The World Health Organization Risk Drinking Levels Measure of Alcohol Consumption: Prevalence and Health Correlates in Nationally Representative Surveys of U.S. Adults, 2001–2002 and 2012–2013

Dvora Shmulewitz, Ph.D., Efrat Aharonovich, Ph.D., Katie Witkiewitz, Ph.D., Raymond F. Anton, M.D., Henry R. Kranzler, M.D., Jennifer Scodes, M.S., Karl F. Mann, M.D., Melanie M. Wall, Ph.D., Deborah Hasin, Ph.D., for the Alcohol Clinical Trials Initiative (ACTIVE Group)

Objective: Little is known about change over time in the prevalence of World Health Organization (WHO) risk drinking levels (very high, high, moderate, low) and their association with health conditions, overall and by gender. The authors used two sets of nationally representative U.S. survey data to determine whether changes over time varied by gender and to examine whether health conditions related to alcohol were associated with WHO risk drinking level within each survey, and whether these associations differed by gender.

Methods: Data on current drinkers from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC; N=26,655) and the 2012–2013 NESARC-III (N=25,659) were analyzed using logistic regression. Prevalence differences between surveys were estimated for each drinking level overall and by gender. Within each survey, prevalence differences by WHO risk drinking level were estimated for alcohol use disorder (AUD), drug use disorders, functional impairment, liver disease, and depressive and anxiety disorders.

Results: In the 2012–2013 survey, the prevalences of moderate, high, and very high risk drinking were 5.9%, 3.2%, and 3.5%, respectively, representing significant increases from the prevalences in the 2001–2002 survey, which were 1.0%, 0.6%, and 0.9%, respectively. The increase for very high risk drinking among men (0.5%) was smaller than the increase among women (1.4%). Within both surveys, compared with low risk, health conditions were significantly associated with very high risk (range of prevalence differences, 2.2%–57.8%), high risk (2.6%–41.3%), and moderate risk (0.6%–29.8%) drinking. Associations were similar by gender, except that there were stronger effects for AUD in men and for functional impairment and depressive and anxiety disorders in women.

Conclusions: The increase in potentially problematic drinking levels among U.S. adults emphasizes the need for better prevention and treatment strategies. The study results support the validity of the WHO risk drinking levels, which show clinical utility as nonabstinent drinking reduction treatment goals. Such goals could engage more people in treatment, improving public health by decreasing personal and societal consequences of risk drinking.

Am J Psychiatry 2021;178:548–559; doi:10.1176/appi.ajp.2020.20050610

Heavy drinking and alcohol use disorder (AUD) contribute substantially to morbidity and mortality worldwide (1, 2), mainly through liver disease, injury, cancer, cardiovascular disease, and impaired psychosocial functioning (3, 4). However, few individuals receive treatment for problematic drinking (5–8), often because they are not interested in abstinence, the goal most commonly offered in treatment settings (9–11). Recently, nonabstinent drinking reduction treatment goals, which may be more attainable and engage more people in treatment, have gained attention (12, 13). Psychopharmacological treatments successfully reduce drinking to nonabstinent levels (14–16), and reductions are maintained over time (17) and are associated with decreased mortality (14), improved health, and reduced negative consequences of drinking in clinical and general population samples (17–23). In these studies, drinking reduction was measured using the World Health Organization (WHO) risk drinking levels, a gender-specific metric indicating the level of risk associated with the average daily amount of alcohol consumed: very high risk, high risk, moderate risk, and low risk (24).

Recent studies and a meta-analysis (25) of time trends in alcohol consumption among U.S. adults show increases in any alcohol use (25–27) and in heavy use (binge drinking) (25, 26), specifically among women (25, 26, 28, 29). However, none of these studies measured consumption using the WHO risk drinking level definitions. What is known about the

prevalences of the WHO levels was estimated in older data (2001–2002), in which 2.5% of current drinkers were at very high risk, 2.5% at high risk, 4.8% at moderate risk, and 90.2% at low risk (18). However, more recent prevalence data are lacking, and whether the prevalences of WHO risk drinking levels have changed over time and whether there are differences between men and women remain unknown. Furthermore, reports on the relationships between the WHO risk drinking levels and clinically important drinking consequences—for example, alcohol dependence (18), drug dependence (23), reduced quality of life (19, 21), mental health functional impairment (18), impaired liver function (17, 21), liver disease (20), and anxiety and depressive disorders (22)—used data collected over 15 years ago. Additionally, the relationships between alcohol use and its consequences differ in men and women (30). Given the many changes in U.S. society and the prevalence of alcohol-related conditions (26, 31–41), updated information is needed on the associations of health conditions with the WHO risk drinking levels, overall and by gender.

To examine these issues, we used data on U.S. adults from two nationally representative surveys, the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (42) and the 2012–2013 NESARC-III (8). First, we determined whether prevalence of WHO risk drinking levels changed between the 2001–2002 and 2012–2013 surveys, as well as whether changes varied by gender. Second, we examined whether health conditions related to alcohol (alcohol dependence, AUD, drug dependence, drug use disorders, functional impairment, liver disease, and depressive and anxiety disorders) were associated with WHO risk drinking level within each survey and whether these associations differed by gender.

METHODS

Sample and Procedures

NESARC (42) and NESARC-III (8) are nationally representative surveys of civilian adults (age ≥18 years), sampled from households and group quarters using multistage probability sampling designs. Sample weights adjusted the data for nonresponse and selection probabilities to represent the U.S. civilian population based on the 2000 Census for NESARC (43) and the 2012 American Community Survey for NESARC-III (44). The surveys utilized similar rigorous field procedures, including structured interviewer training, ongoing supervision, and quality control assurance (8, 42–45). The methodological similarities of the surveys have enabled their use in examining change over time in health outcomes (26, 31–34, 46–48). The National Institute on Alcohol Abuse and Alcoholism (NIAAA) sponsored the surveys, and the field work was carried out by large survey organizations (NESARC by the U.S. Census Bureau and NESARC-III by Westat). Institutional review boards from the U.S. Census Bureau and Office of Management and Budget (for NESARC), NIAAA (for both surveys), and Westat (for NESARC-III) approved the protocol and consent procedures. All respondents gave informed consent after receiving a complete description of the study. Interviews were conducted in 2001 and 2002 for NESARC and in 2012 and 2013 for NESARC-III, with overall response rates of 81.2% and 60.1%, respectively. The total analyzed sample (N=52,314) included current drinkers for whom information about drinks per day was available from NESARC (N=26,655) and NESARC-III (N=25,659). Among all current drinkers (N=52,724), daily drinking information was missing for 410 respondents (0.78%), who were excluded from the analysis.

Measures

Both surveys used the Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS) to assess drinking, AUD, drug use disorders, sociodemographic variables, and other health conditions. The AUDADIS is a fully structured computer-assisted diagnostic interview. AUDADIS-IV (49) was used for NESARC and AUDADIS-5 (50) for NESARC-III.

WHO Risk Drinking Levels

In both surveys, identical questions assessed alcohol use (26), which were used to estimate average ethanol consumed per day in the past year. AUDADIS measures of past-year average daily ethanol consumption showed substantial to excellent reliability (intraclass correlation coefficients, 0.68–0.92) (51–53). Average daily ethanol consumption was used to categorize respondents into the WHO very high risk, high risk, moderate risk, and low risk categories (see Table S1 in the online supplement), as in recent studies (18, 20, 22, 23). For men, very high risk was defined as >100 g/day or >7.1 U.S. standard drinks; high risk as >60 to 100 g/day or >4.3 to 7.1 drinks; moderate risk as >40 to 60 g/day or >2.9 to 4.3 drinks; and low risk as 1 to 40 g/day or 1 to 2.9 drinks. For women, very high risk was defined as >60 g/day or >4.3 standard drinks; high risk as >40 to 60 g/day or >2.9 to 4.3 drinks; moderate risk as >20 to 40 g/day or >1.4 to 2.9 drinks; and low risk as 1 to 20 g/day or 1 to 1.4 drinks.

The WHO risk level variable was the outcome for the first aim (change between surveys in risk level prevalence) and a predictor for the second aim (association with health conditions).

Health Conditions

Alcohol use disorder (AUD). For consistency across surveys, DSM-IV criteria were used, and past-year AUD diagnoses were positive if respondents had alcohol dependence or abuse in the past year. Dependence required at least three of seven DSM-IV dependence criteria, and abuse required at least one of four DSM-IV abuse criteria. Because extensive evidence indicates that all 11 criteria reflect a single continuum (54), dependence and abuse were combined into one variable (AUD). Most of the symptom items used to assess criteria in both surveys were identical, and the few trivial differences could not account for the changes in AUD prevalence across the two surveys (26). Alcohol dependence

was included as a separate outcome because WHO drinking risk levels were previously associated with alcohol dependence (18). The reliability and validity of AUDADIS DSM-IV AUD and alcohol dependence diagnoses have been found to be substantial to excellent (kappa values >0.60) in national and international studies, in general and clinical populations (51–53, 55–61).

Drug use disorders. Similarly, past-year drug use disorders (dependence or abuse) were diagnosed using the DSM-IV criteria for marijuana, cocaine, heroin, prescription opioids, sedative/tranquilizers, hallucinogens, stimulants, inhalants, and club drugs. Respondents who were positive for any drug use disorder were considered positive for the drug use disorder variable. As with alcohol, the small differences in operationalization between the surveys had little effect on prevalence for marijuana (31), heroin (32), prescription opioids (35), and cocaine use disorders (34). Any drug dependence was included as a separate outcome, because WHO drinking risk levels were previously associated with drug dependence (23). In multiple studies, the reliability and validity of any AUDADIS DSM-IV drug use disorder/drug dependence as well as drug-specific disorders have been found generally to be substantial to excellent (52, 53, 55–60).

Functional impairment. Both surveys included the Medical Outcomes Study 12-Item Short Form Health Survey, version 2 (SF-12) (62), a valid measure of general functioning used in clinical (63) and general population surveys (64). The SF-12 was used to calculate a standardized mental component summary score (mean=50; standard deviation=10), shown to be related to AUD (5, 8). Functional impairment was defined as ≥1 standard deviation below the mean, that is, scores ≤40, as has been done previously (18).

Liver disease. The two surveys asked identical questions about whether respondents had cirrhosis of the liver or another form of liver disease in the past year. As has been done previously, liver disease was considered positive if a doctor or health professional confirmed to the respondent that they had cirrhosis or other liver disease (20).

Depressive and anxiety disorders. AUDADIS-IV provided diagnoses of past-year DSM-IV anxiety disorders (generalized anxiety, panic, agoraphobia, social or specific phobia) and depressive disorders (major depression, dysthymia). Reliability was moderate for anxiety disorders (kappa values, 0.40–0.52) (51) and moderate to substantial for depressive disorders (kappa values, 0.50–0.73) (51, 55). AUDADIS-5 provided DSM-5 diagnoses of the depressive and anxiety disorders, which showed fair to moderate reliability (kappa values, 0.39–0.51) (65) and validity (kappa values, 0.32 and 0.40 for any anxiety disorder and any depressive disorder, respectively) (66), but not DSM-IV diagnoses. Because depressive and anxiety disorders show high comorbidity (67–69) and cluster together on the internalizing dimension of the transdiagnostic model (70), they were combined into one variable, any depressive and anxiety disorder, as has been done previously (22). An additional variable was defined as positive for respondents with any depressive and anxiety disorder not due to substances or illness.

Sociodemographic Variables

Covariates were measured identically in both surveys: gender (men, women), age group (18–29 years, 30–44 years, 45–64 years, and ≥65 years), education (less than high school, high school, some college, college degree or higher), race/ethnicity (Hispanic; non-Hispanic: White, Black, American Indian/Alaska Native, Asian/Native Hawaiian/Pacific Islander), current smoking (yes, no), and health insurance (any, none). These covariates were used in previous studies of WHO risk levels in NESARC data (18, 20, 22, 23).

Statistical Analysis

As in previous studies of substance-related trends (26, 31–34, 47, 48), the two data sets were concatenated, and a survey variable (2001–2002 or 2012–2013) was added. SUDAAN, version 11.0.1, was used for analysis to incorporate survey weights and adjust for complex sampling (71). Weighted prevalence was evaluated for WHO risk drinking levels, health conditions, and sociodemographic covariates, by survey.

To test for change in the prevalence of WHO risk levels over time (between surveys), we used multinomial logistic regression to model the risk level variable (outcome) as a function of time (survey), adjusting for covariates (gender, age, race/ethnicity, education, smoking status, insurance). In each survey, weighted model-predicted marginal prevalence estimates (back-transformed from log odds) and standard errors were generated (72) for each risk level. For each risk level, the prevalence difference between the 2012–2013 and 2001–2002 surveys indicated time trends. A prevalence difference significantly greater than 0 indicated that prevalence was higher in the 2012–2013 than the 2001–2002 survey, that is, it increased over time; a prevalence difference significantly lower than 0 indicated a decrease. To determine whether prevalence difference differed by gender, an interaction term of survey by gender was included in the model. Prevalence differences (trends) were estimated for men and women, and the difference in trends for men versus women (difference-in-prevalence differences) was evaluated. A difference-in-differences significantly different from 0 indicated differential trends for men and women. To adjust for potentially different covariate effects in men and women, this model also included gender-by-covariate interaction terms.

To evaluate association of WHO risk level and health conditions within each survey, we used logistic regression to model each health condition (outcome) as a function of WHO risk level, survey, and risk level-by-survey interaction, adjusting for covariates. To adjust for potentially different covariate effects in the different risk levels, risk level-by-covariate interactions were also included. (Both surveys were

TABLE 1. Characteristics of the NESARC and NESARC-III samples in a study of WHO risk drinking levels[a]

	2001–2002 (N=26,655)			2012–2013 (N=25,659)		
		Prevalence			Prevalence	
Measure	N	%	SE	N	%	SE
Gender						
Male	12,886	52.5	0.43	11,935	50.7	0.37
Female	13,769	47.5	0.43	13,724	49.3	0.37
Age group						
18–29 years	6,076	24.3	0.41	6,384	23.8	0.45
30–44 years	9,373	34.0	0.38	7,839	28.2	0.38
45–64 years	7,858	30.5	0.36	8,451	34.7	0.39
≥65 years	3,348	11.2	0.29	2,985	13.3	0.42
Race/ethnicity						
White	16,562	75.3	1.44	14,236	68.5	0.73
Black	4,129	9.0	0.59	5,102	10.7	0.58
Hispanic	4,899	10.6	1.13	4,868	14.3	0.63
Asian/Native Hawaiian/ Pacific Islander	660	3.2	0.41	1,092	4.9	0.42
American Indian/Alaska Native	405	1.9	0.15	361	1.6	0.13
Health insurance						
Any	21,677	81.8	0.55	20,466	82.8	0.48
None	4,978	18.2	0.55	5,193	17.2	0.48
Current smoker						
Yes	8,436	33.0	0.61	8,248	30.9	0.53
No	18,219	67.0	0.61	17,411	69.1	0.53
Education						
Less than high school	1,097	3.4	0.24	858	2.8	0.17
High school	9,499	34.9	0.61	8,604	31.2	0.65
Some college	6,057	22.9	0.39	6,035	22.7	0.36
College degree	10,002	38.8	0.66	10,162	43.3	0.78
WHO risk drinking level						
Low risk	23,984	89.7	0.29	22,202	87.5	0.32
Moderate risk	1,314	4.9	0.17	1,561	5.9	0.19
High risk	686	2.7	0.15	865	3.1	0.16
Very high risk	671	2.7	0.15	1,031	3.4	0.17
Health conditions						
Alcohol dependence	1,457	5.8	0.21	2,493	9.0	0.27
Alcohol use disorder[b]	3,283	12.9	0.35	4,571	17.4	0.40
Any drug dependence[c]	218	0.9	0.08	577	2.1	0.13
Any drug use disorder[b,c]	689	2.8	0.15	1,393	5.1	0.19
Liver disease	154	0.6	0.06	268	1.1	0.09
Functional impairment	2,759	9.5	0.23	3,957	13.7	0.31
Depressive or anxiety disorders[d], any	4,771	17.3	0.40	5,989	22.7	0.44
Depressive or anxiety disorders[d], not substance or illness induced	4,595	16.7	0.39	5,692	21.6	0.42

[a] WHO=World Health Organization. The 2001–2002 data are from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), and the 2012–2013 data are from the NESARC-III. Prevalences are weighted.
[b] Alcohol and drug use disorders include abuse or dependence.
[c] Drug use disorders include marijuana, cocaine, heroin, painkillers (prescription opioids), sedative/tranquilizers, hallucinogens, stimulants, inhalants, and club drugs.
[d] Depressive and anxiety disorders include anxiety (panic disorder, agoraphobia, social phobia/social anxiety disorder, specific phobia, generalized anxiety disorder) and depression (dysthymia/persistent depressive disorder, major depression), based on DSM-IV for the 2001–2002 data and DSM-5 for the 2012–2013 data.

included in the same model so that adjustments would be consistent across surveys.) For each outcome, weighted model-predicted marginal prevalence estimates and standard errors were generated within each survey and each risk level. Within each survey, association is indicated by the prevalence difference between each risk level and the reference (low risk level). To determine whether association differed by gender, a three-way interaction term of risk level by survey by gender was included in the model (as well as survey by gender). In each survey, association was estimated

TABLE 2. Change over time (trend) in WHO risk drinking levels, 2001–2002 (NESARC) to 2012–2013 (NESARC-III), overall[a]

	2001–2002 (N=26,655)		2012–2013 (N=25,659)			
	Prevalence		Prevalence		Prevalence Difference	
WHO Risk Level	%	SE	%	SE	%	95% CI
Very high risk	2.6	0.14	3.5	0.17	**+0.9**	**0.49, 1.31**
High risk	2.6	0.15	3.2	0.16	**+0.6**	**0.17, 1.03**
Moderate risk	4.9	0.16	5.9	0.19	**+1.0**	**0.51, 1.49**
Low risk	89.8	0.28	87.4	0.32	**−2.5**	**−3.34, −1.66**

[a] WHO=World Health Organization. The 2001–2002 data are from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), and the 2012–2013 data are from the NESARC-III. Prevalences are adjusted for sample weights and sociodemographic covariates (gender, age, education, race/ethnicity, health insurance, and current smoking). Prevalences and prevalence differences are rounded, such that subtracting the values may not yield the exact difference reported. The prevalence difference—the prevalence in the 2012–2013 survey minus the prevalence in the 2001–2002 survey—indicates the trend. Prevalence differences whose 95% confidence intervals do not include 0 are statistically significant at $p<0.05$ and are in boldface.

in men and women, and contrasts were used to determine whether these differed.

All tests were two-tailed, with the significance threshold set at 0.05, as indicated by 95% confidence intervals not including 0.

RESULTS

Sample Characteristics

As shown in Table 1, both surveys had ~50% men, ~80% with any insurance, ~30% current smokers, and about two-thirds with at least some college education. The 2012–2013 sample was older on average (~50% ages 18–44) than the 2001–2002 sample (~60% ages 18–44) and had a higher prevalence of minorities (~30%) than the 2001–2002 sample (~25%) and of health conditions (ranging from 1.1% for liver disease to 22.5% for depressive and anxiety disorders) than the 2001–2002 sample (ranging from 0.6% for liver disease to 17.3% for depressive and anxiety disorders).

Prevalence of WHO Risk Drinking Levels Over Time

Overall, compared with the 2001–2002 prevalence, significant increases were observed in the 2012–2013 prevalence of moderate risk (+1.0%), high risk (+0.6%), and very high risk drinking (+0.9%), with a concomitant decrease in prevalence of low risk drinking (−2.5%) (Table 2). Trends over time differed by gender. Among women, there were significant increases in moderate (+1.1%), high (+0.5%), and very high (+1.4%) levels. In contrast, among men, a significant increase was seen in moderate risk (+0.9%). In the very high risk group, the increase among men (0.5%) was significantly smaller (−1.0%) than the increase among women (+1.4%) (Table 3).

Association of WHO Risk Levels With Health Conditions

DSM-IV alcohol use disorders. In the 2001–2002 survey, the prevalence of alcohol dependence was significantly greater among very high risk (+40.4%), high risk (+21.4%), and moderate risk (+12.3%) drinkers than among low risk drinkers (Table 4). Similarly, in the 2012–2013 survey, the prevalence was significantly greater among very high risk (+49.7%), high risk (+32.0%), and moderate risk (+20.1%) drinkers than among low risk drinkers. Significant associations were observed for men and women, with a stronger association for moderate risk among men than women (Table 5). Similar results were observed for AUD (Tables 4, 5, 6).

DSM-IV drug use disorders. In the 2001–2002 survey, the prevalence of any drug dependence was significantly greater among very high (+5.0%) and moderate risk (+0.6%) drinkers than among low risk drinkers (Table 4). In the 2012–2013 survey, the prevalence was significantly greater among very high (+6.1%), high (+2.6%), and moderate (+1.2%) than low risk drinkers. Similar results were observed for any drug use disorder, except that the prevalence was also significantly greater among high risk (+3.7%) than low risk drinkers in the 2001–2002 survey. Similar associations were observed for men and women (Tables 5, 6).

Functional impairment. In the 2001–2002 survey, the prevalence of functional impairment was significantly greater among very high (+13.9%), high (+3.1%), and moderate (+2.6%) drinkers than among low risk drinkers (Table 4). In the 2012–2013 survey, the prevalence was significantly greater among very high (+11.9%) and high (+3.1%) risk drinkers than among low risk drinkers. In men and women, significant associations were observed with very high risk (Tables 5, 6), with a significantly stronger association for women than men (Table 6).

Liver disease. In both the 2001–2002 and 2012–2013 surveys, the prevalence of liver disease was significantly greater among very high risk drinkers (+2.9% and +2.2%, respectively) than among low risk drinkers (Table 4). Differences by gender were not estimated because of the low prevalence of liver disease among women in NESARC.

Any depressive or anxiety disorder. In both the 2001–2002 and 2012–2013 surveys, the prevalence of any depressive or anxiety disorder was significantly greater among very high risk drinkers (+9.2% and +7.1%, respectively) than low risk drinkers (Table 4). Significant associations with very high risk were observed for women in both surveys but for men in the 2001–2002 survey only (Tables 5, 6). Similar results were observed for any depressive or anxiety disorder, excluding

TABLE 3. Trends in WHO risk drinking levels, 2001–2002 (NESARC) to 2012–2013 (NESARC-III), by gender[a]

	Men (N=24,821)						Women (N=27,493)							
	2001–2002 Prevalence		2012–2013 Prevalence		Prevalence Difference		2001–2002 Prevalence		2012–2013 Prevalence		Prevalence Difference		Trend Differences, Men Versus Women[b]	
Very high	3.3	0.19	3.7	0.24	+0.5	−0.09, 1.09	1.8	0.18	3.3	0.17	**+1.4**	**0.93, 1.87**	**−1.0**	**−1.69, −0.31**
High	3.4	0.21	4.0	0.24	+0.6	−0.03, 1.23	1.7	0.15	2.2	0.17	**+0.5**	**0.05, 0.95**	+0.1	−0.59, 0.79
Moderate	4.1	0.21	5.0	**0.25**	**+0.9**	**0.27, 1.53**	5.8	0.25	6.8	0.29	**+1.1**	**0.36, 1.84**	−0.2	−1.16, 0.76
Low	89.2	0.38	87.2	**0.38**	**−2.0**	**−3.02, −0.98**	90.7	0.35	87.7	0.42	**−3.0**	**−4.08, −1.92**	+1.0	−0.27, 2.27

[a] WHO=World Health Organization. The 2001–2002 data are from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (men, N=12,886; women, N=13,769), and the 2012–2013 data are from the NESARC-III (men, N=11,935; women, N=13,724). Prevalences are adjusted for sample weights and sociodemographic covariates (gender, age, education, race/ethnicity, health insurance, and current smoking). The prevalence difference—the prevalence in the 2012–2013 survey minus the prevalence in the 2001–2002 survey—indicates the trend. Prevalences, prevalence differences, and trend differences are rounded, such that subtracting the values may not yield the exact difference reported. Prevalence differences whose 95% confidence intervals do not include 0 are statistically significant at $p<0.05$ and are in boldface.

[b] For each WHO risk drinking level, the trend (prevalence difference) in men minus the prevalence difference in women indicated whether change over time differs by gender.

those occurring only during periods of substance use or illness (Tables 4, 5, 6).

DISCUSSION

In previous studies, the WHO risk drinking levels (very high, high, moderate, and low) were associated with physical, mental, and social functioning and reduction in the WHO risk drinking categories predicted improvement in these conditions (17–23). Thus, the WHO risk levels show potential clinical utility as a treatment outcome measure (14–17, 19, 21). However, important epidemiological information was lacking, namely, whether the prevalence of the WHO risk levels changed over time, associations of these levels with clinical correlates of heavy drinking in newer data, and whether results differed by gender. In adult general population current drinkers, the prevalence of moderate, high, and very high risk levels was significantly greater in the 2012–2013 survey than in the 2001–2002 survey, with a greater increase in prevalence of the very high risk drinking level among women than among men. Health conditions (AUD, drug use disorders, functional impairment, liver disease, depressive and anxiety disorders) were associated with risk levels within each survey, among men and women.

Increases over time in moderate, high, and very high risk drinking are similar to results from other U.S. national studies, which show increases in alcohol consumption, specifically binge drinking (any or weekly), particularly among women (25, 26, 28, 29). Increases in heavy drinking among women are concerning, as women are less likely to receive treatment (73) yet may be more likely than men to develop health consequences at comparable consumption levels (30). Additional studies should identify the drivers of these patterns (41). Inconsistent with previous studies, the present study showed an increase in moderate drinking among men. This study differs from the others in two key ways: an important and widely recognized consumption measure and analysis conducted in current drinkers. One previous study of current drinkers showed no increase in binge drinking in men or women (28), suggesting that binge drinking and the WHO risk drinking levels measure alcohol consumption differently. As a metric of alcohol consumption, the WHO levels are particularly useful, as they categorize drinkers on the basis of intensity and frequency of drinking and identify which drinkers are at greatest risk for alcohol-related consequences (24).

In both surveys, higher WHO risk drinking levels were associated with clinically important health conditions (alcohol dependence/AUD, drug dependence/drug use disorders, functional impairment, liver disease, and depressive and anxiety disorders), similar to previous studies (18, 20, 22, 23), suggesting that they are a valid characterization of alcohol consumption. Alcohol dependence, AUD, drug dependence, and drug use disorders were associated with all three risk levels (moderate, high, and very high versus low). Functional impairment was associated with very high and high risk, the categories of greatest clinical concern (18). Liver disease and depressive and anxiety disorders were associated with very high risk drinking. Generally, the prevalence of these health conditions was greater in the very high and high risk levels, indicating that increased drinking shows increased risk, and suggesting that reducing drinking to moderate or low risk levels could reduce such conditions.

Associations were generally similar for women and men, with some differences, mainly in the 2012–2013 survey. Women showed stronger relationships of very high risk drinking to functional impairment and depressive and anxiety disorders than men, similar to previous studies in AUD samples (74–76). Men showed a stronger relationship of moderate risk drinking to AUD than women. These differences may reflect the fact that, generally, men show higher prevalence of AUD and women show higher prevalence of depression and anxiety, emphasizing the need for further studies in women examining the relationship

TABLE 4. Association of WHO risk drinking level with health conditions, 2001–2002 (NESARC) and 2012–2013 (NESARC-III)[a]

Heath Condition and Risk Level	2001–2002 (N=26,655)				2012–2013 (N=25,659)			
	Prevalence of Condition		Prevalence Difference		Prevalence of Condition		Prevalence Difference	
	%	SE	%	95% CI	%	SE	%	95% CI
Alcohol dependence								
Very high risk	43.4	2.49	**40.4**	**35.56, 45.24**	54.6	2.45	**49.7**	**44.90, 54.50**
High risk	24.4	2.11	**21.4**	**17.24, 25.56**	36.9	2.35	**32.0**	**27.40, 36.61**
Moderate risk	15.3	1.07	**12.3**	**10.21, 14.40**	25.0	1.43	**20.1**	**17.30, 22.90**
Low risk	3.0	0.14	Ref.		4.9	0.19	Ref.	
Alcohol use disorder[b]								
Very high risk	56.6	2.77	**47.7**	**42.29, 53.11**	70.4	2.32	**57.8**	**53.25, 62.35**
High risk	40.9	2.24	**32.0**	**27.55, 36.45**	53.9	2.38	**41.3**	**36.56, 46.04**
Moderate risk	33.2	1.52	**24.3**	**21.40, 27.20**	42.3	1.41	**29.8**	**26.92, 32.68**
Low risk	8.9	0.25	Ref.		12.6	0.34	Ref.	
Any drug dependence[c]								
Very high risk	5.6	0.99	**5.0**	**3.06, 6.94**	7.7	0.96	**6.1**	**4.24, 7.96**
High risk	1.1	0.39	0.6	−0.18, 1.38	4.2	0.79	**2.6**	**1.05, 4.15**
Moderate risk	1.2	0.30	**0.6**	**0.01, 1.19**	2.9	0.38	**1.2**	**0.42, 1.98**
Low risk	0.6	0.07	Ref.		1.7	0.13	Ref.	
Any drug use disorder[b,c]								
Very high risk	13.0	1.48	**11.0**	**8.08, 13.92**	17.4	1.62	**13.1**	**9.96, 16.24**
High risk	5.7	0.98	**3.7**	**1.84, 5.56**	11.1	1.23	**6.8**	**4.37, 9.23**
Moderate risk	4.7	0.74	**2.8**	**1.39, 4.21**	7.9	0.70	**3.6**	**2.23, 4.97**
Low risk	2.0	0.12	Ref.		4.3	0.19	Ref.	
SF-12 functional impairment								
Very high risk	21.9	2.24	**13.0**	**8.57, 17.43**	25.2	1.75	**11.9**	**8.37, 15.43**
High risk	12.0	1.59	**3.1**	**0.01, 6.20**	16.5	1.52	**3.1**	**0.02, 6.18**
Moderate risk	11.4	1.05	**2.6**	**0.54, 4.66**	13.8	0.99	0.4	−1.62, 2.42
Low risk	8.9	0.23	Ref.		13.3	0.33	Ref.	
Liver disease								
Very high risk	3.4	0.98	**2.9**	**0.98, 4.82**	3.1	0.85	**2.2**	**0.51, 3.89**
High risk	0.9	0.37	0.4	−0.33, 1.13	2.3	0.80	1.4	−0.17, 2.97
Moderate risk	0.6	0.28	0.2	−0.35, 0.75	1.1	0.30	0.2	−0.43, 0.83
Low risk	0.5	0.06	Ref.		0.9	0.09	Ref.	
Any depressive or anxiety disorder[d]								
Very high risk	25.8	2.16	**9.2**	**4.95, 13.45**	29.8	1.87	**7.1**	**3.47, 10.73**
High risk	19.5	1.92	2.9	−0.84, 6.64	24.7	1.78	2.0	−1.57, 5.57
Moderate risk	17.6	1.25	1.0	−1.45, 3.45	22.4	1.22	−0.3	−2.81, 2.21
Low risk	16.6	0.36	Ref.		22.7	0.47	Ref.	
Any depressive or anxiety disorder[d], not substance or illness induced								
Very high risk	24.2	2.13	**8.2**	**4.03, 12.37**	28.8	1.80	**7.1**	**3.47, 10.73**
High risk	18.6	1.85	2.7	−0.91, 6.31	23.6	1.74	1.9	−1.61, 5.41
Moderate risk	17.2	1.25	1.2	−1.25, 3.65	21.3	1.20	−0.4	−2.85, 2.05
Low risk	16.0	0.36	Ref.		21.7	0.45	Ref.	

[a] SF-12=12-Item Short Form Health Survey, version 2; WHO=World Health Organization. The 2001–2002 data are from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), and the 2012–2013 data are from the NESARC-III. Prevalences are adjusted for sample weights and sociodemographic covariates (gender, age, education, race/ethnicity, health insurance, and current smoking). The prevalence difference—prevalence in each risk level minus prevalence in the reference risk level (low)—indicates the association at each survey. Prevalences and prevalence differences are rounded, such that subtracting the values may not yield the exact difference reported. Prevalence differences whose 95% confidence intervals do not include 0 are statistically significant at $p<0.05$ and are in boldface.

[b] Alcohol and drug use disorders include abuse or dependence.

[c] Drug use disorders include marijuana, cocaine, heroin, painkillers (prescription opioids), sedative/tranquilizers, hallucinogens, stimulants, inhalants, and club drugs.

[d] Depressive and anxiety disorders include anxiety (panic disorder, agoraphobia, social phobia/social anxiety disorder, specific phobia, generalized anxiety disorder) and depression (dysthymia/persistent depressive disorder, major depression), based on DSM-IV for the 2001–2002 data and DSM-5 for the 2012–2013 data.

TABLE 5. Association of WHO risk drinking level with health conditions in 2001–2002 (NESARC), by gender[a]

Health Condition and Risk Level	Men (N=12,886)				Women (N=13,769)				Difference in Prevalence Differences, Men Versus Women	
	Prevalence of Condition		Prevalence Difference		Prevalence of Condition		Prevalence Difference			
	%	SE	%	95% CI	%	SE	%	95% CI	%	95% CI
Alcohol dependence										
Very high risk	45.7	2.91	**42.0**	**36.32, 47.68**	39.4	3.66	**37.3**	**30.15, 44.45**	4.7	−3.79, 13.29
High risk	27.6	2.64	**23.9**	**18.73, 29.07**	20.6	3.64	**18.5**	**11.37, 25.63**	5.4	−3.38, 14.18
Moderate risk	16.1	1.68	**12.4**	**9.09, 15.71**	14.1	1.37	**12.0**	**9.31, 14.69**	0.4	−3.97, 4.77
Low risk	3.7	0.20	Ref.		2.1	0.17	Ref.			
Alcohol use disorder[b]										
Very high risk	60.7	3.09	**48.8**	**42.72, 54.88**	52.2	4.54	**46.7**	**37.80, 55.60**	2.1	−8.15, 12.35
High risk	48.0	2.91	**36.1**	**30.36, 41.84**	31.9	3.76	**26.4**	**18.97, 33.83**	**9.8**	**0.24, 19.36**
Moderate risk	39.1	2.33	**27.2**	**22.63, 31.77**	26.9	1.70	**21.3**	**18.05, 24.55**	**5.9**	**0.53, 11.27**
Low risk	11.9	0.38	Ref.		5.6	0.27	Ref.			
Any drug dependence[c]										
Very high risk	5.5	1.18	**4.8**	**2.49, 7.11**	5.7	1.47	**5.3**	**2.42, 8.18**	−0.5	−3.99, 2.99
High risk	1.7	0.61	1.0	−0.22, 2.22	0.3	0.19	−0.2	−0.61, 0.21	1.1	−0.19, 2.39
Moderate risk	1.4	0.46	0.8	−0.10, 1.70	0.9	0.34	0.5	−0.21, 1.21	0.3	−0.84, 1.44
Low risk	0.7	0.11	Ref.		0.4	0.07	Ref.			
Any drug use disorder[b,c]										
Very high risk	12.1	1.68	**9.7**	**6.39, 13.01**	13.7	2.39	**12.3**	**7.60, 17.00**	−2.6	−8.24, 3.04
High risk	7.2	1.43	**4.8**	**2.04, 7.56**	3.3	1.20	1.9	−0.45, 4.25	2.9	−0.88, 6.68
Moderate risk	5.1	0.95	**2.7**	**0.84, 4.56**	4.2	0.98	**2.8**	**0.86, 4.74**	−0.2	−2.65, 2.25
Low risk	2.4	0.18	Ref.		1.4	0.13	Ref.			
SF-12 functional impairment										
Very high risk	15.8	2.22	**9.5**	**5.11, 13.89**	25.9	3.38	**14.1**	**7.38, 20.82**	−4.6	−12.05, 2.85
High risk	8.5	1.44	2.2	−0.60, 5.00	16.7	3.21	4.9	−1.45, 11.25	−2.7	−9.64, 4.24
Moderate risk	8.0	1.17	1.6	−0.79, 3.99	15.3	1.73	**3.5**	**0.13, 6.87**	−1.9	−6.00, 2.20
Low risk	6.4	0.25	Ref.		11.8	0.37	Ref.			
Any depressive or anxiety disorder[d]										
Very high risk	18.4	2.07	**7.3**	**3.20, 11.40**	30.5	3.71	**7.8**	**0.49, 15.11**	−0.5	−8.77, 7.77
High risk	13.6	1.79	2.5	−1.03, 6.03	27.0	3.82	4.3	−3.21, 11.81	−1.8	−10.07, 6.47
Moderate risk	11.2	1.39	0.0	−2.70, 2.70	24.6	1.97	1.9	−2.02, 5.82	−1.9	−6.49, 2.69
Low risk	11.1	0.37	Ref.		22.7	0.56	Ref.			
Any depressive or anxiety disorder[d], not substance or illness induced										
Very high risk	16.8	2.03	**6.1**	**2.10, 10.10**	29.5	3.64	**7.6**	**0.43, 14.77**	−1.5	−9.61, 6.61
High risk	13.0	1.73	2.3	−1.11, 5.71	26.0	3.74	4.1	−3.25, 11.45	−1.8	−9.97, 6.37
Moderate risk	11.0	1.38	0.4	−2.29, 3.09	23.8	1.96	2.0	−1.88, 5.88	−1.6	−6.09, 2.89
Low risk	10.7	0.37	Ref.		21.9	0.55	Ref.			

[a] NESARC=National Epidemiologic Survey on Alcohol and Related Conditions; SF-12=12-Item Short Form Health Survey, version 2; WHO=World Health Organization. Liver disease was excluded from this table because of low prevalence in women. Prevalences are adjusted for sample weights and sociodemographic covariates (age, education, race/ethnicity, health insurance, and current smoking). The prevalence difference—prevalence in each risk level minus prevalence in the reference risk level (low)—indicates the association. The difference in prevalence difference—prevalence difference in men minus prevalence difference in women—indicates the differential association by gender. Prevalences, prevalence differences, and differences in prevalence differences are rounded, such that subtracting the values may not yield the exact difference reported. Prevalence differences whose 95% confidence intervals do not include 0 are statistically significant at $p<0.05$ and are in boldface.

[b] Alcohol and drug use disorders include abuse or dependence.

[c] Drug use disorders include marijuana, cocaine, heroin, painkillers (prescription opioids), sedative/tranquilizers, hallucinogens, stimulants, inhalants, and club drugs.

[d] Depressive and anxiety disorders include anxiety (panic disorder, agoraphobia, social phobia, specific phobia, generalized anxiety disorder) and depression (dysthymia, major depression), based on DSM-IV.

between drinking and functional impairment, depression, and anxiety.

While causality cannot be determined in these cross-sectional data sets, modeling alcohol consumption as preceding the outcomes (health conditions) is supported by the following. By definition, drinking precedes AUD. Drinking has an impact on liver function, causes liver disease, and exacerbates liver disease due to other causes (3). Heavy

TABLE 6. Association of WHO risk drinking level with health conditions in 2012–2013 (NESARC-III), by gender[a]

Health Condition and Risk Level	Men (N=11,935)				Women (N=13,724)				Difference in Prevalence Differences, Men Versus Women	
	Prevalence of Condition		Prevalence Difference		Prevalence of Condition		Prevalence Difference			
	%	SE	%	95% CI	%	SE	%	95% CI	%	95% CI
Alcohol dependence										
Very high risk	55.1	3.17	**49.7**	**43.47, 55.93**	54.3	3.18	**49.9**	**43.73, 56.07**	−0.2	−8.16, 7.76
High risk	40.7	2.78	**35.4**	**29.95, 40.85**	32.8	3.39	**28.4**	**21.76, 35.04**	7.0	−0.72, 14.72
Moderate risk	30.2	2.28	**24.9**	**20.41, 29.39**	19.8	1.57	**15.4**	**12.30, 18.50**	**9.5**	**4.21, 14.79**
Low risk	5.3	0.27	Ref.		4.4	0.25	Ref.			
Alcohol use disorder[b]										
Very high risk	73.7	2.86	**58.2**	**52.57, 63.83**	66.9	3.16	**57.6**	**51.33, 63.87**	0.6	−7.19, 8.30
High risk	59.6	2.63	**44.0**	**38.65, 49.35**	48.7	3.70	**39.4**	**32.03, 46.77**	4.7	−3.65, 13.05
Moderate risk	49.1	2.28	**33.5**	**28.84, 38.16**	35.2	1.65	**25.9**	**22.47, 29.33**	**7.6**	**1.82, 13.38**
Low risk	15.5	0.38	Ref.		9.3	0.35	Ref.			
Any drug dependence[c]										
Very high risk	7.7	1.12	**6.0**	**3.86, 8.14**	7.8	1.35	**6.2**	**3.57, 8.83**	−0.3	−3.22, 2.62
High risk	5.2	1.21	**3.4**	**1.01, 5.79**	3.3	0.91	1.8	−0.00, 3.60	1.7	−1.20, 4.60
Moderate risk	3.4	0.65	**1.7**	**0.35, 3.05**	2.2	0.49	0.6	−0.36, 1.56	1.0	−0.80, 2.80
Low risk	1.7	0.18	Ref.		1.5	0.16	Ref.			
Any drug use disorder[b,c]										
Very high risk	16.0	2.08	**10.8**	**6.74, 14.86**	19.0	2.13	**15.8**	**11.64, 19.96**	−5.0	−10.29, 0.29
High risk	12.9	1.78	**7.7**	**4.13, 11.27**	9.4	1.65	**6.2**	**3.01, 9.39**	1.5	−3.24, 6.24
Moderate risk	9.3	1.15	**4.1**	**1.75, 6.45**	6.3	0.80	**3.2**	**1.75, 4.65**	0.9	−1.90, 3.70
Low risk	5.2	0.27	Ref.		3.2	0.21	Ref.			
SF-12 functional impairment										
Very high risk	15.7	1.78	**5.6**	**1.99, 9.21**	36.3	2.91	**19.3**	**13.42, 25.18**	**−13.6**	**−20.26, −6.94**
High risk	13.1	1.58	3.0	−0.19, 6.19	19.8	2.83	2.8	−2.88, 8.48	0.2	−6.39, 6.79
Moderate risk	10.5	1.38	0.4	−2.44, 3.24	17.5	1.50	0.5	−2.54, 3.54	−0.1	−4.37, 4.17
Low risk	10.1	0.43	Ref.		17.0	0.48	Ref.			
Any depressive or anxiety disorder[d]										
Very high risk	18.4	2.07	2.4	−1.28, 6.08	43.3	3.15	**13.0**	**6.57, 19.43**	**−10.6**	**−17.81, −3.39**
High risk	18.9	1.69	3.1	−0.41, 6.61	30.5	3.12	0.2	−5.92, 6.32	2.9	−3.80, 9.60
Moderate risk	17.5	1.71	1.7	−1.79, 5.19	28.1	1.80	−2.2	−5.87, 1.47	3.9	−1.20, 9.00
Low risk	15.8	0.50	Ref.		30.3	0.66	Ref.			
Any depressive or anxiety disorder[d], not substance or illness induced										
Very high risk	17.6	1.77	2.7	−0.83, 6.23	41.7	3.14	**12.6**	**6.41, 18.79**	**−9.9**	**−17.09, −2.71**
High risk	18.0	1.66	3.2	−0.19, 6.59	29.1	3.09	0.1	−6.05, 6.25	3.1	−3.64, 9.84
Moderate risk	16.3	1.66	1.5	−1.85, 4.85	27.0	1.77	−2.1	−5.71, 1.51	3.5	−1.42, 8.42
Low risk	14.9	0.46	Ref.		29.1	0.67	Ref.			

[a] NESARC-III=National Epidemiologic Survey on Alcohol and Related Conditions–III; SF-12=12-Item Short Form Health Survey, version 2; WHO=World Health Organization. Liver disease was excluded from this table because of low prevalence in women. Prevalences are adjusted for sample weights and sociodemographic covariates (age, education, race/ethnicity, health insurance, and current smoking). The prevalence difference—prevalence in each risk level minus prevalence in the reference risk level (low)—indicates the association. The difference in prevalence difference—prevalence difference in men minus prevalence difference in women—indicates the differential association by gender. Prevalences, prevalence differences, and differences in prevalence differences are rounded, such that subtracting the values may not yield the exact difference reported. Prevalence differences whose 95% confidence intervals do not include 0 are statistically significant at $p<0.05$ and are in boldface.

[b] Alcohol and drug use disorders include abuse or dependence.

[c] Drug use disorders include marijuana, cocaine, heroin, painkillers (prescription opioids), sedative/tranquilizers, hallucinogens, stimulants, inhalants, and club drugs.

[d] Depressive and anxiety disorders include anxiety (panic disorder, agoraphobia, social anxiety disorder, specific phobia, generalized anxiety disorder) and depression (persistent depressive disorder, major depression), based on DSM-5.

drinking/AUD leads to functional impairment due to mental health issues (77). Drug use disorders and depressive and anxiety disorders are highly comorbid with alcohol use/AUD (5, 8, 42, 67, 78), with some (but not all) studies showing alcohol use/AUD preceding the comorbid disorders (79). In longitudinal studies, reduction in drinking was found to be associated with reduced likelihoods of these outcomes (18, 20, 22, 23), justifying the inference about directionality

modeled here. Further studies are warranted to better understand the complex and possibly reciprocal relationships between drinking and these conditions.

This study had several limitations. While the direction of effect modeled was well supported, cross-sectional data cannot determine causality. Data were based on self-report, leading to the possibility that response bias could contribute to the findings. A higher response rate for NESARC-III would be preferred, since survey respondents may be healthier than nonrespondents (80), and thus the prevalence of risky drinking and health conditions may be underestimated. Diagnoses were not made by clinicians, because clinician-administered interviews are not feasible in large-scale epidemiological surveys. Future studies of health conditions could incorporate direct examinations or medical record variables. Participants were not asked whether alcohol was the cause of their liver disease, but even in those with liver disease from other causes, alcohol use leads to further damage and a worse prognosis (3). Liver disease had low prevalence, especially among women. For depressive and anxiety disorders, the diagnostic systems could not be perfectly aligned, because DSM-IV diagnoses were used in the 2001–2002 survey and DSM-5 diagnoses in the 2012–2013 survey. However, the effect of these DSM differences should be small for a combined depressive/anxiety disorder variable, because some diagnoses would be made in both systems (81).

The study had several strengths as well: nationally representative data were used, with a sample large enough to include all the WHO risk drinking levels; there was representation of participants by gender, age, race/ethnicity, and socioeconomic status; the assessment of alcohol consumption and health conditions was detailed, rigorous, and consistent; and diagnoses were reliable and valid.

CONCLUSIONS

This study provides important information about the WHO risk drinking levels. The prevalence of moderate, high, and very high risk drinking increased over time, pointing to the increasing public health burden of individuals with potentially problematic drinking. Association of the WHO risk drinking levels with health conditions in both surveys, among men and women, shows their relevance as valid measures of drinking, since increased drinking was associated with increased risk. Thus, from the public health perspective, this metric of alcohol consumption is useful, and it can be adopted internationally by translating amounts of alcohol into country-specific standardized drinks. This metric also has clinical utility, since nonabstinent drinking reduction, that is, reducing consumption by one or two WHO risk drinking levels, leads to significant physical, psychological, and emotional improvement (14, 17–23). If clinicians and the general public became more aware that nonabstinent drinking reduction is feasible, sustainable, and beneficial to health, more individuals could be engaged in treatment, which is of great public health importance. The WHO risk drinking levels can be leveraged in prevention and intervention strategies for the public health goal of decreasing the personal and societal toll of risky alcohol use.

AUTHOR AND ARTICLE INFORMATION

Department of Psychiatry, Columbia University Irving Medical Center, New York (Shmulewitz, Aharonovich, Wall, Hasin); New York State Psychiatric Institute, New York (Shmulewitz, Aharonovich, Scodes, Wall, Hasin); Department of Psychology, University of New Mexico, Albuquerque (Witkiewitz); Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston (Anton); Department of Psychiatry, Perelman School of Medicine, University of Pennsylvania, Philadelphia (Kranzler); Crescenz Veterans Affairs Medical Center, Philadelphia (Kranzler); Central Institute of Mental Health, Medical Faculty Mannheim, Heidelberg University, Mannheim, Germany (Mann); Department of Biostatistics (Wall) and Department of Epidemiology (Hasin), Mailman School of Public Health, Columbia University, New York.

Send correspondence to Dr. Hasin (dsh2@columbia.edu).

Supported by NIH grant 1R01AA025309 (to Dr. Hasin), the New York State Psychiatric Institute, and the Veterans Integrated Service Network 4 Mental Illness Research, Education, and Clinical Center.

Drs. Witkiewitz, Anton, Kranzler, Mann, and Hasin are members of or have participated in meetings sponsored by the American Society of Clinical Psychopharmacology's Alcohol Clinical Trials Initiative (ACTIVE Group), which over the time that this study was conducted was supported by Alkermes, Amygdala Neurosciences, Arbor Pharmaceuticals, Ethypharm, Indivior, Lundbeck, Mitsubishi, and Otsuka. Dr. Anton has received grant funding from Laboratorio Pharmaceutico and has served as a consultant for Allergan, Alkermes, Dicerna, Insys, Laboratorio Pharmaceutico, and Life Technologies. Dr. Kranzler is named as an inventor on PCT patent application 15/878,640 (genotype-guided dosing of opioid agonists). Dr. Hasin has received funding from Campbell Alliance and has a contract with Syneos Health. The other authors report no financial relationships with commercial interests.

Received May 7, 2020; revision received August 26, 2020; accepted October 5, 2020; published online Jan. 21, 2021.

REFERENCES

1. Rehm J, Imtiaz S: A narrative review of alcohol consumption as a risk factor for global burden of disease. Subst Abuse Treat Prev Policy 2016; 11:37
2. World Health Organization: Global Status Report on Alcohol and Health, 2018. Geneva, World Health Organization, 2018. (https://www.who.int/substance_abuse/publications/global_alcohol_report/en/)
3. Rehm J, Shield KD: Global burden of alcohol use disorders and alcohol liver disease. Biomedicines 2019; 7:E99
4. GBD 2016 Alcohol and Drug Use Collaborators: The global burden of disease attributable to alcohol and drug use in 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Psychiatry 2018; 5:987–1012
5. Hasin DS, Stinson FS, Ogburn E, et al: Prevalence, correlates, disability, and comorbidity of DSM-IV alcohol abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 2007; 64:830–842
6. Cohen E, Feinn R, Arias A, et al: Alcohol treatment utilization: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. Drug Alcohol Depend 2007; 86:214–221
7. Shield KD, Rehm J, Rehm MX, et al: The potential impact of increased treatment rates for alcohol dependence in the United Kingdom in 2004. BMC Health Serv Res 2014; 14:53
8. Grant BF, Goldstein RB, Saha TD, et al: Epidemiology of DSM-5 alcohol use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA Psychiatry 2015; 72:757–766

9. Wallhed Finn S, Bakshi AS, Andréasson S: Alcohol consumption, dependence, and treatment barriers: perceptions among non-treatment seekers with alcohol dependence. Subst Use Misuse 2014; 49:762–769
10. Chartier KG, Miller K, Harris TR, et al: A 10-year study of factors associated with alcohol treatment use and non-use in a US population sample. Drug Alcohol Depend 2016; 160:205–211
11. Probst C, Manthey J, Martinez A, et al: Alcohol use disorder severity and reported reasons not to seek treatment: a cross-sectional study in European primary care practices. Subst Abuse Treat Prev Policy 2015; 10:32
12. van Amsterdam J, van den Brink W: Reduced-risk drinking as a viable treatment goal in problematic alcohol use and alcohol dependence. J Psychopharmacol 2013; 27:987–997
13. Mann K, Aubin HJ, Witkiewitz K: Reduced drinking in alcohol dependence treatment: what is the evidence? Eur Addict Res 2017; 23:219–230
14. Roerecke M, Sørensen P, Laramée P, et al: Clinical relevance of nalmefene versus placebo in alcohol treatment: reduction in mortality risk. J Psychopharmacol 2015; 29:1152–1158
15. Aubin HJ, Reimer J, Nutt DJ, et al: Clinical relevance of as-needed treatment with nalmefene in alcohol-dependent patients. Eur Addict Res 2015; 21:160–168
16. Falk DE, O'Malley SS, Witkiewitz K, et al: Evaluation of drinking risk levels as outcomes in alcohol pharmacotherapy trials: a secondary analysis of 3 randomized clinical trials. JAMA Psychiatry 2019; 76: 374–381
17. Witkiewitz K, Falk DE, Litten RZ, et al: Maintenance of World Health Organization risk drinking level reductions and posttreatment functioning following a large alcohol use disorder clinical trial. Alcohol Clin Exp Res 2019; 43:979–987
18. Hasin DS, Wall M, Witkiewitz K, et al: Change in non-abstinent WHO drinking risk levels and alcohol dependence: a 3 year follow-up study in the US general population. Lancet Psychiatry 2017; 4: 469–476
19. Witkiewitz K, Hallgren KA, Kranzler HR, et al: Clinical validation of reduced alcohol consumption after treatment for alcohol dependence using the World Health Organization risk drinking levels. Alcohol Clin Exp Res 2017; 41:179–186
20. Knox J, Wall M, Witkiewitz K, et al: Reduction in nonabstinent WHO drinking risk levels and change in risk for liver disease and positive AUDIT-C Scores: prospective 3-year follow-up results in the US general population. Alcohol Clin Exp Res 2018; 42:2256–2265
21. Witkiewitz K, Kranzler HR, Hallgren KA, et al: Drinking risk level reductions associated with improvements in physical health and quality of life among individuals with alcohol use disorder. Alcohol Clin Exp Res 2018; 42:2453–2465
22. Knox J, Scodes J, Wall M, et al: Reduction in non-abstinent WHO drinking risk levels and depression/anxiety disorders: 3-year follow-up results in the US general population. Drug Alcohol Depend 2019; 197: 228–235
23. Knox J, Wall M, Witkiewitz K, et al: Reduction in non-abstinent World Health Organization (WHO) drinking risk levels and drug use disorders: 3-year follow-up results in the US general population. Drug Alcohol Depend 2019; 201:16–22
24. World Health Organization: International Guide for Monitoring Alcohol Consumption and Related Harm. Geneva, World Health Organization, 2000
25. Grucza RA, Sher KJ, Kerr WC, et al: Trends in adult alcohol use and binge drinking in the early 21st-century United States: a meta-analysis of 6 national survey series. Alcohol Clin Exp Res 2018; 42:1939–1950
26. Grant BF, Chou SP, Saha TD, et al: Prevalence of 12-month alcohol use, high-risk drinking, and DSM-IV alcohol use disorder in the United States, 2001–2002 to 2012–2013: results from the National Epidemiologic Survey on Alcohol and Related Conditions. JAMA Psychiatry 2017; 74:911–923
27. Cheng HG, Kaakarli H, Breslau J, et al: Assessing changes in alcohol use and alcohol use disorder prevalence in the United States: evidence from national surveys from 2002 through 2014. JAMA Psychiatry 2018; 75:211–213
28. White A, Castle IJ, Chen CM, et al: Converging patterns of alcohol use and related outcomes among females and males in the United States, 2002 to 2012. Alcohol Clin Exp Res 2015; 39:1712–1726
29. Hasin DS, Shmulewitz D, Keyes K: Alcohol use and binge drinking among US men, pregnant and non-pregnant women ages 18–44: 2002–2017. Drug Alcohol Depend 2019; 205:107590
30. McHugh RKVV, Votaw VR, Sugarman DE, et al: Sex and gender differences in substance use disorders. Clin Psychol Rev 2018; 66: 12–23
31. Hasin DS, Saha TD, Kerridge BT, et al: Prevalence of marijuana use disorders in the United States between 2001–2002 and 2012–2013. JAMA Psychiatry 2015; 72:1235–1242
32. Martins SS, Sarvet A, Santaella-Tenorio J, et al: Changes in US lifetime heroin use and heroin use disorder: prevalence from the 2001–2002 to 2012–2013 National Epidemiologic Survey on Alcohol and Related Conditions. JAMA Psychiatry 2017; 74:445–455
33. Hasin DS, Shmulewitz D, Sarvet AL: Time trends in US cannabis use and cannabis use disorders overall and by sociodemographic subgroups: a narrative review and new findings. Am J Drug Alcohol Abuse 2019; 45:623–643
34. Kerridge BT, Chou SP, Pickering RP, et al: Changes in the prevalence and correlates of cocaine use and cocaine use disorder in the United States, 2001–2002 and 2012–2013. Addict Behav 2019; 90:250–257
35. Saha TD, Kerridge BT, Goldstein RB, et al: Nonmedical prescription opioid use and DSM-5 nonmedical prescription opioid use disorder in the United States. J Clin Psychiatry 2016; 77:772–780
36. Sacco P, Unick GJ, Kuerbis A, et al: Alcohol-related diagnoses in hospital admissions for all causes among middle-aged and older adults: trends and cohort differences from 1993 to 2010. J Aging Health 2015; 27:1358–1374
37. Doycheva I, Watt KD, Rifai G, et al: Increasing burden of chronic liver disease among adolescents and young adults in the USA: a silent epidemic. Dig Dis Sci 2017; 62:1373–1380
38. National Institute on Alcohol Abuse and Alcoholism: Surveillance Reports. 2018. https://pubs.niaaa.nih.gov/publications/surveillance.htm
39. White AM, Slater ME, Ng G, et al: Trends in alcohol-related emergency department visits in the United States: results from the Nationwide Emergency Department Sample, 2006 to 2014. Alcohol Clin Exp Res 2018; 42:352–359
40. Mojtabai R, Olfson M, Han B: National trends in the prevalence and treatment of depression in adolescents and young adults. Pediatrics 2016; 138:e20161878
41. Keyes KM, Jager J, Mal-Sarkar T, et al: Is there a recent epidemic of women's drinking? A critical review of national studies. Alcohol Clin Exp Res 2019; 43:1344–1359
42. Grant BF, Stinson FS, Dawson DA, et al: Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 2004; 61:807–816
43. Grant BF, Moore TC, Shepard J, et al: Source and Accuracy Statement: Wave 1 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Bethesda, Md, National Institute on Alcohol Abuse and Alcoholism, 2003
44. Grant BF, Chu A, Sigman R, et al: Source and Accuracy Statement: National Epidemiologic Survey on Alcohol and Related Conditions-III (NESARC-III). Rockville, Md, National Institute on Alcohol Abuse and Alcoholism, 2014
45. Grant BF, Stinson FS, Dawson DA, et al: Co-occurrence of 12-month alcohol and drug use disorders and personality disorders in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry 2004; 61:361–368

46. Hasin DS, Sarvet AL, Cerdá M, et al: US adult illicit cannabis use, cannabis use disorder, and medical marijuana laws: 1991–1992 to 2012–2013. JAMA Psychiatry 2017; 74:579–588
47. Olfson M, Blanco C, Wall M, et al: National trends in suicide attempts among adults in the United States. JAMA Psychiatry 2017; 74: 1095–1103
48. Hasin DS, Shmulewitz D, Cerda M, et al: US adults with pain, a group increasingly vulnerable to nonmedical cannabis use and cannabis use disorder: 2001–2002 and 2012–2013. Am J Psychiatry 2020; 177: 611–618
49. Grant BF, Dawson DA, Hasin DS: The Alcohol Use Disorder and Associated Disabilities Interview Schedule–DSM-IV version. Bethesda, Md, National Institute on Alcohol Abuse and Alcoholism, 2001
50. Grant BF, Goldstein RB, Chou SP, et al: The Alcohol Use Disorder and Associated Disabilities Interview Schedule–Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition Version (AUDADIS-5). Rockville, Md, National Institute on Alcohol Abuse and Alcoholism, 2011
51. Grant BF, Dawson DA, Stinson FS, et al: The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV): reliability of alcohol consumption, tobacco use, family history of depression, and psychiatric diagnostic modules in a general population sample. Drug Alcohol Depend 2003; 71:7–16
52. Grant BF, Harford TC, Dawson DA, et al: The Alcohol Use Disorder and Associated Disabilities Interview schedule (AUDADIS): reliability of alcohol and drug modules in a general population sample. Drug Alcohol Depend 1995; 39:37–44
53. Hasin D, Carpenter KM, McCloud S, et al: The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS): reliability of alcohol and drug modules in a clinical sample. Drug Alcohol Depend 1997; 44:133–141
54. Hasin DS, O'Brien CP, Auriacombe M, et al: DSM-5 criteria for substance use disorders: recommendations and rationale. Am J Psychiatry 2013; 170:834–851
55. Canino G, Bravo M, Ramírez R, et al: The Spanish Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS): reliability and concordance with clinical diagnoses in a Hispanic population. J Stud Alcohol 1999; 60:790–799
56. Chatterji S, Saunders JB, Vrasti R, et al: Reliability of the alcohol and drug modules of the Alcohol Use Disorder and Associated Disabilities Interview Schedule–Alcohol/Drug-Revised (AUDADIS-ADR): an international comparison. Drug Alcohol Depend 1997; 47:171–185
57. Cottler LB, Grant BF, Blaine J, et al: Concordance of DSM-IV alcohol and drug use disorder criteria and diagnoses as measured by AUDADIS-ADR, CIDI, and SCAN. Drug Alcohol Depend 1997; 47: 195–205
58. Grant BF: DSM-IV, DSM-III-R, and ICD-10 alcohol and drug abuse/harmful use and dependence, United States, 1992: a nosological comparison. Alcohol Clin Exp Res 1996; 20:1481–1488
59. Hasin D, Grant BF, Cottler L, et al: Nosological comparisons of alcohol and drug diagnoses: a multisite, multi-instrument international study. Drug Alcohol Depend 1997; 47:217–226
60. Ustün B, Compton W, Mager D, et al: WHO study on the reliability and validity of the alcohol and drug use disorder instruments: overview of methods and results. Drug Alcohol Depend 1997; 47: 161–169
61. Vrasti R, Grant BF, Chatterji S, et al: Reliability of the Romanian version of the alcohol module of the WHO Alcohol Use Disorder and Associated Disabilities Interview Schedule–Alcohol/Drug–Revised. Eur Addict Res 1998; 4:144–149
62. Ware J Jr, Kosinski M, Keller SDA: A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996; 34:220–233
63. Kirouac M, Stein ER, Pearson MR, et al: Viability of the World Health Organization quality of life measure to assess changes in quality of life following treatment for alcohol use disorder. Qual Life Res 2017; 26:2987–2997
64. Rubio JM, Olfson M, Villegas L, et al: Quality of life following remission of mental disorders: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. J Clin Psychiatry 2013; 74:e445–e450
65. Grant BF, Goldstein RB, Smith SM, et al: The Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5): reliability of substance use and psychiatric disorder modules in a general population sample. Drug Alcohol Depend 2015; 148:27–33
66. Hasin DS, Greenstein E, Aivadyan C, et al: The Alcohol Use Disorder and Associated Disabilities Interview Schedule-5 (AUDADIS-5): procedural validity of substance use disorders modules through clinical re-appraisal in a general population sample. Drug Alcohol Depend 2015; 148:40–46
67. Hasin DS, Sarvet AL, Meyers JL, et al: Epidemiology of adult DSM-5 major depressive disorder and its specifiers in the United States. JAMA Psychiatry 2018; 75:336–346
68. Hasin DS, Goodwin RD, Stinson FS, et al: Epidemiology of major depressive disorder: results from the National Epidemiologic Survey on Alcoholism and Related Conditions. Arch Gen Psychiatry 2005; 62:1097–1106
69. Hasin DS, Grant BF: The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) waves 1 and 2: review and summary of findings. Soc Psychiatry Psychiatr Epidemiol 2015; 50: 1609–1640
70. Eaton NR, Rodriguez-Seijas C, Carragher N, et al: Transdiagnostic factors of psychopathology and substance use disorders: a review. Soc Psychiatry Psychiatr Epidemiol 2015; 50:171–182
71. RTI International: SUDAAN, release 11.0.1. Research Triangle Park, NC, RTI International
72. Bieler GS, Brown GG, Williams RL, et al: Estimating model-adjusted risks, risk differences, and risk ratios from complex survey data. Am J Epidemiol 2010; 171:618–623
73. Gilbert PA, Pro G, Zemore SE, et al: Gender differences in use of alcohol treatment services and reasons for nonuse in a national sample. Alcohol Clin Exp Res 2019; 43:722–731
74. Peters TJML, Millward LM, Foster J: Quality of life in alcohol misuse: comparison of men and women. Arch Women Ment Health 2003; 6:239–243
75. Karpyak VMGJ, Geske JR, Hall-Flavin DK, et al: Sex-specific association of depressive disorder and transient emotional states with alcohol consumption in male and female alcoholics. Drug Alcohol Depend 2019; 196:31–39
76. Khan S, Okuda M, Hasin DS, et al: Gender differences in lifetime alcohol dependence: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Alcohol Clin Exp Res 2013; 37: 1696–1705
77. Dawson DA, Li TK, Chou SP, et al: Transitions in and out of alcohol use disorders: their associations with conditional changes in quality of life over a 3-year follow-up interval. Alcohol Alcohol 2009; 44: 84–92
78. Grant BF, Saha TD, Ruan WJ, et al: Epidemiology of DSM-5 drug use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions–III. JAMA Psychiatry 2016; 73:39–47
79. Castillo-Carniglia A, Keyes KM, Hasin DS, et al: Psychiatric comorbidities in alcohol use disorder. Lancet Psychiatry 2019; 6: 1068–1080
80. Keyes KM, Rutherford C, Popham F, et al: How healthy are survey respondents compared with the general population? Using survey-linked death records to compare mortality outcomes. Epidemiology 2018; 29:299–307
81. Center for Behavioral Health Statistics and Quality: 2014 National Survey on Drug Use and Health: DSM-5 Changes: Implications for Child Serious Emotional Disturbance (unpublished internal documentation). Rockville, Md, Substance Abuse and Mental Health Services Administration, 2016