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Forget About Forgetting: Structural Barriers and Severe Non-Adherence to Antiretroviral Therapy

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Abstract

HIV infection is now clinically manageable with antiretroviral therapy (ART). However, a significant number of people with HIV do not benefit from ART because of non-adherence. This study examined the use of adherence strategies and barriers to adherence among persons at substantial risk for developing resistant virus (less than 75% adherent). People living with HIV (n = 556) who were less than 95% adherent to ART completed computerized interviews, were screened for active drug use, provided medical records for HIV viral load and completed unannounced pill counts to monitor ART adherence and an assessment of adherence barriers. Based on pill counts, participants were defined as severely non-adherent (< 75% medications taken) and moderately non-adherent (> 75% and < 95% adherent). Results showed a broad array of memory devices were used to no avail across non-adherence groups. Individuals who were severely non-adherent were significantly more likely to attribute missing medications due to substance use and structural barriers, including running out of medications, inability to get to pharmacy, and inability to afford medications. Results suggest that interventions focused on memory lapses will be insufficient and should rather concentrate on substance use treatment and providing case management to resolve structural barriers to adherence.

Antiretroviral therapy (ART) has revolutionized the care of people living with HIV infection. Unfortunately, in the US, many people aware of their HIV infection are not engaged in medical care, of which only a portion receive ART, and one in five people treated fail to achieve complete viral suppression (Gardner, McLees, Steiner, Del Rio, & Burman, 2011). Interventions are needed to improve ART adherence and to address disparities in HIV-related health. Unfortunately, interventions designed to increase ART adherence have often fallen short (Mathes, Pieper, Antoine, & Eikermann, 2013). One reason that ART adherence interventions may have limited impact is their focus on strategies to address memory lapses that result in missing single doses rather than factors resulting in sustained non-adherence. Research shows that adherence of less than 75%, including gaps in adherence rather than sporadic missed doses, increases the risk for viral resistance by more than one and half fold (Genberg et al., 2012).

Strategies commonly used to improve adherence have tended to concentrate on memory aides and are based on the assumption that non-adherence stems from memory lapses

(Maqutu, Zewotir, North, Naidoo, & Grobler, 2011; Zogg, Woods, Saucedo, Wiebe, & Simoni, 2011). However, non-adherence at the most concerning levels is unlikely the result of periodic forgetting. Factors that are more likely associated with low-level adherence are persistent (e.g., depression and stress) and structural (e.g., stigma and poverty). Nevertheless, individuals at any level of non-adherence are instructed to use memory aides (Simoni, Amico, Pearson, & Malow, 2008).

Studies have also typically examined differences between persons who are less than 90% or 95% adherent relative to individuals who are completely (100%) adherent. Examining differences between individuals who are between 80% adherent and 100% adherent may not detect clinically meaningful differences in risks for viral rebound (Amico, Harman, & Johnson, 2006). In addition, comparing persons within the higher levels of adherence will mask factors placing people at greatest risk for treatment failure. The current study sought to bridge these gaps in the literature by examining barriers to adherence and use of adherence strategies among individuals who are severely non-adherent to persons who are moderately non-adherent. We hypothesized the use of memory aides and organizational strategies would be common and would not differentiate severe from moderate non-adherence, whereas severe non-adherence would be associated with a greater number of intrapersonal and structural barriers to adherence.

Methods

Participants

Men and women living with HIV (N= 1101) were recruited in Atlanta, GA through outreach to HIV clinics and services. Participants included were non-adherent to their ART regimen defined as having been less than 95% ART during one month of observation.

Measures

Computerized self-interviews assessed demographic and health characteristics including a measure of 14 HIV-related symptoms of 2-weeks duration (Kalichman, Rompa, & Cage, 2000); ART side-effects (Carrieri, Villes, & 2007); common memory strategies for improving adherence (Catz, Kelly, Bogart, Benotsch, & McAuliffe, 2000); depression using the CESD (Radloff, 1977); experience of 18 stressful life events in the previous month (Chesney, Folkman, & Chambers, 1996); and quantity and frequency of alcohol use with the Alcohol Use Disorders Identification Test consumption subscale (AUDIT-C, Maisto, Conigliaro, McNeil, Kraemer, & Kelley, 2000). Current drug use was determined with a 12-panel urine dip-test (Redwood Toxicology Labs - Reditest-12).

A participant-to-provider form was used to collect HIV viral load and CD4 cell counts from participants' medical records. ART adherence was monitored using phone-based unannounced pill counts (Kalichman et al., 2007). Following an office interview that included a full accounting of all prescription medications and training in the pill counting procedure, participants were called at three unscheduled times over 12 to 16 day intervals to calculate 1-month adherence. At each pill count participants who had missed doses were asked whether they had experienced 15 common barriers, including cognitive and

organizational factors, mental health and, structural barriers, and substance use. Barriers were summed within each category to create indexes.

Data analyses

Participants were grouped on the basis of their pill count adherence, with severe non-adherence defined as <75% medications taken and moderate non-adherence defined as >75% and <95% medications taken. Adherence groups were compared on demographic and health characteristics, adherence strategies, and barriers using chi-square tests for categorical variables and independent t-tests for continuous variables. We used a multiple logistic regression model that entered composites for adherence barriers as predictor variables. To avoid confounding from known correlates of adherence, we included participant age and HIV symptoms in the multivariable model.

Results

Of the 1101 participants, 943 (85%) were currently taking ART. The median adherence was 93%, and the mean was 85% (SD = 17.8). For the purposes of this study, we excluded 387 participants who demonstrated adherence over 95%. As expected, participants with severe non-adherence were more likely to have unsuppressed HIV viral loads and lower CD4 cell counts. In addition, severely non-adherent participants were more likely to screen positive for drugs, were younger, had greater depression, and reported more stressors (see Table 1).

Use of Common Adherence Strategies

Table 2 shows the frequencies of adherence strategies used by the severely and moderately non-adherent groups. Both groups demonstrated high-rates for using an array of adherence tools and strategies. Participants who demonstrated severe non-adherence were slightly more likely to keep a journal or write down medication doses. Thus, adherence strategies were frequently used but not used differentially among individuals characterized as severely and moderately non-adherent.

Intrapersonal and Structural Barriers to Adherence

Participants across adherence groups frequently indicated that their missed medications were attributable to forgetting and being too busy doing other things. However, cognitive and organizational barriers did not differentiate severe and moderate non-adherence. In terms of mental health and wellness, severely non-adherent participants were more likely to feel depressed and overwhelmed and indicate that their medications make them sick as reasons for missing medications. The structural and substance use barriers, however, demonstrated robust differences between severe and moderate non-adherence groups. These factors were more frequently associated with severe non-adherence (see Table 2).

Multivariable logistic regression with all four composites of adherence barriers entered simultaneously, controlling for participant age and HIV symptoms, found that both structural and substance use barriers to medication adherence were significantly associated with severe non-adherence (see Table 3).

Discussion

All of the structural barriers assessed in this study as well as the use of alcohol and other drugs, emerged as barriers to adherence that distinguished persons with severe ART non-adherence. Multivariable models confirmed that structural barriers and substance use clearly differentiated severe and moderate non-adherence. In contrast, we found that forgetting to take medications and other cognitive and personal adherence barriers did not differentiate severe and moderate non-adherence. We found no evidence that cognitive factors, particularly memory lapses to take medications, accounted for the severe levels of non-adherence.

Our findings once again demonstrate that substance use poses substantial challenges to ART adherence. Substance use treatment itself may prove to be among the more effective ART adherence interventions (Durvasula & Miller, 2014). For people with untreated alcohol and drug abuse, interventions should directly address the barriers that substance use poses to both unintentional and intentional non-adherence, particularly strategies for remaining ART adherent while actively using substances. For example, a substantial number of active substance users are intentionally non-adherent out of fear of mixing alcohol and drugs with ART (Kalichman et al., 2013; Kalichman, Kalichman, et al., 2015). In addition, structural barriers, particularly those associated with poverty, including food insecurity, (Kalichman, Washington, Grebler, Hoyt, Welles, Merely, et al., 2015), lack of transportation (Kalichman et al., 2014; Tuller et al., 2009), and unstable housing (Leaver, Bargh, Dunn, & Hwang, 2007; Surratt, O'Grady, Levi-Minzi, & Kurtz, 2015) should be directly addressed by case management interventions.

Use of medication reminders and medication organization strategies were common in this sample of individuals who were non-adherent to ART. Nevertheless, these strategies were clearly not resulting in optimal adherence. It is striking that persons who were severely and moderately non-adherent to ART reported using multiple adherence strategies. Thus, focusing further on memory and organizational strategies in ART adherence interventions would likely yield few improvements, especially for individuals missing more than a quarter of medication doses.

The strengths of this study include the use of a reliable and objective measure of medication adherence and a large sample size. In terms of limitations, we relied on a convenience sample from a city in the southeastern US that cannot be considered representative of people living with HIV. The sample also came from a wide-range of providers that likely varied in their prescription practices. We also used self-report measures to assess barriers to adherence, including substance use, which are subject to under-reporting. Our study did not use a dose-level measure of adherence, precluding our ability to examine true gaps and patterns in adherence. With these limitations in mind, we conclude that the current findings have implications for advancing ART adherence interventions.

Adherence interventions that focus on assisting people living with HIV to remember their medications have often proven ineffective (Amico et al., 2006). While reminders may serve well to correct the occasional missed dose of medications, memory-aides will not likely

correct missing more than 25% of doses. Clinical service providers should routinely screen for and treat alcohol and drug abuse. Interventions should also directly address the barriers that substance use poses to both unintentional and intentional non-adherence. Assuring adequate transportation to pharmacy or home-delivery of ART and drug assistance programs that waive co-pays and other costs are structural interventions that may prove effective. Addressing the underlying sources of ART non-adherence at levels that threaten viral suppression should be the focus of a next generation of medication adherence interventions.

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Demographic and health characteristics of severe and moderate non-adherence groups.

Table 1

Characteristic	Severely Non-Adherent (N = 214)		Moderately Non-Adherent (N = 342)		X ²
	N	%	N	%	
Male	156	73	246	72	
Female	58	27	96	28	0.1
African-American	203	95	313	92	7.4
Income < \$10,000	149	70	210	61	5.0
Drug screen positive	135	63	191	56	5.3*
CD4 count < 200 cells/ml	50	23	61	18	2.7 ⁺
Detectable viral load	68	32	69	20	10.3**
	Mean	SD	Mean	SD	t
Age [years]	43.5	9.8	45.7	9.9	2.5**
Education [years]	12.5	1.8	12.7	1.8	1.1
Years since testing HIV ⁺	12.8	7.6	13.5	8.0	0.9
HIV symptoms score	3.9	3.5	3.6	3.4	0.9
ART side effects score	0.5	0.5	0.4	0.5	1.4
CD4 count cells/cc ³	426.5	277.8	492.1	380.7	2.1*
CESD-Depression score	14.7	9.0	13.2	8.5	1.9*
Stress score	3.9	2.8	3.3	2.3	2.5**
AUDIT-C alcohol score	4.7	2.1	4.5	1.7	0.8

Note

⁺ p < .10,

* p < .05,

** p < .01

Use of ART adherence strategies and adherence barriers encountered during the observation period among severe and moderate non-adherence groups.

Table 2

Adherence Strategy	Severely Non-Adherent (N = 214)			Moderately Non-Adherent (N = 342)			X ²
	N	%	N	%	N	%	
Pill box to organize medications	90	42	134	39	0.5		
Store medicines where they can be easily seen	125	58	191	56	0.4		
Stored medicines in a case, bag or purse	134	63	216	63	0.1		
Use a timer as a reminder to take medications	44	21	64	19	0.3		
Use a device with an alarm as a reminder	49	23	70	20	0.5		
Another person helped remind about doses	83	39	107	31	3.4		
Used mealtimes as a reminder to take medications	131	61	207	61	0.1		
Used bedtime as a reminder	143	67	222	65	0.1		
Used regular daily activity as a reminder	107	50	162	47	0.5		
Kept a journal or recoded each time dose taken	28	13	27	8	4.1*		
Used a calendar to remember	56	26	85	25	0.1		
Put up signs or other reminders to take medicine	43	20	53	15	2.0		
Adherence Barriers							
Cognitive/Organizational Factors							
I forgot to take my HIV drugs	116	54	141	41	0.4		
I did not have the right pill with me at the time.	58	27	66	19	0.5		
I was too busy doing other things.	96	45	104	30	2.7		
I got confused	16	7	13	4	1.5		
Something unexpected came up.	95	44	102	30	2.9		
Mental Health/Wellness							
Making me sick so I chose to skip a dose.	25	12	13	4	8.1**		
I slept through dose time.	71	33	81	24	0.7		
I felt depressed and overwhelmed	41	19	35	10	3.7*		
Structural Barriers							
I did not want someone to see me take them.	25	12	16	5	5.3*		
I ran out of pills.	44	21	32	9	7.4**		

Adherence Strategy	Severely Non-Adherent (N = 214)		Moderately Non-Adherent (N = 342)		X ²
	N	%	N	%	
I could not get to the pharmacy.	38	18	24	7	8.9**
I could not afford my medications.	17	8	7	2	7.4**
Substance use					
I was too drunk or high at the time.	29	14	17	5	7.6**
I had been drinking so I did not take my medications.	36	17	26	8	5.9**
I had been using drugs so I did not take my medications.	16	7	12	4	2.1

Note

* p < .05,

** p < .01

Table 3

Multivariable logistic regression model of adherence barriers during the month observation period differentiating severe and moderate non-adherence groups, controlling for age and HIV symptoms.

Adherence Barrier Composites	Adjusted OR	95%CI
Cognitive/Organizational	1.10	0.95–1.28
Mental Health/Wellness	1.26	0.96–1.67
Structural factors	1.49**	1.17–1.89
Substance use	1.32*	1.02–1.73

Note: Controlling for participant age and HIV symptoms,

* p < .05,

** p < .01