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# Memory-based Strategies for Antiretroviral Medication Management: An Evaluation of Clinical Predictors, Adherence Behavior Awareness, and Effectiveness

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## Abstract

"Forgetting" is the most commonly endorsed reason for missing an antiretroviral therapy (ART) dose, yet little is known about the prevalence, predictors, and effectiveness of the mnemonic strategies to support ART adherence. The current study assessed 28 self-reported memory-based medication strategies in 233 HIV-infected individuals with 30-day ART adherence measured via the Medication Event Monitoring System. Participants endorsed using multiple (8.7 5.6) strategies with the most common being internally-driven. More frequent strategy use was uniquely associated with affective distress, dependent daily functioning, higher non-ART pill burden, and poorer ART adherence. Individuals who used strategies frequently, but perceived them as minimally effective, had more affective, physical, and functional distress. More frequent strategy use was associated with worse ART adherence and was unrelated to perceived effectiveness. Primary reliance on internally-based mnemonic strategies may reflect a lack of awareness of adherence behaviors and may be insufficient to support optimal ART adherence in vulnerable populations.

### Keywords

Infectious disease; self-awareness; mnemonic devices; medications

## Introduction

Despite concerted efforts over the past decade to improve adherence to combination antiretroviral therapy (ART), nonadherence remains common and continues to adversely affect health outcomes in persons living with HIV(1, 2). Importantly, suboptimal adherence to ART regimens is closely associated with viral rebound(3), evolution of drug-resistant HIV strains(1), more rapid progression to AIDS, and death(4). A host of factors have been identified as barriers to successful adherence among persons with HIV; for instance low social support(5, 6), active substance use(7), co-occurring psychiatric conditions(8), environmental factors(1), and high dose frequency (e.g.,(9) are all associated with poor ART adherence. Additionally, neurocognitive impairment, particularly deficits in executive functions(10) and memory(11), are strongly predictive of ART nonadherence. In fact, "forgetting" is the most commonly endorsed reason for missing an ART dose (41–43% of samples(12, 13)), which may be attributable to primary cognitive problems(14) and/or

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environmental (e.g., homelessness) or situational (e.g., do not have medications with them at the time of dosing) influences(15). As such, techniques that aid in the detection and recollection of ART dosing times (via mnemonic devices or overt reminders) may be particularly important to persons living with HIV infection.

Although several mnemonic devices aimed at improving ART adherence have been identified in the intervention literature and have shown generally positive results, there is a paucity of studies examining self-implemented mnemonic adherence strategies in everyday life. For example, electronic devices including one-(16) and two-way(16, 17) pager or text-messaging systems, verbal recorded adherence prompts(18), as well as self-monitoring (via daily adherence diary) and brief educational interventions aimed at retrospective and prospective memory strategies for adherence(19) are all associated with increased ART adherence. These studies suggest that a variety of mnemonic aids may be effective for improving ART adherence; however, it is not yet clear which strategies are actually being used (and are useful) in the everyday lives of persons infected with HIV. Additionally, these adherence strategies were examined in a time-limited fashion (i.e., the longest intervention period in the above studies was 24 weeks), which has important implications for which strategies may be effective on a daily basis across a prolonged period of time in this population.

Therefore, one aim of the current study is to examine patient-implemented ART adherence strategy use – that is, self-report of naturalistic mnemonic strategies utilized to improve adherence in patients' daily lives – and determine the characteristics of HIV+ individuals employing such strategies. By examining which reminder strategies are most frequently utilized, by whom, and with what degree of perceived efficacy, we can gain a better understanding of which strategies may be most appropriate and well-tolerated for a given individual and how the strategy can be best utilized in order to obtain optimal effectiveness in ART treatment. Relatively few prior studies have examined the effectiveness of patient-implemented strategy use among HIV-infected individuals. For instance, Kalichman and colleagues(20) found that adherence strategy use among their cohort of women living with HIV was generally low (e.g., 27% timer/beeper, 27% notes, 15% datebooks), with pillbox organizers being the most commonly used aid (49%). Importantly, however, current ART strategy use did not impact adherence in this cohort, though women who reported prior strategy use were more likely to have recently missed an ART dose. In a more recent study by this group, pillbox users (39% of cohort) were more likely to have self-reported undetectable viral loads, more likely to have used other adherence strategies (i.e., calendars and counting pills), and less likely to report missing their ART medication within a day of the assessment(12). Lastly, Petersen et al.(21) found that self-initiated pillbox use (61% of sample) was more frequent among HIV+ individuals with higher prior adherence rates and among women, but was less frequent among homeless individuals, those who were ART naïve, or had a large number of ART drugs. Importantly, pillbox users showed 4% improved adherence across the study period (12-months) as well as decreased viral loads. These data suggest that self-implemented adherence strategies are being utilized among individuals with HIV-infection, and may be associated with better ART adherence. However, the findings are mixed and a more in-depth examination of reminder strategies beyond pillbox use is warranted in order to determine which strategies are most frequently employed as well as how these strategies may differentially impact successful ART adherence.

One potentially important moderator of such self-initiated adherence strategy use that also warrants examination is individuals' awareness of their ART adherence behaviors; that is, in order to successfully utilize an adherence strategy, an individual must be able to accurately assess if the strategy is helping or not (i.e., improving ART adherence). Notably, accurate awareness of adherence behaviors may have important implications for motivation to self-

initiate changes in adherence behaviors when necessary. This awareness deficit may then impact actual adherence as well as the validity of self-reported adherence abilities for providers. For example, an individual who perceives his ART adherence strategy to be helpful when it is not will be less likely to try a different strategy and may be unable to accurately communicate his adherence abilities to his provider thereby impacting treatment planning (e.g., switching to a less complex regimen). Although the relationship between perceived future ability to adhere and actual ART adherence has been examined in previous studies(22, 23), patients' perceived effectiveness of adherence strategy use on adherence behaviors has been largely overlooked in the ART adherence literature. Of note, among healthy older adults, accurate awareness of the efficacy of adherence behaviors may promote better adherence(24). Although insight into adherence behaviors has not yet been examined in individuals with HIV, previous research suggests that HIV+ individuals show poor awareness of their cognitive abilities (i.e., metacognition)(25–27). For example, only 37% of an HIV+ sample had memory complaints that were consistent with actual memory functioning(28). Given the lack of cognitive awareness in individuals with HIV and significant clinical implications of poor adherence awareness, further investigation into awareness of adherence behaviors is needed.

As such, the current study extends the literature on mnemonic strategy use and ART adherence by: 1) characterizing which adherence reminders are most frequently implemented on a daily basis among individuals with HIV; 2) determining the characteristics of those HIV+ individuals who most often use mnemonic adherence strategies; and 3) examining patient insight into ART adherence behaviors by examining the relationship between perceived effectiveness and frequency of ART reminder use as well as how these measures are associated to objective adherence. Understanding the everyday mnemonic adherence behaviors of HIV+ persons will help to better inform clinicians and researchers alike in identifying those individuals who are likely employing such strategies as well as their effectiveness on actual ART adherence, thereby improving our ability to tailor these strategies to the needs of this population.

## Methods

### Participants

Two-hundred thirty-three HIV-infected individuals were drawn retrospectively from two NIH-funded observational cohort studies that included behavioral measurements of ART adherence using a 30-day medication event monitoring system (MEMS) approach. Inclusion criteria were HIV infection (determined by enzyme linked immunosorbernt assay and confirmed by a Western Blot test), prescription of at least one ART medication, and the ability to provide informed consent on the day of evaluation. The intent of the current study was to retrospectively identify a representative clinic sample in order to enhance generalizability to the HIV epidemic. Therefore exclusion criteria were somewhat liberal: individuals with schizophrenia or other psychotic disorders, neurological disease known to adversely effect cognition (e.g., seizure disorder, traumatic brain injury with loss of consciousness ≥ 15 minutes), or inability to be tested at the time of evaluation were not included in the current study. Demographic, HIV disease, and psychiatric characteristics of the overall study sample are illustrated in Table 1.

### Materials and Procedure

After providing written, informed consent, all participants completed baseline psychiatric, neuropsychological, and standardized medical research evaluations for which they received nominal financial compensation. CD4+ lymphocytes were counted in blood using flow

cytometry and HIV RNA levels were quantified in plasma using RT-PCR (Amplicor, Roche Diagnostics, Indianapolis, IN).

**Measurement of ART adherence strategies—**The Prospective Memory for Medications Questionnaire (PMMQ) was administered to assess utilization of 28 common strategies that can be used to assist adherence to a prescribed medication regimen(24). In the PMMQ, participants indicated how often they used each strategy on a scale ranging from 0 (*Never*) to 4 (*Always*) as well as how effective they perceived the strategy to be for medication adherence, 0 (*Highly Effective*) to 3 (*Highly Ineffective*). Items were categorized into type of adherence strategy: external strategies for a retrospective aspect of adherence (E-R; 7 items; e.g., *"Do you use a dated pillbox to help you make sure you take the right amount of medication per day?"*); external strategy for a prospective aspect of adherence (E-P; 7 items; e.g., *"Do you use a clock or watch alarm to remind you when it is time to take your medication?"*); internal strategy for a retrospective aspect of adherence (I-R; 10 items; e.g., *"Do you regularly repeat to yourself the instructions for taking a prescription that you've been taking for a long time?"*); and internal strategy for a prospective aspect of adherence (I-P; 4 items; e.g., *"At the beginning of the day, do you think about when you need to take your medication so you can include your medication into your day's schedule?"*). If participants were missing one item on a given strategy scale, the individual's mean score for the scale was imputed for that item; if >1 item was missing on a strategy scale, the participant had a missing score for that scale. Scores were determine by adding all of the items together (total possible range for frequency of strategy use = 0–112; total possible range for perceived effectiveness of strategy use = 0–84); a higher score indicates more frequent strategy use for the Frequency scale whereas lower scores indicate higher perceived effectiveness of strategy use for the Effectiveness scale.

**Tracking of ART medication adherence—**The Medication Event Monitoring System (MEMS, AARDEX, Sion, Switzerland) was used to track ART medication adherence over the 30-day study period. MEMS TrackCaps provide an electronic record of the date and time at which the cap was removed. Previous studies support the use of MEMS as a more accurate estimate of adherence than self-report or pill counts (both of which tend to overestimate adherence(29, 30). We selected a "sentinel" ART to be tracked via MEMS. This was largely the participant's protease inhibitor since this is the agent most critically sensitive to non-adherence; however, if a participant was not prescribed a PI, we used the most frequently dosed non-nucleoside reverse transcriptase inhibitor or nucleoside reverse transcriptase inhibitor as the sentinel medication to track. For participants taking a fixed-dose combination tablet (e.g., efavirenz/emtricitabine/tenofovir disoproxil fumerate) we tracked this medication. Percent adherence was calculated as the proportion of correct bottle openings over the 30-day period (i.e., [(Number of recorded bottle openings)/(Number of prescribed doses)]*100%).

**Current affective Distress, Psychiatric and Substance Use Assessment—**Current overall affective distress over the past week was measured via The Profile of Mood States (POMS(31)). The POMS is a 65-item, self-report measure of current mood states in which participants rate various adjectives (e.g., "unhappy") on a five-point Likert scale ranging from 0 (*not at all*) to 4 (*extremely*). The POMS Total score was used for all analyses. Diagnosis of psychiatric, alcohol and/or substance abuse or dependence was obtained using the Composite International Diagnostic Interview (CIDI(32)) or Structured Clinical Interview for DSM Disorders (SCID(33)), where available. The CIDI is a lay administered computerized assessment that follows the diagnostic criteria of the DSM-IV. We used the CIDI to assess for both current and lifetime alcohol, cannabis, cocaine, methamphetamine, and opioid abuse or dependence as well as mood disorders.

**Neuropsychological Functioning—**Four neuropsychological tests were administered to all study participants: the Trail Making Test (Parts A and B(34)), Grooved Pegboard Test (Dominant and Nondominant hands(35)), and Verbal Fluency (Actions(36)). Raw scores for each test variable were converted into demographically corrected T-scores using comprehensive normative standards which corrected for age, education, sex, and ethnicity, as appropriate(37–39). A summary neuropsychological score was achieved by averaging each standardized test score to create a mean neuropsychological T-score for each participant.

The HIV Dementia Scale is a brief (10 minute) cognitive screener for detecting dementia in HIV infected individuals(40). We included the memory subscale of the HDS in analyses to assess for memory impairment (range = 0–4). The Memory for Intentions Screening Test was also administered to measure prospective memory abilities (i.e., remembering to remember future intentions). The MIST is a 30-minute task in which eight different intentions are prescribed while the participant completes a word search. There are four cues based on time (e.g., “In 15 minutes, tell me it is time to take a break.”) and four based on events (e.g., “When I show you a postcard, self address it.”). The following variables were derived from the MIST and included in analyses: 1) time-based score; 2) event-based score; 3) recognition total. Prior studies support the reliability(41) and construct validity(14) of the MIST in HIV.

**Instrumental Activities of Daily Living—**To assess dependence in performing instrumental activities of daily living (IADLs), a modified version of the Lawton and Brody scale was utilized(37). This scale includes 11 items detailing the degree to which individuals independently function in the areas of Financial Management, Home Repair, Medication Management, Laundry, Transportation, Grocery Shopping, Shopping, Housekeeping (Cleaning), Cooking, Work, and Telephone Use. For each activity the participant separately rates his/her current level of independence and highest previous level of independence. IADL dependence is determined if there is decline (i.e., need for increased assistance) in two or more domains and the participant endorses that these difficulties are due at least partially to cognitive problems.

## Statistical Analyses

First, we examined the raw number of reminder strategy categories (e.g., Internal vs. External strategies) that were used (i.e., at least “Sometimes”) versus those that were not used (i.e., “Seldom” or “Never”). Since the PMMQ has an unequal number of strategies within each strategy category (e.g., 4 I-P strategy versus 10 I-R strategy items), we examined the average number of strategy items endorsed at least “Sometimes” per category and divided that by the total number of possible strategy items in the category. In this manner, the relative number of strategies used could be examined.

For all other analyses, to increase interpretability, we transformed the frequency and perceived effectiveness of strategy use scores into population-based z-scores from our cohort in which higher scores reflected more frequent strategy use or perceived effectiveness of strategy use. We next conducted univariate analysis of variance (ANOVA) and chi-square analyses to determine predictors of total frequency of strategy use. Those predictors that reached a significance threshold of $p < 0.10$ were included a multivariable model reflecting the unique characteristics of frequency of strategy use.

Additionally, we examined the relationship between frequency and perceived effectiveness of strategy use using a nonparametric Spearman’s correlation. We further probed this association by dichotomizing the raw scores of strategy use frequency and perceived effectiveness using a median split to create a 2×2 “frequency × effectiveness” variable in

which individuals were separated into: 1) high frequency and high perceived effectiveness of strategy use; 2) high frequency but low perceived effectiveness of strategy use; 3) low frequency but high perceived effectiveness of strategy use; or 4) low frequency and low perceived effectiveness of strategy use. We performed univariate ANOVAs and chi-square analyses to determine how these groups differed from each other across demographic, clinical, and functional characteristics. A multivariable model was then conducted including the significant ($p< 0.10$) univariate predictors of the "frequency × effectiveness" outcome variable.

Lastly, nonparametric Spearman's correlations were utilized to examine the relationship between frequency of strategy use and perceived effectiveness of strategy use with actual ART adherence (MEMS total percent adherence).

## Results

### Number of reminder strategies endorsed

Our sample endorsed an average of 8.7 (out of 28 possible) ART strategies used at least "Sometimes" per participant. The number of strategies endorsed within each category (e.g., number of I-P strategies versus number of E-P strategies endorsed) differed by strategy category ($F(3,228) = 125.8$, $p < 0.001$). Internal-Prospective strategies [47% (1.9/4) of the I-P strategies were endorsed] were the most frequently endorsed (t range($N=231$) = −14.7–8.9, $ps < 0.001$) while External-Retrospective strategies [16% (1.1/7) of the E-R strategies] were the least frequently used (t range = −4.7–19.2, $ps<0.001$; see Figure 1). Descriptively, at the item level, leaving a pill bottle or pillbox in a prominent place was the most common reminder strategy employed (69% endorsed using this strategy at least "Sometimes"; see Table 2). Marking a calendar after medication ingestion was the least common strategy endorsed (2% endorsed using at least "Sometimes"). Strategies related to social support (items #: 22, 24–27; Table 2) were among the least commonly endorsed (6–10% of the sample endorsed using these at least "Sometimes"). Dated pillbox use was the most frequently E-R strategy employed (48% endorsed its use at least "Sometimes").

### Frequency of strategy use predictors

In order to determine the characteristics of individuals using ART adherence strategies, we examined predictors of total frequency of strategy use. Univariate analyses revealed that multiple factors were associated with increased adherence strategy use at the $p<0.10$ level: older age (= 0.19, $p = 0.003$), non-Caucasian individuals ($F(1,229=5.5$, $p = 0.02$), increased number of ART (= 0.11, $p = 0.10$) or non-ART prescriptions (= 0.27, $p < 0.001$), AIDS diagnosis ($F(1, 229)=9.3$, $p = 0.003$), current affective distress (i.e., POMS total; = 0.29, $p < 0.001$), lifetime history of MDD ($F(1, 228)=12.8$, $p < 0.001$), worse global neuropsychological (= −0.12, $p = 0.06$) and MIST event-based (=−0.14, $p = 0.03$) performances, unemployment ($F(1,218)=5.7$, $p = 0.02$), and being IADL dependent ($F(1, 216)= 29.3$, $p < 0.001$). These variables were all included in a multivariable model. The multivariable model significantly accounted for 23% of the variance in frequency of strategy use ($F(11, 184)=6.0$, $p < 0.001$; see Table 4). Only increased number of non-ART pills ($p = 0.02$), current affective distress via POMS total ($p = 0.01$) and IADL dependence ($p = 0.01$) uniquely predicted frequency of strategy use after accounting for the other predictors in the model.

### Frequency versus Perceived Effectiveness of Strategy Use

Total frequency of adherence strategy use was not associated with total perceived effectiveness of strategy use (=−0.09, $p = 0.18$; see Figure 2); none of the strategy types significantly differed from each other across effectiveness ratings ($ps>0.05$). In order to

further examine this unexpected relationship, we used a median split of the raw scores of the total frequency of strategy use (i.e., >30 or ≤30) and perceived effectiveness of strategy use (i.e., >29 or ≤29) to create a "frequency × effectiveness" variable separating individuals with: 1) high frequency and high perceived effectiveness of strategy use (25%); 2) high frequency but low perceived effectiveness of strategy use (24%); 3) low frequency but high perceived effectiveness of strategy use (26%); or 4) low frequency and low perceived effectiveness of strategy use (25%). Univariate analyses revealed that differences between individuals in the two discrepant groups (i.e., those with high frequency but low perceived effectiveness of strategy use versus those with low frequency but high perceived effectiveness of strategy use) were driving most of the differences (see Table 5). Specifically, the high frequency but low perceived effectiveness individuals had a higher non-ART pill burden ($F(1, 103)=12.8$, $p<0.001$), more AIDS diagnoses ($^2 = 4.8$, $p = 0.03$), more prior (i.e., lifetime MDD; $F(1,91)=14.7$, $p<0.001$) and current affective distress ($^2=14.7$, $p<0.001$), and were more likely to be IADL dependent ($^2=12.6$, $p<0.001$) than the individuals endorsing a low frequency but high perceived effectiveness of strategy use. A significant multivariable analysis including these predictors indicated that only lifetime MDD ($^2 =10.6$, $p = 0.01$) uniquely predicted group differences on the frequency × effectiveness variable after accounting for all other predictors in the model ($^2=38.4$, $p < 0.001$, $R^2=0.08$).

### Strategy use and ART adherence

Increased frequency of adherence reminder use was associated with poorer ART medication adherence (=−0.15, $p = 0.02$). Specifically, more frequent use of E-P (=−0.20, $p = 0.002$) and E-R (=−0.13, $p = 0.04$) based strategies were associated with poorer medication adherence. However, perceived strategy effectiveness total score was not related to actual ART adherence (= 0.01, $p = 0.91$).

## Discussion

Antiretroviral nonadherence is highly prevalent and is associated with a multitude of negative HIV disease outcomes, which highlights the importance of understanding self-implemented adherence behaviors among this population. Results from our study suggest that HIV+ individuals tend to employ multiple, internally-based reminder strategies (8.7 strategies per participant on average). However, the individuals endorsing strategy use most frequently also tended to be the individuals most "at-risk" for nonadherence (i.e., greater co-occurring mood and functional distress as well as increased pill burden). In fact, ART adherence was negatively associated with strategy use and was not associated with perceived efficacy of strategy use. These discrepancies between the type, frequency, and perceived effectiveness of strategy use and actual cognitive and adherence abilities have important implications for how ART treatment and adherence behaviors are approached and understood among HIV individuals.

Specifically, participants' reliance on internal memory cues to aid ART adherence (e.g., concentrate when learning a new medication, mentally repeat instructions) has important implications for a population that has high rates of objective memory deficits(42) and reported difficulties remembering when to take ART medications(12); that is, HIV individuals are depending on internal memory strategies (more cognitively effortful than relying on external cues) to maintain successful ART adherence despite commonly observed difficulties with these abilities. These findings further support the metamemory difficulties reported in individuals with HIV (up to 50% of a HIV+ cohorts showed a discrepancy between reported memory abilities and actual memory performance(28)) and extends the everyday implications (i.e., ART nonadherence) of such difficulties.

Given that external memory cues were infrequently used in our study and were not related with objective ART, future adherence interventions targeting external reminder cues (e.g., pager systems) may need to further investigate how to best optimize these types of interventions. It is possible that external cues may not be as easily implemented into individuals' daily lives as internal strategies due to the additional effort and cognitive skills necessary to successfully execute them (e.g., planning ahead for reminder placement and additional materials needed), and/or these strategies may be susceptible to habituation over time even if they are implemented. However, as structured external reminders have been shown to be effective for ART adherence in this population(18), it may be that additional support in implementation and potentially more individualized (e.g., using their own voice, use of personalized messages from loved ones or to themselves, integration of strategy use around their schedule and/or tailored to their particular cognitive strengths and weaknesses) external strategies may be particularly helpful. Additionally of note, reminder strategies employing social support were among the least commonly used. It is not clear from the current data if this is due to a lack of social network in which to employ such strategies or because such strategies are not well tolerated or perceived as ineffective. However, given that poor social support is associated with ART nonadherence(5), adherence interventions aimed at boosting social networks may be warranted.

Furthermore, although scores on the HDS memory subscale were not associated with frequency of memory-based strategy use, HIV individuals who performed poorer on event-based prospective memory tasks (e.g., "when I present you with the pen at a later time, address the envelope") endorsed using memory strategies more frequently. Integrity of prospective memory abilities is strongly associated with successful ART adherence(11). Individuals with deficits in event-based prospective memory therefore may not benefit from the predominant use of internally-based memory strategies, which necessitate such abilities (e.g., remembering to take one's medication each morning with breakfast), thereby impacting successful ART adherence. These findings further support the meta-prospective memory deficit previously reported in HIV individuals in which prospective memory complaints were not predictive of actual prospective memory abilities(27). The lack of awareness regarding prospective memory abilities may therefore increase the risk of ART nonadherence. Focused awareness training particularly targeting prospective memory abilities may be an important construct to integrate into traditional adherence interventions among HIV individuals.

HIV+ individuals who reported employing mnemonic adherence strategies more frequently also endorsed greater levels of functional dependence, current affective distress, and larger non-ART pill burdens, which accounted for about one-quarter of the variance in frequency of strategy use. Since functional dependence, affective distress and regimen complexity are all associated with poorer ART adherence, these results suggest that those participants using strategies may be most "at-risk" for declines in ART adherence, and therefore the most in need of successful adherence strategy utilization. Importantly, however, increased use of adherence strategies was associated with *poorer* actual ART adherence. Therefore, although the individuals most in need of adherence support are employing strategies, these strategies are not entirely effective in helping them to reach optimal levels of actual ART adherence. However, given the cross-sectional design of our current study, it is not clear if the individuals utilizing adherence strategies most frequently have even poorer adherence compared to when they are not employing any strategies. Another possibility may be that the current strategy implementation itself is not precise (due to this cohort's difficulties with everyday functioning and mood) or reliable (i.e., participants are utilizing more internal memory aids despite previously established difficulties remembering when to take ART medications), both due to user-based miscalculations. Regardless, these findings have important implications for ART adherence strategy recommendations given by healthcare

providers. In particular, healthcare providers should ensure that clients understand all steps involved in recommended strategy use and assess for the capacity to successfully implement them.

Additionally, there was no relationship between frequency and perceived effectiveness of strategy use; in fact, half of the cohort showed a discrepancy between frequency of strategy use and perceived effectiveness of the strategy. Those individuals who employed reminder strategies most frequently but did not perceive their strategy use to be effective also reported more physical, affective, and functional distress (e.g., increased lifetime and current affective distress, unemployment, dependence in everyday functioning, increased pill burden, and more severe HIV disease progression) compared to individuals who were using strategies less frequently but perceived them to be effective. In particular, a history of affective distress (i.e., lifetime MDD) uniquely predicted those individuals with high frequency of strategy use but low perceived effectiveness above and beyond other areas of distress. On the other hand, individuals who did not employ adherence strategies frequently but found them effective showed less affective and functional distress (e.g., lifetime MDD, unemployment, functional dependence) than participants with congruent frequency by effectiveness ratings. Therefore, experiencing overall life distress (either high or low), especially affective, is an important predictor of incongruence between strategy use behaviors and perceptions about those behaviors. Importantly, the individuals with low strategy frequency use but high perceived effectiveness may represent a cohort of people who do not need help with ART adherence but recognize the value of such strategies and/or simply employ fewer strategies that they perceive to be highly effective. Whereas the high strategy frequency but low perceived effectiveness group may represent individuals who are experiencing apathy toward their adherence behaviors or amotivation to change them (both apathy and amotivation can be associated with affective distress); therefore, though they recognize which adherence behaviors are optimal, they are reluctant to change strategy use. Or secondly, these individuals may be experiencing a lack of insight into their adherence behaviors (dependence in everyday functioning and mood are also associated to poorer awareness and metacognitive abilities(27)).

Supporting the latter possibility, perceived effectiveness of strategy use was not associated with actual ART adherence. Therefore, as a group, HIV individuals showed a lack of insight into how successful their adherence behaviors actually are. This finding has important implications for the current and future adherence behaviors in these individuals. For instance, individuals who perceive their adherence behaviors to be effective even if they are not are less likely to self-initiate changes (e.g., use of different or additional adherence strategies) and are therefore at risk of continued suboptimal adherence. Additionally, lack of adherence behavior awareness is important for clinicians and researchers when evaluating patients (i.e., accuracy of self-reported adherence behaviors may be biased) and recommending the most appropriate ART regimen or strategy use (e.g., enlisting social support may be most appropriate for a patient with poor insight rather than encouraging the patient to use internal strategies). HIV individuals may be imprecise in determining adherence strategy effectiveness due to concurrent cognitive impairment, which may impact one's ability to objectively assess such abilities(43), or possibly due to lack of feedback from such suboptimal strategy use (i.e., they do not feel sick). Regardless, awareness of functional abilities, including adherence, is an important skill that is necessary for successful independent functioning, and is therefore an important area for intervention in this population (e.g., awareness-training).

There are also several limitations to the current study that should be considered. Most importantly, the cross-sectional design of the study limits interpretation of the findings; we could only examine how people who use strategies differ from those who do not rather than

examining adherence behaviors within participants. In this manner, it is not clear if those participants who report using strategies actually do benefit as compared to when they are not using them. However, our study addresses the characteristics and adherence implications of those individuals who are using everyday adherence strategies, an important and understudied event. As noted earlier, our study was largely inclusive of individuals with HIV infection with few exclusionary criteria; in this manner, our results reflect a heterogeneous population, which are less specific. However, we believe our cohort is representative of the larger HIV population and, therefore, may allow our results to be more generalizable to the population as a whole. Lastly, measurement of adherence strategies use via self-report may have limitations, particularly among a cohort that may be experiencing difficulty in awareness. Ideally, use of an informed observer to either independently identify adherence strategies used or confirm those that the participant endorsed would enhance our confidence in the endorsed strategies being used and could be examined to directly assess participant awareness of adherence behaviors.

Taken together, our findings suggest that individuals with HIV+ employ multiple internal mnemonic strategies; however among those using strategies most frequently, both perceived effectiveness of strategy use and actual adherence are poorest. Our data suggest that these incongruencies may be due to a lack of insight into adherence behaviors. Specifically, HIV individuals tend to employ internal effortful reminder cues (versus external cues) the most, which may have limited effectiveness among a population with prospective memory difficulties; in a larger sense, our data suggest that HIV individuals may, therefore, have difficulty recognizing when their behaviors are contributing to successful adherence or not. Individuals experiencing life distress, particularly affective distress, are most at risk for these awareness difficulties, which may be used by researchers and clinicians as indicators for poor insight in the future. Importantly, assessment and recommendation of ART adherence strategies by healthcare providers should factor for these limitations in awareness and functional difficulties (e.g., use of informant when assessing adherence behaviors, objective measurement of adherence such as pill count, and clear outline/practice with recommended strategy).

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## References


1. Bangsberg DR, Hecht FM, Charlebois ED, Zolopa AR, Holodniy M, Sheiner L, et al. Adherence to protease inhibitors, HIV-1 viral load, and development of drug resistance in an indigent population. AIDS. 2000 Mar 10; 14(4):357–366. [PubMed: 10770537]
2. Bartlett JG. International HIV Workshop on Management of Treatment-Experienced Patients. Hopkins HIV Rep. 2002 Nov; 14(6):4–5. [PubMed: 12491990]
3. Arnsten JH, Demas PA, Farzadegan H, Grant RW, Gourevitch MN, Chang CJ, et al. Antiretroviral therapy adherence and viral suppression in HIV-infected drug users: comparison of self-report and electronic monitoring. Clin Infect Dis. 2001 Oct 15; 33(8):1417–1423. [PubMed: 11550118]
4. Bangsberg DR, Hecht FM, Clague H, Charlebois ED, Ciccarone D, Chesney M, et al. Provider assessment of adherence to HIV antiretroviral therapy. J Acquir Immune Defic Syndr. 2001 Apr 15; 26(5):435–442. [PubMed: 11391162]
5. Simoni JM, Montgomery A, Martin E, New M, Demas PA, Rana S. Adherence to antiretroviral therapy for pediatric HIV infection: a qualitative systematic review with recommendations for research and clinical management. Pediatrics. 2007 Jun; 119(6):e1371–e1383. [PubMed: 17533177]
6. Vyavaharkar M, Moneyham L, Tavakoli A, Phillips KD, Murdaugh C, Jackson K, et al. Social support, coping, and medication adherence among HIV-positive women with depression living in rural areas of the southeastern United States. AIDS Patient Care STDS. 2007 Sep; 21(9):667–680. [PubMed: 17919094]
7. Malta M, Magnanini MM, Strathdee SA, Bastos FI. Adherence to antiretroviral therapy among HIV-infected drug users: a meta-analysis. AIDS Behav. 2010 Aug; 14(4):731–747. [PubMed: 19020970]
8. Tegger MK, Crane HM, Tapia KA, Uldall KK, Holte SE, Kitahata MM. The effect of mental illness, substance use, treatment for depression on the initiation of highly active antiretroviral therapy among HIV-infected individuals. AIDS Patient Care STDS. 2008 Mar; 22(3):233–243. [PubMed: 18290749]
9. Beusterien KM, Davis EA, Flood R, Howard K, Jordan J. HIV patient insight on adhering to medication: a qualitative analysis. AIDS Care. 2008 Feb; 20(2):244–252. [PubMed: 18293136]
10. Hinkin CH, Castellon SA, Durvasula RS, Hardy DJ, Lam MN, Mason KI, et al. Medication adherence among HIV+ adults: effects of cognitive dysfunction and regimen complexity. Neurology. 2002 Dec 24; 59(12):1944–1950. [PubMed: 12499488]
11. Woods SP, Dawson MS, Weber E, Gibson S, Grant I, Atkinson JH. Timing is everything: antiretroviral nonadherence is associated with impairment in time-based prospective memory. J Int Neuropsychol Soc. 2009 Jan; 15(1):42–52. [PubMed: 19128527]
12. Kalichman SC, Cain D, Cherry C, Kalichman M, Pope H. Pillboxes and antiretroviral adherence: prevalence of use, perceived benefits, and implications for electronic medication monitoring devices. AIDS Patient Care STDS. 2005 Dec; 19(12):833–839. [PubMed: 16375615]
13. Miller W, Hecht FM. Adherence to HIV treatment. Clinical Care of AIDS Patients. 1997
14. Woods SP, Iudicello JE, Moran LM, Carey CL, Dawson MS, Grant I. HIV-associated prospective memory impairment increases risk of dependence in everyday functioning. Neuropsychology. 2008 Jan; 22(1):110–117. [PubMed: 18211160]
15. Gifford AL, Bormann JE, Shively MJ, Wright BC, Richman DD, Bozzette SA. Predictors of self-reported adherence and plasma HIV concentrations in patients on multidrug antiretroviral regimens. J Acquir Immune Defic Syndr. 2000 Apr 15; 23(5):386–395. [PubMed: 10866231]
16. Safren SA, Hendriksen ES, Desousa N, Boswell SL, Mayer KH. Use of an on-line pager system to increase adherence to antiretroviral medications. AIDS Care. 2003 Dec; 15(6):787–793. [PubMed: 14617500]
17. Hardy H, Kumar V, Doros G, Farmer E, Drainoni ML, Rybin D, et al. Randomized controlled trial of a personalized cellular phone reminder system to enhance adherence to antiretroviral therapy. AIDS Patient Care STDS. 2011 Mar; 25(3):153–161. [PubMed: 21323532]
18. Andrade AS, McGruder HF, Wu AW, Celano SA, Skolasky RL Jr, Selnes OA, et al. A programmable prompting device improves adherence to highly active antiretroviral therapy in

HIV-infected subjects with memory impairment. Clin Infect Dis. 2005 Sep 15; 41(6):875–882. [PubMed: 16107989]

19. Safren SA, Otto MW, Worth JL, Salomon E, Johnson W, Mayer K, et al. Two strategies to increase adherence to HIV antiretroviral medication: life-steps and medication monitoring. Behav Res Ther. 2001 Oct; 39(10):1151–1162. [PubMed: 11579986]
20. Kalichman SC, Rompa D, DiFonzo K, Simpson D, Austin J, Luke W, et al. HIV treatment adherence in women living with HIV/AIDS: research based on the Information-Motivation-Behavioral Skills model of health behavior. J Assoc Nurses AIDS Care. 2001 Jul-Aug;12(4):58–67. [PubMed: 11486721]
21. Petersen ML, Wang Y, van der Laan MJ, Guzman D, Riley E, Bangsberg DR. Pillbox organizers are associated with improved adherence to HIV antiretroviral therapy and viral suppression: a marginal structural model analysis. Clin Infect Dis. 2007 Oct 1; 45(7):908–915. [PubMed: 17806060]
22. Barclay TR, Hinkin CH, Castellon SA, Mason KI, Reinhard MJ, Marion SD, et al. Age-associated predictors of medication adherence in HIV-positive adults: health beliefs, self-efficacy, and neurocognitive status. Health Psychol. 2007 Jan; 26(1):40–49. [PubMed: 17209696]
23. Johnson MO, Neilands TB, Dilworth SE, Morin SF, Remien RH, Chesney MA. The role of self-efficacy in HIV treatment adherence: validation of the HIV Treatment Adherence Self-Efficacy Scale (HIV-ASES). J Behav Med. 2007 Oct; 30(5):359–370. [PubMed: 17588200]
24. Gould ON, McDonald-Miszczak L, King B. Metacognition and medication adherence: how do older adults remember? Exp Aging Res. 1997 Oct-Dec;23(4):315–342. [PubMed: 9352290]
25. Carter SL, Rourke SB, Murji S, Shore D, Rourke BP. Cognitive complaints, depression, medical symptoms, and their association with neuropsychological functioning in HIV infection: a structural equation model analysis. Neuropsychology. 2003 Jul; 17(3):410–419. [PubMed: 12959507]
26. Moore LH, van Gorp WG, Hinkin CH, Stern MJ, Swales T, Satz P. Subjective complaints versus actual cognitive deficits in predominantly symptomatic HIV-1 seropositive individuals. J Neuropsychiatry Clin Neurosci. 1997 Winter;9(1):37–44. [PubMed: 9017527]
27. Woods SP, Carey CL, Moran LM, Dawson MS, Letendre SL, Grant I. Frequency and predictors of self-reported prospective memory complaints in individuals infected with HIV. Arch Clin Neuropsychol. 2007 Feb; 22(2):187–195. [PubMed: 17289343]
28. Hinkin CH, van Gorp WG, Satz P, Marcotte T, Durvasula RS, Wood S, et al. Actual versus self-reported cognitive dysfunction in HIV-1 infection: memory-metamemory dissociations. J Clin Exp Neuropsychol. 1996 Jun; 18(3):431–443. [PubMed: 8877626]
29. Lu M, Safren SA, Skolnik PR, Rogers WH, Coady W, Hardy H, et al. Optimal recall period and response task for self-reported HIV medication adherence. AIDS Behav. 2008 Jan; 12(1):86–94. [PubMed: 17577653]
30. Vriesendorp R, Cohen A, Kristanto P, Vrijens B, Rakesh P, Anand B, et al. Adherence to HAART therapy measured by electronic monitoring in newly diagnosed HIV patients in Botswana. Eur J Clin Pharmacol. 2007 Dec; 63(12):1115–1121. [PubMed: 17882408]
31. McNair, A.; Lorr, M.; Droppleman, LF. Manual for the Profile of Mood States. San Diego: Educational and Industrial Testing Services; 1981.
32. Wittchen HU, Robins LN, Cottler LB, Sartorius N, Burke JD, Regier D. Cross-cultural feasibility, reliability and sources of variance of the Composite International Diagnostic Interview (CIDI). The Multicentre WHO/ADAMHA Field Trials. Br J Psychiatry. 1991 Nov.159:645–653. 58. [PubMed: 1756340]
33. First, MB.; Spitzer, RL.; Gibbon, M.; WIlliams, JBW. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition. Institute NYSP. , editor. New York: Biometrics Research; 1991.
34. Reitan, RM.; Wolfson, D. The Halstead-Reitan Neuropsychological Test Battery: Theory and clinical interpretation. Tuscon, AZ: Neuropsychology Press; 1985.
35. Kløve, H. Grooved Pegboard. Lafayette, IN: Lafayette Instruments; 1963.
36. Woods SP, Carey CL, Troster AI, Grant I. Action (verb) generation in HIV-1 infection. Neuropsychologia. 2005; 43(8):1144–1151. [PubMed: 15817172]

37. Heaton RK, Marcotte TD, Mindt MR, Sadek J, Moore DJ, Bentley H, et al. The impact of HIV-associated neuropsychological impairment on everyday functioning. J Int Neuropsychol Soc. 2004 May; 10(3):317–331. [PubMed: 15147590]

38. Heaton, RK.; Taylor, MJ.; Manly, J.; Tulsky, DS. Demographic effects and use of demographically corrected norms with the WAIS-III and WMS-III. Clinical Interpretation of the WAIS-III and WMS-III. Burlington: Academic Press; 2003. p. 181-210.

39. Norman MA, Moore DJ, Taylor M, Franklin D Jr, Cysique L, Ake C, et al. Demographically corrected norms for African Americans and Caucasians on the Hopkins Verbal Learning Test-Revised, Brief Visuospatial Memory Test-Revised, Stroop Color and Word Test, and Wisconsin Card Sorting Test 64-Card Version. J Clin Exp Neuropsychol. 2011 Aug; 33(7):793–804. [PubMed: 21547817]

40. Power C, Selnes OA, Grim JA, McArthur JC. HIV Dementia Scale: a rapid screening test. J Acquir Immune Defic Syndr Hum Retrovirol. 1995 Mar 1; 8(3):273–278. [PubMed: 7859139]

41. Woods SP, Moran LM, Carey CL, Dawson MS, Iudicello JE, Gibson S, et al. Prospective memory in HIV infection: is "remembering to remember" a unique predictor of self-reported medication management? Arch Clin Neuropsychol. 2008 May; 23(3):257–270. [PubMed: 18243645]

42. Sacktor N, McDermott MP, Marder K, Schifitto G, Selnes OA, McArthur JC, et al. HIV-associated cognitive impairment before and after the advent of combination therapy. J Neurovirol. 2002 Apr; 8(2):136–142. [PubMed: 11935465]

43. Juengst S, Skidmore E, Pramuka M, McCue M, Becker J. Factors contributing to impaired self-awareness of cognitive functioning in an HIV positive and at-risk population. Disabil Rehabil. 2012; 34(1):19–25. [PubMed: 21870997]

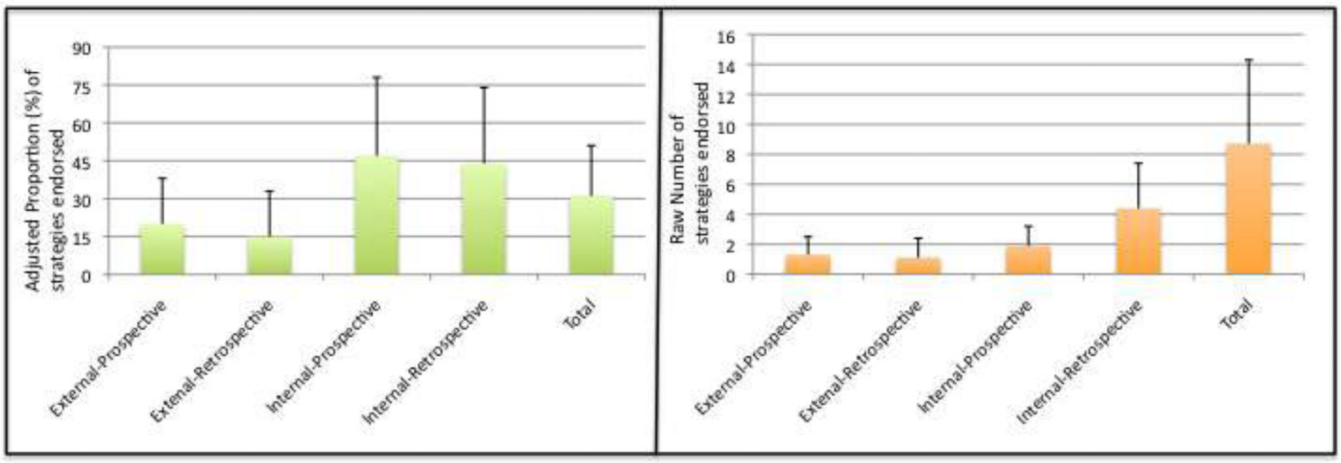


**Figure 1.**

Average strategies endorsed at least "sometimes" across the internal/external and prospective/retrospective dimensions.

**Note (right panel)**. Adjusted proportion indicates adjustment for total number of strategies possible per category. Each proportion of strategy type used significantly differed from each other (ps<0.03).

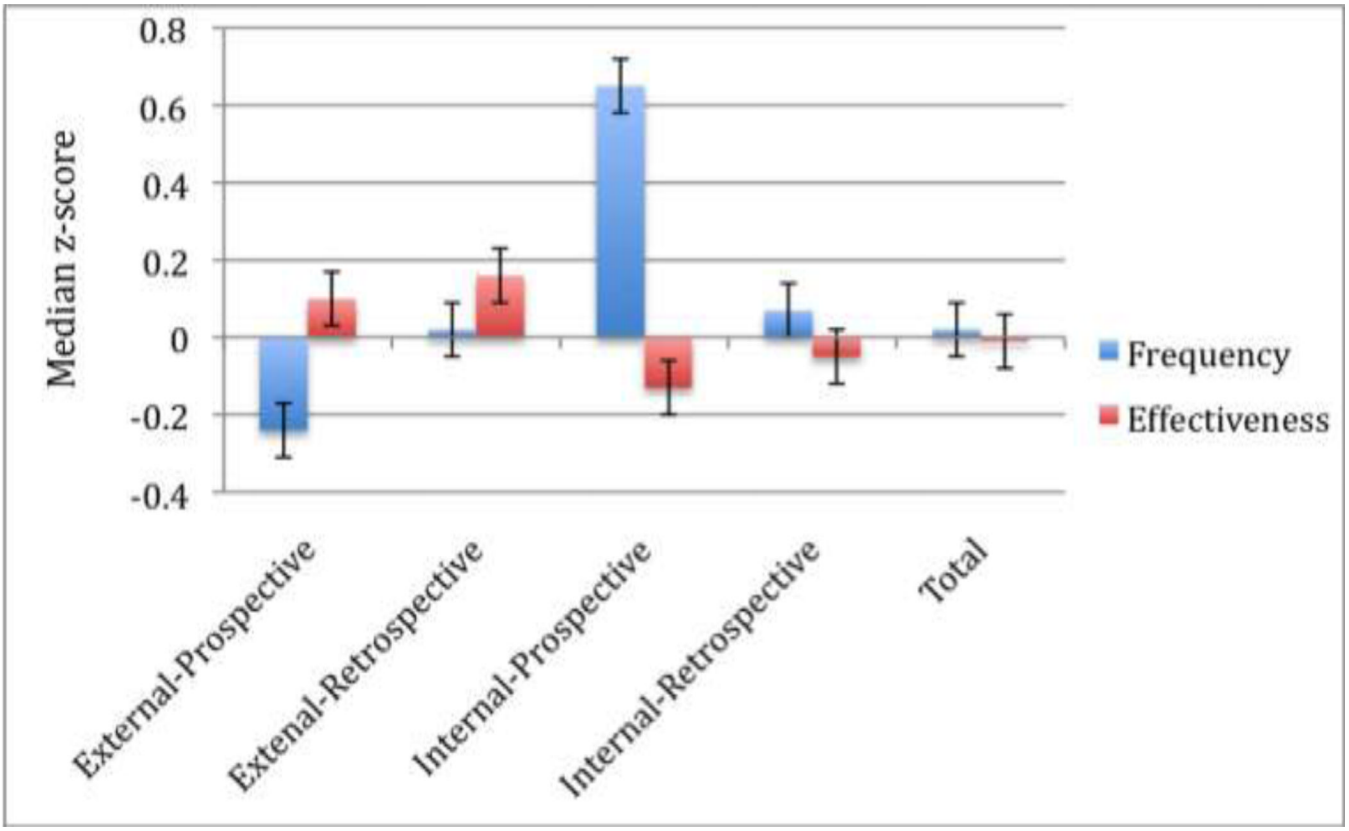


**Figure 2.**
Relative frequency and perceived effectiveness of reminder strategy type (established from median population-based z-scores).

## Table 1

Demographic and clinical characteristics of sample (N = 233).

| Variable | Mean, Median[a], or % | D, IQR, or N |
|---|---|---|
| Age | 47.4 | 10.4 |
| Gender (% M) | 83% | 193 |
| Ethnicity (% Caucasian) | 66% | 153 |
| Education | 13.4 | 2.5 |
| Number of ART rx | 4[a] | 3, 4 |
| Number of non-ART rx | 4[a] | 2, 7 |
| Current CD4 | 546[a] | 338, 733 |
| Nadir CD4 | 150[a] | 48, 259 |
| AIDS | 65% | 152 |
| CSF RNA log10 (n = 174) | 1.69[a] | 1.68, 1.69 |
| % Undetectable viral load in CSF (n = 174) | 88% | 60 |
| Plasma RNA log10 | 1.69[a] | 1.68, 1.69 |
| % Undetectable viral load in plasma | 85% | 131 |
| Profile of Mood States (POMS) total score | 55.5 | 35.2 |
| Lifetime MDD | 55% | 128 |
| Current MDD | 14% | 32 |
| Bipolar disorder | 18% | 42 |
| Lifetime substance dependence | 55% | 127 |
| NP Average T-score | 48.0 | 7.9 |
| Unemployed | 65% | 144 |
| IADL dependent | 21% | 46 |
| MEMS total ART adherence | 85.7 | 22.7 |

[a]Median scores

**Note**. ART = antiretroviral therapy; rx = prescriptions; CSF = cerebrospinal fluid; MDD = Major Depressive Disorder; NP = Neuropsychological; IADL = Instrumental Activities of Daily Living; MEMS = Medication Event Monitoring System

**Table 2**

Frequency of mnemonic adherence strategy use (N = 233).

| **Strategy*** | **Scale** | **Frequency** | | | | | |
|---|---|---|---|---|---|---|---|
| | | ***Always*** | ***Often*** | ***Sometimes*** | ***At Least Sometimes**** | ***Seldom*** | ***Never*** |
| *1. Leave pill bottle/pillbox in prominent place* | E-P | 48% | 12% | 9% | 69% | 6% | 25% |
| *2. Pair medication times to something you do routinely* | I-P | 35% | 19% | 14% | 68% | 4% | 28% |
| *3. Think about when need to take medications at the beginning of the day* | I-P | 33% | 16% | 12% | 61% | 8% | 31% |
| *4. Concentrate when receiving verbal medication instructions* | I-R | 26% | 15% | 20% | 61% | 14% | 25% |
| *5. Read written medication instruction more than once* | I-R | 18% | 16% | 26% | 60% | 20% | 21% |
| *6. Try hard to learn medication amount with new prescriptions* | I-R | 31% | 13% | 13% | 57% | 13% | 29% |
| *7. Read medication instructions slowly* | I-R | 13% | 17% | 25% | 55% | 15% | 30% |
| *8. Dated pillbox* | E-R | 38% | 6% | 4% | 48% | 2% | 51% |
| *9. Relate the medication times to an event specific to that day* | I-P | 12% | 11% | 24% | 47% | 13% | 40% |
| *10. Concentrate when learning times to take new medications* | I-R | 17% | 12% | 17% | 46% | 14% | 40% |
| *11. Mentally repeat medication instructions* | I-R | 10% | 11% | 21% | 42% | 13% | 45% |
| *12. Concentrate when reading medication instructions* | I-R | 13% | 12% | 16% | 41% | 18% | 42% |
| *13. Associate name of medication with name of condition it is treating* | I-R | 18% | 6% | 13% | 37% | 11% | 52% |
| *14. Make mental images/picture when receiving medication instructions* | I-R | 5% | 6% | 14% | 25% | 10% | 65% |
| *15. Clock/watch alarm* | E-P | 9% | 5% | 9% | 23% | 6% | 72% |
| *16. Ask doctor to speak slowly when giving medication instructions* | E-R | 4% | 4% | 13% | 21% | 17% | 63% |
| *17. Written list of time and amount of medication needed* | E-P | 8% | 3% | 5% | 16% | 10% | 73% |
| *18. Spend a lot of time making plans/using memory aids to help take medications on time* | I-P | 3% | 4% | 7% | 14% | 18% | 68% |
| *19. Repeat medication instructions for a prescription you've been taking for a long time* | I-R | 3% | 4% | 7% | 14% | 12% | 74% |
| *20. Leave notes in prominent places* | E-P | 3% | 2% | 8% | 13% | 9% | 78% |
| *21. Write yourself notes of medication instructions* | E-R | 2% | 2% | 7% | 11% | 7% | 82% |
| *22. Ask someone to help remember medication name* | E-R | 1% | 0% | 9% | 10% | 15% | 74% |
| *23. Leave notes in prominent place to remind how to take medications* | E-R | 2% | 0% | 6% | 8% | 7% | 85% |
| *24. Ask someone to help remember when and how to take new prescriptions* | E-P | 1% | 3% | 4% | 8% | 7% | 85% |
| *25. Ask other people to remind you how to take your medications* | E-R | 2% | 0% | 5% | 7% | 7% | 86% |

| Strategy* | Scale | Frequency | | | | | |
|---|---|---|---|---|---|---|---|
| | | *Always* | *Often* | *Sometimes* | *At Least Sometimes*** | *Seldom* | *Never* |
| *26. Ask other people to remind you what time to take your medication* | E-P | 1% | 0% | 5% | 6% | 10% | 84% |
| *27. Ask others to remind you amount of medication to take* | E-R | 1% | 1% | 4% | 6% | 6% | 89% |
| *28. Calendar use* | E-P | 1% | 0% | 1% | 2% | 3% | 95% |

*Strategy descriptions abbreviated; for a full version of the Prospective Memory for Medications Questionnaire, see Gould et al. (1997).

***At Least Sometimes* indicates cumulative proportion of strategy endorsement of "*Sometimes,*" "*Often,*" and "*Always.*"

**Note.** E-P = External-Prospective; E-R = External-Retrospective; I-R = Internal-Retrospective; I-P = Internal-Prospective.

## Table 3

Univariate predictors of total frequency of ART adherence strategy use (z-score).

| Variable | | F | *p*-value |
|---|---|---|---|
| **Age** | **0.19** | | **0.003** |
| **Ethnicity (Caucasian vs. other)** | | **5.5** | **0.02** |
| Gender | | 0.15 | 0.70 |
| Education | 0.05 | | 0.40 |
| **Number of ART rx** | **0.11** | | **0.10** |
| **Number of non-ART rx** | **0.27** | | **<0.001** |
| **AIDS** | | **9.3** | **0.003** |
| CSF RNA log10 | 0.05 | | 0.51 |
| Plasma RNA log10 | −0.006 | | 0.93 |
| Current CD4 | −0.01 | | 0.86 |
| **Profile of Mood States (POMS) total** | **0.29** | | **<0.001** |
| **Lifetime MDD** | | **12.8** | **<0.001** |
| Bipolar Disorder | | 1.0 | 0.33 |
| Lifetime substance dependence | | 0.62 | 0.43 |
| **NP Average T-score** | **−0.12** | | **0.06** |
| HDS Memory | 0.02 | | 0.73 |
| **MIST Event-based Score** | **−0.14** | | **0.03** |
| MIST Time-based Score | −0.08 | | 0.24 |
| MIST Recognition | −0.02 | | 0.82 |
| **Unemployment** | | **5.7** | **0.02** |
| **IADL dependence** | | **29.3** | **<0.001** |

**Note**. **Bold** indicates p<0.10. ART = antiretroviral; rx = prescriptions; CSF = cerebrospinal fluid; MDD = major depressive disorder; NP = neuropsychological; IADL = Instrumental Activities of Daily Living

## Table 4

Multivariable regression model predicting total frequency of ART adherence strategy use (z-score).

| Variable | Model | Parameter (t ratio) | p-value | 95% CI |
|---|---|---|---|---|
| Adjusted $R^2$ | 0.23 | | | |
| F | 6.0 | | <0.001 | |
| Age | | 0.36 | 0.72 | −1.88, 0.74 |
| Ethnicity (non-Caucasian) | | −0.40 | 0.69 | −0.18, 0.12 |
| Number of ART rx | | 0.26 | 0.79 | −0.14, 0.18 |
| **Number of non-ART rx** | | **2.36** | **0.02** | **0.008, 0.09** |
| AIDS | | 0.77 | 0.45 | −0.09, 0.21 |
| **Profile of Mood States (POMS) total** | | **2.48** | **0.01** | **0.001, 0.01** |
| Lifetime MDD | | −1.75 | 0.08 | −0.26, 0.02 |
| NP Average T-score | | 0.57 | 0.57 | −0.01, 0.02 |
| MIST Event-based Score | | −1.77 | 0.08 | −0.15, 0.008 |
| Unemployment | | 0.30 | 0.77 | −0.13, 0.18 |
| **IADL dependence** | | **2.46** | **0.01** | **0.05, 0.43** |

**Note**. ART = antiretroviral; rx = prescriptions; MDD = major depressive disorder; NP = neuropsychological; IADL = Instrumental Activities of Daily Living

**Table 5**

Demographic and clinical characteristics between frequency of strategy use and perceived effectiveness.

| | **Hi Frequency/ Hi Perceived Effective n=53 (a)** | **Hi Frequency/ Lo Perceived Effective n=51 (b)** | **Lo Frequency/ Hi Perceived Effective n=54 (c)** | **Lo Frequency/ Lo Perceived Effective n=52 (d)** | ***p*-value** | **Pairwise differences** |
|---|---|---|---|---|---|---|
| Age | 48.2 (10.5) | 49.4 (9.6) | 46.2 (9.9) | 46.1 (10.1) | 0.27 | |
| Ethnicity (% Caucasian) | 72% | 67% | 55% | 69% | 0.31 | |
| Gender (% M) | 85% | 78% | 80% | 90% | 0.33 | |
| Education | 13.8 (2.4) | 13.4 (2.4) | 13.0 (2.3) | 13.3 (2.7) | 0.40 | |
| Number of ART rx | 3.9 (1.0) | 4.0 (0.80) | 3.7 (0.96) | 3.7 (0.87) | 0.43 | |
| Number of non-ART rx | 5.2 (4.3) | 6.2 (4.6) | 3.5 (3.1) | 4.9 (3.8) | 0.006 | b,d > c |
| AIDS | 72% | 73% | 52% | 67% | 0.09 | b > c |
| CSF RNA log10 | 1.8 (0.33) | 1.8 (0.31) | 1.7 (0.34) | 1.9 (0.67) | 0.44 | |
| Plasma RNA log10 | 1.9 (0.73) | 1.8 (0.63) | 1.9 (0.63) | 2.1 (1.0) | 0.53 | |
| Current CD4 | 572.7 (363.6) | 587.0 (356.4) | 598.6(321.0) | 513.4 (275.5) | 0.73 | |
| Profile of Mood States (POMS) total | 56.2 (35.1) | 75.3 (42.7) | 46.3 (29.4) | 51.4 (31.4) | <0.001 | b > a,c,d |
| Lifetime MDD | 58% | 78% | 33% | 52% | <0.001 | b > a,c,d; a>c |
| Bipolar Disorder | 50% | 68% | 53% | 59% | 0.68 | |
| Lifetime substance dependence | 51% | 67% | 54% | 52% | 0.33 | |
| NP Average T-score | 48.3 (8.1) | 46.6 (7.7) | 48.7 (7.8) | 49.1 (8.4) | 0.30 | |
| HDS Memory | 3.6 (0.7) | 3.5 (0.7) | 3.6 (0.6) | 3.5 (1.0) | 0.65 | |
| MIST Event-based Score | 5.8 (2.0) | 5.8 (2.1) | 6.2 (1.6) | 6.4 (1.7) | 0.28 | |
| MIST Time-based Score | 5.6 (1.7) | 5.3 (1.9) | 5.5 (1.8) | 5.5 (1.4) | 0.80 | |
| MIST Recognition | 7.6 (0.6) | 7.4 (0.9) | 7.6 (0.7) | 7.6 (0.6) | 0.46 | |
| Unemployment | 77% | 69% | 56% | 59% | 0.10 | a > c |
| IADL dependent | 27% | 40% | 9% | 12% | <0.001 | b > c,d; a>c |

**Note**. ART = antiretroviral; rx = prescriptions; CSF = cerebrospinal fluid; MDD = major depressive disorder; NP = Neuropsychological; IADL = Instrumental Activities of Daily Living