or using illicit drugs	0.038	#6 Problems with pharmacy/insurance	0.062	#6 Day-to-day life	0.050
#7 Felt sick or ill	0.011	#7 Felt sick or ill	0.034	#7 Asleep/slept through dose time	0.030
#8 Wanted to avoid side-effects	0.006	#8 Felt depressed/overwhelmed	0.020	#8 Problems with pharmacy/insurance	0.011
#9 Ran out of pills	0.004	#9 Wanted to avoid side-effects	0.000	#9 Ran out of pills	0.007
Young Adults (*n* = 104) 18-29 yrs.		Middle-aged Adults (*n* = 590) 30-49 yrs.		Older Adults (*n* = 524) >50 yrs.	
Adherence Barrier	Dominance Weights	Adherence Barrier	Dominance Weights	Adherence Barrier	Dominance Weights
#1 Alcohol or using illicit drugs	0.521	#1 Felt depressed/overwhelmed	0.454	#1 Asleep/slept through dose time	0.580
#2 Felt sick or ill	0.183	#2 Day-to-day life	0.187	#2 Problems with pharmacy/insurance	0.230
#3 Simply forgot	0.081	#3 Alcohol or using illicit drugs	0.119	#3 Alcohol or using illicit drugs	0.057
#4 Wanted to avoid side-effects	0.066	#4 Wanted to avoid side-effects	0.096	#4 Wanted to avoid side-effects	0.042
#5 Felt depressed/overwhelmed	0.051	#5 Problems with pharmacy/insurance	0.077	#5 Felt depressed/overwhelmed	0.040
#6 Day-to-day life	0.050	#6 Asleep/slept through dose time	0.027	#6 Simply forgot	0.033
#7 Asleep/slept through dose time	0.030	#7 Ran out of pills	0.021	#7 Day-to-day life	0.015
#8 Problems with pharmacy/insurance	0.011	#8 Felt sick or ill	0.020	#8 Ran out of pills	0.007
#9 Ran out of pills	0.007	#9 Simply forgot	0.008	#9 Felt sick or ill	0.004

Note. The most-to-least important adherence barriers are ranked by their dominance weights. Adherence barrier names are abbreviated (see Table 2 for full descriptions). Standardized dominance weights reflect how important each barrier was to a 4-day treatment interruption. The three shades of gray correspond to the three most important barriers from the total sample (#1 Fell asleep; #2 Felt depressed; #3 Day-to-Day life) to show how they vary by race/ethnicity and age.

Table 4

Path model odds ratios of the five most important adherence barriers in the total sample (N = 1,217)

Outcome: Treatment Interruption*	**OR**	**Estimate/Std. Error**	**p**
Adherence Barriers			
#1 Asleep/slept through dose	1.45	2.01	0.04
#2 Felt depressed	2.60	7.58	0.01
#3 Day-to-day life	1.34	2.96	0.003
#4 Side-Effects	0.75	−0.09	0.37
#5 Alcohol and Drugs	1.46	3.13	0.002
Outcome: Detectable Viral Load†	OR	Estimate/Std. Error	p
Treatment Interruption	1.16	2.07	0.04
Age	0.74	−4.31	0.001
Sex at birth (male vs. female)	1.29	1.14	0.25
#1 Asleep/slept through dose	1.05	0.29	0.77
#2 Felt depressed	1.35	1.97	0.049
#3 Day-to-day life	0.73	−2.68	0.01
#4 Side-Effects	0.76	−1.02	0.31
#5 Alcohol and Drugs	0.73	−1.88	0.06

Note.

*OR = Odds of a treatment interruption if specific barrier was endorsed, holding all other barriers constant.

†OR = Odds of a detectable VL if specific barrier was endorsed, holding other barriers and covariates constant. Covariates are age and self-reported sex at birth. The adherence barriers were the five with the largest standardized dominance weight in the total sample.