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## 90-90-90-Plus: Maintaining Adherence to Antiretroviral Therapies

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### Abstract

Medication adherence is the “Plus” in the global challenge to have 90% of HIV-infected individuals tested, 90% of those who are HIV positive treated, and 90% of those treated achieve an undetectable viral load. The latter indicates viral suppression, the goal for clinicians treating people living with HIV (PLWH). The comparative importance of different psychosocial scales in predicting the level of antiretroviral adherence, however, has been little studied. Using data from a cross-sectional study of medication adherence with an international convenience sample of 1811 PLWH, we categorized respondent medication adherence as None (0%), Low (1–60%), Moderate (61–94%), and High (95–100%) adherence based on self-report. The survey contained 13 psychosocial scales/indices, all of which were correlated with one another ( $p < 0.05$  or less) and had differing degrees of association with the levels of adherence. Controlling for the influence of race, gender, education, and ability to pay for care, all scales/indices were associated with adherence, with the exception of Berger’s perceived stigma scale. Using forward selection stepwise regression, we found that adherence self-efficacy, depression, stressful life events, and perceived stigma were significant predictors of medication adherence. Among the demographic variables entered into the model, nonwhite race was associated with double the odds of being in the None rather than in the High adherence category, suggesting these individuals may require additional support. In addition, asking about self-efficacy, depression, stigma, and stressful life events also will be beneficial in identifying patients requiring greater adherence support. This support is essential to medication adherence, the Plus to 90-90-90.

**Keywords:** adherence, 90-90-90, ART, predictors

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## Introduction

THE 90-90-90 UNAIDS PROPOSAL recommends that by 2020, 90% of HIV-infected persons globally know their positive status; 90% of those with positive status be receiving antiretroviral therapy (ART) and 90% of those receiving treatment be virally suppressed.<sup>1</sup> The research demonstrating the effectiveness of ART, when taken appropriately, in preventing transmission to uninfected partners raised the hopes of scientists, clinicians, and those infected with HIV that transmission could be prevented.<sup>2,3</sup> However, previous research has found that 22% of those who were prescribed ART were not virally suppressed and attribute this to a lack of adherence.<sup>4,5</sup> Consequently, promoting ART adherence is a central concern of clinicians caring for people living with HIV (PLWH) both for the patient's health and well-being and for the prevention of transmission to uninfected partners.

In the early days of the HIV pandemic, PLWH in San Francisco would maintain adherence to ART by setting their technical devices to ring every 4 h. With limited options and the specter of death prevalent, those who had access to medications, largely azidothymidine (AZT) in the mid-1980s, were eager to maintain adherence given the alternative. More than 30 years later, PLWH have many more options and most drug regimens are once per day and at the most twice a day.<sup>6</sup> The number of pills that need to be ingested at any one time are far reduced given the coformulation of a number of drugs into one pill. Nonetheless, medication adherence remains a challenge in HIV care just as it does in the care of people living with diabetes and hypertension. Recent reports suggest that medication adherence has been estimated to be "as low as 55%" across all populations.<sup>7,8</sup> Marcum et al. report that 30–50% of US adults are not adherent to their medications for chronic health-related conditions.<sup>9</sup>

### *Factors associated with adherence*

Sociodemographic factors associated with adherence include higher annual income (>\$20,000 per year) and increased treatment self-efficacy.<sup>10</sup> The base income for higher annual income of greater than \$20,000 is of interest given that the US Census Bureau indicates that for 2015, for individuals younger than 65 years of age, the poverty level is \$12,331 and for those older than 65, that sum is \$11,367.<sup>11</sup> For a family of four (two adults and two children), the sum is \$24,036, and for a family with one adult and two children, the figure is \$19,096. In the article by McCoy et al., the figure cited for higher annual income as noted is above the US poverty level.<sup>10</sup> Participants in that study were 50 years and older and 80% had an income of less than \$20,000. The 20% with an income of \$20,000 or greater were the individuals who were more adherent. In the McCoy et al. study, there were no statistically significant differences by race in treatment self-efficacy and adherence.<sup>10</sup>

### *Challenges to adherence*

Beer and Skabinski describe challenges to adherence as falling into four categories, including demographic (<40 years of age, being female), psychosocial (depression, use of stimulants), characteristics of the regimen (side effects, frequency of medications), and patient beliefs (medication characteristics, beliefs about ability to adhere).<sup>4</sup> When these researchers ex-

amined dose, schedule, and instruction adherence, they found that although 86% were dose adherent, only 72% were schedule adherent and 69% were instruction adherent. This percentage slipped to 60% when all three factors were considered. Saberi et al. reported the following as having the highest relative importance in explaining a patient's detectable viral load: too many pills to take, wanted to avoid side effects, felt drug was toxic/harmful, felt sick/ill, and felt depressed/overwhelmed.<sup>8</sup> Interestingly, "simply forgot," often given as a response to such queries, was ninth in importance in this study.

PLWH give many reasons for a lack of adherence to ART. Okonsky et al. found forgetting was the most common reason cited for nonadherence in women.<sup>12</sup> The authors caution, however, that forgetting may be a shorthand response reflecting a more complex issue. They urge clinicians to investigate "what forgetting actually means" (p. 1022). Forgetfulness was the most common reason given for missing a dose of medication in studies in Tanzania, Uganda, Zambia,<sup>13</sup> and Ethiopia.<sup>14</sup> The variables that had a statistically significant relationship with nonadherence in Ethiopia, however, were age, employment, HIV disclosure, and "comfortability to take ART in the presence of others" (p. 373). The concern about taking medications in front of others who may not know of the individual's HIV status connotes fear of stigmatization.<sup>15,16</sup> Employment may make it more challenging to take one's medication surreptitiously, whereas lack of economic resources, and in particular food insecurity resulting from lack of employment, may impede ART adherence.<sup>17,18</sup> Food insecurity has been observed to be "an important barrier to ART adherence."<sup>18</sup>

Depression has frequently been explored in relation to nonadherence to ART.<sup>19</sup> Gonzalez et al. assert that far more attention has been given to depression in the literature than other mental health conditions.<sup>20</sup> They suggest that it is the degree of symptom severity and not just meeting given depression diagnostic criteria that is associated with adherence. Citing Leserman,<sup>21</sup> they emphasize that "Stress and trauma have been consistent risk factors for HIV disease progression" (p. 6).<sup>20</sup>

One of the other mental health conditions or psychosocial factors associated with impaired ART adherence is substance abuse.<sup>22</sup> Impairment from the abuse of substances varies with the substances used. In a study conducted in New York City, ARV adherence was poorest for those using alcohol and cocaine/crack.<sup>23</sup> Cocaine use also was implicated as a barrier to adherence in a study providing cognitive behavioral therapy (CBT) to promote ARV adherence in those suffering from depression.<sup>24</sup> It was reported that cocaine use at baseline limited the effectiveness of the (CBT) intervention. These studies and others highlight the numerous factors such as substance abuse and violence associated with unacceptable levels of adherence.<sup>25</sup> The question remains as to how these variables, and in particular psychosocial variables, relate to one another and the various levels of adherence.

This article reports the results of an investigation with a focus on the relationships of selected psychosocial variables and self-compassion with levels of ART adherence in varied settings, including resource limited settings. Numerous scales and indices have been used to measure the well-being of PLWH,<sup>26</sup> but the comparative importance of many of these measures in predicting medication adherence has not been fully explored. This article reports on an investigation as to whether there were differences by psychosocial variables and

the level of ART adherence. Further, given the significance of some of these variables in previous research, we also investigated the impact of these variables in discriminating different levels of adherence.

## Methods

Following review and approval of site-specific Institutional Review Boards, 1181 PLHV from 30 clinics in 4 countries, (Canada, Namibia, Thailand, and the United States) and the Commonwealth of Puerto Rico, were enrolled in a convenience sample. The research for this article excludes participants who stopped taking medications on the advice of their healthcare provider (HCP). Among those who were currently taking ART or who had stopped on their own, 36% had some college education, 24% were white, 71% were male, and 40% reported having been unable to get healthcare because of their inability to pay (Table 1).

### Instruments

**Sociodemographic questionnaire.** This questionnaire has been used numerous times in our previous studies and consists of 20 items including age, gender, race, ethnicity, level of education, adequacy of income, health insurance, date of HIV diagnosis, route of HIV transmission, current CD4 count, viral load, other health conditions, and general health.<sup>27,28</sup>

**Engagement with HCP scale.** The HCP scale is a 13-item, 4-point scale (1 = always true to 4 = never true), which queries research participants about their interactions with their HCP(s). A low score reflects greater provider engagement. Cronbach's  $\alpha$  reliability was 0.96 in this sample.<sup>29</sup>

**Rosenberg self-esteem scale.** This measure of feelings of self-worth consists of 10 items, on a 4-point Likert-type

scale (0 = strongly agree to 3 = strongly disagree).<sup>30</sup> Cronbach's  $\alpha$  reliability was 0.85 in this sample.

**Perceived stigma scale.** The perceived stigma scale (PSS) measures perceived stigma by PLWH.<sup>31</sup> The scale consists of 40 items using 4-point Likert-type response options from 0 (strongly disagree) to 3 (strongly agree). The higher the score, the greater the perceived stigma. The Cronbach's  $\alpha$  reliability score was 0.96.

**Social capital scale.** The social capital scale is a 36-item scale with 8 subscales.<sup>32</sup> The social capital scale was modified by Webel et al. with the consent of the authors of the scale. Items were rated on a 4-point Likert-type scale and higher scores indicate greater social capital. Reliability for the revised social capital scale as measured by Webel et al. was 0.88.<sup>33</sup>

**Sense of coherence scale.** The sense of coherence (SOC) scale is a 13-item scale with 4 items concerned with meaningfulness, 5 items with comprehensibility, and 4 items with manageability. The 7-point scale has two anchors namely 1 = very often and 7 = very seldom/never. The SOC scale scores range from 16 to 91, with a higher score indicating a lower SOC. Cronbach's  $\alpha$  has ranged between 0.74 and 0.95.<sup>34,35</sup>

**HIV adherence self-efficacy.** The HIV adherence self-efficacy scale (HIV-ASES) measures the confidence of the respondent in completing treatment-associated behaviors and incorporating those behaviors into daily life as appropriate.<sup>36</sup> The scale consists of 12 items using a 10-point range of options from 1 (cannot do it) to 10 (certain can do it). The higher the score, the greater the perceived adherence self-efficacy. "The HIV-ASES demonstrates robust internal consistency ( $\rho$ 's > 0.90) and 3-month ( $r$ 's > 0.70) and 15-month ( $r$ 's > 0.40) test-retest reliability" (p. 359).

**Chronic disease self-efficacy scale.** The chronic disease self-efficacy scale was modified from the 6-item scale.<sup>37</sup> The 6-item scale was derived from a 33-item scale with the following subscales: exercise regularly; obtain help from community, family friends; communicate with physician; manage disease in general; do chores; social/recreational activities; manage symptoms; control/manage depression; and one item each on get information about disease; and manage shortness of breath. The 6-item scale contained items from the manage symptoms scale and the manage disease in general scale. Four additional items were added and pilot tested by Webel (2009, pers. comm.). All items are rated on a 1–10 scale, where 1 = not at all confident and 10 = totally confident. Alpha reliability of the scale was found to be 0.92.

**Stressful life events scale.** The list of threatening experiences scale consisted of 12 stressful life events scales such as experience of a serious illness, death of a loved one, and assault, requiring a yes/no response.<sup>38,39</sup> Holzemer revised the questionnaire adding eight items related to HIV disease such as queries on abuse of alcohol and stigma.<sup>40</sup> The revised scale had a Cronbach's  $\alpha$  of 0.88.

TABLE 1. SAMPLE CHARACTERISTICS

	No.	Percentage
Total	1811	100
Adherence (self-report past 30 days)		
0% or stopped on their own	109	6.0
1–60%	151	8.3
61–94%	603	33.3
95–100%	948	52.3
Education		
HS graduate or less	1154	64.2
Some college or more	643	35.8
Missing	14	
Race		
White	422	23.6
Nonwhite	1369	76.4
Missing	20	
Gender		
Male	1273	71.0
Female	519	29.0
Missing	19	
Ever needed healthcare but could not pay		
No	664	60.4
Yes	1014	39.6
Missing	133	

Self-compassion scale. The self-compassion scale short form adapted from the Neff 26-item scale measures self-kindness and self-judgment.<sup>41,42</sup> The 12 items are measured on a scale ranging from 1 (almost never) to 5 (almost always). The self-kindness items are worded positively, whereas the self-judgment items are worded negatively. The Cronbach's  $\alpha$  reliability value in a study by Eller et al. was 0.78 for self-kindness and 0.83 for self-judgment.<sup>19</sup>

The revised sign and symptom checklist (SSC-rev.) for persons with HIV disease. The revised sign and symptom checklist measures the intensity of symptoms that may be experienced by the PLWH<sup>43</sup> The SSC-rev. is composed of three parts. Part 1 is composed of 45 questions regarding the presence and severity of symptoms; Part 2 contains 19 symptoms that did not cluster into factor scores; and Part 3 consists of queries about 8 gynecological symptoms. The 64-item scale is generally used unless the focus is on HIV-infected women. Cronbach's  $\alpha$  reliability for the 64-item scale was reported to be 0.92 by Wantland et al.<sup>44</sup>

Center for epidemiologic studies depression (CESD) scale. This 20-item scale serves as a screen for the presence of symptoms of depression in a community sample.<sup>45</sup> Participants can rate items from 0 (rarely or none of the time) to 3 (most or all of the time). The higher the score, the more the symptoms are present. The  $\alpha$  reliability value was 0.90 in a study of PLWH.<sup>46</sup>

Anxiety instrument of the symptom checklist-90-R instrument. The 10-item anxiety instrument<sup>47</sup> is part of the symptom checklist-90-R instrument that measures degree of distress associated with psychological problems such as somatization, interpersonal sensitivity, depression, and anxiety. The anxiety instrument is rated on a 5-point scale ranging from 0 (not at all) to 4 (extremely).

The 30-Day Visual Analog Scale for Medication Adherence. The *30-Day Visual Analog Scale for Medication Adherence* is a one-item scale adapted from Walsh et al.<sup>48</sup> Participants are queried about their medication use and asked to indicate on a scale of 0% to 100% how much of the time in the past 30 days they have taken their medications.

Adherence in the HIV literature is categorized with a variety of approaches. We followed a consensus pattern for cutoffs at 95% and 60% adherence. In our sample, this yielded 52.3% in the High (95–100%) adherence category, 33.3% in the Medium (61–94%) category, 8.3% in the Low adherence (1–60%) category, and 6% in the None adherence category (Table 1). We also conducted sensitivity analysis with the cutoffs at 90% and 40% adherence.

*Analytic method*

We compared the predictive value of 13 different scales containing 267 questions. The distribution of missing values in the scales would have reduced the valid sample substantially, so we employed the SPSS missing values module. This software first determines whether values are missing at random or following a pattern and then uses multiple imputations to replace missing data. This process resulted in a valid sample of 1811 participants. The means, standard distribution, and Cronbach's  $\alpha$  are reported in Table 2. The reliability

TABLE 2. SCALE PROPERTIES AND CORRELATION MATRIX

	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)	(10)	(11)	(12)	(13)
Healthcare provider engagement scale (1)	<b>0.95</b>												
Self-esteem scale (Rosenberg) (2)	-0.15	<b>0.86</b>											
Perceived stigma scale (Berger) (3)	0.15	-0.33	<b>0.96</b>										
Marginalization and social capital scale (4)	-0.19	0.37	-0.28	<b>0.89</b>									
Sense of coherence scale (5)	0.22	-0.54	0.41	-0.42	<b>0.72</b>								
Adherence self-efficacy scale (6)	-0.27	0.28	-0.14	0.28	-0.33	<b>0.95</b>							
Chronic disease self-efficacy scale (7)	-0.24	0.35	-0.23	0.37	-0.43	0.54	<b>0.93</b>						
Stressful life events index (8)	0.13	-0.22	0.18	-0.11	0.33	-0.20	-0.21	<b>0.88</b>					
Self-compassion scale (9)	-0.17	0.61	-0.30	0.39	-0.62	0.32	0.41	-0.22	<b>0.74</b>				
Center for epidemiologic studies depression scale (10)	0.22	-0.55	0.37	-0.35	0.64	-0.32	-0.42	0.32	-0.58	<b>0.87</b>			
Anxiety instruments of the symptom checklist (11)	0.19	-0.38	0.35	-0.29	0.48	-0.21	-0.33	0.31	-0.41	0.61	<b>0.97</b>		
Health status (VA-SF12) (12)	0.21	-0.42	0.37	-0.35	0.60	-0.30	-0.48	0.30	-0.47	0.64	0.52	<b>0.89</b>	
Sign and symptom checklist, intensity (13)	0.22	-0.26	0.29	-0.20	0.39	-0.27	-0.34	0.29	-0.28	0.51	0.58	0.55	<b>0.95</b>

Cronbach's  $\alpha$  is presented on the diagonal in bold, italicized text.

of each of the scales, as measured by Cronbach's  $\alpha$ , was appropriate for research purposes.

$\chi^2$  was used to analyze adherence category by respondent demographics, *t*-tests to compare scale means by adherence category, and correlation to explore the relationships between the scales. We conducted two forms of multinomial logistic regression to test the association between scale items and reported adherence. First we tested each of the scales sequentially (i.e., one at a time) and then used a forward selection stepwise function to choose which scales to include in the model. In both forms of regression, we required all models to include sex, education, ability to pay for care, and race. All analyses were conducted with SPSS Version 21.

## Results

All scales were significantly correlated with one another (Table 2). Of the 78 possible associations between the scales, nearly half were weak with a correlation less than 0.3; nearly half were moderate with a correlation between 0.3 and 0.5; and 10 associations were strong with correlations more than 0.5. The strongest associations were between health status and depression ( $r=0.64$ ) and between health status and SOC ( $r=0.64$ ).

In bivariate analysis, education and race were associated with the adherence category, whereas gender and ability to pay were not (Table 3). Among those in the None adherence category, 16.7% were white compared with 27.9% in the High adherence category. Among those in the High adherence category, 38.5% had some college education compared with 29.4% in the None adherence category and 27% in the Low adherence category.

With the exception of the PSS and the stressful life events inventory, all scales showed differences in means between the High and None adherence categories (Table 4). Interestingly, the means in the "Low" adherence group were often lower than those in the "None" adherence group, including self-esteem, social capital, and self-compassion as well as the self-efficacy scales. Scale means were also substantially

different between the Medium and High adherence groups, with the exception of perceived stigma.

Each scale was tested in a multinomial logistic regression predicting adherence category and adjusting for sex, race, education, and ability to pay for healthcare (Table 5). All 13 of the models were significant at  $p<0.001$  and within the models the scales were significant predictors at  $p<0.001$ , with the exception of Berger's PSS, which was significant at 0.027. The scale with the strongest predictive association with adherence, as measured by Nagelkerke pseudo R square, was adherence self-efficacy. For every one point increase in this scale, the odds of being in the None adherence category decreased by 6% as compared with the High adherence category. A one point increase in adherence self-efficacy was associated with 7% lower odds of being in the Low adherence category and 3% lower odds of being in the Medium adherence category.

Finally, the stepwise multinomial logistic regression forced the demographic variables into the model and then chose among the scales in a forward selection stepped manner (Table 6). Adherence self-efficacy, the CESD depression scale, stressful life events, and perceived stigma were significant in this model along with race. Nonwhite race doubled the odds that the respondent was in the None adherence category compared with High adherence category, whereas education, gender, and ability to pay were not significant.

The impact of adherence self-efficacy and CESD depression was similar in both multinomial regression analyses. The role of stressful life events was decreased in these analyses. Although an additional life event increased the odds of being in the None or Low adherence category by 10% and 11%, respectively, when tested individually, an additional life event increased the odds of being in the None or Low adherence category by 5% in the stepwise analysis. More surprising was the emergence of perceived stigma as a weak predictor in the stepwise model. For every one point increase in the PSS, there was a 1% decrease in the odds of being in the None adherence category as opposed to the High adherence category. This may seem counter-intuitive, nonetheless the

TABLE 3. DEMOGRAPHICS BY ADHERENCE CATEGORY

	Total, n (%)	None, n (%)	Low, n (%)	Medium, n (%)	High, n (%)	Significance
Education						
HS graduate or less	1154 (64.2)	77 (70.6)	108 (73.0)	390 (65.2)	579 (61.5)	0.016
Some college or more	643 (35.8)	32 (29.4)	40 (27.0)	208 (34.8)	363 (38.5)	
Total	1797 (100)	109 (100)	148 (100)	598 (100)	942 (100)	
Race						
White	422 (23.6)	18 (16.7)	30 (20.3)	113 (18.9)	261 (27.9)	0.000
Nonwhite	1369 (76.4)	90 (83.3)	118 (79.7)	485 (81.1)	676 (72.1)	
Total	1791 (100)	108 (100)	148 (100)	598 (100)	937 (100)	
Gender						
Male	1273 (71.0)	74 (67.9)	99 (67.8)	420 (70.6)	680 (72.2)	0.587
Female	519 (29.0)	35 (32.1)	47 (32.3)	175 (29.4)	262 (27.8)	
Total	1792 (100)	109 (100)	146 (100)	595 (100)	942 (100)	
Ever needed healthcare but could not pay						
No	1014 (60.4)	55 (52.4)	87 (58.4)	332 (61.1)	540 (61.3)	0.116
Yes	664 (39.6)	50 (47.6)	62 (41.6)	211 (38.9)	341 (38.7)	
Total	1678 (100)	105 (100)	149 (100)	543 (100)	881 (100)	

Significance is tested with Mantel-Haenszel's  $\chi^2$ .

TABLE 4. SCALES BY ADHERENCE

	<i>None, 0% or stopped on their own</i>	<i>Low, 1–60%</i>	<i>Medium, 61–94%</i>	<i>High, 95–100%</i>
Healthcare system scale				
Healthcare provider engagement scale	20.68b,c	20.54d,e	17.97b,d,f	16.36c,e,f
Psychosocial scales				
Rosenberg self-esteem scale	18.86a,c	17.37a,d,e	18.79d,f	20.22c,e,f
Perceived stigma scale (Berger)	94.29	99.15d,e	94.26d	92.56e
Social capital scale	81.34a,c	74.72a,d,e	82.78d,f	85.65c,e,f
Sense of coherence	51.14b,c	53.45d,e	48.53b,d,f	45.21c,e,f
Adherence self-efficacy	79.13a,b,c	71.28a,d,e	92.43b,d,f	105.61c,e,f
Chronic disease self-efficacy	64.40a,b,c	58.18a,d,e	72.80b,d,f	79.27c,e,f
Stressful life events	7.71b	7.51d,e	5.94b,d,f	5.03e,f
Self-compassion scale	37.85a,c	35.85a,d,e	38.26,d,f	40.08c,e,f
Psychological health scales				
Center for epidemiologic studies depression scale	25.23b,c	27.75d,e	22.60b,d,f	19.05c,e,f
Anxiety	20.04b,c	20.58d,e	18.17b,d,f	16.88c,e,f
Physical health scales				
VA-SF12	33.32b,c	34.62d,e	30.41b,d,f	28.35c,e,f
Sign and symptom checklist, intensity	40.33b,c	45.50d,e	33.84b,d,f	27.85c,e,f
Sign and symptom checklist, frequency	24.03,c	26.78d,e	21.33d,f	17.42c,e,f

Statistically significant differences ( $p < 0.05$ ) are represented by a, between None and Low; b, between None and Medium; c, between None and High; d, between Low and Medium; e, between Low and High; f, between Medium and High.

result suggests that perceived stigma predicted a separate and distinct source of variance in adherence although the result may also be an artifact. The direction of the relationship in the multinomial regression is opposite to the relationship in the bivariate tables and it is only present in the Low versus High comparison.

## Discussion

This research tested the influence of 13 psychosocial scales/indices for adherence and found that all scales/indices were associated with adherence in bivariate analysis and that this association was robust for gender, race, education, and ability to pay for care, with the exception of stigma. We also found that all scales/indices were correlated with one another. This raises the prospect that research may aid clinicians by guiding their interview to those questions most closely associated with adherence. We found those to be the questions about self-efficacy, depression, stressful life events, and stigma.

The importance of the association of depression with antiretroviral adherence, found in prior research, was also found in this study. Magidson et al. have a potential explanation for this finding.<sup>49</sup> While conducting their investigation of data from the California Collaborative Treatment Group 578 study, they found that although there was not a relationship between depression and dose taking adherence, there was a significant relationship of depression with dose timing. PLWH took their medications but not at the indicated time. The explanation was what these investigators term “lifestyle structure” (p. 36). This was measured by a 9-item 5-point scale<sup>50,51</sup> with items such as “my days consist of doing the same things at the same time” and “I get up nearly at the same time each day” (p. 36).<sup>49</sup>

Beer et al. addressed the importance of obtaining multiple measures of nonadherence, including dose nonadherence,

schedule nonadherence, and instruction nonadherence.<sup>52</sup> All of these forms of nonadherence can contribute to a less than desirable level of adherence and need to be addressed by the HCP as was noted previously.

Hughes et al. estimate that 1 in 20 adults in the United States who initiated ART subsequently discontinued therapy.<sup>53</sup> Younger age was associated with both patient- and provider-initiated discontinuation of ART. Other variables associated with discontinuation included female gender, injection drug use, incarceration, and lack of supportive services to mention a few. Adverse events and intolerability were also factors that accounted for change or discontinuation of ART in a study by Mirjam-Colette et al.<sup>54</sup> They observed that of the 631 PLWH, 53% of the males and 54.4% of the females discontinued therapy within 12 months of beginning ART. This high proportion underscores the importance of addressing the question of adherence.

These results demonstrated that the psychosocial outcome measures differed between those who had discontinued therapy (the None group) and those whose adherence was Low, as well as those who had Moderate or High adherence. In many instances, those in the None adherence category had more beneficial psychosocial scores than those in the Low adherence category and often were midway between the Low and the Moderate adherence categories. Although those in the Low adherence category appeared to have access to medications, their ability to maintain adherence was decidedly less than those with Moderate adherence. This suggests that providers will need to access other members of the healthcare team to enhance the support such individuals require to maintain adherence. Those in the Moderate adherence category may have needs for education or other support that do not require the same degree of intervention as for those in the Low adherence category. Individuals currently in the None group require a collaborative approach to determine why they are not taking medications and what would help them to be

TABLE 5. MULTINOMIAL REGRESSION COMPARING SCALES

	<i>None, 0% or stopped on their own</i>	<i>Low, 1–60%</i>	<i>Medium, 61–94%</i>	<i>High, 95–100%</i>	$\chi^2, p$	<i>Nagelkerke pseudo R square</i>
Healthcare system scale	1.07 (1.05, 1.10)	1.07 (1.05, 1.10)	1.04 (1.02, 1.06)	Reference	88.23, <0.001	0.059
Healthcare provider engagement scale						
Psychosocial scales						
Self-esteem scale (Rosenberg)	0.94 (0.91, 0.98)	0.90 (0.87, 0.93)	0.95 (0.93, 0.97)	Reference	86.72, <0.001	0.058
Perceived stigma scale (Berger)	1.00 (0.99, 1.01)	1.01 (1.00, 1.02)	1.00 (1.00, 1.01)	Reference	39.92, <0.001	0.027
Marginalization and social capital scale	0.99 (0.97, 1.00)	0.96 (0.95, 0.97)	0.99 (0.98, 0.99)	Reference	85.43, <0.001	0.057
Sense of coherence scale	1.04 (1.02, 1.06)	1.06 (1.05, 1.08)	1.03 (1.02, 1.03)	Reference	110.75, <0.001	0.073
Adherence self-efficacy scale	0.94 (0.94, 0.95)	0.93 (0.93, 0.94)	0.97 (0.96, 0.97)	Reference	416.62, <0.001	0.252
Chronic disease self-efficacy scale	0.97 (0.96, 0.97)	0.95 (0.94, 0.96)	0.98 (0.98, 0.99)	Reference	189.56, <0.001	0.122
Stressful life events index	1.10 (1.06, 1.14)	1.11 (1.08, 1.15)	1.04 (1.02, 1.06)	Reference	81.66, <0.001	0.055
Self-compassion scale	0.96 (0.93, 0.99)	0.92 (0.90, 0.95)	0.96 (0.95, 0.98)	Reference	86.51, <0.001	0.058
Psychological health scales						
Center for epidemiologic studies depression scale	1.05 (1.03, 1.07)	1.07 (1.05, 1.08)	1.03 (1.02, 1.04)	Reference	122.69, <0.001	0.081
Anxiety instruments of the symptom checklist	1.03 (1.01, 1.06)	1.04 (1.02, 1.06)	1.02 (1.01, 1.03)	Reference	56.10, <0.001	0.038
Physical health scales						
Health status (VA-SF12)	1.06 (1.04, 1.09)	1.08 (1.06, 1.11)	1.03 (1.02, 1.05)	Reference	111.46, <0.001	0.074
Sign and symptom checklist, intensity	1.02 (1.01, 1.02)	1.02 (1.01, 1.03)	1.01 (1.01, 1.01)	Reference	89.39, <0.001	0.060

Results reported as odds ratios and 95% confidence intervals. All models control for gender, race, education, and ability to pay for care and have 15 degrees of freedom.



TABLE 6. MULTINOMIAL REGRESSION STEPWISE

	<i>None 0% or stopped on their own</i>	<i>Low, 1–60%</i>	<i>Medium, 61–94%</i>	<i>High, 95–100%</i>	<i>Significance</i>
<b>Forced variables</b>					
Nonwhite (vs. white)	2.06 (1.17, 3.63)	1.75 (1.07, 2.87)	1.65 (1.25, 2.17)	Reference	0.001
Female (vs. male)	1.39 (0.86, 2.22)	1.34 (0.87, 2.08)	1.1 (0.85, 1.42)	Reference	0.422
High school or less (vs. college or more)	1.02 (0.63, 1.63)	1.19 (0.76, 1.86)	0.95 (0.75, 1.21)	Reference	0.780
Unable to get care because of cost (vs. able to get care despite cost)	1.33 (0.85, 2.1)	0.89 (0.59, 1.36)	0.91 (0.71, 1.16)	Reference	0.352
<b>Stepwise variables</b>					
Adherence self-efficacy scale	0.95 (0.94, 0.96)	0.94 (0.93, 0.95)	0.97 (0.96, 0.97)	Reference	0.000
Center for epidemiologic studies depression scale	1.03 (1.00, 1.05)	1.03(1.01, 1.05)	1.02 (1.00, 1.03)	Reference	0.002
Stressful life events index	1.05 (1.01, 1.10)	1.05 (1.01, 1.09)	1.01 (0.98, 1.03)	Reference	0.031
Perceived stigma scale (Berger)	0.99 (0.98, 1.00)	1.00 (0.99, 1.01)	1.00 (0.99, 1.00)	Reference	0.047

Results reported as odds ratios and 95% confidence intervals. Model  $\chi^2=450.845$ ;  $p<0.001$  with Nagelkerke  $r^2$  0.270.

adherent if they were to initiate ART. Finally those in the High adherence group need praise for accomplishing the challenge of maintaining adherence to ART. These individuals can, if interested, mentor others in becoming highly adherent. It is important to note that technology-based methods for improving adherence including mobile devices have been shown to be effective.<sup>55</sup> Depending on the individual and the particular circumstances, the use of technology-based reminders, particularly if creatively constructed and aligned with the individual's interests, may prevent adherence fatigue.

#### Limitations

There are several limitations to this research. First, the adherence measure we used was self-reported and not independently verified. Although we did have a measure of viral load, the outcome measure that adherence seeks to improve, it was inconsistently available in the data set and consequently was not used in this analysis. Previous research into the measurement of adherence has found discrepancies between self-report and objective measures such as pill counts or electronic medication monitors. In addition, comorbid substance use may be a confounding variable when addressing self-reported adherence. Although we acknowledge these issues and the benefit of objective adherence measures, we also recognize that many clinicians rely on self-report of adherence verified by periodic CD4 counts and viral load testing. The number of research participants willing to acknowledge no or low adherence gives us some reason to have confidence in these findings.

The 90-90-90 UNAIDS proposal notes some of the challenges for HIV testing and ART prescription, but is largely silent on the issue of adherence and the factors that contribute to its maintenance.<sup>1</sup> The proposal does indicate an expectation that 73% of the PLWH will be virally suppressed when 90-90-90 is achieved. Our data indicate that 52% of our sample is 95–100% adherent and thus likely are virally suppressed. Of note, is the fact that with the emergence of newer regimens, 80–85% adherence is usually sufficient for viral suppression. In our study, high adherence was categorized as 95–100%, thus some individuals who were sufficiently virally suppressed were categorized as moderately

adherent. However, when during our initial statistical analysis we examined whether there would be a different result if the High adherence group were categorized as 90% or higher, our findings did not differ. Consequently, we elected to remain with the most stringent category for highly adherent. As noted, this decision may have omitted some individuals who would have been considered highly adherent, given the more recent ART and viral load findings on level of adherence required for viral suppression. Further, given that the data were collected at many university-affiliated clinics, there may be greater support services available to the PLWH, and consequently these data may represent a better, although not best, case scenario.

As we have seen, factors such as self-efficacy, stigma, depression, and stressful life events all have implications for the ability to maintain adherence. Each of these variables collectively or independently as in the case of stigma was correlated with whether viral suppression was maintained and consequently the last “90” of the 90-90-90 triad. Unless clinicians inquire about such factors in a routine, nonjudgmental manner, PLWH may not share the challenges they are confronting in maintaining their adherence. And as indicated by Beer and Skarbinski, adherence to dose may not be equivalent to adherence to schedule or instruction, requiring adroit questioning by the clinician.<sup>4</sup> Such questioning may result in distinguishing those who would benefit from additional support, thereby improving their ability to maintain adherence to ARVs and consequently suppression of viral load: 90-90-90 Plus.

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### References

- UNAIDS. 90-90-90 An Ambitious Treatment Target to Help End the AIDS Epidemic. Joint United Nations Programme on AIDS. Geneva, Switzerland. 2014.
- Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med* 2011;365:493–505.
- Rodgers AJ, Cambiano V, Bruun T, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA* 2016;316:171–181.
- Beer L, Skarbinski J. Adherence to antiretroviral therapy among HIV-infected adults in the United States. *AIDS Educ Prev* 2014;26:521–537.
- Gardner EM, McLees MP, Steiner JF, et al. The spectrum of engagement in HIV and its relevance to test and treat strategies for prevention of HIV infection. *Clin Infect Dis* 2011;52:793–800.
- Panel on Antiretroviral Guidelines for Adults and Adolescents Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. 2016. Available at: <http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf> (Last accessed July 14, 2016).
- Mills EJ, Nachega JB, Buchan I, et al. Adherence to antiretroviral therapy in sub-Saharan Africa: A meta-analysis. *JAMA* 2006;296:679–690.
- Saberi P, Neilands TB, Vittinghoff E, et al. Barriers to antiretroviral therapy adherence and plasma HIV RNA suppression among AIDS Clinical Trials Group Study Participants. *AIDS Patient Care STDs* 2015;29:111–116.
- Marcum ZA, Sevick MA, Handler SM, et al. Medication non-adherence, a diagnosable and treatable medical condition. *JAMA* 2013;309:2105–2106.
- McCoy K, Waldrop-Valverde D, Balderson BH, et al. Correlates of antiretroviral therapy adherence among HIV-infected older adults. *J Int Assoc Prov AIDS Care* 2016;15:248–255.
- U.S. Census Bureau. Poverty Thresholds 2015. U.S. Department of Commerce. 2016. Available at: <https://www.census.gov/data/tables/time-series/demo/income-poverty/historical-poverty-thresholds.html> (Last accessed May 12, 2017).
- Okonsky JG, Webel A, Rose CD, et al. Appreciating reasons for non-adherence in women. *Health Care Women Int* 2015;36:1007–1025.
- Koole O, Denison JA, Menten J, et al. Reasons for missing antiretroviral therapy: Results from a, multi-country study in Tanzania, Uganda, and Zambia. *PLoS One* 2016;11:e0147309.
- Tsega B, Srikanth BA, Shewamene Z. Determinants of non-adherence to antiretroviral therapy in adult hospitalized patients, Northwest Ethiopia. *Patient Pref Adherence* 2015;9:373–380.
- Treves-Kagan S, Steward WT, Ntswane L, et al. Why increasing availability of ART is not enough: A rapid, community-based study on how HIV-related stigma impacts engagement to care in rural South Africa. *BMC Public Health* 2016;16:87.
- Katz IT, Ryu AE, Onuegbu AG, et al. Impact of HIV-related stigma on treatment adherence: Systematic review and meta-synthesis. *J Int AIDS Soc* 2013;16:18640.
- Weiser SD, Tuller DM, Frongillo EA, et al. Food insecurity as a barrier to sustained antiretroviral therapy adherence in Uganda. *PLoS One* 2010. Available at: <http://dx.doi.org/10.1371/journal.pone.0010340> (Last accessed May 12, 2017).
- Singer AW, Weiser, SD, McCoy SI. Does food insecurity undermine adherence to antiretroviral therapy? A systematic review. *AIDS Behav* 2015;19:1510–1526.
- Eller LS, Rivero-Mendez M, Voss J, et al. Depressive symptoms, self-esteem, HIV-symptom management self-efficacy and self-compassion on people living with HIV. *AIDS Care* 2014;26:795–803.
- Gonzalez JS, Batchelder AW, Psaros C, et al. Depression and HIV/AIDS treatment non-adherence: A review and meta-analysis. *J Acquir Immune Defic Syndr* 2011;58:181–187.
- Leserman J. Role of depression, stress, and trauma in HIV disease progression. *Psychosom Med* 2008;70:539–545.
- Cohn SE, Jiang H, McCutchan JA, et al. Association of ongoing drug and alcohol use with non-adherence to antiretroviral therapy and higher risk of AIDS and death: Results from ACTG 362. *AIDS Care* 2011;23:775–785.
- Parsons JT, Starks TJ, Millar BM, et al. Patterns of substance use among HIV-positive adults over 50: Implications for treatment and medication adherence. *Drug Alcohol Depend* 2014;139:33–40.
- Dale SK, Traeger L, O'Cleirigh C, et al. Baseline substance use interferes with maintenance of HIV medication adherence skills. *AIDS Patient Care STDs* 2016;30:215–220.
- Sullivan KA, Messer LC, Quinlivan EB. Substance abuse, violence, and HIV/AIDS (SAVA) syndemic effects on viral suppression among HIV positive women of color. *AIDS Patient Care STDs* 2015;29(Suppl 1):S42–S48.
- Corless IB, Guarino AJ, Nicholas PK, et al. Mediators of Antiretroviral Medication Adherence: A Multisite International Study. *AIDS Care* 2013;25:364–377.
- Kemppainen J, Johnson MO, Phillips JC, et al. A multinational study of self-compassion and HIV-related anxiety. *Int Nurs Rev* 2013;60:477–486.
- Corless IB, Voss J, Guarino AJ, et al. The impact of stressful life events, symptom status, and adherence concerns on quality of life in people living with HIV. *J Assoc Nurses AIDS Care* 2013;24:478–490.
- Bakken S, Holzemer WL, Brown MA, et al. Relationships between perception of engagement with health care provider and demographic characteristics, health status, and adherence to therapeutic regimen on persons with HIV/AIDS. *AIDS Patient Care STDs* 2000;14:189–197.
- Rosenberg M. *Society and Adolescent Self-Image*. Middletown, CT: Wesleyan University Press, 1989.
- Berger BE, Ferrans CE, Lashley FR. Measuring stigma in people with HIV: Psychometric assessment of the HIV stigma scale. *Res Nurs Health* 2001;24:518–529.
- Onyx J, Bullen JP. Measuring social capital in five communities. *J Appl Behav Sci* 2000;36:23–42.
- Webel AR, Phillips JC, Dawson-Rose C, et al. A cross-sectional description of social capital in an international

- sample of persons living with HIV/AIDS (PLWH). *BMC Public Health* 2012;12:188.
34. Antonovsky A. The structure and properties of the sense of coherence scale. *Soc Sci Med* 1993;36:725–733.
  35. Kontinen H, Haukala A, Uutela A. Comparing sense of coherence, depressive symptoms and anxiety, and their relationships with health in a population-based study. *Soc Sci Med* 2008;66:2401–2412.
  36. Johnson MO, Neillands TB, Dilworth SE, et al. The role of self-efficacy in HIV treatment adherence. Validation of the HIV Treatment Self-Efficacy Scale (HIV-ASES). *J Behav Med* 2007;30:359–370.
  37. Lorig K, Stewart A, Ritter P, et al. *Outcome Measures for Health Education and Other Health Care Interventions*. Thousand Oaks, CA: Sage Publications, 1996.
  38. Brugha TS, Bebbington PE, Tennant C, et al. The List of Threatening Experiences: A subset of 12 life event categories with considerable long-term contextual threat. *Psychol Med* 1985;15:189–194.
  39. Brugha TS, Cragg D. The List of Threatening Experiences: The reliability and validity of brief life events questionnaire. *Acta Psychiatr Scand* 1990;82:77–81.
  40. Corless IB, Voss J, Guarino AJ, et al. The impact of stressful life events, symptom status, and adherence concerns on quality of life in people living with HIV. *JANAC* 2013;24:478–490.
  41. Neff KD. The development and validation of a scale to measure self-compassion. *Self Identity* 2003;2:233–250.
  42. Raes F, Pommier E, Neff KD, et al. Construction and factorial validation of a short form of the Self-Compassion Scale. *Clin Psychol Psychother* 2011;18:250–255.
  43. Holzemer WL, Hudson A, Kirksey KM, et al. The revised Sign and Symptom Checklist for HIV (SSC-HIVrev). *J Assoc Nurses AIDS Care* 2001;12:60–70.
  44. Wantland DJ, Holzemer WL, Moezzi S, et al. A randomized controlled trial testing the efficacy of an HIV/AIDS symptom management manual. *J Pain Symptom Manage* 2008;36:235–246.
  45. Radloff L. The CES-D scale: A self-report depression scale to research with the general population. *Appl Psychol Meas* 1977;1:385–401.
  46. Holzemer WL, Henry SB, Nokes KM, et al. Validation of the Sign and Symptom Check-List for persons with HIV disease (SSC-HIV). *J Adv Nurs* 1999;30:1041–1049.
  47. Derogatis LR. *Symptom Checklist-90-R (SCL-90-R): Administration, Scoring and Procedures Manual* (3rd ed.). Minneapolis: NCS Pearson, Inc., 1994.
  48. Walsh JC, Mandalia S, Gazzard BG. Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. *AIDS* 2002;12:269–277.
  49. Magidson, JF, Blashill AJ, Safren SA, et al. Depressive symptoms, lifestyle structure, and ART adherence among HIV-infected individuals: A longitudinal mediation analysis. *AIDS Behav* 2015;19:34–40.
  50. Wagner GJ, Remien RH, Carballo-Diequez A, et al. Correlates to adherence to combination antiretroviral therapy among members of HIV-positive mixed status couples. *AIDS Care* 2002;14:105–109.
  51. Wagner GJ, Ryan GW. Relationship between routinization of daily behaviors and medication adherence in HIV-positive drug-users. *AIDS Patient Care STDS* 2004;18:385–393.
  52. Beer L, Heffelfinger J, Frazier E, et al. Use of and adherence to antiretroviral therapy in a large U.S. sample of HIV-infected adults in care, 2007–2008. *Open AIDS J* 2012; 6:213–223.
  53. Hughes AJ, Mattson CI, Scheer S, et al. Discontinuation of antiretroviral therapy among adults receiving HIV care in the United States. *J Acquir Immune Defic Syndr* 2014;66: 80–89.
  54. Mirjam-Collette K, Pisu M, Dumcheva A, et al. Gender differences in discontinuation of antiretroviral treatment regimens. *J Acquir Immune Defic Syndr* 2009;52:336–341.
  55. Rana AI, van den Berg JJ, Lamy E, et al. Using a mobile health intervention to support HIV treatment adherence and retention among patients at risk for disengaging from care. *AIDS Patient Care STDs* 2016;30:178–184.

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