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Medication Adherence Mediates the Relationship between Adherence Self-efficacy and Biological Assessments of HIV Health among those with Alcohol Use Disorders

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Abstract

The current study examines the relationship between negative consequences of alcohol use, adherence self-efficacy, medication adherence, and biological markers of HIV health (CD4 count and viral load). A total of 275 HIV-positive men and women with alcohol use disorders were surveyed using Audio-CASI measures and time line followback interviews. Findings from a structural equation model suggest that negative consequences related to alcohol use did not directly impact HIV health. Adherence self-efficacy had direct effects on viral load, but not CD4 count. Mediation analyses indicated that self-reported adherence partially mediated the relationship between adherence self-efficacy and viral load. Cognitive-oriented interventions aimed at facilitating adherence self-efficacy may be effective in improving both medication adherence and HIV health. If facilitating confidence improves HIV health, then health care providers can make a strong impact by spending a few short minutes themselves and/or partnering with behavioral health clinicians using techniques like motivational enhancement.

Keywords

Adherence; Alcohol; Self-efficacy; Viral load; CD4

Introduction

Since highly active anti-retroviral therapy (HAART) was introduced into clinical practice in 1996, people living with HIV have shown dramatic reductions in viral load and have begun to live longer and more productive lives. HAART has been the single most important treatment for people with HIV, but patients must maintain a high rate of adherence—95% or better—in order to optimize their chance at viral suppression, slowing disease progression, and reducing the risk of developing drug resistance (Kitahata et al., 2004; Paterson, 2000; Piacenti, 2006). Unfortunately, poor adherence to medication regimens is pervasive. As many as half of people

taking antiretroviral medication are non-adherent (Ammassari et al., 2001; Bangsberg et al., 2001; Howard et al., 2002; Ickovics et al., 2002). Non-adherence may result in failure to achieve viral suppression, increased HIV replication, and drug resistance (Murphy et al., 2001; Powderly, Landay, & Lederman, 1998; Vittinghoff et al. 1999). Because of the individual and public health implications, an entire body of HIV adherence research has been dedicated to looking at predictors of adherence. Areas heavily studied include social support, side effects of medication, self-efficacy (confidence) for adherence, drug and alcohol use, depression, anxiety, quality of provider-patient relationship, and regimen complexity.

Cognitive processes are believed to guide health behaviors, such as adherence to medication, and have been widely implicated in health behavior research. Aspects of the cognitive process explain health related behavior in the four most common health behavior theories: Health Belief Model (Becker, 1974; Rosenstock, 1974), Theory of Reasoned Action (Ajzen & Fishbein, 1980), Theory of Planned Behavior (Ajzen & Madden, 1986), and the Social Cognitive Theory (Bandura, 1986). While each theory uses its own terminology and constructs, there are core concepts that are, for the most part, common to these health behavior theories. As described by Noar and Zimmerman (2005) these concepts include *attitudinal beliefs* (appraisal of the positive and negative consequences of the behavior and expected outcome), *self-efficacy* (confidence or ability to engage in the health behavior), *normative and norm-related beliefs and activities* (belief that others want you to engage in the behavior and/or belief that others are engaging in the behavior), *risk-related beliefs* (belief that one is at risk if one does not engage in the behavior—explained only as part of the Health Belief Model), and *intention/planning* (intention to perform the behavior/setting of realistic goals to engage in the behavior—a construct in all but the Health Belief Model).

There is evidence that cognitive factors, including self-efficacy, directly impact HIV health. Strengthening perceived self-efficacy in coping with stressors has been shown to improve immune function (Wiedenfeld et al., 1990). The appraisal process is a cognitive response to stress and research has demonstrated that it can have distinctive physiological effects (Tomaka & Blascovich, 1994). Specifically, negative disease-specific (as opposed to dispositional) expectancies have been shown to predict HIV disease course. Negative expectancies predicted decreased survival time in 74 gay men with AIDS (Reed, Kemeny, Taylor, Wang, & Visscher, 1994) and predicted negative immunologic changes when negative disease expectancies were combined with exposure to an AIDS-related death in a sample of 128 men without AIDS (Kemeny, 2003). Less disease-specific factors have also have shown to impact HIV progression. One study found that negative attributions—such as negative beliefs about self, the future, and control—predicted faster CD4 decline (Segerstrom, Taylor, Kemeny, Reed, & Visscher, 1996). Laboratory studies have linked cortisol levels (Leserman et al., 2000) and activation of the sympathetic nervous system (Cole et al., 2001) to HIV progression. There has been an on-going debate about the role of psychosocial factors on disease progression in HIV (Kemeny, 2003), a debate that is grounded in Bandura's notion of self-efficacy and the power of belief in health.

Studies have shown some connections between medication adherence and these cognitive concepts. In our own previous work investigating these cognitive components, we found that adherence self-efficacy predicted adherence behavior over and above any other cognitive processes (Parsons, Rosof, & Mustanski, 2007). Similarly studies have found patients who believe they are able to take their medications (have high adherence self-efficacy) are more likely to be adherent (Ammassari et al., 2002; Ickovics et al., 2002; Molassiotis et al., 2002). Those who believe in the effectiveness of their HAART medication are more likely to adhere (Wagner et al., 2002); whereas nonadherent patients tend to perceive fewer benefits of HAART (Deschamps et al., 2004). Both of these attitudinal factors can promote self-efficacy for adherence. Perhaps one reason cognitive factors play a central role in the HIV medication

adherence literature is that interventions targeting attitudes and self-efficacy through increasing motivation and goal setting offer a real solution to improving adherence.

Yet interventions targeting cognitions and adherence alone may not be sufficient to address other behavioral factors, such as alcohol use, which may negatively impact both cognitive function as well as adherence. This is important given that alcohol consumption is common among people infected with HIV, with rates of heavy and problem drinking ranging from 8 to 41% (Cook et al., 2001; Lefevre et al., 1995). In a study of 267 people with a history of alcohol problems who were taking HAART, alcohol consumption was the most significant predictor of adherence (Samet, Horton, Meli, Freedberg, & Palepu, 2004). Samet and his colleagues also found that better adherence was associated with recent abstinence from alcohol compared with moderate and at-risk level of alcohol use. In another study, after adjusting for potentially confounding clinical and demographic factors, alcohol use was independently associated with poor adherence (Golin et al., 2002). However, the nature of the relationship between alcohol use and adherence is poorly understood and has not been studied in relation to the cognitive aspects of adherence behavior.

Impairment due to alcohol use has an immediate effect on cognitive functioning that may impede self-efficacy for adherence and adherence behaviors. For example, HIV-positive men and women have been shown to feel less confident in taking their HIV medications as prescribed when drinking because of concerns regarding potential negative interactions between the medication and the alcohol (Rosof, Punzalan, & Parsons, 2004). However, findings are mixed when it comes to the assertion that alcohol use proximally influences other HIV-related health behaviors such as condom use (Weinhardt & Carey, 2000). A recent study examining the distal role of alcohol use on intentions and attitudes of condom use found no such relationship (Bryan, Rocheleau, Robbins, & Hutchison, 2005). Unfortunately, no such studies have been published for HIV medication adherence and the underlying agent connecting cognitive correlates of medication and alcohol use remains unclear.

Apart from its role in adherence, both alcohol use and adherence self-efficacy have been shown to impact biological measures of HIV health (viral load and CD4 counts). Alcohol consumption has also been shown to have direct effects on HIV disease progression. In two laboratory-based studies, alcohol use was associated with greater HIV viral replication in cell cultures (Bagasra, Kajdacsy-Balla, Lischner, & Pomerantz, 1993; Bagby et al., 2003). More recent studies have shown heavy alcohol consumption to be associated with higher levels of HIV viral load and lower CD4 counts (Miguez, Posner, Morales, Rodriguez, & Burbano, 2003; Samet, Horton, Traphagen, Lyon, & Freedberg, 2003).

In the present study, we explore the relationship between alcohol use and adherence self-efficacy on the two primary virologic and immunologic markers of HIV progression—viral load and CD4 count. Our previous work has shown that of all the cognitive processes identified across health behavior theories, only adherence self-efficacy was a significant predictor of medication adherence (Parsons et al., 2007). It was hypothesized that negative consequences associated with alcohol use and adherence self-efficacy would have significant effects on these biological markers, and that these effects would be mediated by self-reported HIV medication adherence.

Methods

Participants

Participants were 275 HIV-positive men and women who were currently taking HAART, reported alcohol use disorders, and agreed to be part of Project PLUS, a randomized clinical trial comparing Motivational Interviewing (MI) and Cognitive Behavioral Therapy (CBT) to

didactic health education for increasing medication adherence and reducing alcohol use. Two recruitment methods were used: (1) interested participants contacted the project in response to flyers placed in AIDS service organizations, HIV clinic waiting rooms, community-based organizations, and other venues, and were then screened by telephone ($n = 179$, 65.8%) and (2) interested participants completed an on-site screener during HIV-related community events ($n = 93$, 34.2%). Inclusion criteria were: age greater than 18 years, a score of eight or above on the Alcohol Use Disorder Identification Test (AUDIT), and currently on a HAART regimen. A score of eight on the AUDIT suggests problem-level drinking (Maisto, Carey, Carey, Gordon, & Gleason, 2000). People with significant drug problems other than alcohol, and those with active psychosis were excluded.

A total number of 1,285 participants phoned the project line for screening. Of these, 898 were excluded because they failed to meet eligibility criteria at the time of phone screening or upon secondary screening during the initial visit. The most common reasons for ineligibility were greater problems associated with other drug use compared to alcohol ($n = 564$), score of less than eight on the AUDIT ($n = 308$), and no alcohol use in the past 30 days ($n = 61$). A total of 105 failed to show for their first appointment, resulting in 282 eligible participants. However, seven of these had incomplete baseline data, so the final sample for analysis was 275.

The sample was predominantly male (76.7%, $n = 211$) and was ethnically diverse with 55.6% ($n = 153$) of the sample identifying as African American and 23.7% ($n = 65$) as Latino/a. Over half the sample (59.3%, $n = 163$) identified as gay or bisexual. Mean age was 43.7 (SD = 7.25) and ranged from 26 to 66. Over half the sample (57.1%, $n = 157$) had never been treated for alcohol use. Mean number of HAART medications taken was 2.85 (SD = 1.16) and the sample had been taking HIV medications for an average of 7.54 (SD = 6.51) years. Based on HIV PCR analyses done at the baseline assessment and transformation into log₁₀, the mean log₁₀ HIV viral load was detected at an average of 3.28 copies/ml (SD = 1.48). The logarithmic transformation of the absolute number of copies has become the preferred unit of measurement for viral load. Mean CD4 counts were 421.44 (SD = 298.12).

Measures

Demographics—Participants were asked a series of demographic questions including age, gender, ethnicity, relationship status, sexual identity and employment status.

Confidence for Adherence—This measure consists of 11-items that were specifically developed for HIV medication adherence self-efficacy based on Bandura's (1986) theory of self-efficacy and pilot work with HIV-positive adults (Parsons, Rosof, Punzalan, & DiMaria, 2005). The measure asks participants to rate on a five-point scale how confident they are that they could take their HIV medications on time under several circumstances (e.g. on vacation; out at night). The final scale consisted of one factor accounting for 46% of the variance with $\alpha = 0.91$.

Alcohol Related Problems—The Alcohol Use Disorder Identification Test (AUDIT), a 10-item survey, measures alcohol consumption, dependence symptoms, and personal and social harm reflective of drinking over the past 30 days. It was administered during the screening to determine eligibility. The AUDIT has demonstrated good content, criterion, and construct validity (NIAAA, 1995) and reliability (alphas from .77 to .83) (Bohn et al., 1995). Total current alcohol consumption was assessed using a timeline follow-back (Allen & Litten, 1992; Sobell & Sobell, 1992) during which an assessor asked participants to reflect back on the past thirty days, mark memorable events on the calendar as anchor points and then recall day by day number of standard drinks consumed. This calendar technique has been used to improve reliability and validity (Weinhardt et al., 1998). For purposes of our model, the Drinker

Inventory of Negative Consequences (DrinC) was used to assess negative consequences of drinking for the past 90 days. Because the sample was comprised of those meeting criteria for alcohol use disorders, it was believed that negative consequences associated with drinking would provide a more comprehensive picture of alcohol use problems than would amount of alcohol consumption. The DrinC has demonstrated excellent psychometric properties in previous work (Miller, Tonigan, & Longabaugh, 1995; Parsons et al., 2007).

Medication Adherence—Self-reported HAART adherence was assessed using a timeline follow-back (Sobell & Sobell, 1992) during which an interviewer asked participants to reflect back on the past fourteen days, mark memorable events on the calendar as anchor points and then recall day by day all missed HAART medication doses. Fourteen days was used to capture two weeks of both weekday and weekend activity so as to capture consistent and inconsistent patterns that may be missed with a one week or three day measure, which is often used (Simoni et al., 2006).

Biological assessments of HIV health—Viral load and CD4 counts were obtained through an onsite blood draw by a certified phlebotomist. CD4 levels were reported as the absolute number of CD4 T-lymphocytes per cubic millimeter. HIV selectively infects CD4 T-cells killing these cells. Viral load is a measure of HIV RNA in peripheral blood. Viral load numbers can reach into the millions, so to adjust for skew, viral load was log transformed.

Procedure

All participants underwent a baseline interview intended to examine socio-demographic and biopsychosocial variables such as mental health, adherence related social support and social norms, decision making processes regarding adherence and alcohol use, regimen characteristics, motivation to change current behavior, viral load and CD4 counts. The findings reported in this article represent data from the baseline interviews. All participants reviewed and signed a written informed consent before participating in the study. The majority of the assessment was completed on a computer assisted survey interview (ACASI) in which the participant responded to automated questions on a computer screen that they could either read or listen to with headphones. ACASI has been found to be an effective interview method for people of diverse educational backgrounds by providing audio assistance, thereby eliminating the effects that reading ability has on internal validity (Gribble, Miller, Rogers, & Turner, 1999). Recent studies have shown that ACASI increases the proportion of individuals truthfully endorsing drug use (Tourangeau & Smith, 1996) because ACASI allows greater respondent privacy and removes barriers to honest responding, such as embarrassment, feedback from facial expressions of the interviewer, and other social influences (Gribble et al., 1999). The interview lasted about 3 hours and subjects were paid \$30.

Analytic Strategy

Following recommendations by Bryan, Schmiede, and Broaddus (2007) we conducted mediation analysis using path analytic models in a structural equation modeling (SEM) framework. Data management and descriptive statistics were performed with SPSS 12.0. Data preparation and screening was conducted in Prelis and the SEM was conducted with Lisrel 8.54. Model fit was assessed using a variety of fit indices recommended by Kline (2005), including: the Root Mean Square Error of Approximation (RMSEA; Browne & Cudeck, 1993), which should be less than .05 for close fit, less than .08 for reasonable fit, and have the lower bound of the 90% confidence interval less than .05; The Standardized Root Mean Square Residual (SRMR), which should be less than .10 for favorable fit (Kline, 2005); The Comparative Fit Index, which should be greater than .90 (Hu & Bentler, 1999). Nested sub-models are compared using a likelihood ratio chi-square test—a significant change in chi-

square, based on the difference of the degrees of freedom between the nested models, indicates that the model with the fewer degrees of freedom should be adopted.

Path analysis was used to test for mediation by Medication Adherence of the effect of the cognitive (adherence self-efficacy) and alcohol (the DrinC) variables on the biological HIV health outcomes (CD4 and Viral Load). Following recommendations by MacKinnon, Fairchild, and Fritz (2007), we tested the significance of mediation effects based on distribution of the products confidence limits. The PRODCLIN program (MacKinnon et al., in press) was used to find critical values of the distribution of the products and to compute confidence limits. If the 95% confidence intervals of the product do not include zero, then the mediation effect is considered significant at $P < .05$. Complete versus partial mediation was explored, when mediation was found to be significant, by dropping the direct effect of the predictor from the model and using a chi-square difference test to determine if there was a significant decrease in model fit. A significant decrease is consistent with complete mediation.

Results

Descriptive Statistics

The sample reported consuming an average of 84.9 standard drinks over the thirty days prior to the baseline interview and on the AUDIT scored significantly higher ($M = 18.58$) than the established cutoff of 8 which is suggestive of problem drinking. Mean self-reported adherence of the sample was 84.4%, which is below the recommended 95% required for optimal viral suppression. Mean CD4 and viral load (log transformed) was 421.4 and 3.3, respectively. Healthy adults usually have a CD4 count of at least 800 cells per cubic millimeter of blood. Correlations between the scores on the DrinC and medication adherence and adherence self-efficacy were significant, although correlations with HIV biological outcomes were nonsignificant (See Table 1). Adherence self-efficacy showed significant correlations with medication adherence and both HIV biological outcomes. Medication adherence was significantly correlated with viral load, but not with CD4 count.

Structural Equation Model

Mardia statistics revealed significant departures from univariate normality for each of the variables included in the model. Accordingly, ML estimation was used to compute the Satorra-Bentler chi-square, which is the most preferred method for adjusting goodness-of-fit and standard error statistics for inflation due to non-normality (Kline, 2005).

The initial model fit to the data was saturated, and contained paths from the two exogenous variables (DrinC and Adherence Self-Efficacy) to Medication Adherence and to the HIV biological outcomes (CD4 and Viral Load), as well as paths from Medication Adherence to the HIV biological outcomes. The paths from scores on the DrinC to Medication Adherence and HIV biological outcomes were not significant, so they were subsequently dropped from the model. Table 2 indicates that dropping these paths from the model did not significantly decrease model fit, based on a chi-square difference test ($P = .47$).

To test for mediation of the association between Adherence Self-Efficacy and Viral Load through Medication Adherence, the PRODCLIN program (Mackinnon et al., 2007) was used to find critical values of the distribution of the products and to compute confidence limits. The 95% confidence interval was $-.009$ to $-.001$; that it did not include zero indicates significant mediation. To test for partial versus complete mediation, the direct path from Adherence Self-Efficacy to Viral Load was dropped from the model. As shown in Table 2, this resulted in a significant degradation of model fit ($P < .01$) and indicated that the mediation was partial. The confidence interval of the product term testing the significance of mediation of the association

between Adherence Self-Efficacy and CD4 count through Medication Adherence was $-.020$ to $.002$, which was not significant. Table 2 contains the fit statistics for a model that did not contain a significant direct path from Adherence Self-Efficacy to CD4 count. While the parameter estimates for the paths leading to CD4 count were non-significant based on t -tests ($t = 1.55$ for confidence; $t = 1.51$ for adherence), dropping either of these paths resulted in a significant degradation of model fit, so they were retained in the final model (see Figure 1). The final model explained 10% of the variance in medication adherence, 6.5% of Viral Load, and 1.8% of CD4. To assure that the limited effects on CD4 were not due to a suppression effect resulting from the correlation with Viral Load, we re-estimated the final model without Viral Load. The parameter estimates in this model were identical to those reported in Fig. 1. Differences in these parameter estimates would have been suggestive of a suppression effect.

Discussion

We set out to test a structural equation model of the relationship between alcohol (specifically, negative consequences associated with alcohol use) and a cognitive process (self-efficacy for medication adherence), on biological aspects of HIV Health (assessed via viral load and CD4 counts) through the mediating effects of self-reported HAART medication adherence. The model fit to the data showed that adherence self-efficacy predicted viral load, while alcohol did not. Further analysis found that self-efficacy had direct effects on viral load, but not CD4 counts. We next sought to determine whether the relationship between self-efficacy and viral load was mediated by adherence to medication and found that adherence significantly, but only partially, mediated the relationship. In other words, self-efficacy for adherence to HIV medications had a direct effect on viral load that was not explained by self-reported medication adherence. However, we found that adherence did not mediate the relationship between self-efficacy and CD4 counts, which was explained by the fact that none of the paths to CD4 counts were significant.

The construct of self-efficacy, or confidence, hinges on a belief in oneself, a self-belief that one can accomplish even the most difficult tasks of tasks, such as taking the often complex regimens of HAART. Bandura (1994) speaks directly to this in terms of suggesting that high levels of self-efficacy enhance well being in several ways. Health benefits appear to come from adopting an attitude of “I can do it,” or in this case, “I can take my HIV medications consistently.” The health specific self-efficacy literature would view these findings as additional evidence that positive thinking can improve health. Even though several studies have previously pointed to the beneficial effects of self-efficacy and positive health expectancies on health, most of these studies have used HIV immunologic outcomes, and not virologic ones (Kemeny, 2003; Segerstrom et al., 1996; Wiedenfeld et al., 1990). This study demonstrates the connection between self-efficacy and viral load, such that confidence about one's ability to adhere to their HIV medications may have an effect on limiting viral reproduction.

Given the previous research on self-efficacy and immunologic outcomes, it is not clear why adherence self-efficacy did not directly impact CD4 count in the way it affects viral load in our sample. CD4 counts are indicative of immunologic health, while viral load is indicative of virologic health. In our model, adherence self-efficacy had a direct effect on virologic, but not on immunologic, functioning. This was not expected because CD4 and viral load are both markers of HIV health and in our analyses show a moderate correlation. However, one recent paper suggests that CD4 counts are not as effective as viral load in determining treatment failure among HIV-positive persons on HAART (Chaiwarith et al., in press).

Several limitations should be considered when interpreting this data. First, the sample was comprised entirely of HIV-positive men and women with alcohol problems and those taking

HAART. Those without alcohol use problems, those who reported greater problems associated with drugs other than alcohol, those not currently on HAART, and those with severe psychiatric histories were excluded, so results may not generalize to HIV-positive individuals in general. Second, self-efficacy was measured as directly related to adherence and not as a general measure of self-efficacy or decision-making regarding one's health. There is an assumption that it is a proxy measure of confident health attitudes, which may or may not be the case. The limited range of alcohol use, due to the skewed rates of problems found in the sample, may have restricted our findings for the alcohol factor and could explain why negative consequences associated with alcohol use failed to predict medication adherence or HIV health outcomes.

The findings described here reveal that factors other than adherence to medication can predict variability in HIV health. It adds to a growing body of evidence that cognitive factors, particularly self-efficacy, impact biological processes associated with physical health. Thus, future interventions should include enhancing self-efficacy and strengthening beliefs in the benefits of taking medication and maintaining good health. Clearly, cognitive interventions, which emphasize boosting confidence in one's ability to take medication and confidence in the effects of medication, are implicated. Motivational therapies can address self-efficacy directly by simply asking patients about their level of confidence. Health care providers could engage their patients in a brief conversation about confidence to adhere to their HAART medications that could be highly motivational and lead to higher confidence levels. Similarly, providers could partner with behavioral health clinicians to deliver adherence interventions that include motivational components. Our findings suggest that these approaches could positively impact health, and a recent pilot test of an intervention using Motivational Interviewing, coupled with cognitive skills building, to promote adherence and reduce substance abuse among those living with HIV provides further support for this (Parsons et al., 2005). Health professionals should use motivational techniques to also explore ambivalence about medication taking and attempt to assist the patient in resolving this ambivalence. Additionally, cognitive behavioral therapy could offer a way to improve self-efficacy by setting goals that are accomplishable and challenging thinking that interferes with confidence. Given that there is yet to be a cure for those with HIV, any findings that suggest ways to limit HIV progression and maintain higher levels of immune functioning are useful and encouraging.

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Fig. 1. Path analysis testing mediation effects of Adherence Self-Efficacy on HIV Health (CD4 counts and Viral Load) through Medication Adherence. * indicates $P < .05$, two tailed

Table 1

Zero order correlations and descriptive statistics

	1	2	3	4	5
1. DrinC	1.00				
2. Adherence Self-efficacy	-.21*	1.00			
3. CD4	.03	.12*	1.00		
4. Log viral load	.07	-.25*	-.41*	1.00	
5. Medication adherence	-.18*	.30*	.11	-.18*	1.00
Mean	34.98	33.88	421.44	3.28	84.38
SD	24.20	11.73	298.12	1.49	23.07

Note: * $P < .05$

Table 2

Fit of path models testing mediation effects

Model	Model Fit			Model Comparison							
	χ^2	df	p	RMSEA	95% CIRMSEA	SRMR	CFI	Comparison	$\Delta\chi^2$	Δdf	p
1. Saturated model	0.00	0	1.00								
2. Drop paths from DrinC	2.55	3	.47	.00	.00--.10	.03	.98	1 vs 2	2.55	3	.47
3. Drop adherence self-efficacy to CD4 counts	6.84	4	.15	.05	.00--.11	.04	.97	2 vs 3	4.29	1	.04
4. Drop adherence self-efficacy to viral load	15.70	4	.04	.10	.05--.16	.06	.88	2 vs 4	13.15	1	<.01