Using the AUDIT-PC to Predict Alcohol Withdrawal in Hospitalized Patients

Anna Pecoraro, PsyD^{1,2}, Edward Ewen, MD³, Terry Horton, MD^{2,3}, Ruth Mooney, PhD, MN, BSN⁴, Paul Kolm, PhD⁵, Patty McGraw, MS RN³, and George Woody, MD^{1,2}

¹Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, USA; ²NIDA Clinical Trials Network, Delaware Valley Node, Philadelphia, PA, USA; ³Department of Medicine, Christiana Care Health System, Newark, DE, USA; ⁴Department of Nursing, Christiana Care Health System, Newark, DE, USA; ⁵Center for Outcomes Research, Christiana Care Health System, Newark, DE, USA.

BACKGROUND: Alcohol withdrawal syndrome (AWS) occurs when alcohol-dependent individuals abruptly reduce or stop drinking. Hospitalized alcohol-dependent patients are at risk. Hospitals need a validated screening tool to assess withdrawal risk, but no validated tools are currently available.

OBJECTIVE: To examine the admission Alcohol Use Disorders Identification Test-(Piccinelli) Consumption (AUDIT-PC) ability to predict the subsequent development of AWS among hospitalized medical-surgical patients admitted to a non-intensive care setting.

DESIGN: Retrospective case-control study of patients discharged from the hospital with a diagnosis of AWS. All patients with AWS were classified as presenting with AWS or developing AWS later during admission. Patients admitted to an intensive care setting and those missing AUDIT-PC scores were excluded from analysis. A hierarchical (by hospital unit) logistic regression was performed and receiver-operating characteristics were examined on those developing AWS after admission and randomly selected controls. Because those diagnosing AWS were not blinded to the AUDIT-PC scores, a sensitivity analysis was performed.

PARTICIPANTS: The study cohort included all patients age ≥ 18 years admitted to any medical or surgical units in a single health care system from 6 October 2009 to 7 October 2010.

KEY RESULTS: After exclusions, 414 patients were identified with AWS. The 223 (53.9 %) who developed AWS after admission were compared to 466 randomly selected controls without AWS. An AUDIT-PC score ≥ 4 at admission provides 91.0 % sensitivity and 89.7 % specificity (AUC=0.95; 95 % CI, 0.94–0.97) for AWS, and maximizes the correct classification while resulting in 17 false positives for every true positive identified. Performance remained excellent on sensitivity analysis (AUC=0.92; 95 % CI, 0.90–0.93). Increasing AUDIT-PC

scores were associated with an increased risk of AWS (OR=1.68, 95 % CI 1.55–1.82, $p<0.001$).

CONCLUSIONS: The admission AUDIT-PC score is an excellent discriminator of AWS and could be an important component of future clinical prediction rules. Calibration and further validation on a large prospective cohort is indicated.

KEY WORDS: alcoholism; addictive behavior; screening; risk assessment; hospital medicine.

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INTRODUCTION

Between 17 %¹ and 20 %^{2,3} of medical inpatients are unhealthy drinkers, and approximately 77 % of those patients are alcohol-dependent.¹ Alcohol-dependent patients admitted to the hospital experience abrupt cessation of alcohol use and are at risk for alcohol withdrawal syndrome (AWS),⁴ a dangerous constellation of symptoms associated with significant morbidity, and safety concerns for patients and staff. Unidentified and/or under-treated AWS can, in up to 20 % of such patients, result in severe withdrawal including the onset of delirium tremens (DTs),⁵ which can require transfer to intensive care settings to manage potentially life-threatening complications.^{6,7} Severe AWS including DTs can be prevented if those at risk are identified, monitored and treated aggressively once symptoms appear. A screening tool applicable to busy inpatient services would be beneficial. Screening medical/surgical inpatients for unhealthy alcohol use is advocated nationally as an extension of Screening and Brief Intervention (SBI) and Screening, Brief Intervention, and Referral to Treatment (SBIRT) efforts. Based in part on the success of SBI with primary care outpatients with “risky drinking”,⁸ the Joint Commission is developing hospital-based alcohol screening performance measures.⁹ Although screening efforts associated with SBI and SBIRT are geared toward identifying moderate users for brief intervention and referring dependent patients to treatment, this study explores the feasibility

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of broadening its role to include the early identification of those at risk for alcohol withdrawal during hospitalization, providing a better opportunity to prevent the devastating consequences of untreated AWS.¹⁰

In response to concerns brought to light after several AWS-associated adverse safety events, Christiana Care Health System (CCHS), a large Mid-Atlantic healthcare provider, implemented a standardized, system-wide AWS screening and treatment protocol in October of 2009. The initiative consists of an alcohol withdrawal risk assessment administered by nurses to all medical or surgical patients on admission. Positive screens initiate a treatment algorithm that includes standardized ordering and monitoring using a CIWA-Ar (Clinical Institute Withdrawal Assessment for Alcohol-Revised; CIWA-Ar) triggered model¹¹ (algorithm details available in online [appendix](#)).

An initial challenge faced by the development team tasked with designing the protocol concerned the choice of screening instrument. No tool was validated to screen for alcohol withdrawal in hospitalized medical or surgical inpatients. Furthermore, a successful tool would need to be short, require minimal training to use, and be easily given by any of our 2,500 nursing staff without interfering with existing workflows. There were several potential candidates. The Alcohol Use Disorders Identification Test (AUDIT;¹¹ Table 1), a ten-item instrument, was developed to detect “hazardous and harmful alcohol consumption” in outpatient primary care. It was developed in the context of the World Health Organization (WHO) Collaborative Project,¹² is culturally sensitive, widely applicable, and has good psychometric qualities.¹³ Two studies have examined its usefulness in predicting AWS in different

inpatient populations: Reoux et al.¹⁴ evaluated the AUDIT’s ability to predict clinically significant AWS among alcohol-dependent patients in inpatient detoxification, and found that a cut point of 27 showed 98 % sensitivity and a specificity of 24 %. Dolman and Hawkes⁴ combined the AUDIT with blood tests (GGT, ALT, AST, MCV) to predict medical inpatients’ withdrawal risk. They found that a score ≥ 8 , plus two or more abnormal blood tests had a sensitivity of 94.1 % and a specificity of 97.9 %. These results suggest that the AUDIT has promise as a predictor of AWS.

In busy hospital environments, time is a precious resource, necessitating brevity. Several abbreviated versions of the AUDIT are available, including the AUDIT-3,¹⁵ the AUDIT-C,¹⁵ and the AUDIT-PC^{16–18} (Table 1). The AUDIT-3 has a single item (AUDIT item 3) that measures binge drinking. The AUDIT-C consists of the first three items contained in the original AUDIT survey. The AUDIT-PC was designed to screen for hazardous alcohol intake, consists of five AUDIT items, including the first, which asks how often the patient drinks, and has similar psychometric characteristics to the AUDIT.¹⁸ Based on existing research with the AUDIT,^{4,19} the desire for a briefer instrument, and the importance of the frequency of prior alcohol use in the development of AWS, we chose the AUDIT-PC for study.

Because the AUDIT-PC was developed to identify problem drinkers in outpatient primary care, and not to predict the risk of AWS in medical/surgical inpatients, and a literature review revealed no studies examining the AUDIT-PC’s efficacy as a predictor of AWS, we conducted the present study. Our primary objective was to examine the test characteristics of the AUDIT-PC in terms of its ability to

Table 1. AUDIT, AUDIT-PC*, AUDIT-3*, and AUDIT-C* Items

0	1	2	3	4
1. How often do you have a drink containing alcohol? ¹				
Never	≤ Monthly	2–4 times a month	2–3 times a week	> 4 times a week
2. How many drinks containing alcohol do you have on a typical day when you are drinking? ¹				
1 or 2	3 or 4	5 or 6	7 or 9	≥ 10
3. How often do you have six or more drinks on one occasion? ^{2,3}				
Never	< Monthly	Monthly	Weekly	Daily or almost daily
4. How often during the last year have you found that you were not able to stop drinking once you had started? ¹				
Never	< Monthly	Monthly	Weekly	Daily or almost daily
5. How often during the last year have you failed to do what was normally expected from you because of drinking? ^{1,3}				
Never	< Monthly	Monthly	Weekly	Daily or almost daily
6. How often during the last year have you needed a first drink in the morning to get yourself going after a heavy drinking session?				
Never	< Monthly	Monthly	Weekly	Daily or almost daily
7. How often during the last year have you had a feeling of guilt or remorse after drinking?				
Never	< Monthly	Monthly	Weekly	Daily or almost daily
8. How often during the last year have you been unable to remember what happened the night before because you had been drinking? ³				
Never	< Monthly	Monthly	Weekly	Daily or almost daily
9. Have you or someone else been injured as a result of your drinking?				
Never		Yes, but not in the last year		Yes, during the last year
10. Has a relative, friend, doctor or other health worker been concerned about your drinking or suggested you should cut down? ^{1,3}				
Never		Yes, but not in the last year		Yes, during the last year

AUDIT Alcohol Use Disorders Identification Test

Note: All items are included in the AUDIT

* Abbreviated versions of the AUDIT

¹Included in the AUDIT-PC

²Included in AUDIT-3

³Included in AUDIT-C

predict the development of AWS occurring after admission among hospitalized medical-surgical inpatients.

METHODS

Design

This was a retrospective case-control study of adult patients admitted to a non-intensive care unit (ICU) medical or surgical unit and discharged with a diagnosis of AWS during hospitalization. The study cohort included all patients age ≥ 18 years admitted to any one of 38 CCHS medical-surgical units from 1 October 2009 to 1 October 2010. Patients admitted from the emergency department to an ICU setting were frequently unable to complete the survey, and so were excluded from further analysis. In addition, hospital discharge data were examined from 1 January 2001 through 31 December 2012 to determine underlying rates of and trends in AWS diagnosis.

The AUDIT-PC was administered by the admitting nurse beginning in October 2009, as part of the standard CCHS admission process for all adult patients capable of completing the survey. Demographic data, admission unit, and discharge diagnoses were extracted from the administrative database. AWS was defined as alcohol withdrawal and/or delirium tremens. Cases were identified by principal and secondary discharge ICD-9 codes of Alcohol Withdrawal (291.81) or Alcohol Withdrawal Delirium (291.0). A discharge diagnosis of AWS was based solely on the attending physician's diagnoses at the conclusion of the visit. Caregivers were not blinded to the admission AUDIT-PC score. The study was approved by the University of Pennsylvania and CCHS institutional review boards, and procedures followed institutional guidelines.

We selected all patients from the study cohort with a discharge diagnosis of AWS and 500 randomly selected controls without AWS. Two physicians performed a chart review on the cases and controls. All AUDIT-PC scores were reviewed and any miscalculations were corrected by the reviewers. A diagnosis of AWS was confirmed upon review of the hospital discharge summary. Cases were further categorized as having AWS on admission versus developing AWS later during the hospital stay based on the presence of any one of the following criteria in the admitting history and physical: 1) a diagnosis of AWS by the admitting physician, 2) seizures in a patient without a known history of seizure disorder, 3) otherwise unexplained delirium or tremors. A randomly selected 25 % sample of cases was reviewed by both physicians, and an inter-rater reliability analysis using the Kappa statistic²⁰ was performed to determine consistency among reviewers (Kappa=0.75, 95 % CI 0.66–0.84, $p < 0.001$). The reviewers were unaware of which cases were selected for reliability analysis. Cases with missing AUDIT-PC scores were excluded from further analysis.

Analysis

Descriptive statistics were examined with Chi-square and Mann-Whitney U tests. A hierarchical (hospital unit), logistic regression was performed using the controls and those cases developing AWS after admission. Regression models, including the AUDIT-PC score alone and with the addition of age, sex, and race, were examined and compared using the likelihood ratio test. A hierarchical model was used to correct for potential differences between hospital units in the application of the AUDIT-PC.

A receiver operating characteristics (ROC) curve was plotted and a smooth curve fitted using the maximum likelihood estimation of the binormal ROC curve.^{21,22} The area under the curve (AUC) was estimated using Wilcoxon's rank-sum test statistic²³ and asymmetric 95 % confidence intervals (CI) for the AUC were calculated.^{24,25} The optimal cut-point was estimated using the Youden index (the point on the curve furthest from chance),^{26,27} and the positive predictive value (PPV) and number needed to screen (NNS) were calculated for each score based on the incidence in the eligible population.

Sensitivity Analysis

Because the physicians caring for the patients were not blinded to the result of the AUDIT-PC survey, it is possible that they were influenced by the score and thus more likely to diagnose AWS. We performed a sensitivity analysis examining the potential impact of this review bias. The rate of AWS diagnoses was examined in the years preceding and following the study year using linear regression and comparisons made by analysis of covariance. This incremental increase in rate beyond that projected for the study year was used to estimate the increase in AWS identification resulting from the available AUDIT-PC scores. In order to simulate physicians being blinded to the AUDIT-PC score, we randomly selected a proportion of cases equal to that represented by the rate increase and reclassified them as controls, and then calculated the AUC. This random reclassification was repeated 1,000 times to estimate the AUC, 95 % CI, sensitivity and specificity.

Descriptive statistics were performed in SPSS (Chicago, IL) version 15.0, and all other analyses were performed using STATA (College Station, TX) version 12.0.

RESULTS

Of the 40,908 patients hospitalized between 6 October 2009 and 7 October 2010, 589 (1.4 %) were discharged with a diagnosis of AWS. After excluding the 4,577 ICU admissions (11.2 % of the total), there remained 36,331 hospitalizations eligible for study, and within this group we identified 466 patients with AWS (1.3 % of the non-ICU admission population). On chart review, six (1.3 %) of the 466 patients were incorrectly classified as having AWS. Of the remaining 460 cases, 221 (48.0 %) had

AWS on admission, while 239 (52.0 %) developed AWS later in their hospital stay. When comparing the randomly selected controls to all of those without AWS in the eligible population, there was no significant difference in age ($p=0.98$) or sex ($p=0.83$); however, the selected controls did have significantly fewer patients of white race (68.6 % vs. 73.8 %, $p=0.004$). AUDIT-PC scores were missing in 30 (13.6 %) who presented with AWS, 16 (6.7 %) who developed AWS later in their hospital stays, and 34 (6.8 %) randomly selected controls (Figure 1). There were no significant differences in those missing AUDIT-PC scores in age, sex and race distributions for either the selected controls (age $p=0.91$, sex $p=0.24$, race $p=0.84$) or those developing AWS after admission (age $p=0.43$, sex $p=0.57$, race $p=0.17$).

Within the 36,331 eligible hospitalizations, those discharged with a diagnosis of AWS were younger (mean age 52.8 [SD 12.9] vs. 61.8 [SD 18.4] years, $p<0.001$) and more frequently male (76.3 % vs. 45.5 %, $p<0.001$) than

those without AWS. In multivariate analysis adjusted for age, sex, and race, those <65 years old (OR 3.48, 95 % CI 2.76–4.39, $p<0.001$), males (OR 3.56, 95 % CI 2.87–4.42, $p<0.001$), and white race versus all other races (OR 1.40, 95 % CI 1.13–1.75, $p=0.002$) were at significantly greater risk of AWS. The AWS and the control groups are compared in Table 2. Those presenting with AWS were also more likely to be diagnosed with delirium tremens than those developing AWS later during hospitalization (30.9 % vs. 20.6 %, $p=0.017$).

The hierarchical logistic regression with AUDIT-PC score, age, race and sex included in the model as covariates demonstrated an increased risk of AWS developing subsequent to admission with each incremental increase in AUDIT-PC score (OR 1.68, 95 % CI 1.55–1.82, $p<0.001$). Age, sex and race did not contribute significantly to the model (Table 3). A simplified model using the AUDIT-PC score alone predicted the later development of AWS as well as the model containing age, sex and race covariates

Figure 1. Study cohort selection process. *The final receiver operating characteristics analysis was performed on the 466 controls and 223 cases presenting with alcohol withdrawal syndrome (AWS) after admission. Patients admitted directly to the ICU, either from home or the emergency department, and those missing AUDIT-PC scores were excluded from further analysis.

Table 2. Characteristics of the Study Cohort*

	Control n=466	AWS after Admission n=223	AWS on Admission n=191
Age, mean (SD)	61.7 (18.4)	54.7 (14.2)	49.9 (11.2)
Male, n (%)	215 (46.1)	160 (71.7)	155 (81.2)
Race–Ethnicity, n (%)			
White	319 (68.5)	164 (73.5)	160 (83.8)
Black	127 (27.3)	45 (20.2)	22 (11.5)
Hispanic	13 (2.8)	13 (5.8)	8 (4.2)
Other	7 (1.5)	1 (0.4)	1 (0.5)
AUDIT-PC Score, mean (SD)	1.1 (2.4)	10.5 (5.2)	12.5 (4.9)

* All comparisons are significant at $p < 0.001$

($p=0.69$), and all subsequent ROC analyses were performed using this simplified model.

The non-parametric ROC curve demonstrated the AUDIT-PC score's excellent discriminating ability (AUC 0.952, 95 % CI 0.935–0.968). The binormal smoothed ROC curve performed equally well (AUC 0.959, 95 % CI 0.945–0.972), and the results for the combined approaches are illustrated in Fig. 2. Table 4 provides the sensitivities, specificities, number needed to screen (NNS), positive predictive value (PPV), and Youden index associated with this model based on the observed incidence of AWS of 0.66 % (239 of 36,110 hospitalizations). An AUDIT-PC score of 4 provides the greatest balance between true and false-positive rates based on the highest Youden Index, with a sensitivity of 91.0 % and a specificity of 89.7 %.

The trend analysis examined a total of 483,144 hospitalizations, including 5,319 diagnosed with AWS, over a 12-year period from 2001 through 2012. The overall rate of AWS diagnoses was 11 per 1,000 hospital admissions. The rate of AWS increased steadily at a rate of 0.6 per 1,000 admissions per year ($p < 0.001$) from 2001 to 2008, and this same rate continued from 2009 through 2012. However, in 2009 (the intervention year) the rate increased by 3.1 per 1,000 admissions, an increase of 2.5 per 1,000 greater than projected for that single year (trend figure available in online [appendix](#)). Assuming similar proportions of patients admitted to a non-ICU setting and subsequently developing AWS after admission, this represents an additional 41 patients identified as developing AWS after admission than expected based on the preceding and following years. In the sensitivity analysis, we randomly selected 41

Figure 2. Receiver operating characteristics of the AUDIT-PC score in patients developing AWS after hospital admission. The receiver operating characteristics of the AUDIT-PC score are based on the binormal model obtained from the hierarchical (by hospital unit) logistic regression. The dashed lines indicate the 95 % confidence limits of the binormal curve. The markers indicate the points on the non-parametric or empiric curve, and value labels indicate specific AUDIT-PC score cutoff points and their respective true and false-positive fractions. The area under the curve (AUC) for the binormal model was 0.96 (95 % CI 0.95–0.97). The non-parametric AUC was 0.95 (95 % CI 0.94–0.97).

cases without replacement and reclassified them as controls, and then recalculated the AUC using the simplified model described above. This random selection and analysis was repeated 1,000 times, resulting in a mean AUC of 0.92, 95 % CI 0.90–0.93 (ROC curve available in online [appendix](#)).

DISCUSSION

The admission AUDIT-PC score is an excellent discriminator of those developing AWS in hospitalized, non-ICU, medical-surgical patients, and could be an important component of future clinical prediction rules. An AUDIT-PC score ≥ 4 appears to be the optimal cut point in terms of maximizing the correct classification of patients^{28,29} with a sensitivity of 91.0 % and a specificity of 89.7 %. The PPV or post-test probability of developing AWS at this cut point is 5.6 %, or eight times the baseline incidence in our population, with 17 patients screened for every one correctly identified. Increasing the threshold to 5 results in a substantial increase in PPV (to 9.7 %), while decreasing the NNS to 9; however, nearly twice as many patients would be falsely classified as low risk (41 versus 21 false negatives). The optimal threshold would ultimately depend on the cost in clinical and economic terms of a false-positive versus a false-negative designation. The cost of a false-positive result is largely confined to the nursing time needed to perform the CIWA-Ar assessments, while the cost of missing impending AWS is unknown, but likely to be considerably larger.

Table 3. Risk of Developing AWS During Hospitalization*

Patient Characteristic	Adjusted Odds Ratio (95 % CI)	p value
Age, years	1.01 (0.99, 1.02)	0.52
Male	1.28 (0.73, 2.23)	0.39
White	1.26 (0.67, 2.35)	0.47
AUDIT-PC Score	1.68 (1.55, 1.82)	< 0.001

* Excludes patients with a diagnosis of, or findings consistent with, AWS on admission

Table 4. Test Characteristics of the AUDIT-PC Score in Patients Developing AWS After Admission

AUDIT-PC score	Sensitivity	Specificity	NNS*	PPV†	Youdin Index‡
0	100.0 %	0.0 %	152	0.7 %	0.00
1	97.8 %	64.4 %	55	1.8 %	0.62
2	96.0 %	77.7 %	35	2.8 %	0.74
3	93.3 %	84.3 %	26	3.8 %	0.78
4	91.0 %	89.7 %	17	5.6 %	0.81
5	83.0 %	94.9 %	9	9.7 %	0.78
6	78.9 %	95.9 %	8	11.4 %	0.75
7	73.5 %	96.4 %	8	11.8 %	0.70
8	66.8 %	96.8 %	7	12.1 %	0.64
9	61.0 %	97.0 %	8	11.9 %	0.58
10	55.2 %	97.4 %	7	12.5 %	0.53
11	51.6 %	97.6 %	7	12.7 %	0.49
12	46.2 %	98.5 %	5	17.0 %	0.45
13	38.1 %	98.9 %	4	19.2 %	0.37
14	33.2 %	99.1 %	4	20.5 %	0.32
15	28.7 %	99.6 %	2	30.8 %	0.28
16	24.7 %	100.0 %	1	100.0 %	0.25
17	14.8 %	100.0 %	1	100.0 %	0.15
18	8.5 %	100.0 %	1	100.0 %	0.09
19	4.0 %	100.0 %	1	100.0 %	0.04

All calculations based on the results of the non-parametric ROC curve and an incidence of 0.66 % for developing AWS during admission

*NNS = number needed to screen, in this setting, the number of false-positive patients requiring monitoring for 72 hours for each true-positive patient

† PPV = positive predictive value

‡ Youden Index = the higher the number, the better the classification rate

Our results with the AUDIT-PC are comparable to those examining the AUDIT survey.^{4,13} Our sensitivity and specificity are lower than those reported in these studies, perhaps because we conducted our study in a general medical-surgical population and we used the AUDIT-PC rather than the AUDIT. Reoux et al.'s study was conducted with patients hospitalized for the treatment of alcohol dependence, rather than with medical inpatients at risk for alcohol abuse or dependence. Dolman and Hawkes combined the AUDIT with blood tests, which likely increased their predictive power over the AUDIT alone. While this may be favorable in a study environment, it may not be practical. In a busy inpatient medical environment, administering and waiting for the results of multiple blood tests as a universal screen before initiating enhanced surveillance for AWS could prevent patients from being identified in a timely fashion.

The major strengths of this study are the novel use of the AUDIT-PC to predict AWS among hospitalized patients and the excellent discriminating ability that was demonstrated. In addition, the test retains this discriminating ability during simulation where over 18 % of cases were in effect misclassified as controls. The AUDIT and its derived instruments were originally designed to identify problem drinking; however, to prevent the development and consequences of severe AWS, hospitals need a validated brief screening tool to assess withdrawal risk in recently admitted patients. This study specifically addresses this need by examining the performance characteristics of such an instrument. Despite these strengths,

however, there are important limitations to consider. First, the study was conducted in a single healthcare system during a single year after implementation of an AWS protocol. This system, however, serves a diverse population using a typical healthcare delivery model that is likely generalizable to much of the US. Second, the physicians making the diagnosis of AWS were not blinded to the AUDIT-PC scores. So even though the scores were not used by coders in medical records to assign an AWS ICD-9 code, it is likely that elevated scores resulted in heightened physician awareness for the potential for AWS, leading to a higher probability of diagnosis in these patients. This would result in fewer false-positive identifications, thus increasing the apparent specificity of the test. We attempted to mitigate this bias by performing the sensitivity analysis described. Third, the survey depends on patients accurately representing their alcohol use history. In our population, relatively few AWS patients denied any alcohol use (2.2 %). However, based on the frequency of scores <5, a large proportion may have underrepresented their alcohol use, reducing test sensitivity. Fourth, the case-control study design itself introduces bias that can lead to overestimating the AUC. In addition, even though demographic characteristics did not contribute significantly to our regression model, there may still be important differences in the AUDIT-PC performance by age and/or gender. Our study did not have sufficient power to resolve these potential differences.

The AUDIT-PC shows considerable promise as a predictor of AWS in hospitalized medical patients. In addition, it appears that a cut-point of ≥ 4 provides the best balance between true and false positives, but a lower score may be more appropriate if there are significant costs associated with developing AWS. Further research is needed, including calibration, validation, and cost-benefit analysis of this tool on a large prospective cohort, possibly including patients from multiple hospital systems in diverse geographic locations. It would also be useful to compare the AUDIT-PC's ability to predict AWS with the other brief instruments derived from the AUDIT.

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administered by Denver Health to study abuse liability of prescription drugs that is funded by contracts with pharmaceutical companies. Drs. Pecoraro, Horton, and Mooney, and Ms. McGraw declare they have no conflicts of interest.

Corresponding Author: Edward Ewen, MD; Department of Medicine, Christiana Care Health System, John H Ammon Medical Education Center, Suite 2E70 19718, Newark, DE, USA (e-mail: eewen@christianacare.org).

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