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Predictive Utility of Brief AUDIT for HIV Antiretroviral Medication Nonadherence

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Abstract

Alcohol use negatively affects adherence to antiretroviral therapy (ART), thus HIV/AIDS providers need accurate, efficient assessments of alcohol use. Using existing data from an efficacy trial of two cognitive-behavioral ART adherence interventions, we sought to determine if results on two common alcohol screening tests (Alcohol Use Disorders Identification Test—Consumption (AUDIT-C) and its binge-related question (AUDIT-3)) predict ART nonadherence. Twenty seven percent of the sample (n=308) were positive on the AUDIT-C and 34% were positive on the AUDIT-3. In multivariate analyses, AUDIT-C positive status predicted ART nonadherence after controlling for race, age, conscientiousness, and self-efficacy (p=.036). While AUDIT-3 positive status was associated with ART nonadherence in unadjusted analyses, this relationship was not maintained in the final multivariate model. The AUDIT-C shows potential as an indirect screening tool for both at-risk drinking and ART nonadherence, underscoring the relationship between alcohol and chronic disease management.

Keywords

Patient adherence; Alcohol consumption; Mass screening; HIV Infection; Acquired Immunodeficiency Syndrome

INTRODUCTION

Accurate, efficient assessment of alcohol risk behavior is an important issue for HIV/AIDS care providers, particularly for individualized antiretroviral therapy (ART) adherence counseling (1,2). One alcohol screening instrument with the advantages of brevity and sensitivity is the three-item Alcohol Use Disorders Identification Test—Consumption (AUDIT-C) (3), an abbreviated version of the ten-item AUDIT (4). The AUDIT-C assesses frequency of drinking, number of drinks per drinking occasion, and frequency of binge

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drinking (≥ 6 drinks/occasion) over the past year. The third question, on binge drinking, has also generated interest as a single-item alcohol screening question termed the AUDIT-3 (5). Binge questions similar to the AUDIT-3 have been recently investigated as useful screening tests for at-risk alcohol consumption (6,7), and the AUDIT-C has been adopted as a standard questionnaire for screening of alcohol assessment in primary care settings in large health care systems, including the Veterans Health Administration.

Recent studies have detected significant relationships between positive AUDIT-C or full AUDIT scores with several medical outcomes, including risk of hospitalizations for gastrointestinal conditions (8), post-surgical complications (9), as well as general health status and mortality (10–12). Despite these relationships, little investigation has occurred on AUDIT-C screening status and its prediction of health outcomes more immediately relevant to the context of chronic disease management. Two groups of investigators have reported relationships between AUDIT-C or full AUDIT scores and medication adherence, i.e., adherence to statin, antihypertensive, and ART medications (1,13). However, despite having large samples and/or comprehensive analyses, neither study used electronic event monitoring (EEM), the “gold standard” for medication adherence measurement (14).

In the context of a regular alcohol screening program, increased attention to the intersection of alcohol use and chronic medical illness would remind clinicians to be alert to the greater risk of suboptimal adherence, particularly for those who *screen* positive for at-risk drinking yet are not *diagnosed* with at-risk drinking behavior. At the same time, alcohol use must be considered in light of the numerous other individual factors long associated with ART adherence to varying degrees, for example, self-efficacy for medication adherence (15,16); depressive symptoms (15,17); social support (15,16); and personality characteristics (18). The aim of this study was to determine if positive screening results on the AUDIT-C and/or AUDIT-3 provide additional prediction of ART adherence based on electronic event monitoring (EEM), after controlling for selected sociodemographic and psychosocial variables commonly associated with ART adherence and possibly with positive AUDIT-C and/or AUDIT-3 status.

METHODS

Design and Procedure

This study is a secondary analysis of baseline data of 308 subjects from Phase II of a randomized clinical trial (the “parent study” [PS]), which tested the efficacy of two cognitive-behavioral ART adherence interventions over 18 months and examined the impact of adherence on clinical outcomes and quality of life. Phase II of the study (2003–2008) mirrored Phase I (1998–2002), previously described (19).

Parent study participants were required to be ≥ 18 years old, on combination HIV therapy, administering their own medications, English-speaking, free from significant cognitive impairment, and community-dwelling with telephone access. Participants were recruited from multiple sites (a university-based clinic, community hospitals, and comprehensive care centers) in western Pennsylvania and eastern Ohio. Individuals were excluded from participation if they were living with another individual already enrolled in the study, had upper extremity or visual impairments which precluded self-administration of medication, or had hearing difficulties without adaptive telephone equipment for possible delivery of the telephone intervention.

In summary, after obtaining informed consent, subjects in the PS were randomized to usual care, a structured adherence intervention, or an individualized adherence intervention. Baseline adherence was determined from data gathered during the last two weeks of the one-

month induction phase, during which participants used an electronic event monitor (EEM) (MEMS 6 TrackCap, AARDEX, Ltd.) attached to the ART medication bottle. EEM uses a special medication container cap which electronically records and stores each time the cap on the medication bottle is opened. Data from the cap are then downloaded for analysis. The PS and the current study's secondary data analysis were approved by the University of Pittsburgh Institutional Review Board.

Variables and Measures

Adherence—For the current study, the outcome variable was adherence for the monitored drug, which we defined as the percentage of prescribed medication administrations taken during the two-week period at the end of the one-month study induction phase. Adherence was calculated by dividing the number of doses taken by the number of doses prescribed, multiplied by 100.

Alcohol screening status—The primary independent variable, alcohol screening status, had two dimensions based on responses to the AUDIT-C. The PS used the full AUDIT to assess alcohol use; PS participants completed the AUDIT independently. AUDIT-C items were extracted from these data (Cronbach's $\alpha = .838$). Based on a five-point Likert-scale, a range of 0–4 points is possible for each item; total scores are calculated by summing the three items and thus range from 0–12 (3).

We defined AUDIT-C positive as a positive screen for at-risk alcohol drinking if the total AUDIT-C score for men was ≥ 4 or for women, ≥ 3 for women (20). We defined AUDIT-3 positive as any positive response to binge drinking; scores from 1 (less than monthly) to 4 (daily or almost daily) were considered an AUDIT-3 positive screen for at-risk alcohol drinking (5,21). The overall item-total correlation for the AUDIT-3 and the total AUDIT-C score was .788.

Additional independent variables—Sociodemographic data and disease- and regimen-related data (e.g., CD4 count, viral load, medication dosing) were collected during baseline assessments and medical record reviews. Several psychosocial variables previously demonstrated to be related to adherence were also assessed. Current drug use was assessed through questions related to the frequency of use for tobacco and various illicit substances (marijuana/hashish, cocaine, crack, heroin, “ecstasy,” “poppers,” stimulants, opioids, hallucinogens, inhalants) which were added to the full AUDIT by the PS. For the current analysis, responses to the drug use items were dichotomized as “use”/“no use” for each drug. Self-efficacy for ART medication-taking was assessed using the 26-item HIV Self-Efficacy Scale (SES) (22). Subjects rated their confidence from one (not at all confident) to ten (totally confident) in their ability to follow the overall medication regimen and to take their monitored medication as prescribed in a variety of settings (Cronbach's $\alpha = .946$). Higher scores reflect greater self-efficacy. Depressive symptoms were measured with the Beck Depression Inventory II (BDI-II) (Cronbach's $\alpha = .940$) (23). Personality characteristics were measured using the NEO Five-Factor Inventory (NEO-FFI), consisting of five 12-item scales measuring Neuroticism (Cronbach's $\alpha = .854$); Extroversion (Cronbach's $\alpha = .796$); Openness (Cronbach's $\alpha = .629$); Agreeableness (Cronbach's $\alpha = .657$); and Conscientiousness (Cronbach's $\alpha = .831$) (24). Social support was measured with the 40-item Interpersonal Support Evaluation List (ISEL), which assesses four dimensions of perceived social support (25). For this study, only the total ISEL score was used (Cronbach's $\alpha = .951$).

Analytic Sample

Individuals removed from medications during the induction phase ($n=6$) and those who did not return the EEM cap ($n=2$) were omitted from the current analysis due to lack of adequate

adherence data. PS participants with missing (n=6) or invalid (n=18) data on the AUDIT-C items at baseline were also removed from the analytic sample. The final sample included 308 individuals.

Statistical Analyses

All data analysis was performed in SPSS. Descriptive statistics were used to characterize the sample. In order to reduce the influence of extreme univariate outliers, the three lowest scores for the HIV Self-efficacy Scale total score (scores of 31, 44, and 54) were increased via score alteration, to 90, 91, and 92, respectively, just slightly lower than the next-lowest score of 93. A reflected square root transformation was applied to the adherence data.

Bivariate analyses were performed to identify possible confounders and covariates; the nonparametric Mann Whitney U test was used to assess associations between continuous variables and each of the two binary alcohol screening status measures. Additionally, Chi-square tests of independence, Fisher's exact test, and Spearman's rank-order correlation coefficient were used to assess relationships between the binary alcohol screening statuses and categorical variables. Across analyses, p-values <.05 were considered statistically significant.

A series of sequential multiple linear regression analyses were performed to determine if a positive AUDIT-C or a positive AUDIT-3 screening test result improved the prediction of adherence after controlling for various sociodemographic and psychosocial variables. Separate regression analyses were performed by group (AUDIT-C positive/negative, AUDIT-3 positive/negative), controlling for potentially confounding variables and covariates.

Potential confounding variables were required to demonstrate a relationship in bivariate analysis at $p \leq .10$ with both AUDIT-C status and adherence, or with both AUDIT-3 status and adherence. The following variables entered one or both sets of the original regression models as potential *confounders*: crack use/nonuse; marijuana use/nonuse; agreeableness score (NEO-FFI); conscientiousness score (NEO-FFI); and self-efficacy (HIV Self-Efficacy Scale total score). Variables were considered potential *covariates* if, in bivariate analysis, they demonstrated a significant or trend ($\leq .10$) relationship with adherence only. The following variables entered one or both of the initial regression models as potential covariates in a single block which included any significant confounding variables from the previous analyses: age, race (white= 0, non-white = 1), and health insurance status (uninsured = 0, insured =1). Although viral load and CD4 count demonstrated significant relationships with adherence, they were not included as potential covariates in the regression models insofar as they are most commonly considered *outcomes* of adherence.

Potential confounding variables and covariates identified via bivariate analyses were then entered as a single block into a backward regression model using a p-value of .10 for exclusion; variables that were significant at this step were retained in the first block, and AUDIT-C or AUDIT-3 status was entered as the second block. P-values <.05 were considered statistically significant. All models were estimated hierarchically yielding incremental R-squared and F-test statistics as well as adjusted R-squared values and adjusted, unstandardized regression coefficients with 95% confidence intervals, and partial F-test statistics. Model assessment included multicollinearity, residual, influential case and sensitivity analyses.

RESULTS

Sample Characteristics and Univariate Analysis

Sample characteristics are presented by AUDIT-C status in Table 1. The total sample was approximately two-thirds male, over half self-identified as non-white ethnicity, and the median age was 44 years. Mean AUDIT-C score was 2.15 ($SD=2.59$); 26.9% ($n=83$) and 34.1% ($n=105$) of the total sample were classified as AUDIT-C positive and AUDIT-3 positive, respectively. Compared to AUDIT-C negative participants, AUDIT-C positive individuals had significantly fewer years of formal education and were significantly more likely to have health insurance. Adherence and psychosocial characteristics are presented in Table 2.

Compared to AUDIT-C negative participants, AUDIT-C positive individuals were also significantly more likely to use drugs overall and to use marijuana, crack, cocaine, “poppers,” and tobacco; had significantly more depressive symptoms; had significantly higher neuroticism scores and lower agreeableness and conscientiousness scores; and had significantly less social support. AUDIT-C positive individuals had significantly lower adherence than AUDIT-C negative individuals (78% versus 89%, Mann-Whitney $U=7292.5$, $p=.003$).

By AUDIT-3 status, groups were significantly different in essentially parallel fashion (data not shown); however, AUDIT-3 positive individuals were significantly more likely to be men, and slightly more likely to be insured. AUDIT-3 positive individuals had significantly lower adherence than AUDIT-3 negative individuals (71% versus 79%), Mann-Whitney $U=8825.5$, $p=.013$). Additionally, in contrast to AUDIT-C status, only marginally significant differences emerged for stimulant use and depressive symptoms ($.05 \leq p < .10$), while differences in opioid use were nonsignificant ($p > .10$).

Multivariate Analysis

In the final multivariate regression model controlling for race, age, conscientiousness, and self-efficacy (Table 3), positive AUDIT-C status significantly added to the prediction of ART nonadherence ($p=.036$). The overall regression equation with confounding variables and covariates was statistically significant, $F(5, 299) = 8.708$, $p=.000$, and accounted for 12.7% of the variance in ART nonadherence. In the first block, non-white race, younger age, lower conscientiousness scores, and lower self-efficacy remained significant independent predictors of nonadherence. As the second block, AUDIT-C status increased the model R^2 by approximately 1%. In contrast, in the final multivariate model controlling for race, conscientiousness, and self-efficacy, positive AUDIT-3 status did not add to the prediction of ART nonadherence ($p=.203$). However, non-white race, lower conscientiousness, and lower self-efficacy remained significant independent predictors of ART nonadherence.

Post Hoc Analyses

We anticipated that a different cut point for AUDIT-3 positive/negative categorization might yield greater sensitivity for the detection of an effect on adherence. When repeating the aforementioned regression analysis with AUDIT-3 positive status defined as only those individuals binge drinking “weekly” or “daily or almost daily,” the additional prediction of nonadherence by AUDIT-3 status approached significance ($p=.072$), however, using this more stringent categorization, only 18 individuals were represented as AUDIT-3 positive.

Because “over-adherence” could arguably be considered a form of nonadherence, we conducted post hoc analyses on the 89 individuals who had $>100\%$ adherence as detected by EEM (28.8% of the sample). Over-adherence was treated as a dichotomous variable and we

conducted Mann Whitney U tests and chi square tests of independence to assess potential differences between over-adherers and those with <100% adherence. Compared to individuals with <100% adherence, over-adherers were significantly less likely to be AUDIT-C positive ($p=.024$) and somewhat less likely to be AUDIT-3 positive ($p=.054$). Additionally, over-adherers had significantly greater conscientiousness ($p=.005$), agreeableness ($p=.002$) and self-efficacy scores ($p<.001$); had significantly higher CD4 counts ($p=.023$) and were more likely to have undetectable viral load ($p=.003$) than individuals with <100% adherence. Finally, over-adherers were significantly more likely to be white ($p=.041$), and significantly less likely to use opioids ($p=.042$) than individuals with <100% adherence.

DISCUSSION

Primary care and HIV care providers are encouraged to screen patients for hazardous alcohol use and adherence on an ongoing basis. The validity, predictive ability, and brevity of the AUDIT-C and AUDIT-3 make them particularly appealing for use in clinical care settings (3,21). This study used AUDIT-C data to categorize alcohol consumption for the prediction of ART nonadherence. We found that AUDIT-C positive status significantly predicted ART nonadherence after controlling for the effects of race, age, and conscientiousness. Additionally, while AUDIT-3 positive status was associated with ART nonadherence in unadjusted analyses, this relationship was not maintained in the final multivariate model.

To our knowledge, this study is the first to consider the ability of positive AUDIT-C and AUDIT-3 screening results to predict medication adherence as measured by EEM. In doing so, our results reflect the “gold standard” for adherence measurement (14) while demonstrating results relatively similar to those of previous investigators who measured medication adherence with pharmacy (13) or self-report data (1). These results also add to the growing body of work exploring the clinical utility of alcohol screening results outside of their initially intended function (8–13). Additionally, these findings reflect a baseline, one-month “snapshot” of adherence *prior to* the parent study’s comprehensive 12-week adherence intervention. While medication adherence over the long term is of greatest importance in the management of HIV/AIDS, other studies have demonstrated the predictive ability of AUDIT-C scores up to one-year prior to the outcome of study (9). This suggests that similarly, AUDIT-C positive status may also predict nonadherence over time, particularly in the absence of other adherence-enhancement interventions.

Alcohol use is generally associated with decreased ART adherence and a dose-response effect appears to exist where greater alcohol consumption is associated with greater likelihood of taking medications off-schedule or missing medication doses/days (26–28). The exact mechanisms through which this nonadherence occurs are unspecified but presumably involve the interplay of numerous interrelated factors in addition to alcohol and medication-taking. Low conscientiousness has previously been associated with alcohol abuse/dependence (29) and with slower HIV disease progression at one year (30) and at four years (31). Importantly, neither adherence nor depression has significantly mediated this latter relationship (30), but the possibility remains that conscientiousness exerts its influence on HIV/AIDS disease progression through other mediational pathways which incorporate these variables, including alcohol use (30,31). Our findings further substantiate the need for mediational analyses to explore the specific mechanisms through which adherence, alcohol use, psychosocial, and disease-related factors exert their influence on one another.

The lesser ability of the AUDIT-3 to provide additional prediction of adherence was somewhat surprising given its embeddedness within the AUDIT-C. As reflected in our post

hoc analyses, narrowing the responses constituting an AUDIT-3 positive categorization suggested a trend toward additional prediction of adherence by AUDIT-3 status; however, the few number of individuals meeting this criterion suggests that additional analysis is required in the future with larger samples of frequent binge drinkers. Proponents of single question alcohol screening have noted improvements in sensitivity for the detection of hazardous drinking and/or alcohol use disorders when such questions are modified to inquire about ≥ 5 drinks per occasion for men and ≥ 4 drinks for women (3).

The clinical outcomes, substance use, and psychosocial profile of over-adherent individuals parallel those of the overall model predicting adherence. We thus included them in the analysis without recalculating their adherence score based on an absolute deviation from 100%. The fact that these individuals possessed high conscientiousness, agreeableness, and self-efficacy, as well as positive clinical indicators of disease, suggests that the additional EEM cap openings may reflect behavior such as extra pill counting or checking to see if doses were taken.

The results of this study require consideration of several limitations. The amount of variability in alcohol use was relatively low. Additionally, effect sizes were small, reflecting that alcohol screening status explained only an additional 1% of the variance in nonadherence after controlling for confounders and covariates. The corresponding clinical significance varies according to the medication regimen considered. AUDIT-C and AUDIT-3 responses were extracted from responses to the full AUDIT, and may have been different were these items administered independently. Additionally, generalizability of the findings is potentially limited by the sample's relatively high mean rates of adherence at baseline (76.32 ± 29.52), however, similar rates of mean dose adherence (70–80%) have been reported in other ART adherence studies using EEM (32–34). The general rate of any alcohol consumption (62%) appears to be higher than rates of alcohol use among persons with HIV/AIDS (40–55%) previously reported (1,27,28,35). Placing the rates of AUDIT-C positive (26.9%) and AUDIT-3 positive (34.1%) screens in the context of previous research is considerably more challenging due to wide variation in definition and determination of alcohol use patterns (17). Published rates of hazardous use and/or binge use generally range from 10–30% (1,2,27).

CONCLUSION

Within the context of a systematic alcohol screening program, positive screens on the AUDIT-C can potentially serve as a legitimate cue to action for primary care and HIV care providers to inquire further not only about alcohol use, but about possible adherence challenges as well. Providers could also utilize this information in the context of brief interventions for hazardous drinking in order to provide risk feedback to patients, emphasizing the links between alcohol consumption and risks to the management of chronic diseases such as HIV/AIDS (8,10). The AUDIT-C shows potential as an indirect screening tool for both at-risk drinking and ART nonadherence, understanding that by nature, this screening function implies the need for further, more in-depth assessment of both behaviors.

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Table 1

Sociodemographic, Clinical, and Substance Use Characteristics of the Sample

	AUDIT-C positive (n=83)	AUDIT-C negative (n=225)	p [*]
Sociodemographic			
Sex, Female, n (%)	22 (27)	76 (34)	.27
Race, Nonwhite, n (%)	49 (59)	131 (58)	.90
Age, Median [IQR]	43 [10]	44 [10]	.17
Education, years, Median [IQR]	12 [2]	13 [2]	.003
Primary language English, n (%)	83 (100)	219 (97)	.20
Marital status, Married/partnered, n (%)	15 (18)	9 (22)	.53
Employment, Currently employed, n (%)	13 (16)	43 (19)	.51
Active health insurance, n (%)	82 (99)	205 (91)	.02
Clinical			
HIV Exposure category, n (%) ^a			
MSM	34 (45)	101 (52)	.42
Heterosexual contact	19 (26)	64 (33)	.45
IVDU	14 (18)	23 (12)	.30
IVDU + MSM	4 (5)	2 (1)	.12
Other/Unknown	4 (5)	4 (2)	.29
Viral load undetectable, n (%) ^b	43 (54)	124 (58)	.60
CD4 count, Median [IQR] ^c	350 [374]	397 [428]	.32
Substance Use			
Drinking status, n (%)			
Nondrinkers	--	117 (52)	
Drinkers	83 (100)	108 (48)	<.001
AUDIT-C score, Median [IQR]	5 [3]	0 [2]	<.001
Positive AUDIT-3 screen, n (%)	79 (95)	26 (12)	<.001
Drug Use, n (%) ^d			
Any	57 (69)	87 (39)	<.001
Marijuana	41 (49)	64 (28)	.001
Crack	25 (30)	24 (11)	<.001
Cocaine	15 (18)	19 (8)	.02
“Poppers”	12 (15)	14 (6)	.02
Tobacco Use, n (%)	63 (76)	130 (58)	.004

Note.

AUDIT-3: Item 3 on the Alcohol Use Disorders Identification Test; AUDIT-C: Alcohol Use Disorders Identification Test—Consumption; CD4 count: Cluster of differentiation 4 cell count; IVDU: Intravenous drug use; IQR: Interquartile range; MSM: Men who have sex with men; p: significance level

^a n=269.

^b n = 293.

^c_n = 287.

^d Illicit drugs for which there were no significant differences in use between the two groups and/or drugs used by less than 5% of the group are not presented; these include heroin, opioids, stimulants, hallucinogens, inhalants, and ecstasy.

* Significance testing for differences between AUDIT-C positive/negative groups, assessed with Mann-Whitney U tests for continuous variables and chi-square tests or Fisher exact test, where appropriate

Table 2

Adherence and Psychosocial Characteristics of the Sample

	AUDIT-C positive (n=83) Median [IQR]	AUDIT-C negative (n=225) Median [IQR]	p [*]
% Adherence	79 [43]	89 [38]	.003
BDI-II, Total score ^a	17 [21]	12 [17]	.03
ISEL, Total score	72 [36]	79 [31]	.03
Neuroticism ^a	25 [11]	23 [11]	.004
Extroversion ^a	26 [8]	26 [9]	.40
Openness ^a	25 [5]	26 [8]	.97
Agreeableness ^a	27 [8]	30 [6]	.001
Conscientiousness ^a	30 [10]	33 [9]	.02
HIV-SES, Total score	215 [55]	229 [47]	.01

Note.

AUDIT-C: Alcohol Use Disorders Identification Test—Consumption; IQR: Interquartile range; BDI-II: Beck Depression Inventory II; HIV-SES: HIV Self Efficacy Scale; ISEL: Interpersonal Support Evaluation List; Neuroticism, Extroversion, Openness, Agreeableness, Conscientiousness: respective scales on NEO-Five-Factor Inventory; p: significance level

^a n = 304

* Significance testing for differences between AUDIT-C positive/negative groups, assessed with Mann-Whitney U tests for continuous variables and chi-square tests or Fisher exact test, where appropriate.

Linear Regression Results for Nonadherence Predicted by AUDIT-C and AUDIT-3 Status Controlling for Confounding Variables and Covariates

Table 3

Variable	Block	Predictor	b	95% CI for b	p	R ²	Δ R ²
AUDIT-C							
1		Age	-.045	(-.074 to -.0150)	.003		
		Race	.538	(.070 to 1.007)	.025		
		Conscientiousness	-.047	(-.082 to -.012)	.008		
		Self-efficacy	-.007	(-.014 to -.001)	.032	.114	
2		AUDIT-C positive status	.564	(.036 to 1.092)	.036	.127	.013
AUDIT-3							
1		Race	.605	(.130 to 1.080)	.013		
		Conscientiousness	-.045	(-.080 to -.009)	.013		
		Self-efficacy	-.009	(-.015 to .002)	.012	.086	
2		AUDIT-3 positive status	.330	(-.179 to .838)	.203	.091	.005

Note.

AUDIT-3: Item 3 on the Alcohol Use Disorders Identification Test; AUDIT-C: Alcohol Use Disorders Identification Test—Consumption; b: Regression coefficient; p: Significance level;

R²: Correlation coefficient, squared; R²Δ = Change in R² with addition of AUDIT-C or AUDIT-3 screening status in Block 2.