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Antiretroviral therapy adherence in youth living with HIV: Exploring the role of risk behaviors, health promotion behaviors and depressive symptoms

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ANTIRETROVIRAL THERAPY ADHERENCE IN YOUTH LIVING WITH HIV: EXPLORING THE ROLE OF RISK BEHAVIORS, HEALTH PROMOTION BEHAVIORS AND DEPRESSIVE SYMPTOMS

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Antiretroviral therapy adherence in youth living with HIV: Exploring the role of risk behaviors, health promotion behaviors and depressive symptoms

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Abstract

Youth living with HIV are often inconsistent with their HIV medication adherence. HIV medication adherence is critical for the treatment of HIV and prevention for future transmission. Understanding associated behaviors that may impact adherence for individuals living with HIV is necessary for their continued care. The current study aimed to more fully identify the influences engaging in risk behaviors, health promoting behaviors and experiencing depressive symptoms have on HIV medication adherence in adolescents and young adults with HIV. Participants were 92 adolescents and young adults with HIV living in the mid-south region of the United States. Individuals completed surveys about demographics, psychosocial behaviors, depressive symptoms and antiretroviral therapy (ART) medication adherence during a clinic visit. Path analyses were conducted to measure the model fit of the Reflective-Impulsive theory on ART adherence. Results did not support any significant path coefficients, variance explained, or mediation effects. These findings suggest limited insight into health and risk factors related to ART adherence in youth living with HIV, but may offer some suggestions for future research. Further study is warranted to understand the relationship among these factors in order to improve ART adherence and health outcomes.

Key words: HIV, Adherence, Youth, Health behaviors, Risk Behaviors, Path analysis

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INTRODUCTION

The United States Center for Disease Control and Prevention estimates that 1.2 million Americans are living with HIV with approximately 50,000 new infections annually[1]. Youth living with HIV aged 13-24 in the United States have been identified as a special group that often struggles with both antiretroviral therapy (ART) adherence and increased engagement in risk behaviors, both of which are linked with lower life expectancy and HIV transmission.[2-7] Less than 1 out of 5 youth living with HIV currently adhere to ART and have a suppressed viral load, the lowest rate of any age group.[1] To complicate this problem, the number of youth living with HIV has been steadily growing in number and currently account for over 20% of individuals with new infections.[1] The seriousness of this problem is reflected in the National HIV/AIDS Strategy for the United States through 2020, which has focused efforts on funding community-based organizations that provide prevention programs to reduce sexually transmitted infections (STIs), substance use and mental health issues and increasing health promoting behaviors.[5] Efforts to identify areas to intervene and increase ART adherence are a critical component to furthering this strategy.

While many research studies have identified factors independently related to ART adherence, no study has put forth a model integrating risk behaviors, depressive symptoms and health promotion behaviors as they relate to an individual's ART adherence.[3,4,8-10] Health promotion behaviors, such as physical activity and nutrition, are relatively new additions to the interventions focused on increasing ART adherence.[11,12] Furthermore, continued efforts to identify health behaviors, and their relation to ART adherence, falls in line with the CDC and National HIV/AIDS Strategy goals of increasing ART adherence in youth while preventing the spread of HIV to currently uninfected individuals. Given this troubling lack of ART adherence

and its consequences for youth living with HIV as well as HIV prevention efforts, the research reported here tested predictive models of adherence that included the new health promotion factors, as well as already established constructs, in an effort to better understand their interrelationship and identify areas of potential intervention.

Theoretical Framework

Informed by decades of dual-process theories in social psychology concerning decision making and behavior, the Reflective-Impulsive Model (RIM) explained information processing by theorizing two systems, reflective and impulsive .[13,14] The model outlined how behavior can be instigated by both a thoughtful and deliberate choice (the reflective system) and by a more automatic and want-based reflex (the impulsive system). For example, "How can it be that one decides to eat a healthy lunch but still reaches out for the sweet muffin?"[13] In this example, the reflective system is illustrated by a thoughtful and deliberate choice to eat a healthy lunch, while eating the sweet muffin illustrates the more automatic, and want-based, impulsive system. The RIM model incorporates both the reflective and impulsive systems in an integrated dual-process model that encompasses components of behavior, knowledge and affect to explain the actions an individual takes.[13]

The Reflective-Impulsive Model (RIM) is well suited to help explain the relationship between health-related behaviors and affect in adolescents and young adults, including their medication adherence.[13,14] The impulsive system is always active and directs behavior through "what feels good/is habitual," seeking pleasure and avoiding pain, and is less reasoned and conscious (e.g., "I have unprotected sex when I'm living in the moment"). Conversely, the reflective system is not automatic and includes judgments, evaluations of pros and cons, and intentions.[15] The reflective system is characterized by reasoned, conscious and intentional plans

and decisions that activate behaviors (e.g., "I'm going to take my medication to improve my health"). Products from the two systems interacting help determine an individual's behavior.

According to work by Hofman, Friese and Strack[16] the reflective system has less influence on decision-making when an individual is experiencing limiting factors like high cognitive load, alcohol consumption, lower capacity for self-control, low working memory, when behavior is habitual, and when affect is reactive. Previous research has used the RIM to conceptualize the relationships and impact of these limiting factors on predicting health-related behaviors. For example, one set of studies used measures of impulsivity, controlled behavior and cognitive capacity to successfully predict three distinct behavioral situations: 1.) Choice of fruit versus chocolate, 2.) potato chip consumption and 3.) beer drinking.[17] Results supported impulsivity and controlled behavior as independent and unique predictors of health behaviors when cognitive capacity was within normal functioning. However, when cognitive capacity was lowered (i.e., watching highly emotional movie clips of violence and aggression) impulsivity was found to have more influence in predicting behavior.[17] In applying the RIM framework to the current research, we propose that ART adherence in an individual living with HIV is, at least in part, determined by the interaction between affect and impulsive and reflective health behaviors.

Health-risk and impulsive behaviors such as substance use and unprotected sex are often framed as "barriers" to a healthy lifestyle and are inconsistent with ART adherence. Known barriers to ART adherence include engaging in risk behaviors such as risky sexual behaviors (e.g., low or no condom use).[8,9,18-20] For instance, one survey of over 350 youth in the United States found that 42% of their youth sample reported engaging in sexual risk behaviors, and of that 42% over half endorsed also experiencing inconsistent ART adherence.[19] Substance use,

and substance use-related factors, have also been found to be significant barriers to ART adherence for adolescents.[10,18] Youth diagnosed with HIV who report cannabis abuse have been found to have poorer ART adherence for multiple reasons such as forgetting to take their ART, and a lack of motivation to take ART after cannabis use.[21] Moreover, higher rates of cannabis use and depressive symptoms were significant predictors of non-adherence in youth with HIV.[3] While the research on the RIM has measured the impulsivity and reflective components more in-depth, including measurement of affect and its role within the model remains largely unexplored.

Health promoting behaviors such as engaging in physical activity and consuming nutritional diet are more likely to be products of the reflective system in that they are conscious and reasoned decisions. The limited existing research in this area has shown that engaging in physical activity and consuming nutrition are associated with reducing negative affect and increasing ART adherence.[11,12] The integration of physical activity and nutritional diets into behavioral intervention models focused on improving ART adherence for adolescents has shown promising results.[22] Specific forms of physical activity including walking, swimming and rollerblading were reported and perceived as helpful in self-care by individuals with HIV, with and without a depressive symptoms.[23]

In general, the RIM focuses on reflective and impulse behaviors as they relate to health choices such as medication adherence but little research on this framework has attempted to integrate affect into the research. The inclusion of affect is particularly important because individuals living with HIV are significantly impacted by depressive and anxiety symptoms. Youth living with HIV often struggle with learning about their HIV diagnosis and depressive symptoms concurrently and as a result have negative outcomes related to their psychosocial

functioning and health.[3,24,25] Depressive symptoms along with anxiety symptoms significantly predict lower ART adherence, accounting for over 20% of the variance in individuals' ART adherence.[3]

The purpose of the current study was to conduct a set of secondary analyses testing theory-based predictive models of adherence that include established predictors, the new health promotion factors, as well as affective factors, in an effort to better understand their interrelationship and identify areas of potential intervention for youth living with HIV. Our study focused specifically on ART adherence outcomes because of the critical impact medication has on individuals' physical and mental health outcomes. Given the RIM literature, we hypothesized that antecedent components such as nutrition, physical activity, unprotected sex, substance use and depressive symptoms would both directly and indirectly impact ART adherence. Our conceptual model, adapted from previous work by Hofmann, Friese and Wiers[26], provides a framework for examining available health behavior variables and additional affect hypotheses. See Figures 1 -3 below.

Study Purpose and Models

The purpose of this study was to examine three alternative models of the relationships between risk behaviors, health promotion behaviors, depressive symptoms and ART adherence indicators. The three alternative models and their comparison can help better understand variable relationships and potential causal effects impacting ART adherence in youth.

Model 1 (shown in Figure 1) examined 1) direct relationships from risk behaviors and health promotion behaviors to depressive symptoms and from depressive symptoms to ART adherence, and 2) indirect relationships from risk behaviors and health promotion behaviors to ART adherence, both through the mediation of depressive symptoms.

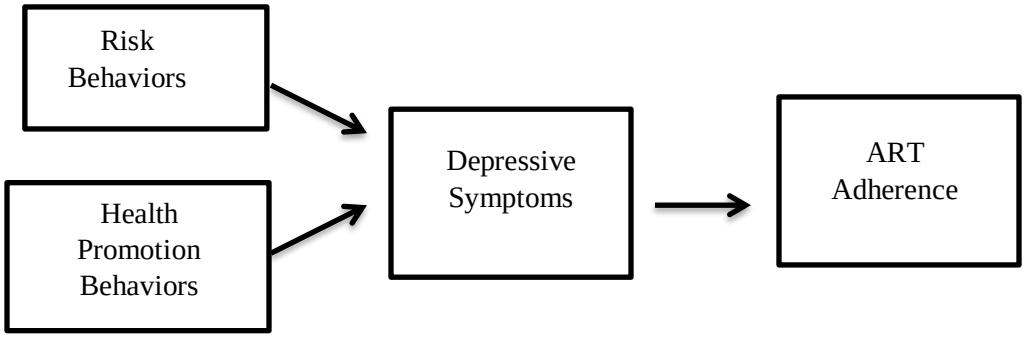

Figure 1.

Model 2 (shown in Figure 2) also examined the same relationships as specified in Model 1; In addition, based on empirical evidence, direct relationships from risk behaviors and health promotion behaviors to ART adherence will be added and tested.

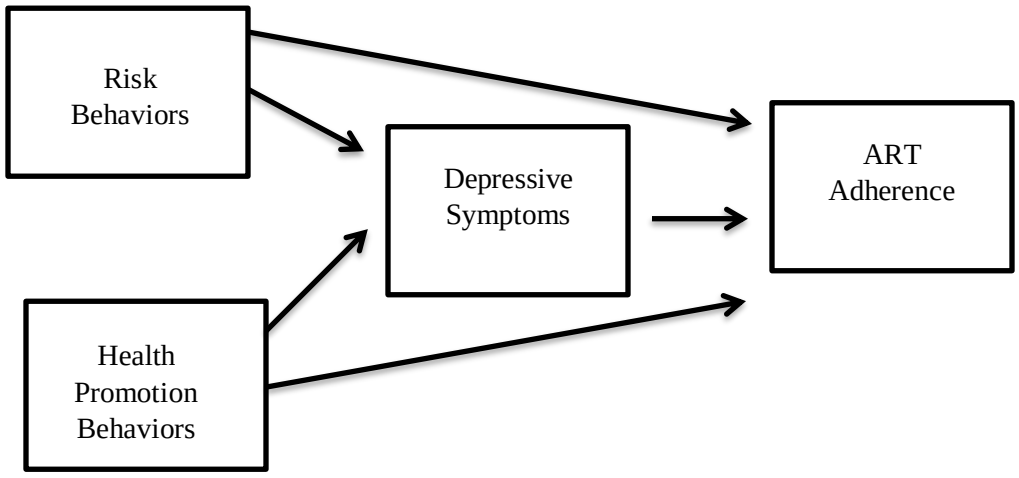

Figure 2.

Model 3 (shown in Figure 3) examined 1) direct relationships from depressive symptoms to risk behaviors and health promotion behaviors, and from both risk behaviors and health promotion behaviors to ART adherence; 2) As such, the model also tested the direct relationships from depressive symptoms to ART adherence, and the mediation of risk behaviors and health promotion behaviors.

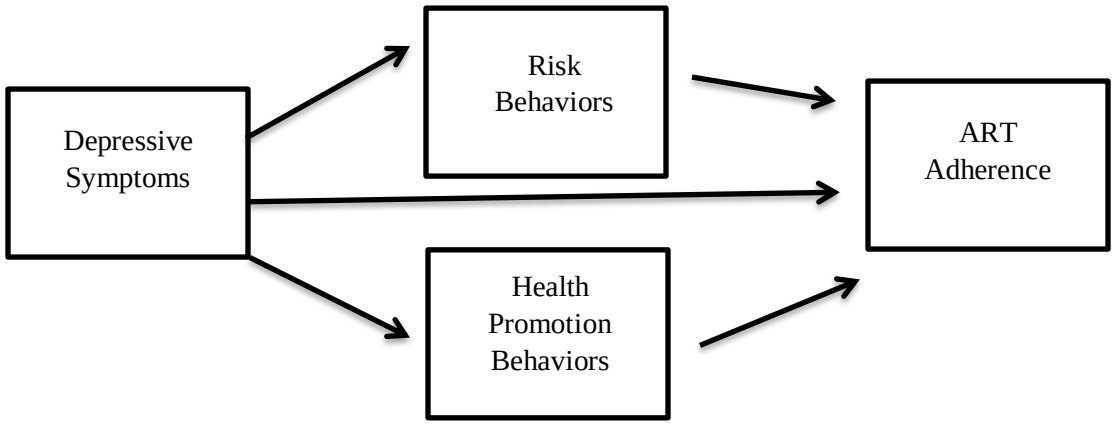
Depressive Symptoms
Risk Behaviors
Health Promotion Behaviors
ART Adherence

Figure 3.

METHODS

Participants and recruitment

The data were collected from youth (ages 16-24) living with HIV in care at a hospital clinic in the Mid-south region of the United States. Recruitment was for an exploratory study on body image.[27] All participants consented themselves, or had parental consent if under 18 years old. Participants were eligible for approach if they were aware of their diagnosis, their primary language was English, they were between the ages of 16-24, and were not pregnant. Additional exclusion criteria included diagnosis of an intellectual disability or a significant motor or sensory impairment, or known acute psychiatric illness, including active suicidal ideation, homicidal ideation or psychosis. In addition, participants needed to have been prescribed an ART regimen. No other limits were set in terms of sexual orientation, education, or other demographic information in order to increase the generalizability of the results. A total of 92 participants fit the inclusion criteria and completed the questionnaires for the proposed study.

Study procedures

Youth with vertically and behaviorally acquired HIV were approached for study participation during their routine infectious disease clinical visit. After obtaining informed consent, participants completed an Audio Computer Assisted Self-Interview (ACASI) in a private clinic room. Additional clinical information was abstracted from the participant's medical record by study staff. The clinic's Institutional Review Board (IRB) approved the current study with agreement from governing University.

Measures

Demographic characteristics. Each participant was asked various demographic questions, including their gender, marital status, education level, employment status and income level.

Social and environmental questions were also asked about utilization of public assistance programs (e.g., food stamps). Additional clinical values such as HIV viral load and CD4 cell count/% were obtained in a medical record review and are presented in Table 1.

Risk Behaviors and Health Promotion Behaviors. Previous risk behaviors were assessed using the Youth Risk Behavior Surveillance System (YRBSS)[28], a survey developed by the Centers for Disease Control and Prevention (CDC) to gather educational and health information for government agencies. The YRBSS monitors six categories of health-risk behaviors among youth and young adults including: behaviors that contribute to unintentional injuries and violence; tobacco use; alcohol and other drug use; sexual behaviors related to unintentional pregnancy and sexually transmitted diseases including HIV; unhealthy dietary behaviors; and physical inactivity. The individual items vary on type and number of responses; for example, "*Did you drink alcohol or use drugs before you had sexual intercourse the last time*? A. I have never had sexual intercourse, B. Yes, or C. No" while another item reads, "*During the past 7 days, how many times did you eat other vegetables?* (Do not count green salad, potatoes, or carrots.) A. I did not eat other vegetables during the past 7 days, B. 1 to 3 times during the past 7 days, C. 4 to 6 times during the past 7 days, D. 1 time per day, E. 2 times per day, F. 3 times per day, or G. 4 or more times per day" For the purposes of the current study, questions pertaining to risk behaviors were selected (i.e., Number of sexual partners in past 3 months; condom use at last sexual encounter; alcohol or substance use during last sexual encounter) as well as the health promotion behaviors (i.e., Physical activity in last 7 days; Vegetables in last 7 days). Previous reliability tests demonstrated Cohen's kappas ranging from 23.6% to 90.5%, with a mean of 60.7% and a median 60.0%, indicating moderate reliability.[29,30]

Depressive symptoms. Symptoms of depression were assessed by the Center for

Epidemiological Studies Depression Scale-10 (CESD-10)[31]. The CESD-10 is a short form that consists of ten items that asks the patient to rate symptoms (e.g., "I felt lonely"; "I could not "get going") over the last week. Each item is scored 0 to 3 [0=Rarely or none of the time (less than 1 day); 1=Some or a little of the time (1-2 days); 2=Occasionally or a moderate amount of time (3-4 days); 3=Most or all of the time (5-7 days)]. Total scores range from 0-30, and higher scores indicated higher depressive symptoms. Cronbach's alpha for the CESD-10 has been measured as α=.72 in the general population[32] and α=.88 in an HIV-specific sample[33].

ART Adherence. Three measures of ART adherence were used. The first measure of ART adherence was a self-reported estimate of adherence using the Visual Analog Scale (VAS) which remains widely used with individuals living with HIV.[34-36] The VAS for ART adherence appears as a continuous scale representing the percent of ART taken relative to that which has been prescribed, for a given HIV medication, during a month long period. Patients are presented with a line anchored at 0% and 100% and asked to assess their own ART adherence. The second indicator was a single item asking "When was the last time you missed a dose of your HIV medication?" with response options of: "Today, Yesterday, Earlier this week, Last week, Less than a month ago, More than a month ago, and Never." The third measure was the adherence rates provided by the clinic's pharmacy pill count (PPC). The PPC is a hybrid adherence measure using pill count and pharmacy refill, both of which are usually classified as "objective measures" and deemed acceptable and valid measures of adherence in the general population and in HIV-specific samples.[37,38] It is clinic policy for patients to bring their HIV medications to all appointments in the clinic. The patient is instructed to drop-off their ART bottles or pillboxes at the pharmacy which is housed within the clinic building. During their appointment, the pharmacists or pharmacy technicians count the pills left and enter the values into the patient's

medical chart. This number is compared to last refill of the HIV medication, giving the clinic a number and percentage of pills taken compared to the amount prescribed that should remain.

Statistical Analyses

All descriptive and correlational statistics were conducted using IBM SPSS Statistics for Macs, Version 24.0 (IBM Corp., 2017, Armonk, NY). First, descriptive analyses were conducted to describe participant characteristics. Second, zero-order correlations were performed to examine relationships between all model variables. Researchers planned to combine the three adherence indicators to measure adherence as a latent variable. However, very low factor loadings demonstrated no evidence to support their combination as measuring one overarching construct. Given the statistical support, the three adherence outcome variables were kept independent and ran as separate path analyses. This changed the proposed three models to a total of nine models. Third, path analyses were conducted using the structural equation modeling (SEM) software package M*plus*, Version 8.0, to jointly model the direct and indirect relationships in the proposed models that examine relationships between the health and risk behaviors, depressive symptoms, and the three adherence outcome variables. See figures 4 – 6 for conceptual illustrations.

Since all available variables for analysis were observed rather than latent, and the goal of this analysis was to use the general SEM framework to test the fit of nine path analysis models. Maximum likelihood (ML) was used for model estimation. Model fit indices were only used in three of the models (i.e., models 1a, 1b, and 1c) of the current study because the other six models (i.e., models 2a-c and 3a-c) proposed prespecified, fully saturated path analysis models. This is a result of utilizing RIM theory and the limited observed variables in the available and pre-existing data set. For a fully saturated model, the global model fit is perfect (i.e., 0.00 or 1.00) and does

not inform us on how well the current study data fits the pre-specified measurement model. Standardized beta (β) regression coefficients are reported for each direct and indirect effect.

The "gold" standard recommends that the smallest acceptable sample size in studies using structural equation modeling is approximately 200.[39] However, because the proposed study is a secondary analysis, the sample size is predetermined and falls below 200. Given this, a second method of determining sample size was based on Kline's (2010) sample size recommendations that uses the ratio of cases (*n*) to the number of parameters that require statistical estimates (q); (*n*:q), with an ideal ratio being 20:1 and less ideal being 10:1 and 5:1 being unacceptable. In the proposed study, there are 92 cases (*n*) and ten parameters (q), (~ 10:1). As such, this study has an acceptable ratio of cases to parameters, which supports the use of SEM as an appropriate analysis.

This study examined the relationships between risk behaviors, health promotion behaviors, depressive symptoms and ART adherence. It investigated the impact of risk behaviors and health promotion behaviors on ART adherence, as well as the impact of depressive symptoms on ART adherence for youth living with HIV. The first two models evaluated whether depression mediates the relationship between both risk behaviors and health promotions and ART adherence. As a possible alternative, the final model evaluated whether risk behaviors and/or health promotion behaviors mediate the relationship between depressive symptoms and ART adherence.

RESULTS

Participant characteristics

The mean age of the sample was 20.9 years (standard deviation = 1.93). The majority of participants identified as male (76.3%), Black (95.9%), gay (46.4%), men who have sex with

men (66.0%), single (94.8%), pursuing education (51.5%) and employed (54.6). Table 1 provides full participant demographic data.

Table 1.

Sample Characteristics

Characteristic	Mean	SD	n	%
Age	20.8	1.96		
CD4 Absolute	636.25	327.50		
CD4 Percentage	30.40	10.78		
HIV Viral Load (copies/ml)	11724.05	35075.53		
Gender				
Male			71	77.2
Female			21	22.8
Race				
Black			88	95.7
White			4	4.3
Transmission Route				
Vertical			14	15.2
Horizontal			78	84.8
Sexual Orientation				
Straight			28	30.4
Gay			43	46.7
Lesbian			1	1.1
Bisexual			17	18.5
Other			3	3.3
Education				
12^{th} grade or less			17	18.5
High School Diploma/GED			36	39.2
Some College			27	29.3
College or more			12	13
Student status				
Not currently enrolled			45	48.9
Full/part-time			47	51.1
Employment status				
Full-time			32	34.8
Part-time			20	21.7
Not employed			40	43.5

Prior to conducting model estimation, we prepared the data in three steps. First, we checked for missing values. It was found that our data had limited missing values. Specifically, one case was missing values on the Visual Analog Scale, Substance use during last sexual encounter, and the Health Risk Behavior mean variables, which reduced the *n* from 92 to 91 on those three variables. Also, the pharmacy pill count only had data available for 71 of the participants. Second, in order to assess univariate normality, we computed skewness and kurtosis, and it was found that all interval and ratio variables in our data were statistically non-significant. Due to the data including two binary items (Condom use during last sexual encounter; Alcohol or substance use during last sexual encounter), the assumptions of multivariate normality cannot be met. Third, correlations between each of our variables were analyzed. Table 2 presents item means, scale means, and standard deviations for all variables of interest, including the ART adherence indicators [1.Visual Analog Scale (VAS) self-report, 2. Time since last missed dose self-report, 3. Pharmacy pill count (PPC)], CESD-10 scores, health promoting behaviors (i.e., Physical activity in last 7 days; Vegetables in last 7 days), and the risk behaviors (i.e., Number of sexual partners in past 3 months; condom use at last sexual encounter; alcohol or substance use during last sexual encounter). Zero-order correlations were also examined between the constructs of interest and are presented in Table 2.

Table 2.

Descriptives and correlations of predictor, mediation, and outcome variables

	1	2	3	4	5	6	7	8	9	10	11
1. Visual Analog Scale (VAS)	-										
2. Time since last missed dose		.43**									
3. Pharmacy Pill Count (PPC)	.50**	.47**									
4. CESD-10 score	-.10	-.15	.06								
5. Physical Activity in last 7 days	.04	.07	.11	-.08							
6. Vegetables in the last 7 days	.13	.08	.21	-.18	.40**						
7. Health Promotion Behaviors Means	.09	.09	.18	-.14	.90**	.76**					
8. Number of sexual partners in the past 3 months	-.06	-.19	-.08	-.09	.28*	.11	.21*				
9. No condom use last sexual encounter	.07	-.07	.07	.14	-.12	-.07	-.11	.05			
10. Alcohol or substance use during last sexual encounter	.01	-.16	.17	.12	.00	-.06	-.03	.19	-.05		
11. Health Risk Behavior Mean	-.04	-.25*	-.07	-.03	.00	.07	.15	.95**	.26*	.41*	-
N	91	92	71	92	92	92	92	92	92	91	91
Mean	82.3	4.9	89.8	9.4	3.15	1.88	2.5	1.75	0.20	0.29	1.8
Range	0-100	0-7	0-100	0-24	0-7	0-7	0-7	0-99	0-1	0-1	0-99
SD	25.9	1.9	15.3	6.0	2.5	1.9	1.8	1.8	0.4	0.5	0.7

Note. *p < at 0.05 level. **p at 0.01 level.

Path Model Estimation

Model construction and evaluation were completed using structural equation modeling (SEM). Data were analyzed using Mplus 7.4 (Muthen & Muthen, 2015) statistical software. When possible, model fit was tested using Chi-square statistics and common fit indices, such as Comparative Fit Index (CFI), Tucker Lewis Index (TLI), Standardized Root Mean Square Residual (SRMR), and Root Mean Square Error of Approximation (RMSEA). Good model fit indices were specified by a CFI and TLI of at least .95, a RMSEA of <. 06, a SRMR of <. 08, and non-significant Chi-square statistic (Weston, Gore, Chan, & Catalano, 2008). Additionally, parameter estimates were estimated using 5000 bootstrap samples. The bootstrapping method has been suggested in mediation models to better assess indirect effects with bias-corrected 95% confidence intervals (Hayes, 2009).

The a priori models were specified and estimated first to assess for multivariate outliers. No participants were identified as multivariate outliers based on Cook's distance and Mahalanobis distance. After the models were estimated, path coefficients were evaluated for statistical significance.

Several path models were structured to evaluate the study's hypotheses. A priori models were specified and included model 1 (Figure 4): health promotion behaviors, health risk behaviors variables as indirect predictors, depressive symptoms as a mediator and the three ART adherence indicators (i.e., Visual Analog Scale [monthly self-report], last missed dosage and pharmacy pill count) as the endogenous measure in the three separated models; model 2 (Figure 5): health promotion behaviors, health risk behaviors variables as direct predictors, depressive symptoms as a mediator and ART adherence indicators (i.e., Visual Analog Scale [monthly self-report], last missed dosage and pharmacy pill count) as outcomes; model 3 (Figure 6): depressive symptoms as a predictor, health promotion behaviors (HPB) and health risk behaviors as

mediators and adherence indicators as outcomes.

All model parameters are presented in Tables 3 through 8. In models 1a-c, health promotion behaviors, health risk behaviors variables are the exogenous variables, depressive symptoms is a mediator and an endogenous/exogenous variable, and the three measures of ART adherence indicators, including Visual Analog Scale [monthly self-report], last missed dosage and pharmacy pill count are each used as the endogenous variable in three separated models. The relationships tested were direct: 1.) from impulsive risk behaviors to depressive symptoms, 2.) from HPBs to depressive symptoms, and 3.) from depressive symptoms to ART adherence. The indirect and mediation relationships tested were: 1.) role of depressive symptoms between risk behaviors and 2.) ART adherence as well as 3.) between HPBs and ART adherence. The indirect relationships tested were: 1.) from risk behaviors to ART adherence and 2.) from HPBs to ART adherence. In comparison to models 2a-c and 3a-c that will be discussed next, only model 1a-c posits the reflective and impulsive behaviors best explain ART adherence indirectly (through affect) as opposed to directly explaining the influence of impulsive and reflective behaviors on ART adherence.

Model 1a was not supported by the data. Although data demonstrated a perfect model fit indicator (RMSEA = .00), this value should be attributed to X^2 being less than *df* and a low sample size, both of which are known to set RMSEA at zero.[40] No other fit indices were available. There were no statistically significant path coefficients between risk behaviors, health promotion behaviors, depressive symptoms, and monthly adherence. Depressive symptoms explained 1% (R^2 = .01), and risk and health behaviors explained < 1% (R^2 = <.01) of the variance in predicting monthly adherence. Model 1b was not supported by the data. Although data demonstrated an acceptable model fit indicator (RMSEA = .07), it is more likely that this

was due to the minimal difference between X^2 and *df*.[40] No other fit indices were available. There were no statistically significant path coefficients between risk behaviors, health promotion behaviors, depressive symptoms, and time since last missed dose. Depressive symptoms explained 3% (R^2 = .03), and risk and health behaviors explained 2% (R^2 = .02) of the variance in predicting time since last missed dose. Model 1c was not supported by the data as evidenced by a poor model fit indicator (RMSEA = .13). No other fit indices were available. There were no statistically significant path coefficients between risk behaviors, health promotion behaviors, depressive symptoms, and pharmacy pill count. Depressive symptoms explained <1% (R^2 = .00), and risk and health behaviors explained 2% (R^2 = .02) of the variance in predicting pharmacy pill count.

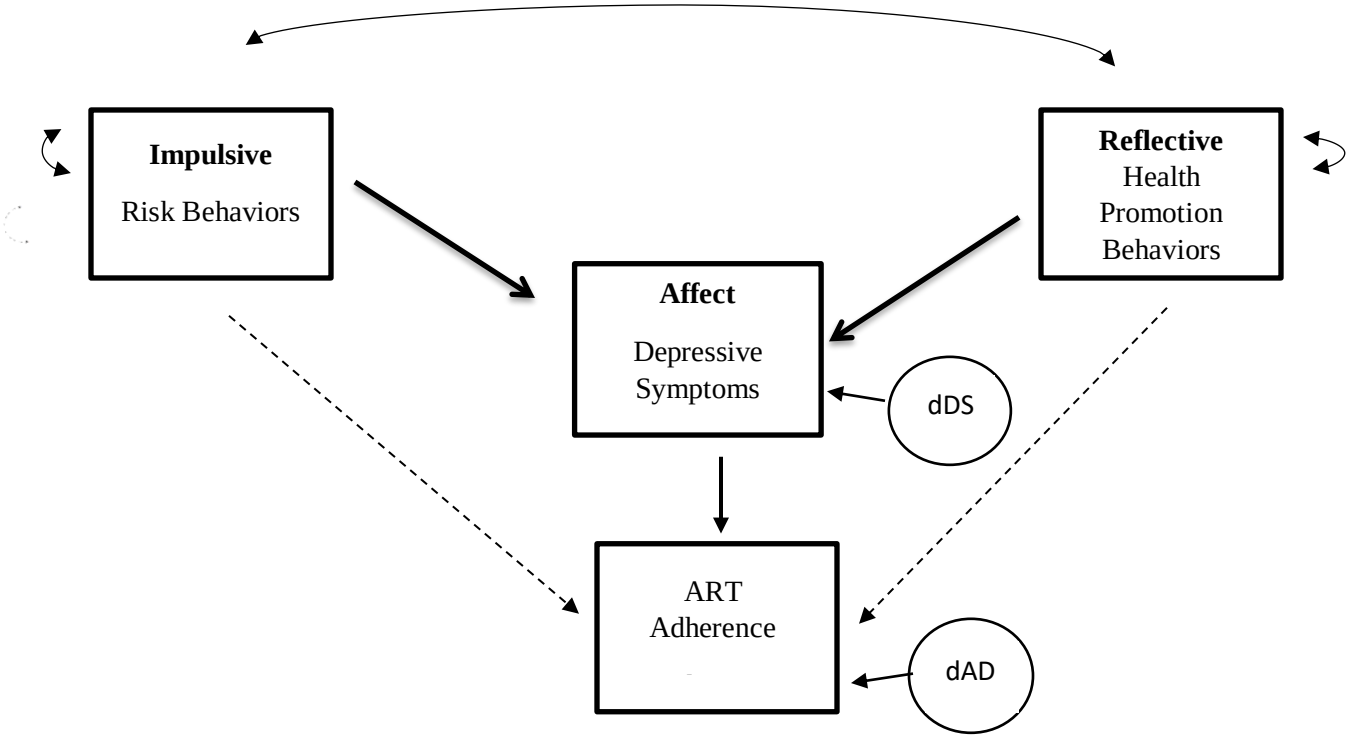

Figure 4.
The a priori model 1 for path analysis including all predictors, mediators, and outcomes. *Note*. Model 1 tested three ART adherence indictors: a. Visual Analog Scale (self-report monthly adherence), b. time since last missed dose, c. pharmacy pill count

Table 3.

Values of Selected Fit Statisics for the full model 1a, 1b, and 1c.

Model	X^2	*df*	X^2/df	RSMEA	CFI	SRMR
Model 1a.) ART Adherence Visual Analog Scale	1.41	2	0.7	.00	1.00	0.03
Model 1b.) ART Adherence Time since last missed dose	3.09	2	1.5	.07	0.64	0.05
Model 1c.) ART adherence Pharmacy Pill count	4.95	2	2.5	.13	0.00	0.07

Table 4.

Standardized and Unstandardized Coefficients for the models 1a, 1b, and 1c.

		Maximum likelihood Estimates From 5000 Bootstrap Samples				
Dependent Variable	Independent Variable	Unstandardized Est.	Standard Est.	S.E.	P-value	R^2
Model 1a.) ART Adherence Visual Analog Scale	CESD-10	-0.42	-0.10	0.11	.35	0.00
Model 1b.) ART Adherence Time since last missed dose	CESD-10	-0.05	-0.17	0.11	.13	0.03
Model 1c.) ART adherence Pharmacy Pill count	CESD-10	0.16	0.06	0.44	.66	0.00
*CESD-10	Health Behaviors	-0.49	-0.14	0.10	.13	0.02
	Risk Behaviors	0.57	0.07	0.09	.43	

*Note. * same values for models 1a, 1b, and 1c.*

In models 2a-c, health promotion behaviors and health risk behaviors variables are the exogenous variables, depressive symptoms is a mediator, and the three measures of ART adherence indicators: Visual Analog Scale [monthly self-report], last missed dosage and pharmacy pill count) were individual endogenous variables for models 2a-c. The relationships tested were direct 1.) from impulsive risk behaviors to affect/depressive symptoms, 2.) from impulsive risk behaviors to ART adherence, 3.) from health promotion behaviors to depressive symptoms, 4.) from health promotion behaviors to ART adherence, and 5.) from depressive symptoms to ART adherence. The indirect and mediation relationships tested are: 1.) role of depressive symptoms between risk behaviors and ART adherence as well as 2.) between HPBs and ART adherence. The indirect relationships tested are: 1.) from risk behaviors to ART adherence and 2.) from HPBs to ART adherence. The relationships tested are unique relative to models 1a-c and 3a-c in that only model 2a-c posits the reflective and impulsive behaviors that best explain ART adherence both directly and when mediated by depressive symptoms as opposed to only explaining the influence of impulsive and reflective behaviors when mediated by depressive symptoms on ART adherence.

Model 2 was just-identified, the number of free parameter equals the number of known values; thus, fit indices were known to be limited. Model 2a was not supported by the data. As expected, data demonstrated a perfect model fit indicator (RMSEA = .00), which is attributed to X^2 being equal to *df* and a low sample size.[40] No other fit indices were available. There were no statistically significant path coefficients between risk behaviors, health promotion behaviors, depressive symptoms, and monthly adherence. Depressive symptoms, health promotion behaviors, and risk behaviors only explained 3% (R^2 = <.03) of the variance in predicting monthly adherence. Model 2b was not supported by the data and demonstrated the default

perfect fit (RMSEA = .00). No other fit indices were available. There were no statistically significant path coefficients between risk behaviors, health promotion behaviors, depressive symptoms, and time since last missed dose of ART. Depressive symptoms, health promotion behaviors, and risk behaviors only explained 6% (R^2 = <.06) of the variance in predicting the time since last missed dose. Model 2c was not supported by the data. Results revealed the default perfect fit (RMSEA = .00). No other fit indices were available. There were no statistically significant path coefficients between and from risk behaviors, health promotion behaviors, depressive symptoms, and pharmacy pill count. Depressive symptoms, health promotion behaviors, and risk behaviors only explained 7% (R^2 = <.07) of the variance in predicting pharmacy pill count percentage.

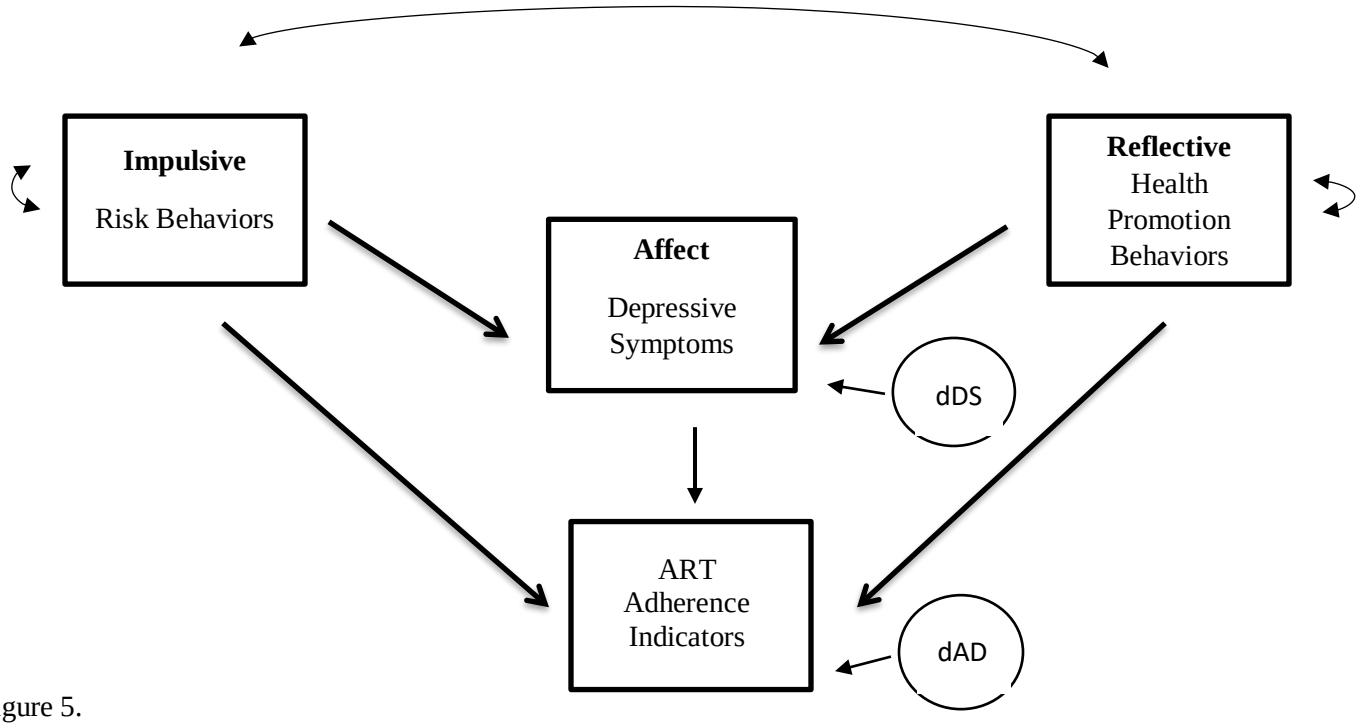

Figure 5.
The a priori model 2 for path analysis including all predictors, mediators, and outcomes. *Note*. Model 1 tested three ART adherence indictors: a. Visual Analog Scale (self-report monthly adherence), b.Time since last missed dose, c. pharmacy pill count

Table 5.

Values of Selected Fit Statisics for the full model 2a, 2b, and 2c.

Model	X^2	*df*	X^2/df	RSMEA	CFI	SRMR
Model 1a.) ART Adherence Visual Analog Scale	0.00	0	0	.00	1.00	0.00
Model 1b.) ART Adherence Time since last missed dose	0.00	0	0	.00	1.00	0.00
Model 1c.) ART adherence Pharmacy Pill count	0.00	0	0	.00	1.00	0.00

Table 6.

Standardized and Unstandardized Coefficients for the models 2a, 2b, and 2c.

		Maximum likelihood Estimates From 5000 Bootstrap Samples				
Dependent Variable	Independent Variable	Unstandardized Est.	Standard Est.	S.E.	P-value	R^2
Model 1a.) ART Adherence Visual Analog Scale	CESD-10	-0.35	-0.08	0.11	.46	0.03
	Health Behaviors Risk Behaviors	1.31	0.09	0.12	.46	
		-3.35	-0.10	0.11	.38	
Model 1b.) ART Adherence Time since last missed dose	CESD-10	-0.05	-0.15	0.11	.18	0.06
	Health Behaviors Risk Behaviors	0.03	0.03	0.10	.74	
		-0.44	-0.19	0.11	.08	
Model 1c.) ART adherence Pharmacy Pill count	CESD-10			0.14	.54	0.07
	Health Behaviors Risk Behaviors	0.22	0.09	0.10	.04	
		1.84	0.21	0.10	.07	
		-3.66	-0.18			
*CESD-10	Health Behaviors Risk Behaviors			0.36	.13	0.02
		-0.49	-0.14	0.85	.43	
		0.57	0.07			

Note. * same values for models 2a, 2b and 2c.

In models 3a-c, affect is defined as depressive symptoms and is the exogenous variable, while risk behaviors and health promotion behaviors are the mediators, and the ART adherence indicators (i.e., Visual Analog Scale [monthly self-report], last missed dosage and pharmacy pill count) are the endogenous outcome variables, respectively for models a-c. The variable type is different from models 1a-c and 2a-c in that depressive symptoms is now the exogenous variable and the risk behaviors and health behaviors are mediating the relationship between affect (depressive symptoms) and the ART adherence indicators.

The relationships tested are direct 1.) from depressive symptoms to risk behaviors, 2.) from depressive symptoms to health promotion behaviors, 3.) from health promotion behaviors to ART adherence, 4.) from risk behaviors to ART adherence. The indirect and mediation relationships tested are: 1.) role of risk behaviors between depressive symptoms and ART adherence as well as 2.) the role of health promotion behaviors between depressive symptoms and ART adherence. The indirect relationships tested are: 1.) from depressive symptoms to ART adherence through risk behaviors and 2.) from depressive symptoms to ART adherence through health promotion behaviors. The relationships tested are unique relative to models 1a-c and 2a-c in that only model 3a-c posits that ART adherence is best explained by measuring affect (depressive symptoms) as mediated by reflective and impulsive behaviors.

Model 3 was also just-identified; thus, fit indices were known to be limited. Model 3a was not supported by the data. Data demonstrated a perfect model fit indicator (RMSEA = .00), which was attributed to X^2 being equal to *df* and low available sample size.[40] No other fit indices were available. There were no statistically significant path coefficients between depressive symptoms, risk behaviors, health promotion behaviors, and monthly adherence. Depressive symptoms, health promotion behaviors, and risk behaviors only accounted for 3% ($R^2 = <.03$) of

the variance in predicting monthly adherence. Model 3b was not supported by the data, and demonstrated the default perfect fit (RMSEA = .00). No other fit indices were available. There were no statistically significant path coefficients between risk behaviors, health promotion behaviors, depressive symptoms, and the time since last missed dose of ART. Depressive symptoms, health promotion behaviors, and risk behaviors only accounted for 7% (R^2 = <.07) of the variance in predicting the time since last missed dose. Model 3c was not supported by the data, and demonstrated the default perfect fit (RMSEA = .00). No other fit indices were available. There were no statistically significant path coefficients between risk behaviors, health promotion behaviors, depressive symptoms, and pharmacy pill count. Depressive symptoms, health promotion behaviors, and rick behaviors only accounted for 8% (R^2 = <.08) of the variance in pharmacy pill count.

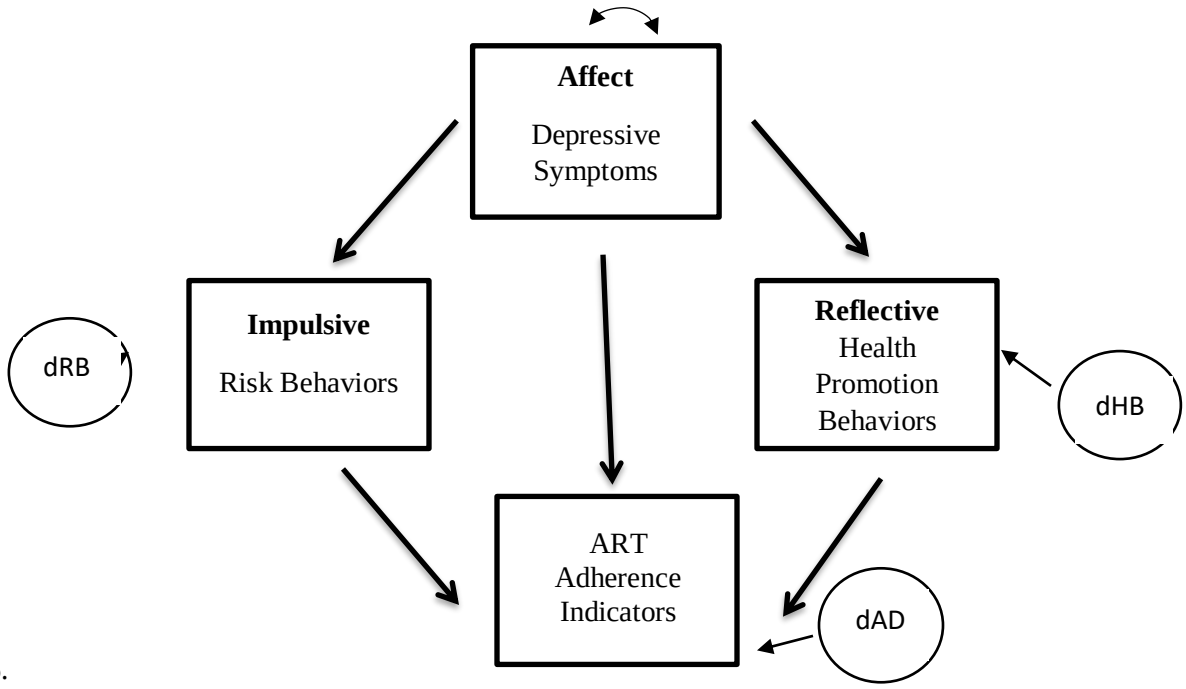

Figure 6.
The a priori model 3 for path analysis including all predictors, mediators, and outcomes. *Note*. Model 3 tested three ART adherence indictors: a. Visual Analog Scale (self-report monthly adherence), b. Time since last missed dose, c. pharmacy pill count.

Table 7.

Values of Selected Fit Statisics for the full model 3a, 3b, and 3c.

Model	X^2	*df*	X^2/df	RSMEA	CFI	SRMR
Model 1a.) ART Adherence Visual Analog Scale	0.98	1	0.98	.00	0.00	0.00
Model 1b.) ART Adherence Time since last missed dose	0.98	1	0.98	.00	0.00	0.00
Model 1c.) ART adherence Pharmacy Pill count	0.98	1	0.98	.00	0.00	0.00

Table 8.

Standardized and Unstandardized Coefficients for the models 3a, 3b, and 3c.

		Maximum likelihood Estimates From 5000 Bootstrap Samples				
Dependent Variable	Independent Variable	Unstandardized Est.	Standard Est.	S.E.	P-value	R^2
Model 1a.) ART Adherence Visual Analog Scale	CESD-10	1.31	0.09	0.12	.46	0.02
	Health Behaviors	-3.35	-0.10	0.11	.38	
	Risk Behaviors	-0.35	-0.08	0.11	.46	
Model 1b.) ART Adherence Time since last missed dose	CESD-10	0.03	0.03	0.10	.74	0.06
	Health Behaviors	-0.44	-0.19	0.11	.08	
	Risk Behaviors	-0.05	-0.15	0.11	.18	
Model 1c.) ART adherence Pharmacy Pill count	CESD-10			0.10	.04	0.07
	Health Behaviors	1.84	0.21	0.10	.07	
	Risk Behaviors	-3.66	-0.18	0.14	.54	
		0.22	0.09			
*Health Behaviors	CESD-10	-0.04	-0.14	0.09	.15	0.02
*Risk Behaviors	CESD-10	0.01	0.06	0.09	.52	0.00

*Note. * same values for models 3a, 3b, and 3c.*

Additional mediation effect analyses were planned to investigate relationships between predictor variables, mediation variables and outcome variables. However, the poor model fit of the data did not warrant further examination of these variable relationships.

Summary

These results do not support the idea that engagement in risk behaviors and health promoting behaviors of the sample significantly contributed toward their ART adherence, as measured by patient monthly self-report (VAS), patient report of time since last missed dose and pharmacy pill count (PPC). In addition, the mediation effects remained unexamined due to the poor data-model fit.

DISCUSSION

Given the current health challenges and consequences that youth living with HIV face, increasing their adherence to Antiretroviral Therapy (ART) is critical and warrants closer examination. This is particularly important given that the sample used is predominately gay, MSM, horizontally infected youth living with HIV in the Southern U.S. region, and are a group disproportionately impacted and underserved. In this research we tested predictive statistical models of ART adherence with the hope of better identifying, understanding and intervening on the behaviors, situations and related factors that influenced health consequences including premature mortality.[12,41-44] Based on previous literature, we conceptualized adherence to ART to be the result of certain health promotion and risk behaviors as well as an individual's affect.[13,14,17,26] In an effort to further understand the relationships among these variables we tested three path models that used risk behaviors, health promotion behaviors, and depressive symptoms in a sample of youth (ages 16-24) living with HIV in care at a hospital clinic to predict three individual measures of ART adherence. These results were inconsistent with the existing

literature on which the models were based, and did not support any of the proposed models. Given the lack of significant findings, the following sections will exam two probable explanations for our findings.

Insufficient model

In this research we used the Reflective-Impulsive Model (RIM) as a theoretical framework for constructing our predictive models. However, given that we fit existing data into the model, some components of the Reflective-Impulsive Model (RIM) framework were not measured or assessed as suggested by model creators. The Reflective-Impulsive Model (RIM) postulates three important domains that should be measured to best predict a health behavior, 1.) reflective precursors and 2.) impulsive precursors, and related 3.) situational and dispositional boundaries.[26]

The first domain that should be assessed is the reflective precursors (reasoned attitudes, restraint standards, and cognitive constructs) associated with conscious goal-pursuit. Based on the Reflective-Impulsive Model (RIM) these reflective components should be measured with explicit self-report measures. Although the current study utilized self-reports to assess the reflective precursors, it is probable that information gathered on nutritional diet and physical activity did not tap into all of the cognitive processes needed to predict ART adherence. For example, reasoned attitudes would be an important variable to include to significantly predict the relationship between reflective variables and ART adherence.

The second domain that should be assessed is impulsive precursors such as automatic affective reactions and automatic behavioral tendencies of approach/avoidance. In the Reflective-Impulsive Model (RIM) a "good measure" of the impulsive system should tap into the "hedonic or behavioral reactions" triggered in decision-making. Given the automatic and often

unconscious nature of impulsive decisions, recommended assessment of the impulsive domain are implicit tests including Implicit Association Test[45], the Affect Misattribution Procedure[46]. Given that the archival data available for this study only used explicit self-report measures to gather information, it is possible that the measurement of the risk behaviors was insufficient and therefore unable to significantly predict ART adherence from risk behaviors.

Lastly, the third domain that should be measured according to Reflective-Impulsive Model (RIM) is the situational and dispositional boundaries such as coping resources and individual differences. Fewer recommendations are made concerning the assessment of the situation or individual differences. In the present study, we measured depressive symptoms utilizing self-report but did not capture situational components or personality factors such as conscientiousness. As a result, the omission of this type of information may have negatively impacted the model's ability to predict adherence to ART.

Given the Reflective-Impulsive Model (RIM) recommendation's to assess all three of these domains and to use implicit and explicit tests, the proposed model was likely deficient in capturing all of the necessary information to accurately and significantly predict the health behavior of ART adherence.

Inadequate Data and Statistics

The current study also had inadequate data and statistical power. The gathered data, although available on an important, and underserved/under researched population, were restricted by both range and type (i.e., dichotomous). Regarding restricted range, the health promotion behavior mean was low (2.5 on a 7-point scale), which suggests that the sample was mostly made up of individuals who do not engage in many health promoting behaviors. This sample limitation likely inhibited the ability to test the inverse relationship between individuals

engaging in a high amount of health promoting behaviors and their experience of depressive symptoms. This may be characteristic of the sample collected in that older African American youth living in the Southern United States are more likely to engage more sedentary activities and to be overweight compared to their counterparts in other regions of the country.[47,48]

In addition, the data set had two dichotomous variables (alcohol and/or substance use during last sexual encounter; condom use during last sexual encounter) contributing to the risk behavior mean, which only allowed a range of (0-2). Beyond the restricted range issues, dichotomous variables are historically not well suited for path analyses using ML, as they do not meet the multivariate normality assumption and may not produce accurate regression coeffients.[49] It is likely that increasing the binary answer range to interval or ratio options would have added a larger range, and broader variance to measure more accurate relationships between risk behaviors, depressive symptoms, and ART adherence.

Finally, the overall small sample size of 92 participants limited the statistical power of the analyses, which undoubtedly contributed toward the lack of significant findings. While the sample was small it was uniquely defined by the youth to young adult age range, inclusion of vertically and horizontally infected, as well as the multiple types of ART adherence indicators (self-report and objective). Perhaps adding older individuals may have increased sample size but it would take away from our specific aim of addressing this gap in adolescents and young adults.

Secondary findings

Primary results of the current study were not significant; however, some secondary findings are useful for discussion of ART adherence and are interpreted below.

A significant positive relationship between physical activity and intake of vegetables (r = .40) was found. This means that individuals in our sample who reported more physical activity were

more likely to eat more vegetables, which is consistent with current literature.[12,50-52] These findings may also provide support for a collective construct of reflective behaviors (deciding to exercise and healthy eating) being related to one another.

Regarding risk behaviors and ART outcomes, a significant negative correlation between the risk behavior mean score and the self-reported time since last missed dose (r = -.25, p = .05) revealed that the more risk behaviors endorsed, the more likely the individual was to have recently missed a dose of their ART. Although not causal, this correlation is meaningful and supports that when acted on the relationship between impulsive precursors, defined as risk behaviors, also have influence on decision-making related to ART adherence.

Strengths and Limitations

Although our results were disappointing and inconclusive, this study was important to conduct and had several strengths. First, we collected data from the predominately gay, MSM, horizontally infected youth living with HIV in the Southern U.S. region, which is a disproportionately impacted and often invisible population. Second, our study aim was aligned with the National HIV/AIDS Strategy for the United States through 2020, which encourages government support for research and resources for individuals living with HIV. Third, our strength-based approach to incorporating health promotion behaviors assists in a non-pathologizing narrative consistent with patient-centered care. Lastly, the path models we put forth aimed to map behaviors and depressive symptomsof youth living with HIV onto a relatively new theory, which aimed to deepen the health-behavior decision making and HIV adherence literature.

As aforementioned, there are also several limitations of the research which should be discussed. First, the sample size was low, and did not meet best practice guidelines (N=200) per

Kline.[39] Having a limited and predetermined sample size reduced the power in our path models to find significance. In order to address this, continued enrollment and increasing sample size above 200 individuals would strengthen the statistical power and the findings. The second limitation was the inability to obtain fit indices, which reduced the ability to compare models on fit between each other. In the future, additional parameters should be added to create an unsaturated model, which would provide us with the standard fit indices (e.g., CFI, GFI) to compare our models to the index standards and to one another in determining the best model to fit our data.[53] Third, given the Reflective-Impulsive Model framework applied, the current data does not include indicators or the recommended measurement types for all of the model components. Therefore, adding measures that capture all components of the theory could strengthen the model.[13,14] Fourth, our findings may not generalize to all youth living with HIV in that our sample was predominately African American and living in the South. The Southern U.S. is unique in the disproportion of HIV infections and limited resources for support compared to more metropolitan settings, which could play a role in medication access and adherence.[1] Lastly, our research relied predominately on self-report, which can be subject to social desirability and biases related to self-judgment. Incorporation of more objective measures (e.g., electronic monitors of adherence), could increase our information to better aggregate the data to more accurately predict behaviors.

Future Directions

The present study provides limited insight into health and risk factors related to adherence to ART in youth living with HIV, but may offer some suggestions for future research. Other researchers working on similar aims have found that a variety of factors including but not limited to negative affect, substance use, younger age, physical activity, and regimen

simplification, contribute to nonadherence of ART.[3,41,54] Based on the majority of the literature, increased efforts are needed to identify predictors that maintain and/or increase adherence as well as barriers to adherence. More specifically, researchers should continue their efforts to expand targeted interventions aligned with the current "prevention of HIV by treatment of HIV" to address adherence while also preventing the spread of HIV.

Future studies would benefit from a sample size larger than 200 individuals, and from an a priori approach in which all of the components of the Reflective-Impulsive Model (RIM) are measured. For instance, adding cognitive components such as an individual's cognitive ability, cognitive load, and self-control would add components that have been identified as important to include in the model.[16,26] The use of implicit tests to measure impulsive precursors is also warranted. An experimental design involving both self-report and the Implicit Association Task could shed light on how risk behaviors are best measured to predict ART adherence in youth living with HIV.

It would also be advantageous for future research to expand the range of items and scales collected for each predictor and indicator. Specifically, inclusion of Likert-type items involving multiple risk (e.g., unprotected sex, substance use) and health promoting behaviors (e.g., physical activity, nutritional eating) would address the restricted range and likely generate more item variance. In doing this, we would capture a broader range of behaviors that represent the constructs of "risk" and "health promotion," which would also lead to more accurate measurements within the model and improved validity and reliability. Research examining youth living with HIV should also examine within group differences by utilizing measures that account for important individual differences. For instance, it would be important to differentiate types of ART regimen (e.g., 1 pill versus 2 pills or multiple administrations a day), which is known to

uniquely predict adherence.[41] Another influential, and emphasized, construct in the ART adherence literature is an individual's experience of stigma and life and social stressors.[43,55] Measurement of these commonly-related constructs could provide us with more information about the psychological process of youth living with HIV, and insight into the best predictors of their adherence.

Lastly, a logical expansion of this project would also be to include a personality measure to capture conscientiousness, defined as the propensity to follow socially prescribed norms for impulse control, to be goal directed, to plan, and to be able to delay gratification.[56] Inclusion of this construct would add the measurement of a possibly important individual difference in youth living with HIV. These results could help researchers further understand characteristics of their sample, while drawing on a potentially independent and unique predictor of ART adherence related to multiple variables in the current study (reflective cognitions, health promotion behaviors, and inversely with risk behaviors). For example, one meta-analysis found small to medium effect sizes in the majority of studies investigating individuals who were high in conscientiousness related to physical activity (r^b = -.03 to .42), unhealthy eating (r^b = -.03 to -.37), excessive alcohol use (r^b = -.07 to -.69), and substance use (r^b = -.06 to .60). These highlight the role conscientiousness could play if added to the current models.[26,57]

Clinical Implications

Given the lack of significant findings and the limitation of the study, there is little that can be said about clinical implication from our findings. Since the participants in this sample came from a hard to study sample of young individuals engaged in treatment, our findings suggest that it will be important to do a more comprehensive clinical interview when evaluating this groups ART adherence. Also these results, and current literature, strongly indicate that

healthcare providers in the Southern U.S. may also face more barriers to facilitating health promotion behaviors.

Conclusion

After testing our hypothesized models, it was found that risk behaviors, health promotion behaviors, and depressive symptoms did not appear to be significant predictors of three ART adherence indicators (self-reported VAS, self-reported last missed dosage, and pharmacy pill count) in this sample. Additionally, depressive symptoms did not appear to mediate the relationship between our predictor variables (risk and health promotion behaviors) and the ART adherence indicators. One plausible explanation for these findings is that we were not able to identify or measure sufficient predictors in our model that could have accounted for significant variance in predicting the ART adherence. For instance, in the past researchers have used cognitive processes, social support, and experience of stigma as predictors of ART adherence.[12,41,55] Researchers should further examine a broader range of risk and health promoting behaviors and cognitive processes and how these interact within a decision-making model. In addition, because our sample was predominately gay, MSM, horizonally horizontally-infected youth living in the Southern U.S., perhaps other variables could have been explored within the hypothesized model. For instance, measuring types of stigma (self, perceived, and enacted), disclosure of status to social support (friends, family, and spiritual leaders) could potentially serve as constructs that identify community-defined values and mediate or moderate transactions occurring within models of ART adherence. This would provide us with a developmental and community-specific model and more insight into youth living with HIV and their decision-making regarding ART adherence.

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