RUNNING HEAD: COGNITIVE ESCAPE AND HIV TREATMENT ADHERENCE

A longitudinal analysis of HIV treatment adherence among men who have sex with men:
a cognitive escape perspective

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Abstract

HIV is best managed by adhering to both medication and HIV care appointment schedules. Nonetheless, many HIV positive men who have sex with men (MSM) report low levels of adherence to both. To explain this, we tested a cognitive escape model whereby drug and alcohol use mediate the effects of depression on HIV medication and appointment adherence. We used longitudinal data ($n=856$) from a behavioral intervention promoting increased treatment adherence among HIV positive MSM. All model variables predicted appointment adherence, and our mediation hypotheses were supported. Conversely, although depression related to medication adherence, substance use did not mediate this relationship, as predicted. Self-reported appointment, but not medication, adherence related to changes in viral load over time. Therefore, cognitive escape characterizes appointment, but not medication, adherence within this sample. Future behavioral interventions for this population should target HIV appointment adherence, given its relationship to important clinical, psychological, and behavioral outcomes.

Key words: HIV treatment adherence, appointment adherence, medication adherence, cognitive escape, MSM

Introduction

For HIV positive men who have sex with men (MSM), adherence to an HIV treatment regimen is crucial for staying healthy and keeping sexual partners healthy. Optimal treatment adherence levels lead to decreased viral loads, and individuals with decreased viral loads are less likely to transmit HIV (Paterson et al., 2000). HIV positive MSM have unprotected sex with potentially serodiscordant partners more than other MSM, on average (Chen, Gibson, Weide, & McFarland, 2003). Therefore, understanding and increasing HIV treatment adherence rates among MSM may benefit both those with HIV and their sexual partners.

Most HIV adherence research has focused on medication, i.e., taking Antiretroviral Therapy (ART) when prescribed. Among MSM, medication adherence is often suboptimal and associated with risky sexual behavior (Halkitis, Parsons, Wolitski, & Remien, 2003; Remien et al., 2007). Notably, low adherence to HIV care appointment schedules – a second component of adherence – also is common among HIV patients, and is related to negative health outcomes such as unprotected sex and virologic failure (Diamond et al., 2005; Mugavero et al., 2009).

Data and theory are lacking that simultaneously address adherence to HIV medication and care appointments. Converging evidence indicates some psychosocial and behavioral variables may relate to both, including depression, drug use, and alcohol use (Carrieri et al., 2003; Holzemer et al., 1999; Mugavero et al., 2009; Turner et al., 2001; Vyavaharkar et al., 2001). Each of these adherence correlates may be more common in, and problematic for, MSM compared to the general population (Martin, Pryce, & Leeper,

2005; Mills et al., 2004; Stall et al., 2001). Here, we link these correlates among MSM, using cognitive escape theory.

Cognitive escape models have been applied to health outcomes such as sexual risk (McKirnan, Vanable, Ostrow, & Hope, 2001) and binge eating (Heatherton & Baumeister, 1991), but not to treatment adherence. These models propose that people confronted with persistent or unmanageable psychosocial stressors may experience negative affect. This dysregulated emotional state may lead to avoidant coping behaviors, such as substance use, which promote cognitive disengagement, or *escape*, from persistent self-awareness of stress. In these models, substance use mediates the effect of negative affect on the health outcome.

Escape models may explain HIV treatment adherence. The treatment regimen requires consistent self-regulation and repeated, effortful cognitive awareness, e.g. taking daily medication and attending HIV care appointments. Following this regimen, or simply being HIV positive, may constitute a “long-term stressor” that for some leads to escape (see Figure 1).

INSERT FIGURE 1 ABOUT HERE

A mediation model including both psychological and behavioral constructs may characterize HIV treatment adherence among MSM (Halkitis & Palamar, 2008). Past research supports the proposed individual relationships in this model. Both MSM and HIV patients report depression disproportionately (Perkins et al., 1994; Williams et al., 2005), suggesting that it is a relevant variable to examine in MSM HIV treatment adherence. Depression relates to suboptimal HIV treatment adherence (Starace,

Ammassari, & Trotta, 2002) and substance use (Angelino & Treisman, 2001). And, alcohol and drug use relate to suboptimal medication and appointment adherence (Golin et al., 2002; Mugavero et al., 2009).

This study addresses several shortcomings of past HIV treatment adherence research. By testing a theoretically- and empirically-based cognitive escape model to explain HIV treatment adherence among MSM, we hope to fill a void of accurate, explanatory theoretical models of HIV treatment adherence among this population (Simno, Frick, & Huang, 2006). Further, research has focused on medication, not appointment, adherence. We plan to address both as outcome variables, to assess whether appointment adherence is a viable measure of HIV treatment adherence. Also, relatively few studies have investigated HIV treatment adherence longitudinally (Mugavero et al., 2009), despite adherence being a lifelong endeavor. Here we use longitudinal data to understand adherence over time. Lastly, few studies have used both self-reported and clinically-obtained data to test the internal and external validity of their measures simultaneously. We test the external validity of our self-reported adherence measures by comparing them to clinically-obtained viral load measures.

We hypothesize decreases in depression over time will predict decreases in drug and alcohol use, and increases in medication and appointment adherence. We believe changes in substance use will mediate the association between depression and adherence over time. We also expect changes in adherence to relate to changes in viral load over time.

Methods

Participants

Participants were recruited from a sample of HIV positive men ($N=945$) attending their HIV care visits at three clinics in/near Chicago between May 2004 – July 2005. Screeners assessed interest in study participation and if potential participants met study inclusion criteria, which included identifying as 18 years or older, male, HIV positive, and engaging in sexual behavior with men in the last six months. This study is a secondary analysis to an intervention study described below. Data collection was part of the intervention evaluation. There inclusion criteria for our study and the intervention were the same.

Procedure

The Treatment Advocacy Program (TAP) was a behavioral intervention designed to increase sexual safety and treatment adherence among HIV positive MSM. Participants were randomized to the intervention or contrast (delayed treatment) group. All participants completed an audio computer-assisted self-interview (ACASI) at baseline, 6-, and 12-month visits, which inquired about the last 6-12 months. Participants received a \$25 stipend for each visit. The intervention consisted of peer-delivered, motivational interviewing-based interactive modules focusing on sexual safety and HIV treatment adherence (see Raja, McKirnan, & Glick, 2007).

Measures

Demographic & personal characteristics

We used standard, face-valid items to assess race/ethnicity, age, socioeconomic status, education, annual income, participants' HIV clinic, and years since HIV diagnosis.

Medication adherence

At each wave, we divided each participant's total number of doses missed in the last week by his total number of weekly doses (both self-reported via ACASI) to produce a percentage representing weekly medication adherence rate (Knafl et al., 2008).

Published clinical recommendations for ART call for 95% adherence (Paterson et al., 2000); thus, we created a dichotomous variable reflecting at/above 95% adherence versus below 95%.

Appointment adherence

We used a dichotomous appointment adherence index classifying each participant as adherent – missing no scheduled appointments – or non-adherent – missing one or more, in the last 12 months. This operationalization is consistent with our dichotomous medication adherence variable. Further, an alternative operationalization, missed visit percentage (MVP; e.g. Mugavero et al., 2009), fails to differentiate potentially heterogeneous patterns. A participant struggling with his regimen and missing 4 of 10 scheduled visits would warrant a lower MVP than someone doing well but missing one of two scheduled visits (40% v. 50%). We perceive these percentage scores to be ambiguous; therefore, we used the simpler index of any missed visit, independent of number of visits scheduled.

Depression

We assessed depressive symptoms with the 15 negative items from the 20-item Center for Epidemiological Studies Depression scale (CES-D; $\alpha = .93$). Items such as “Over the past week, I felt sad” were rated on 4-point frequency scales ranging from “Rarely or none of the time” to “Most or all of the time.” Mean scores were calculated to produce a depression composite score.

Alcohol and drug use

We assessed alcohol and drug use individually, given that past research shows these have differential effects on adherence (Hinkin et al., 2004).

To assess alcohol use we used the CAGE (e.g. Dhalla & Kopec, 2007), which consists of four questions, including: “Have people ever *annoyed* you by criticizing your drinking?” Scores represented the number of items the participant endorsed. We characterized scores of 0 or 1 as non-alcohol-abusing and 2 or more as abusing, consistent with Buchsbaum et al. (1991).

We assessed the frequency of participants’ use of powdered cocaine, crack cocaine, heroin, methamphetamine, club drugs, and poppers, using individual measures on a 5-point frequency scale ranging from “Never” to “About every day.” Mean scores were calculated to produce a substance use composite score.

Viral load

Each participant’s viral load was obtained within two weeks of each study visit, via blood draw by a qualified medical professional. We expressed these using a continuous log₁₀ viral load index.

Analysis

We report two levels of analysis: baseline demographics and adherence behaviors, and a longitudinal test of our proposed model using all data points available for each participant at any wave, $n = 312$ at baseline, $n = 254$ at 6-months, and $n = 290$ at 12-months. Total N for appointment adherence outcomes = 856; for medication adherence, 639, due to some participants not taking ART. We conducted longitudinal analyses using Generalized Estimating Equations (GEE) in SPSS 16.0 (Kinnear & Gray, 2009). The

underlying correlation matrix was auto-regressive, evidenced by higher correlations between measures taken at baseline and 6 months, and at 6 months and 12 months, than at baseline and 12 months. Maximum likelihood estimators of variances were used. Psychosocial and substance use variables were entered as time-varying covariates; intervention group was entered as a covariate.

Mediation model testing was conducted using MacKinnon and colleagues' (2007) cross-products approach, which produces a confidence interval for the cross-product mediation effect at a given alpha level (in this case, $p < .05$). Intervals excluding zero indicate a statistically significant effect. To determine the proportion of the mediated effect, we entered the a , b , and c' mediation path betas into the equation $(ab)/(ab + c')$. Here, the numerator represents the indirect, i.e., mediating effect, and the denominator represents the total (indirect plus direct) effect.

Prior to baseline, participants were randomly divided into intervention ($n=164$) and contrast ($n=148$) groups. The groups did not differ on any clinical or demographic variable at baseline, $ps > .10$. Therefore, we merged these data and conducted aggregated analyses.

Results

Sample characteristics

Of all participants screened, 411 were eligible. Of these, 320 chose to enroll in TAP. Eight participants did not complete the intervention due to death or disqualification, leaving a final $N=312$ participants that completed the baseline ACASI. Retention rates were as follows: Six-month = 81.4% (M follow-up time = 5.9 months), 12-month = 92.9% (M follow-up time = 11.4 months). We obtained data at all three time-points from

250 participants (80.1% of the original sample). The only demographic or model variable that predicted dropout throughout the study was Latino ethnicity, $X^2(2, n=305) = 10.2, p < .00$. Otherwise the 250 men who attended all intervention sessions did not differ from the baseline sample of 312. Mean time for intervention completion was four months.

Table 1 presents participant demographics and baseline health indicators, including relatively high proportions of non-adherence to medication (20.5%, $n=64$) and appointment schedules (34.9%, $n=109$). The mean number of scheduled HIV care appointments was 4.83 ($SD=4.15$); the median and mode 4, and the range 0 ($n=9$) – 30 ($n=3$). Number of scheduled HIV care appointments did not differ by levels of depression, alcohol or drug use, or viral load ($ps > .10$).

INSERT TABLE 1 ABOUT HERE

Longitudinal results

Changes in study variables over time

Medication adherence did not change over time, $X^2(2, n=639) = .729, ns$, while appointment adherence increased, $X^2(2, n=856) = 33.60, p < .001$. Over time our sample became less depressed, $X^2(2, n=856) = 13.75, p = .01$; reported lower CAGE, $X^2(2, n=856) = 11.79, p < .01$ and drug use scores, $X^2(2, n=856) = 24.64, p < .001$; and had decreased viral loads, $X^2(2, n=883) = 46.75, p < .001$.

Predictors of adherence over time

We tested our model with medication adherence as the dependent variable, wave as the factor and within subjects variable, and aforementioned time-varying covariates. Reduced depression over time predicted greater medication adherence, $X^2(2, n=639) = 5.67, p = .017$. Conversely, changes in CAGE and drug use scores did not predict

changes in medication adherence, $ps > .05$. Changes in medication adherence over time did not predict changes in viral load, $X^2(2, n=620) = 3.72, ns$.

Each model variable independently predicted changes in appointment adherence over time: depression, $X^2(2, n=856) = 18.28, p < .001$; CAGE score, $X^2(2, n=856) = 10.92, p = .001$; and drug use score, $X^2(2, n=856) = 11.89, p = .001$. Changes in appointment adherence over time predicted changes in viral load, $X^2(2, n=852) = 12.00, p = .001$. Results for both outcome variables did not differ by group membership (intervention v. contrast; $ps > .10$).

Longitudinal mediation analysis

Because alcohol and drug use were not associated with medication adherence, we did not test these variables as possible mediators of the depression – adherence effect. We did test whether substance use mediated the effect of depression on appointment adherence over time. Changes in depression predicted CAGE score over time, $X^2(1, n=856) = 40.92, p < .001$ and drug use score over time, $X^2(1, n=856) = 18.92, p < .001$. Further, after controlling for depression, changes in both drug use score, $X^2(1, n=856) = 13.83, p < .001$, and CAGE score, $X^2(1, n=856) = 5.52, p = .019$, predicted changes in appointment adherence. Figure 2 reports betas for these regression analyses.

We conducted two follow-up mediation analyses. The first, testing changes in CAGE score as a mediator, produced a 95% confidence interval of .002—.032 for the product of coefficients of depression. The second, testing changes in drug use over time as a mediator, yielded a 95% confidence interval of .007—.036. Changes in CAGE scores mediated 16.8% of the effect of depression on appointment adherence over time, and changes in drug use scores mediated 20.1% of this effect.

INSERT FIGURE 2 ABOUT HERE

Discussion

Many HIV positive MSM show suboptimal HIV treatment adherence, which affects their health and the infection risk of their sexual partners. Both theory (McKirnan, Vanable, Ostrow, & Hope, 2001) and past empirical evidence (Halkitis & Palamar, 2008) suggest substance use mediates the relationship between psychological states and health outcomes among MSM. Guided by cognitive escape theory, and using longitudinal data, we predicted depression would relate to medication and appointment adherence, and these effects would be mediated by alcohol and drug use. Many participants reported suboptimal medication and appointment adherence, and our cognitive escape hypotheses were supported regarding appointment, but not medication, adherence.

There are several possible explanations that our health behavior model did not predict HIV medication adherence. First, our model simply may not characterize medication adherence in this sample; participants may not have perceived medication adherence as a long-term stressor from which they “escaped.” Or, this sample perceived medication adherence as a stressor, but did not cope with this stress by using substances. Alternatively, our measurement of adherence may not match the daily reality of HIV medication regimens. We examined these psychosocial predictors and outcomes in six-month blocks. Insofar as medication adherence is influenced by acute stressors and transient life events, six-month assessments may be less sensitive than momentary measures. In support of this, evidence shows that acute effects of intoxication, but not more stable traits that may underlie substance use, relate to medication non-adherence (Hinkin et al., 2007). Recognizing this, we used longitudinal analyses that modeled

coping as a dynamic process. This is a significant improvement over past studies that used cross-sectional analyses. We recommend future adherence researchers simultaneously use longitudinal analyses and ACASI questions that assess the influence of acute stressors on adherence.

Unlike medication adherence, appointment adherence was predicted by our escape-oriented variables. Our measurement of appointment adherence differed from that of some past studies (e.g. Mugavero et al., 2009). Two findings supported the legitimacy of our approach. First, dichotomous coding of appointment adherence related to participants' clinically measured viral load, indicating external validity of this important clinical outcome. Second, appointment adherence behaved like other psychological and behavioral model variables, in that it co-varied with key constructs over time.

Our results have implications for future adherence research and interventions. It appears that treatment adherence is not a unitary phenomenon. Rather, it represents a complex of at least two behaviors – medication and appointment adherence. We believe both types of adherence should be investigated more systematically. This study suggests that appointment adherence, in particular, may be an effective point of intervention for HIV positive MSM. Therefore, targeting and increasing appointment adherence may be an efficient means of decreasing viral load and improving other health indices.

The effect of substance use, escape coping, or any other variable on regimen adherence is due to concrete behaviors that this study did not address. People who use drugs or alcohol to cope with stressors may exhibit a range of behaviors –intoxication, “motivated forgetting” of regimen requirements, disrupted sleep-wake cycles, personal disorganization, memory impairment – that can interfere with attending medical visits or

taking medication doses. Future studies should address this very concrete level of “mediators” and their related psychological states and health behaviors. Further, our findings indicate the outcomes of substance use and depression are not always specific and concrete, e.g., missing medication doses. Instead they may contribute to a more global disenfranchisement from the healthcare system, e.g. missing schedule HIV care visits. Accordingly, clinicians must be aware of and emphasize to their patients the potential for substance use and depression to interfere with their healthcare.

This study has several limitations. Our results may not generalize to all HIV positive MSM, but instead to ongoing MSM HIV patients currently receiving treatment. Also, our cognitive escape model tested the relationship between a (depression) and c (adherence), mediated by b (substance use). However, as is the case with any mediating model, the a and b variables could be transposed: Substance use could be the core psychosocial predictor of non-adherence, with depression mediating this effect. While we cannot differentiate these models statistically, both theory (McKirnan et al., 2001) and empirical evidence (Halkitis & Palamar, 2008; Marks, Bingman, & Duval, 1998; Piasecki, Kenford, Smith, Fiore, & Baker, 1997) support our perspective that negative affect can induce substance use as an escape oriented “self-medication,” that itself leads to problematic health behaviors.

Overall, our findings suggest that considering the influence of cognitive escape on attending HIV care appointments may advance our understanding of HIV treatment adherence, and promote viral load maintenance among HIV positive MSM.

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Table 1. Sample demographics and health indicator frequencies at baseline.

Demographic	n (%)	Demographic	n (%)	Indicator	n (%)
Race		Income		Medication adherence	
African American	98 (31.4)	None	11 (3.5)	95% or above	160 (51.3)
White	146 (46.8)	\$1-9,999	84 (26.9)	Below 95%	64 (20.5)
Hispanic/Latino	54 (17.3)	\$10,000-19,999	84 (26.9)	No regimen	88 (28.2)
Other	14 (4.5)	\$20,000-29,999	41 (13.1)	Appointment adherence	
Sexual Orientation		\$30,000+	92 (29.6)	Missed none	203 (65.1)
Heterosexual	3 (1.0)	Highest Education Level		Missed 1 or more	109 (34.9)
Gay	279 (89.4)	8th grade or less	9 (2.9)	Depression symptoms^c	
Bisexual	23 (7.4)	Some high school	22 (7.1)	0-4	209 (67.0)
Other	7 (2.2)	Diploma or GED	49 (15.7)	5-9	68 (21.8)
Age^a		Some college	121 (38.8)	10+	35 (11.2)
18-29	41 (13.1)	BA/BS	75 (24.0)	CAGE symptoms	
30-39	94 (30.2)	Post BA/BS	36 (11.5)	0 or 1	213 (68.3)
40-49	136 (43.6)	Employment status		2+	99 (31.7)
50+	41 (13.1)	Unemployed	153 (49.0)	Drugs used^d	
Time Since Diagnosis^b		Full/partial	147 (47.1)	0	126 (40.4)
0-3 years	94 (30.9)	Occasional	12 (3.8)	1-2	137 (43.9)
4-9 years	91 (29.9)			3+	49 (15.7)
10+ years	119 (39.1)				

^a $M = 40.3$, $SD = 8.97$ ^b $M = 8.31$ yrs, $SD = 6.09$ yrs^cParticipants indicated these occurred “a moderate amount...” or “most...” of the time^dExcluding marijuana

Figure 1. The proposed cognitive escape model, in which substance use mediates the effect of depression on a health behavior.

Figure 2. Longitudinal association of depression and HIV care appointments, partially mediated by substance use.