



## Comorbid mental health disorders in persons living with HIV: Adherence to antiretroviral therapy

Anna B. Smith\*, Paul F. Cook

University of Colorado College of Nursing, United States of America



### ARTICLE INFO

#### Keywords:

Antiretroviral therapy  
HIV  
Mental health  
Substance use

### ABSTRACT

This is a secondary data analysis exploring adherence to antiretroviral therapy (ART) in persons living with HIV (PLWH) with a comorbid mental health disorder. Logistic regression analyses indicated that PLWH who had reliable housing were over six times more adherent than those with unreliable housing. Descriptive odds ratio analyses showed directional relationships for ART adherence with coping, employment, and social support. These results indicate areas for future investigation in PLWH and comorbid mental health disorders, and the potential to find ways to foster certain emotional or living conditions that promote ART adherence.

### Introduction

Antiretroviral therapy (ART) was introduced in the 1980's as a promising treatment for human immunodeficiency virus (HIV). ART remains the first line of treatment for HIV and is recommended for all persons living with HIV (PLWH) (Gunthard et al., 2014). The goals of ART are to reduce the amount and transmission of the virus, improve immune system function, reduce morbidity and mortality, and improve quality of life (Pau & George, 2014). Since the original approval of ART, therapies have progressively become more effective and less toxic. However, the amount of HIV that is detectable in serum rebounds when ART medications are stopped (Pau & George, 2014). Accordingly, maintaining the drug regimen is extremely important to facilitate the best outcomes for PLWH. This can be done when there is clear identification of what hinders and what helps ART adherence.

#### Optimal adherence

Historically, research suggested that ART adherence of 95% was the standard for achieving and sustaining an undetectable viral load (Cruess, Minor, Antoni, & Millon, 2007; Tugenberg, Ware, & Wyatt, 2006). More recently, though, a large study by Viswanathan et al. (2015) indicated that newer ART drugs show similar viral load suppression with 85–89% adherence in comparison to the ≥95% adherence that has previously been suggested. While these findings are exciting, individual and viral differences affect treatment enough that perfect adherence is still recommended (Viswanathan et al., 2015). This level of adherence can be challenging for PLWH, and many barriers can

adversely affect adherence. One in ten PLWH who are actively taking ART are still not virally suppressed according to the current national statistics on the HIV care continuum, indicating that optimal adherence levels are not being reached by a substantial portion of PLWH (The White House, 2017). This has severe implications for disease outcome in PLWH and warrants additional exploration.

#### Antiretroviral therapy adherence measurement

There are several ways in which ART adherence can be measured. Researchers have employed methods such as self-report, physician report, pharmacy claims, antiretroviral drug plasma concentrations, viral load measurements, returned pill counts, and electronic monitoring (DeMasi et al., 2001; Kagee & Nel, 2012). Often, more than one of these methods will be combined in a single study. Chesney (2006) indicates that there is no “gold standard” for measuring adherence to ART. There are problems inherent in each method of measuring ART adherence, and one method may be more valid than another for a certain situation or population. Cook, Schmiede, Reeder, Horton-Deutsch, and Lowe's (2018) version of Two Minds Theory suggests that, based on the idea of temporal immediacy, behaviors like adherence are best studied in real time and without relying on participant self-report. For that reason, adherence in the current study was measured using pill bottle sensors that recorded when PLWH opened the cap to take their medication.

#### Factors affecting antiretroviral adherence

Identifying and understanding factors that affect ART adherence has

\* Corresponding author.

E-mail address: [anna.smith@uchealth.org](mailto:anna.smith@uchealth.org) (A.B. Smith).

the potential to improve the lives of PLWH. Adherence to ART leads to an enhanced quality of life, better mental health, increased CD4 cell counts, decreased overall healthcare spending, lower transmission rates, and improved life expectancy (Nel & Kagee, 2013; The White House, 2015; Wang et al., 2009). Evidence can help providers identify individuals at risk for poor adherence or better understand key factors in maintaining optimal adherence.

Identification of specific factors that might improve adherence of individual patients can be difficult, however, because of the immense number of social, physical, and psychological factors that influence ART adherence. Personal support systems and stigmas related to HIV are social mediators of ART adherence (Katz et al., 2013). Demographic variables such as age, poverty, race, and geographic location have an influence on adherence rates, as well (Katz et al., 2013; O'Connor et al., 2013; Silverberg, Leyden, Quesenberry Jr., & Horberg, 2009). Zhang, Terry, and McHorney (2014) found that health literacy, which often varies across ages, cultures, and living situations, seems to have an effect on ART adherence when acting in combination with other factors.

The prescribed drug regimens of ART affect how well PLWH adhere to the treatment. O'Connor et al. (2013) found that protease inhibitor regimens, increased numbers of doses, increased numbers of pills per dose, and additional prescription medications taken concurrently with ART can lead to poor adherence rates. Symptoms of the disease as well as side effects of drugs decrease ART adherence (Gonzalez et al., 2007). Newer ART drug regimens that have single-pill doses and lower toxicity seem to promote better, although not perfect, adherence (Viswanathan et al., 2015).

#### *Mental health and persons living with HIV*

Mental health disorders are already much more prevalent in PLWH than in the general population, with depression as the leading comorbidity (Springer, Dushaj, & Azar, 2012). Pence et al. (2012) report that overall mood and anxiety disorders are five to 10 times more likely in an HIV-infected person compared to someone who is not infected. Substance use is also very common in PLWH. HIV itself causes neurocognitive decline when untreated, and drugs such as cocaine and heroin may further that impairment (Meade, Conn, Skalski, & Safren, 2011).

#### *Mental health impacts on adherence*

##### *Behavioral*

Mental health issues can have individual or synergistic impact on adherence to ART regimens. Depression reduces adherence to ART, and increased severity of depression may further increase nonadherence to treatment (Cruess et al., 2007). Nel and Kagee (2013) found that, along with depression, generalized anxiety disorder and panic disorder are associated with reduced adherence. Negative feelings and poor psychological states have been associated with ART non-adherence (Batchelder et al., 2013). Psychological distress from circumstances such as food or housing insecurity can contribute to lower ART adherence as well (Surratt, O'Grady, Levi-Minzi, & Kurtz, 2014). Emotional states like shame, lack of a strong sense of self, feeling alone, and denial are not only associated with lower ART adherence rates, but also with drug addiction (Batchelder et al., 2013).

##### *Substance use*

Past or current substance use may contribute to poor ART adherence. PLWH that became infected with HIV via intravenous drug injection are more likely to be nonadherent to ART than are PLWH who obtained the virus by sexual transmission (Cantudo-Cuenca, Jimenez-Galan, Almeida-Gonzalez, & Morillo-Verdugo, 2014). Tugenberg et al. (2006) found that drug use was a reason for missed doses of ART, perhaps due to prioritization of substance use over ART. In PLWH who were actively using drugs, Batchelder et al. (2013) found an interaction between drug use, negative affect, and nonadherence. Alcohol use

disorders are also common in PLWH and can lead to nonadherence, followed by subsequent poor health outcomes (Kader, Govender, Seedat, Koch, & Parry, 2015). Cocaine, heroin, and methamphetamine use negatively affect ART adherence due to a complicated interaction of neurocognitive decline from both the use of those substances and from HIV infection (Anderson, Higgins, Ownby, & Waldrop-Valverde, 2015; Meade et al., 2011; Moore et al., 2012).

#### *Discrepancies in the literature*

Much of the literature indicates poor adherence to ART in PLWH with comorbid mental health disorders, but there are some inconsistencies. Springer et al. (2012) found depression to be significantly related to lower adherence, but the associations between anxiety disorders, borderline personality disorder, and adherence were inconsistent. They also found no relationship between adherence and agoraphobia. Tests of the association of post-traumatic stress disorder (PTSD) and adherence in PLWH have shown mixed results (Nel & Kagee, 2011). This may be due in part to what Nel and Kagee (2011) described as attitudes of “self-protection” and “vigilance to health” exhibited by many persons with PTSD. Nel and Kagee (2011) also suggested that ART may be the cause of some psychological problems, which adds an additional layer of complexity to the interactions between mental health and ART compliance.

#### *Treatment of mental health issues*

Targeting and treating mental health issues can be beneficial for ART adherence. Behavioral recovery programs or counseling may help to increase ART adherence rates, specifically by lowering depression severity (Lopez, Jones, Ishii, Tobin, & Weiss, 2007; Pence et al., 2012). Substance use treatment also can increase adherence (Batchelder et al., 2013). Some of the benefit that such programs confer may be due to an increase in social support (Lopez et al., 2007). Targeting the cognitive impairment that accompanies some substance use through behavioral interventions and with psychotropic medications may improve adherence to ART (Moore et al., 2012).

#### *The gap in mental health and ART adherence research*

A significant amount of literature addresses the effects of mental health on ART adherence. The majority of this research focuses on factors that negatively affect adherence, such as depression severity or food insecurity. This is very important knowledge to have in order to identify those who are at risk for decreased adherence to ART. There is also research on what makes PLWH who are not adherent become more adherent, such as treatment programs or psychotropic medication. This, too, is essential information to help those who struggle with ART adherence. Fewer publications focus on factors that promote ART adherence in PLWH with mental health comorbidities. We propose that certain common characteristics of this population facilitate maintenance of ART adherence. The identification of adherence factors in a group that is more often nonadherent will advance our understanding of ART adherence in PLWH with a mental health or substance use disorder, which in turn can improve their quality of life and health outcomes.

## **Materials and methods**

### *Participants*

This study employed secondary data analysis. In the parent study (1R21NR012918-01A, PI: Cook), medication adherence data were collected from persons living with HIV (PLWH) from 2012 to 2015. Participants were recruited from an outpatient clinic in Denver, Colorado, that specializes in infectious disease. All of the participants

provided written informed consent, and the study was approved by the Colorado Multiple Institutional Review Board. The participants were recruited during regularly scheduled appointments for HIV primary care. When patients came in to see their typical care provider at the clinic, the provider outlined the basic protocol for the study and subsequently referred interested patients to the research team to complete informed consent.

The study *inclusion criteria* were: (a) documented HIV infection and current antiretroviral therapy (ART) based on medical records; (b) ability to speak, read, and write English as either a first or second language; (c) aged 18 to 81 years; and (d) demonstrated ability to use a smartphone after initial training. *Exclusion criteria* were any level of current substance abuse, cognitive impairment, major psychiatric disorder, comorbid medical disorder, or other condition that would, in the judgment of the referring clinician, interfere with study participation. The clinic providers spoke to 158 PLWH about the study, and 87 patients decided to participate. There were 7 exclusions based on serious physical illness (e.g. hepatitis C, kidney failure), or severe mental illness that would preclude participation (e.g. bipolar disorder, schizophrenia). An additional 17 patients were excluded because they did not manage their own medication, did not speak English, or were not taking ART. Another 47 patients declined to participate, with the most common reasons being that they were too busy or did not want to talk about adherence.

For this sub-study, 41 of the 87 parent study participants had a comorbid mental health or substance use condition, and were included in the analyses. This subgroup was identified by the PI and the parent study investigator through a review of diagnoses collected from participants' medical records during the parent study. Each author read the diagnoses independently and then discussed the participant's classification as a patient with a mental health diagnosis, substance abuse diagnosis, neither, or both, with 100% agreement on the classifications. The 41 participants selected for secondary analysis were any PLWH who had a comorbidity of a mental health disorder (e.g. depression, anxiety, mental retardation), substance use disorder (alcohol use disorder and/or illicit drug use of any kind; not to include nicotine), or both. Of the 41 participants included in analyses, 7 had a documented substance use disorder only, 11 had a documented mental health disorder only, and 23 had both.

#### Procedure

##### Data collection

The participants completed an intake session in which they responded to self-report questionnaires on demographic data and psychological status. The session was done at the same outpatient clinic where the participants received primary care for HIV. The session was completed with a professional research assistant who was trained in the study protocol and HIPAA regulations. Most of the intake sessions occurred at the same time as study enrollment, but some were scheduled for another time. For completion of the intake, the participants earned \$25. Information was then obtained daily for 10 weeks from participants by Medication Event Monitoring System (MEMS) pill bottles (see Fig. 1) and from smartphone surveys. The MEMS bottles use micro-electronic technology in the pill bottle cap in order to record the date and time of each bottle opening. The bottle opening data was downloaded to a computer for compilation at a follow-up study visit. The smartphone survey data are not included in this sub-study.

#### Measures

##### Demographic and clinical data

Demographic information was obtained during the intake by participant self-report on age, gender, sexual orientation, level of education, employment, race/ethnicity, housing/homelessness, and insurance/access to care. Participants' medical records were used for



Fig. 1. Medication Event Monitoring System (MEMS) pill bottles with micro-electronic technology in cap to record bottle openings.

gathering information on HIV viral load, CD4+ T cell labs, ART medication regimen, years since diagnosis, date since the start of treatment, comorbid medical conditions, comorbid mental health conditions, and substance use.

##### Predictors of adherence

The intake documents garnered self-report information from participants on coping, motivation, social support, mood, and stress. The tools used were: 1) Brief COPE (Carver, 1997) to assess coping; 2) Stages of Change (SOC: Herzog & Blagg, 2007) to assess motivation; 3) Multi-dimensional Scales of Perceived Social Support (MSPSS: Stanley, Beck, & Zebb, 1998) to assess social support; 4) Center for Epidemiological Studies Depression scale (CES-D: Hann, Winter, & Jacobsen, 1999) to assess mood; and 5) HIV/AIDS-Targeted Quality of Life instrument (HAT-QoL: Holmes & Shea, 1998) to assess stress. These measures all showed internal consistency reliability of  $\alpha = 0.71$  or higher, as well as predictive or concurrent validity from the studies referenced. Coping, motivation, social support, and mood were all used in analyses with the total scores calculated for each of the tools. For stress, the HAT-QoL scores across five areas of worry (overall functioning, mental health, physical health, financial, ART medication) were averaged into a composite score. This was done in order to generate a variable that captured stress in various aspects of life.

##### Medication adherence

Participants received a MEMS bottle and were instructed on its use during the intake session. The participants were told to open the bottle only when they were taking the medication it held, which was supposed to be their most frequently taken ART medication. Participants received a written instructional aid for MEMS bottle use as well as a telephone number to call if they had any issues or questions. While the measure does not necessarily equate to actual use, MEMS bottles have been shown to be a good indication of medication adherence (Chesney, 2006). There are some drawbacks to MEMS bottles, such as potential underestimation of adherence, but MEMS are accepted as a valid and reliable measure for adherence (Bova et al., 2005). For this dataset, there was a preliminary 6-week period of MEMS use to control for any initial reactivity in which participants responded to the use of the bottles with better adherence; previous research showed that adherence returned to baseline levels after this amount of time using MEMS (Cook, Schmiege, McClean, Aagaard, & Kahook, 2011). The data from this 6-week period showed limited reactivity that did not affect results. Therefore, the whole dataset, including the 6-week run-in period, was used for adherence analyses.

**Table 1**  
Missing trait-level predictor data for which imputation was performed.

Trait-level predictor	Missing data points n	Percent %
Age	3	7.32
Coping	2	4.88
Mood	1	2.44
Motivation	3	7.32
Social support	1	2.44
Stress	1	2.44
Years since diagnosis	7	17.07
Years since start of treatment	9	21.95

### Data analysis

#### Preliminary data analysis

Demographic and clinical data were analyzed descriptively. We examined means and standard deviations and tested variables for normality. We also examined the amount and pattern of missing data, which ranged from 2.44% to 21.95% per variable. All of these variables had percentages of missing data that fell below the 30% missing data cutoff that allows for unbiased imputation (see Table 1; Collins, Schafer, & Kam, 2001), and the data appeared to be missing at random based on the pattern of responses, so we used multiple imputation in NORM (Schafer, 1997).

This was done prior to analysis to compensate for the missing data points, and subsequent analyses were based on the imputed complete data set. Imputation involves replacing missing data points with estimated values. The NORM program specifically fills in missing data based off of a multivariate normal distribution.

#### Outcome measurement

The level of adherence for each of the 41 participants was computed based on a count of MEMS bottle openings divided by the number of days of monitoring, and multiplied by 100 in order to get a percentage. For participants with twice-daily regimens of ART, each bottle opening was counted as 0.5, which allowed us to avoid over-weighting these participants' data based on the fact that they had more scheduled doses. MEMS data were missing for 31.7% of participants. This percentage is slightly above the 30% threshold that allows for imputation without bias (Collins et al., 2001). However, the missing data seemed to be random in regard to demographics, and other methods for imputing missing data such as casewise deletion are even more likely to bias the results, so imputation was still performed using the NORM program to generate MEMS data for all participants. Participants were dichotomously classified as *adherent* or *non-adherent* as the outcome variable for logistic regression. *Adherent* participants were those who had an adherence level of  $\geq 85\%$ , whereas *non-adherent* participants had an adherence level of  $< 85\%$ . Eighty-five percent adherence for newer ART regimens is indicated in recent literature as providing approximately the same level of viral suppression, which is the ultimate goal of ART, as the traditional standard of  $\geq 95\%$  adherence (Viswanathan et al., 2015).

#### Predictors of adherence

Logistic regression analyses were completed to predict medication adherence (dichotomous). The following variables were tested for their relation to adherence, as potential covariates: *age*, *mood*, *stress*, *years since diagnosis*, *years since treatment start*, *number of medical comorbidities*, and *health insurance*. Each of these was considered a potential confound based on previous ART adherence research. Any of these variables that showed significant relationships to adherence were included as covariates in subsequent analyses. Five predictors of adherence were then analyzed in separate analyses, after controlling for those variables that emerged as potential confounds in the previous

step. *Housing* (stable vs. unstable), and *employment* (employed vs. unemployed) were analyzed as nominal predictor variables. *Motivation*, *coping*, and *social support* were analyzed as interval-level predictor variables.

#### Power analysis

Post hoc analysis was done and showed power = 0.80 to detect effects of  $\phi > 0.46$  at  $\alpha = 0.05$  based on the final sample size of 41 PLWH. This effect size indicates that if 95% of participants with a particular characteristic met the criterion for adherence to ART, this would necessitate that only 55% or fewer of those participants without the characteristic be adherent in order to demonstrate statistical significance. Because this difference is quite large, and it is not possible to increase the sample size with a secondary data set, the study was likely underpowered. However, any significant results would indicate a potentially large effect size for those specific predictor variables, and the results may provide useful information to guide future research.

## Results

### Participant demographics

The study population of PLWH with a comorbid mental health or substance use disorder consisted of 12 women and 28 men, with 1 participant undocumented for gender. This gender breakdown shows a higher prevalence of women and a lower prevalence of men in comparison to both the national and Colorado gender breakdown of PLWH (Table 2).

This disparity may be in part due to the fact that women are more likely to seek out mental health care, and therefore obtain a mental health diagnosis that allowed for inclusion in this study (Pattyn, Verhaeghe, & Bracke, 2015). The average age of participants was  $M = 31.9$  years ( $SD = 9.1$ ), which was slightly younger than the average age of participants in the full sample from which this subsample was obtained,  $M = 40.0$  years ( $SD = 8.84$ ).

Participants included in the subsample were 21 White non-Hispanic, 9 Hispanic/Latino, 5 Asian/Pacific Islander, 2 Native American, 1 African-American, 1 African-American/Hispanic, and 2 other/unidentified participants. While this population does not necessarily reflect the breakdown of PLWH within the United States as a whole, it is loosely reflective of the population of PLWH in Colorado (Table 3; Kaiser Family Foundation, 2017).

The race breakdown of PLWH in the current study exhibits two main trends in PLWH in Colorado as compared to the United States as a whole: 1) a much higher proportion of White PLWH; and 2) a

**Table 2**

Comparison between United States, Colorado, and current study for gender and race/ethnicity in persons living with HIV (PLWH).

	United States %	Colorado %	Current study %
Gender			
Male	81.0	87.0	68.3
Female	19.0	13.0	29.3
Other/unidentified	N/A	N/A	2.4
Race/ethnicity			
African-American	44.3	18.0	2.4
American Indian/Alaskan Native	0.5	0.2	4.9
Asian/Pacific Islander/Native Hawaiian	2.5	2.0	12.2
Hispanic/Latino	23.2	29.4	19.5
White	27.3	48.6	51.2
Mixed race/other	2.2	1.5	9.8

Note. 2014 data from Henry J. Kaiser Family Foundation.

**Table 3**  
Logistic regression results for potential covariates.

Variable	B	OR	p
Age	0.09	1.09	0.04*
Mood	0.03	1.03	0.16
Stress	1.21	3.36	0.06
Years since diagnosis	0.00	0.99	0.93
Years since treatment start	0.00	1.00	0.99
Number of comorbidities	−0.54	0.95	0.95
Health insurance	−20.75	0.00	0.99

\* Significant at  $p < 0.05$ .

significantly lower percentage of African-American PLWH. We did not see quite as high of a percentage of Hispanic/Latino PLWH in the current study as in the state of Colorado as a whole, but of those who are placed in the “Mixed/Other” category, there was one other participant with Hispanic/Latino heritage. The relative under-representation of Latino/Latina PLWH in the current study may also be related to disparities in access to mental health care among minority groups (McGuire & Miranda, 2014).

#### Screening analyses for potential covariates

We conducted initial analyses of multiple variables that were seen as potentially confounding to results and found two that were considered potentially important to include in subsequent analyses (Table 4).

Based on these analyses, we included age,  $p = 0.04$ , and stress,  $p = 0.06$ , as covariates when we conducted the primary analyses reported below. We decided to include stress as a covariate even though it did not reach conventional levels for statistical significance because it was nearly significant and we believed that it was a potentially important confound that could still affect results.

#### Primary tests of hypothesized predictor variables

After controlling for the covariates, logistic regression analyses showed that housing status affected adherence in our subpopulation,  $p = 0.04$ . Those who had reliable housing were significantly more adherent to ART than those with unreliable housing,  $OR = 6.85$ . Additionally, odds ratios suggested a relationship in the expected direction between ART adherence and social support,  $OR = 1.63$ , as well as between ART adherence and employment,  $OR = 3.39$ . Consistent with predictions, those participants who had higher levels of social support or were employed were more likely to be adherent to ART. Even though these results were not statistically significant, that result could be due to limited sample size available for secondary data analysis, and awareness of these relationships may be helpful in guiding future research. Other logistic regression and odds ratio analyses did not show any meaningful findings for the other hypothesized predictors of adherence: motivation or coping.

**Table 4**  
Logistic regression results for hypothesized predictor variables.

Variable	B	OR	p
Housing	1.93	6.85	0.04*
Employment	1.22	3.39	0.22
Motivation	−0.04	0.97	0.97
Coping	−1.22	0.29	0.08
Social support	0.49	1.63	0.18

\* Significant at  $p < 0.05$ .

## Conclusions

The results of this study give insights into a particularly at-risk subpopulation of PLWH. Those PLWH with mental health or substance use disorders have various additional stressors that may affect ART adherence as compared to PLWH who do not suffer from a mental health or substance use disorder.

This study indicates that stable housing is a very important factor in maintaining adherence to ART in PLWH with a comorbid mental health or substance use disorder. This finding fits well with the most recent National HIV/AIDS Strategy for the United States (The White House, 2015). This document outlines the national plans for HIV/AIDS prevention and care through 2020. One of the overall objectives that the document outlines is “increasing access and improving overall health outcomes” for PLWH (The White House, 2015). The means of achieving this goal include tackling issues of access to basic needs among PLWH, including housing. The strategy presents a target of reducing homelessness to no > 5% among PLWH receiving medical care for HIV (The White House, 2015). Another portion of this same goal addresses screening for mental health and substance use disorders in PLWH. The current study results indicate the imperative nature of following through on these goals, especially for a population of PLWH with a comorbid mental health or substance use disorder.

Our results also indicate that social support and employment may be helpful for ART adherence in PLWH with a comorbid mental health or substance use disorder. While these results did not reach conventional levels for statistical significance, the odds ratios indicate a potential relationship that may simply have been difficult to detect in an underpowered secondary data analysis. Those participants with social support and those who were employed, even part-time, were more likely to be adherent to ART.

Employment also has been shown to be associated with higher adherence to ART in the general population of PLWH (Nachega, Peltzer, & Mills, 2015). It seems likely that this may also apply to those PLWH with a mental health or substance use disorder. Unfortunately, persons with a mental health or substance use disorder and those with HIV, independently, have lower employment rates than the general population in the United States (The United States Department of Labor, 2017). Reducing disparities in employment for both persons with mental health or substance use and PLWH is a major aim of the Department of Labor. Additionally, the National HIV/AIDS Strategy includes goals to improve leadership and cites the issue of unemployment in PLWH. Fostering programs that support employment may be important in adherence to ART in our study population, probably by a complicated relationship between several factors. Employment opens many doors by providing an income for important life activities, including the ability to obtain housing, transportation, healthcare, and medication.

For coping, the results actually suggested a relationship in the opposite direction from what was predicted, indicating that increased coping was actually detrimental to ART adherence. The Brief COPE measured coping in a manner that gave higher coping scores to people who used more coping mechanisms when confronted with stressful situations. Based on the nature of this tool and the obtained direction of the odds ratio for coping, this finding may suggest that having multiple coping mechanisms can be detrimental to adherence in our study population. Participants with high coping scores may not focus their skills to adequately cope.

Our finding on coping in this subsample was similar to an inverse effect of coping in a published analysis of the entire sample from the parent study, which reported the same potential issue with the coping measure (Cook, Schmiede, Starr, Carrington, & Bradley-Springer, 2017). However, a lack of effect for motivation in the current study was particularly noteworthy because findings in the parent study indicated that motivation was the single strongest predictor of adherence for PLWH overall (Cook et al., 2017). This difference may be due to people

with a mental health diagnosis having either higher or lower levels of motivation than other PLWH, so that there was insufficient variability to detect a relationship between motivation and adherence in the subsample. However, as the sample size and power of the study were small, we cannot definitively determine or rule out relationships between coping and motivation with ART adherence.

#### Limitations and directions for future research

As noted above, there were limitations in this study. The sample size was small, which negatively affected the power of the study. Additionally, there were several missing data points for which we used imputation. This was done after deliberate assessment of missing data points. The missing data seemed to be at random, and the amounts of missing data were below or just marginally above the 30% threshold for unbiased imputation (Collins et al., 2001). However, with all of the limitations in mind, the results of this study need to be considered carefully, and the findings must be verified and explored with future research. Our results indicate directions in which research on ART adherence in PLWH with a comorbid mental health or substance use disorder should proceed.

#### Conclusion and implications for practice

Finding effective methods to provide and support housing of this subpopulation of PLWH will be an important step towards bettering adherence to ART. Also, determining more definitive relationships of ART adherence with employment and social support may be fruitful in discovering methods to increase adherence in PLWH with a comorbid mental health or substance use disorder.

#### Acknowledgements

Funding for the parent study was provided by National Institutes of Health (NIH)/National Institute of Nursing Research grant # R21 NR012918, with additional infrastructure support from the NIH/National Center for Research Resources Colorado CTSI, grant # UL1 RR025780.

#### References

- Anderson, A. M., Higgins, M. K., Ownby, R. L., & Waldrop-Valverde, D. (2015). Changes in neurocognition and adherence over six months in HIV-infected individuals with cocaine or heroin dependence. *AIDS Care*, 27(3), 333–337. <https://doi.org/10.1080/09540121.2014.985183>.
- Batchelder, A. W., Brisbane, M., Litwin, A. H., Nahvi, S., Berg, K. M., & Arnsten, J. H. (2013). "Damaging what wasn't damaged already": Psychological tension and antiretroviral adherence among HIV-infected methadone-maintained drug users. *AIDS Care*, 25(11), 1370–1374. <https://doi.org/10.1080/09540121.2013.766303>.
- Bova, C. A., Fennie, K. P., Knafl, G. J., Dieckhaus, K. D., Watrous, E., & Williams, A. B. (2005). Use of electronic monitoring devices to measure antiretroviral adherence: Practical considerations. *AIDS and Behavior*, 9(1), 103–110. <https://doi.org/10.1007/s10461-005-1685-0>.
- Cantudo-Cuenca, M. R., Jimenez-Galan, R., Almeida-Gonzalez, C. V., & Morillo-Verdugo, R. (2014). Concurrent use of comedication reduces adherence to antiretroviral therapy among HIV-infected patients. *Journal of Managed Care and Specialty Pharmacy*, 20(8), 844–850.
- Carver, C. S. (1997). You want to measure coping but your protocol's too long: Consider the brief COPE. *International Journal of Behavioral Medicine*, 4(1), 92–100. [https://doi.org/10.1207/s15327581ijbm0401\\_6](https://doi.org/10.1207/s15327581ijbm0401_6).
- Chesney, M. A. (2006). The elusive gold standard. Future perspectives for HIV adherence assessment and intervention. *Journal of Acquired Immune Deficiency Syndromes*, 43(1), S149–S155. <https://doi.org/10.1097/01.qai.0000243112.91293.26>.
- Collins, L., Schafer, J., & Kam, C. (2001). A comparison of inclusive and restrictive strategies in modern missing data procedures. *Psychological Methods*, 6, 330–351.
- Cook, P. F., Schmiede, S. J., McClean, M., Aagaard, L., & Kahook, M. Y. (2011). Practical and analytic issues in the electronic assessment of adherence. *Western Journal of Nursing Research*, 34, 598–620. <https://doi.org/10.1177/0193945911427153>.
- Cook, P. F., Schmiede, S. J., Starr, W., Carrington, J. M., & Bradley-Springer, L. (2017). Prospective state and trait predictors of daily medication adherence behavior in HIV. *Nursing Research*, 66, 275–285. <https://doi.org/10.1097/NNR.0000000000000216>.
- Cook, P. F., Schmiede, S. J., Reeder, B., Horton-Deutsch, S., & Lowe, N. K. (2018). Temporal immediacy: A two-system theory of mid for understanding and changing health behaviors. *Nursing Research*, 67(2). <https://doi.org/10.1097/NNR.0000000000000265>.
- Crues, D. G., Minor, S., Antoni, M. H., & Millon, T. (2007). Utility of the Millon Behavioral Medicine Diagnostic (MBMD) to predict adherence to highly active antiretroviral therapy (HAART) medication regimens among HIV-positive men and women. *Journal of Personality Assessment*, 89(3), 277–290. <https://doi.org/10.1080/00223890701629805>.
- DeMasi, R. A., Graham, N. M., Tolson, J. M., Pham, S. V., Capuano, G. A., Fisher, R. L., ... Eron, J. J., Jr. (2001). Correlation between self-reported adherence to highly active antiretroviral therapy (HAART) and virologic outcome. *Advances in Therapy*, 18(4), 163–173.
- Gonzalez, J. S., Penedo, F. J., Llabre, M. M., Duran, R. E., Antoni, M. H., Schneiderman, N., & Horne, R. (2007). Physical symptoms, beliefs about medications, negative mood, and long-term HIV medication adherence. *Annals of Behavioral Medicine*, 34(1), 46–55. <https://doi.org/10.1080/08836610701495565>.
- Gunthard, H. F., Aberg, J. A., Eron, J. J., Hoy, J. F., Telenti, A., ... Benson, C. A. Volberding (2014). Antiretroviral treatment of adult HIV infection: 2014 recommendations of the International Antiviral Society-USA Panel. *Jama*, 312(4), 410–425. <https://doi.org/10.1001/jama.2014.8722>.
- Hann, D., Winter, K., & Jacobsen, P. (1999). Measurement of depressive symptoms in cancer patients: Evaluation of the Center for Epidemiological Studies Depression Scale (CES-D). *Journal of Psychosomatic Research*, 46(5), 437–443.
- Herzog, T. A., & Blagg, C. O. (2007). Are most precontemplators contemplating smoking cessation? Assessing the validity of the stages of change. *Health Psychology*, 26(2), 222–231. <https://doi.org/10.1037/0278-6133.26.2.222>.
- Kader, R., Govender, R., Seedat, S., Koch, J. R., & Parry, C. (2015). Understanding the impact of hazardous and harmful use of alcohol and/or other drugs on ARV adherence and disease progression. *Public Library of Science ONE*, 10(5), e0125088. <https://doi.org/10.1371/journal.pone.0125088>.
- Kagee, A., & Nel, A. (2012). Assessing the association between self-report items for HIV pill adherence and biological measures. *AIDS Care*, 24(11), 1448–1452. <https://doi.org/10.1080/09540121.2012.687816>.
- Kaiser Family Foundation (2017). State health facts: HIV/AIDS. Retrieved from <http://kff.org/state-category/hiv/aids/hiv-diagnoses/>.
- Katz, I. T., Ryu, A. E., Onuegbu, A. G., Psaros, C., Weiser, S. D., Bangsberg, D. R., & Tsai, A. C. (2013). Impact of HIV-related stigma on treatment adherence: Systematic review and meta-synthesis. *Journal of the International AIDS Society*, 16(3 Suppl 2), 18640. <https://doi.org/10.7448/ias.16.3.18640>.
- Lopez, E., Jones, D. L., Ishii, M., Tobin, J. N., & Weiss, S. M. (2007). HIV Medication Adherence and Substance Use: The Smartest Women's Project. *American Journal of Infectious Diseases*, 3(4), 240–247.
- McGuire, T. G., & Miranda, J. (2014). Racial and ethnic disparities in mental health care: Evidence and policy implications. *Health Affairs (Millwood)*, 27(2), 393–403. <https://doi.org/10.1377/hlthaff.27.2.393>.
- Meade, C. S., Conn, N. A., Skalski, L. M., & Safren, S. A. (2011). Neurocognitive impairment and medication adherence in HIV patients with and without cocaine dependence. *Journal of Behavioral Medicine*, 34(2), 128–138. <https://doi.org/10.1007/s10865-010-9293-5>.
- Moore, D. J., Blackstone, K., Woods, S. P., Ellis, R. J., Atkinson, J. H., Heaton, R. K., & Grant, I. (2012). Methamphetamine use and neuropsychiatric factors are associated with antiretroviral non-adherence. *AIDS Care*, 24(12), 1504–1513. <https://doi.org/10.1080/09540121.2012.672718>.
- Nachege, Uthman, Peltzer, Richardson, Mills, Amekudzi, & Ouédraogo (2015). Association between antiretroviral therapy adherence and employment status: Systematic review and meta-analysis. *Bulletin of the World Health Organization*, 93(1), 29–41. <https://doi.org/10.2471/BLT.14.138149>.
- Nel, A., & Kagee, A. (2011). Common mental health problems and antiretroviral therapy adherence. *AIDS Care*, 23(11), 1360–1365. <https://doi.org/10.1080/09540121.2011.565025>.
- Nel, A., & Kagee, A. (2013). The relationship between depression, anxiety and medication adherence among patients receiving antiretroviral treatment in South Africa. *AIDS Care*, 25(8), 948–955. <https://doi.org/10.1080/09540121.2012.748867>.
- O'Connor, J. L., Gardner, E. M., Mannheimer, S. B., Lifson, A. R., Esser, S., Telzak, E. E., & Phillips, A. N. (2013). Factors associated with adherence amongst 5295 people receiving antiretroviral therapy as part of an international trial. *Journal of Infectious Diseases*, 208(1), 40–49. <https://doi.org/10.1093/infdis/jis731>.
- Pattyn, E., Verhaeghe, M., & Bracke, P. (2015). The gender gap in mental health service use. *Social Psychiatry and Psychiatric Epidemiology*, 50(7), 1089–1095. <https://doi.org/10.1007/s00127-015-1038-x>.
- Pau, A. K., & George, J. M. (2014). Antiretroviral therapy: Current drugs. *Infectious Disease Clinics of North America*, 28(3), 371–402. <https://doi.org/10.1016/j.idc.2014.06.001>.
- Pence, B. W., Gaynes, B. N., Williams, Q., Modi, R., Adams, J., Quinlivan, E. B., ... Mugavero, M. J. (2012). Assessing the effect of measurement-based care depression treatment on HIV medication adherence and health outcomes: Rationale and design of the SLAM DUNC study. *Contemporary Clinical Trials*, 33(4), 828–838. <https://doi.org/10.1016/j.cct.2012.04.002>.
- Schafer, J. L. (1997). NORM: Multiple imputation of incomplete multivariate data under a normal model, version 2.03 (computer software). Available from <http://www.stat.psu.edu/~jls/misofswa.html>.
- Silverberg, M. J., Leyden, W., Quesenberry, C. P., Jr., & Horberg, M. A. (2009). Race/ethnicity and risk of AIDS and death among HIV-infected patients with access to care. *Journal of General Internal Medicine*, 24(9), 1065–1072. <https://doi.org/10.1007/s11606-009-1049-y>.
- Springer, S. A., Dushaj, A., & Azar, M. M. (2012). The impact of DSM-IV mental disorders on adherence to combination antiretroviral therapy among adult persons living with HIV/AIDS: A systematic review. *AIDS Behavior*, 16(8), 2119–2143. <https://doi.org/>

- 10.1007/s10461-012-0212-3.
- Stanley, M. A., Beck, J. G., & Zebb, B. J. (1998). Psychometric properties of the MSPSS in older adults. *Aging & Mental Health, 2*(3), 186–193.
- Surratt, H. L., O'Grady, C. L., Levi-Minzi, M. A., & Kurtz, S. P. (2015). Medication adherence challenges among HIV positive substance abusers: the role of food and housing insecurity. *AIDS Care, 27*(3), 307–314. <https://doi.org/10.1080/09540121.2014.967656>.
- The United States Department of Labor (2017). *Office of disability employment policy*. Washington, DC: Author. Retrieved from <https://www.dol.gov/odep/topics/>.
- The White House (2015). *National HIV/AIDS strategy for the United States: Updated to 2020*. Washington, DC: Author. Retrieved from <https://www.aids.gov/federal-resources/national-hiv-aids-strategy/nhas-update.pdf>.
- The White House (2017). *HIV/AIDS care continuum*. Washington, DC: Author. Retrieved from <https://www.aids.gov/federal-resources/policies/care-continuum/>.
- Tugenberg, T., Ware, N. C., & Wyatt, M. A. (2006). Paradoxical effects of clinician emphasis on adherence to combination antiretroviral therapy for HIV/AIDS. *AIDS Patient Care and STDs, 20*(4), 269–274. <https://doi.org/10.1089/apc.2006.20.269>.
- Viswanathan, S., Justice, A. C., Alexander, G. C., Brown, T. T., Gandhi, N. R., McNicholl, I. R., ... Jacobson, L. P. (2015). Adherence and HIV RNA suppression in the current era of highly active antiretroviral therapy. *Journal of Acquired Immune Deficiency Syndromes, 69*(4), 493–498. <https://doi.org/10.1097/qai.0000000000000643>.
- Wang, H., Zhou, J., He, G., Luo, Y., Li, X., Yang, A., ... Williams, A. B. (2009). Consistent ART adherence is associated with improved quality of life, CD4 counts, and reduced hospital costs in central China. *AIDS Research and Human Retroviruses, 25*(8), 757–763. <https://doi.org/10.1089/aid.2008.0173>.
- Zhang, N. J., Terry, A., & McHorney, C. A. (2014). Impact of health literacy on medication adherence: A systematic review and meta-analysis. *Annals of Pharmacotherapy, 48*(6), 741–751. <https://doi.org/10.1177/1060028014526562>.