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Heterogeneous Dose-Response and College Student Drinking: Examining Problem Risks Related to Low Drinking Levels

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Abstract

Background and aims—Previous research demonstrates that the number of problems related to each additional drink consumed on any drinking occasion, dose-response, varies nonlinearly across average drinking quantities. We test predictions from a dynamic model of drinking behavior that locates this heterogeneity in drinkers' efforts to equilibrate between costs and benefits of use.

Design—Equations derived from the theoretical model are used to assess dose-response across drinking quantity subgroups using censored regressions.

Setting—Fourteen California, USA college campuses surveyed from 2003–2011.

Participants—37,762 undergraduate college students 18 years of age and older.

Measurements—Drinking patterns, five physiological problems related to alcohol use (hangover, memory loss, medical treatment for overdose, nausea/vomiting, passing out) and student demographics.

Findings—Number of physiological problems related to each additional drink consumed was an inverse function of average drinking quantities ($b=0.2947$, $z=21.92$, $p<0.001$), differed by drinker age (of-age drinker $b=-0.1144$, $z=-3.95$, $p<0.001$) and gender (male $b=-0.3379$, $z=-18.56$, $p<0.001$) and, at the population level, drinking three drinks per occasion was associated with the greatest number of problems.

Conclusions—Among US college students, all drinkers exhibit greater risks for physiological problems related to alcohol use (hangover, memory loss, medical treatment for overdose, nausea/vomiting, passing out) when drinking greater amounts of alcohol, but heavier drinkers, (those who consume more on average) exhibit fewer problems for each additional drink consumed (less dose-response) than light and moderate drinkers. Light and moderate drinkers exhibit greater dose-response, with three drinks per occasion associated with the greatest number of problems.

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The amount of alcohol a drinker consumes on any drinking occasion is generally believed to be a function of real and perceived benefits and costs related to use (1, 2). Benefits include factors like neurophysiological responses to ethanol (3) and social amenities related to drinking (4). Costs include direct physiological consequences of use (e.g., hangovers), economic costs, and other potential problems (e.g., motor vehicle crashes). In a naïve way, drinkers can be viewed as trying to achieve a balance of benefits and costs related to drinking that enables them to drink with a minimum of negative consequences (2). While a strict behavioral economic treatment of drinking ignores many complexities of alcohol use, abuse, and addiction (5), this simple observation points toward a gap in the research literature: Epidemiological assessments of drinking and problems do not incorporate the implications of these dynamic processes in specifying statistical models of alcohol effects. Here we show that a model of these dynamics allows us to identify structural relationships between drinking and problems that can be assessed using cross-sectional data. This leads to a more informed approach by which to interpret results of epidemiologic assessments of problems related to alcohol use.

The proposed model assumes that drinkers experience different costs and benefits related to the amounts they consume on any occasion; variations in these costs and benefits lead them to drink different average quantities. At any average drinking quantity, say three drinks, one drinker may report many problems and another very few. Heterogeneous response to alcohol effects is reflected in differences in numbers of problems reported by drinkers who otherwise consume the same amounts of alcohol and differences in reported rates of problems associated with heavy drinking (6,7,8). All other things being equal, the drinker who experiences many problems related to consuming three drinks is less likely to continue to drink beyond this level than the drinker who experiences very few (2,9,10).

Theoretical Approach

We assume the number of problems that arise on any drinking event, P_{ε} , is proportional to the quantity of alcohol consumed on that occasion, $P_{\varepsilon} = \beta Q_{\varepsilon}$. β is a measure of dose-response, the additional number of problems that result from an increase in drinking quantity. We further assume that drinkers limit the amounts they consume conditional upon previous drinking problems, $Q_{\varepsilon} = K - \alpha P_{\varepsilon-1}$, where K is the number of drinks a drinker would consume if no problems occurred or if these problems did not affect subsequent decisions to drink and α is the proportional reduction in drinks related to problems. Combining equations, current drinking quantities are autoregressive functions of prior drinking levels, $Q_{\varepsilon} = K - \alpha \beta Q_{\varepsilon-1}$, as shown in prior work examining temporal feedback between drinking and problems (9,10,11). As shown in the Appendix, this system comes into equilibrium at drinking level Q^* :

$$Q^* = K / (1 + \alpha \beta) \quad (1)$$

Solving for β :

$$\beta = (K/\alpha)(1/Q^*) - (1/\alpha) \quad (2)$$

dose-response is inversely related to equilibrium drinking quantities, Q^* . Thus, although problems are linearly related to drinking quantities, $P_e = \beta Q_e$, dose-response is nonlinearly related to equilibrium drinking levels, Q^* . Since interpretations of the results of all cross-sectional analyses of drinking data rest on the assumption that equilibration has taken place between drinking and problems, this nonlinear relationship underlies all drinking-problem analyses. β will also be directly affected by covariates representing benefits associated with drinking, K , but these are not central to the current argument.

Empirical Approach

Empirical estimates of β may be obtained using methods that relate the number of self-reported drinking problems to self-reported drinking quantities (8). These methods are fully described in the Appendix and outlined here. We assume that number of problems that arise from drinking are proportional to the number of occasions on which different numbers of drinks are consumed, E_n , where $n = 1, 2, 3, \dots, N$ drinks. Drinking frequency, F , is the sum of drinking occasions on which 1 through n drinks are consumed, $F = E_1 + E_2 + E_3 + \dots + E_N$, and drinking volume, V , is the weighted sum of these occasions, $V = E_1 + 2E_2 + 3E_3 + \dots + NE_N$. The number of problems related to drinking, R , accumulated over time is assumed proportional to frequencies of drinking each different quantity, E_n :

$$R = \alpha_1 E_1 + \alpha_2 E_2 + \alpha_3 E_3 + \dots + \alpha_N E_N \quad (3)$$

with the α_n representing the number of problems that arise from each occasion of drinking n drinks. The α_n may take on any number of functional forms over n . If we assume all values of α_n are equal, $\alpha = \alpha_n$, then $R = \alpha F$; numbers of problems are proportional to drinking frequency. If we assume values of α_n are linear increasing so that $\alpha_n = n\beta$, then $R = \beta V$; numbers of problems are a linear function of drinking volume. If we assume that risks associated with the first drink are conflated with other non-drinking risks (12, 13), effects related to drinking frequencies, α , can be distinguished from those associated with greater volumes, β , by assessing dose-response in terms of increased risks for problems beyond the first drink, incorporating a measure of continued volume, $V - F$:

$$R = \mu + \alpha F + \beta (V - F) \quad (4)$$

This formulation has proven to be an adequate model of relationships between drinking and problems, but does not capture observed decreases in dose-response at higher drinking quantities. This effect has been empirically identified using a power exponent that represents decreases in dose-response at higher drinking levels (ζ , see Appendix) (8). Alternatively, equation 2 provides a theoretical basis and functional form for this effect; dose-response should decline as an inverse function of average drinking levels (Q), $\beta = a + b(1/Q)$:

$$R = \mu + \alpha F + a(V - F) + b(1/Q)(V - F) \quad (5)$$

We refer to the expected reciprocal relationship between β and Q^* as “heterogeneous dose-response” because β will vary as a function of equilibrium levels of alcohol use.

We use replicated cross-sectional data from a sample of college drinkers to assess whether dose-response is an inverse function of average drinking levels. We assume that self-reports of use and problems are in quasi-stable equilibrium and that observed average drinking quantities, Q , roughly approximate equilibrium drinking levels, Q^* . Our goals are to determine whether the heterogeneous dose-response model (equation 5) captures nonlinear patterns of dose-response observed in previous studies (8), show how measures of heterogeneous dose-response enable us to distinguish individual from population distributions of problem risks, and illustrate the impacts of heterogeneous dose-response on distributions of problems across gender and age groups. Since greater dose-response among lighter drinkers may be due to occasional heavy drinking, an alternative explanation for the expected dose-response effects, we also test whether those who exclusively drank less than four drinks on all occasions exhibited greater dose-response than those who sometimes drank more.

Methods

Survey data came from the Safer California Universities evaluation of community-based environmental alcohol risk management strategies to reduce campus drinking problems. Eight University of California and six California State University campuses were included in the study with survey data collected from random cross-sections of undergraduate students during fall semesters from 2003 to 2011 (14). This sample represented students from all university and most state campuses in California. The sample included 60,898 students, with 37,762 drinkers providing complete data on measures of drinking patterns, alcohol-related problems, and demographics. Response rates ranged from 50% in 2003 to 39% in 2008. Since these were less than optimal, post-hoc sample weights correcting for gender, ethnic group, age and grade distributions by campus were developed to adjust for differences in non-response. Interventions were implemented in seven campuses in 2005 and in the remaining seven campuses in 2008.

Drinking data were collected using a method designed to estimate relative frequencies of use across drinking quantities (16). Respondents indicated the number of times they consumed 1+, 2+, 3+, 6+, and 9+ drinks in the previous 28 days or, for low frequency drinkers, since the beginning of the semester (the latter were rescaled to the 28-day metric and so resulted in fractional values). A drink was defined as a 12-ounce glass or bottle of beer, 5-ounce glass of wine, or 1-ounce shot of spirits. The continued drinking data from each respondent were fit using a log-logistic model (with average R^2 values of 0.98) used to estimate the number of drinking occasions on which drinkers consumed 1 through 12 drinks over 28 days. Drinking measures derived from this procedure exhibit good reliability (16). Here we use measures of 28-day drinking frequency, F , average quantities used per occasion, Q , and a measure of continued drinking volume, $V-F$ (volume consumed beyond the first drink), to assess risks for drinking problems. Detailed information on distributions of use provided by this procedure allowed us to assess low dose effects predicted from the heterogeneous dose-response model; drinkers were segregated into those who drank no more than 3 drinks on 95% of all occasions and exhibited no evidence of heavy drinking vs. all other users.

The survey instrument asked students to assess drinking problems using a procedure common to college drinking studies for some decades (17). Students reported the number of times problems related to drinking had occurred between the beginning of the current semester and the time of the survey. These reports were converted to problem rates per 28 days. In this study we focused upon five physiological problems related to use because drinking is necessary and sufficient to produce these problems and we wished to avoid outcomes strongly affected by drinking contexts. Among drinkers, 53.1% reported hangovers in the previous 28 days, 25.3% reported forgetting some aspect of the drinking event, 0.6% reported medical treatment for overdose, 40.7% reported nausea/vomiting in response to use, and 22.2% reported passing out. Other measures included campus (dummy variables), gender, age (21+ vs. under 21), intervention campus (which varied by year) (yes/no), race (white vs. non-white), class (freshman, sophomore, junior, senior), current living situation (off-campus vs. on campus), use of a motor vehicle on campus (yes/no), marital status (married/not), employment (full/part time vs. none), and membership in a fraternity or sorority (yes/no).

Statistical Approach

Since the dependent measure represented rates of problems per 28 days, coefficients of equation 5 were directly estimated using generalized least squares regression procedures suitable for censored dependent variables. We assumed that equilibrium drinking levels, Q^* , were represented by average drinking levels, Q . F , V , and $V-F$ were given by self-reports. We used likelihood ratio tests to compare the performance of the heterogeneous dose-response model (equation 5) to a linear model in which $b = 0$ and a best fitting nonlinear dose-response model in which rates of problems are a power function of quantities consumed per drinking occasion (see reference 8 and Appendix, nonlinear coefficients estimated from a simplex search of the parameter space).

Each dose-response model provided estimates of the number of problems associated with a single occasion of drinking at each drinking quantity. These estimates were multiplied by observed average frequencies of drinking at each quantity to portray average risks for problems at each drinking quantity in the drinking population (the risk distribution). The mode of each risk distribution represents that quantity at which greatest numbers of problems appear in the population of drinkers. Weighting these values by population size then gives the population weighted risks for problems among college drinkers (the population weighted risk distribution).

Analyses were conducted using Tobit models with controls for heteroskedasticity related to frequency and continued volumes using the `tobithetm` command in Stata v.13.1 (see Appendix) (18). Models used population weights to ensure generalizability to all students attending university and state campuses. Subgroup analyses were conducted among men and women and drinkers under or of legal drinking age. The control covariate representing intervention effects and all other covariates were included in all analysis models. Campus membership was treated as a fixed effect; results assuming random campus effects were much the same so we report the unbiased fixed effects specification.

Results

Descriptive statistics for the sample and covariates appear in Table 1. Statistics for Q, F, and V–F are presented for the full sample and by subgroups. V–F represents the number of drinks consumed beyond the first drink across drinking occasions.

Figure 1 presents the average number of drinking days on which 1 through 12 drinks were consumed by all drinkers (top), the number of drinking days on which 1 through 12 drinks were consumed by subgroups of drinkers binned by average drinking quantities Q = 2, 4, 6, 8, and 10 drinks (middle), and those distributions weighted by subgroup population size (per 1000 college drinkers, bottom). The first graph shows that 1–4 drinks were consumed on a majority of drinking occasions across all college students. Heavier drinking was evident but less frequent. The second graph shows that heavier drinking subgroups drank more alcohol more frequently (F = 4.8, 5.6, 7.0, 8.8 and 11.2 days per month) and spread their drinking across a wider range of drinking quantities. The third graph shows that in the population of drinkers more drinking took place at lower quantities due to the large numbers of drinkers consuming at those levels.

Coefficient estimates for the linear, nonlinear, and heterogeneous dose-response equations are presented in Table 2. Coefficient estimates for the parameters of each dose-response model were different from zero and demonstrated expected relationships in each case: linear increasing ($\beta > 0.0$) for the linear dose-response model, nonlinear increasing and decelerating ($\beta > 0.0$, $\delta < 1.0$) for the nonlinear dose-response model, and linear increasing ($a > 0.0$) with decreasing slope ($b > 0.0$) for the heterogeneous dose-response model. Replicating earlier work, the nonlinear model significantly outperformed the linear model ($X^2 = 238.40$, $df = 1$, $p < 0.001$). The heterogeneous dose-response model also outperformed the linear model ($X^2 = 524.95$, $df = 1$, $p < 0.001$) and was a substantial improvement over the nonlinear model ($X^2 = 286.55$, non-nested X^2) with improved values for the Akaike Information Criterion (AIC) and pseudo- R^2 . Separate heterogeneous dose-response models for men vs. women and under vs. of-age drinkers also demonstrated linear increasing dose-response ($a > 0.0$) with decreasing slope ($b > 0.0$) and negative, significant interactions with decreasing slope for male gender and of-age status, respectively.

Figure 2 presents the linear, nonlinear, and heterogeneous dose-response functions estimated from the statistical analyses in Table 2. Noting that the heterogeneous dose-response model best fits the available data, the figure shows that the linear dose-response function overestimated problem risks at low and high drinking quantities. The improved fit of the nonlinear model is due to reduced risk estimates at low and high quantities and the improved fit of the heterogeneous dose-response model is due a further correction at high drinking quantities. As the standard error bars indicate, distinctions between the nonlinear and heterogeneous dose-response models were substantively small. Multiplying the three dose-response functions by the distribution of drinking levels (Figure 1), the risk distribution of problems related to drinking is given in the lower graph. These functions peak at two drinks for linear and nonlinear models but at three drinks for the better fitting heterogeneous dose-response model.

The top graph in Figure 3 presents the estimated dose-response function from the heterogeneous dose-response model averaged across all drinkers (gray line) and separated into linear components specific to average quantity subgroups defined in Figure 1; for clarity, the functions are trimmed to those drinking quantities which constituted 5% or more of each group's drinking events. As shown, the slopes of the separate dose-response functions decrease across heavier drinking groups. This illustrates the expected reduction in dose-response among heavier drinkers. Greater dose-response among lighter drinkers was not due to occasional heavy drinking events; those drinkers who consumed 3 or fewer drinks on 95% of their drinking occasions had much greater dose-response than other who sometimes consumed more ($b=0.0740$, $z=3.149$, $p=0.003$).

The second graph of Figure 3 displays the risk distributions for each subgroup obtained by weighting each dose-response function in the first graph of figure 3 by the drinking distributions shown in the second graph of Figure 1. As shown, drinkers who consumed more alcohol on average had much greater risks for problems than lighter drinkers. But when these distributions were further weighted by the population size of each subgroup (third graph of Figure 3) it appears that overall population risks for problems were dominated by low quantity drinkers. This was due to the much larger number of drinkers who consumed at lower average drinking levels.

Two examples of the implications of these observations for assessments of problems related to drinking are presented in Figure 4. The top two graphs show dose-response functions for men vs. women on the left and underage vs. of-age drinkers on the right. Women exhibit more problems per drinking occasion across all drinking quantities greater than one. Underage and of-age drinkers have largely the same dose-response as one would expect. The middle two graphs show the distributions of drinking days at each drinking level. Men drink more often at greater drinking quantities than women. Of-age drinkers drink far more often at low drinking levels than underage drinkers, representing an influx of lower quantity drinkers into the drinking population at age 21. The lower two graphs show the population risk distributions per 1000 persons for each of these groups. Women exhibit greater risks at lower drinking quantities, men exhibit greater risks at higher drinking quantities, of-age drinkers exhibit greater risks at lower quantities (because so many drinking events take place at these drinking quantities), and underage drinkers exhibit greater risks at higher drinking levels (because underage drinkers consume more often at these higher quantities).

Discussion

The data, models and methods presented in this paper demonstrate that risks related to drinking are nonlinearly related to standard measures of drinking frequency, volume and average drinking quantity. Greater numbers of physiological problems appear related to the consumption of greater amounts of alcohol by every drinker, but the strength of these relationships vary as a function of average drinking levels. Drinkers who consume more on average have fewer problems related to each additional drink consumed than those who consume less; in other words, they are less dose-responsive. The two empirical consequences of these observations are: (1) although risks related to drinking might arguably be linearly related to drinking frequencies and volumes, they are nonlinearly

related to average drinking levels and (2) aggregate population risks related to drinking peak at relatively modest drinking quantities, 2 to 3 drinks.

The central theoretical argument of this paper is that the dynamic determinants of drinking behaviors have direct implications for assessments of risks for problems related to alcohol use. We start with a simple dynamic model of how costs and benefits associated with alcohol use affect drinking over time. We show, first, that a linear discrete event formulation of these dynamics can be used to derive equilibrium conditions that relate drinking to problems and, second, that the derived dose-response relationships are nonlinear and contingent upon equilibrium drinking levels, Q^* . Q^* is unobservable, so we assume that this theoretical quantity is roughly equivalent to observed average drinking levels, Q , and that drinking levels and associated problems are in equilibrium. This is a strong assumption, but one commonly assumed without remark in the alcohol epidemiology literature. With this in mind, we show that it is possible to estimate nonlinear dose-response relationships using common drinking measures, that dose-response is reciprocally related to average drinking quantities, and that the resulting dose-response model performs better than previous models. We furthermore demonstrate that observed problems among lighter drinkers are not mainly due to occasional heavy drinking in these subgroups, and that the model can be used to provide detailed analyses of both individual and population distributions of problems related to drinking.

Differences in the individual vs. population distributions of problems related to drinking are often discussed in the literature but rarely quantitatively distinguished. We provide a quantitative expression of these differences that supports important contrasts between individual and population risks for problems suggested by the public health (19) and substance abuse (20) literatures. At the individual level problem risks increase monotonically over drinking quantities, and greater numbers of problems are associated with greater quantities consumed. However, at the population level numbers of problems peak at about three drinks and decline thereafter (Figure 2). The practical importance of these differences are striking when considering differences between men and women (Figure 4); at the individual level numbers of problems associated with greater drinking quantities grow more rapidly for women than men and at the population level women exhibit many more problems associated with drinking at moderate drinking levels (two through four drinks). Thus, there are two different definitions of “risky” drinking to be considered: At the individual level, greater drinking quantities pose greater risks for problems to individual drinkers. At the population level, greater drinking quantities pose greater risks for problems at moderate drinking levels. At the individual level, recommendations to curtail heavier drinking are the obvious messages to send to college drinkers. But at the population level, these messages may be to no avail, having little effect on the bulk of drinkers or drinking problems. For this reason, broad-based prevention programs incorporating efforts to reduce individual and population risks, particularly risks related to moderate drinking, will be most effective (21, 22).

Our model-based arguments are limited by the fact they are indeed model-based. Only limited empirical research is available by which to justify our dynamic formulation of drinking and problems. While many alcohol researchers may agree with this minimal

formulation, the underlying dynamic processes relating drinking to problems and problems to drinking are largely unknown and unidentified. Available studies indicate that these dynamics are much more detailed and complex; at the least these dynamics include context-specific drinking expectations, periodicities in drinking behaviors, and other autoregressive effects (9, 10, 11, 12, 13). It is also arguable that the survey drinking measures are not observed in equilibrium, especially in a cohort of college students undergoing rapid developmental change. More likely, college drinkers achieve temporary states of equilibrium that span several months then change as conditions warrant. Thus, the estimates provided here represent approximations to those that would be obtained under true equilibrium conditions (a limitation common to all statistical analyses of cross-sectional data).

Two final contributions of this study recommend new directions for research into drinking and problems. First, previous dose-response studies have shown that very detailed data on the distribution of drinking quantities across drinking occasions are required to identify nonlinear relationships between drinking and problems. We show here that that this level of detail is not required for a general assessment of nonlinear relationships between drinking quantities and drinking problems. In the absence of detailed individual drinking data, standard measures of F, V, and Q (e.g., any measure of average or typical quantity) can be used to assess overall problem risks (Figure 2) and heterogeneities in dose-response (Figure 3). When weighted by population distributions of average drinking levels, these can provide marginal assessments of individual and population risks related to use. Second, improved models of dynamic relationships between drinking and problems can inform future individual and population models of problem risks. While moment-to-moment relationships between drinking and problems can only be studied using time series data, equilibrium relationships derived from dynamic models can inform cross-sectional analyses of drinking problems enabling, for example, detailed examinations of quantitative relationships between drinking contexts and drinking problems (12, 13) and assessments of neurocognitive characteristics of drinkers (e.g., depression, impulsivity) as they affect problem response and subsequent use (3, 5).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix

Derivation of equilibrium conditions for the heterogeneous dose-response model proceeds by defining dose-response, β , as the number of problems, P_ε , that arise in response to drinking different quantities of alcohol, Q_ε , on successive drinking events, ε :

$$P_\varepsilon = \beta Q_\varepsilon \quad \text{A.1}$$

β is in the metric of number of problems per drink consumed. We assume that K drinks would be consumed in the absence of the occurrence of any problems associated with use and that current drinking quantities are conditional upon the numbers of problems that occurred on previous drinking events, $\varepsilon - 1$:

$$Q_\varepsilon = K - \alpha P_{\varepsilon-1} \quad \text{A.2}$$

α is in the metric of drinks per unit problem. Thus, numbers of problems that arose on previous drinking events affect current drinking quantities. Substituting A.1 into A.2, current drinking quantities are an autoregressive function of previous drinking quantities:

$$Q_\varepsilon = K - \alpha \beta Q_{\varepsilon-1} \quad \text{A.3}$$

In equilibrium current and past drinking quantities are equal, $Q^* = Q_\varepsilon = Q_{\varepsilon-1}$, and:

$$Q^* = K / (1 + \alpha \beta) \quad \text{A.4}$$

which can be solved for β :

$$\beta = (K/\alpha)(1/Q^*) - (1/\alpha) \quad \text{A.5}$$

The model predicts that dose-response will be an inverse function of equilibrium quantities, Q^* .

This simplest of models is discrete (i.e., each event is separable from every other), interprets time in terms of succession rather than duration (i.e., the length of time between events is immaterial to the autoregressive adjustment process), and focuses only upon the negative feedback relating numbers of problems to subsequent drinking quantities. The model is deliberately impoverished in these respects. A more realistic model would allow drinking events to arise continuously in time and enable both positive and negative feedback to affect use. Varying inter-arrival times between drinking events and continuous time periodic and autoregressive effects may be incorporated by shifting from event, ε , to continuous time, t . The discrete formulation can be extended to incorporate benefits related to alcohol use that either affect K , the target level of the adjustment process, or Q_ε , direct impacts of benefits on subsequent drinking decisions. These different assumptions have theoretical implications, but importantly neither of these enhancements would alter the relationship between dose-response, β , and equilibrium quantities, Q^* , expressed in equation A.5.

Although it is possible to empirically assess the degree to which observed average drinking quantities, Q , approximate equilibrium drinking levels, Q^* , by a direct examination of the autoregressive processes outlined by equation A.3, β remains unmeasurable without a more detailed formal analysis of empirical drinking-problem data. In previous work we have shown how this may be accomplished. Estimates of β , the increase in the number of problems related to a unit increase in number of drinks consumed, can be obtained from statistical analyses of drinking data using a formal measurement model (8), an analysis of quantitative relationships between drinking and problems that provides a measure of differences in numbers of problems related to differences in drinking quantities consumed over time. Critically, although drinking and problems may be linearly related one to the other on an event-to-event basis as expressed in equation A.1, relationships between drinking and problems in aggregate survey data are not. The alcohol problems reported in epidemiologic survey data accumulate across many different drinking events at many different levels of use. Therefore, aggregate relationships between measures of use and problems must be formally identified in order to extract estimates of dose-response from survey data.

We accomplish this objective by explicitly modeling “exposures” to alcohol and their relationships to problems using a quantitative dose-response model (8). We define monthly drinking frequencies, F , as the sum of days on which $n = 0, 1, 2, 3, \dots, N$ drinks are consumed so that $F = E_1 + E_2 + E_3 + \dots + E_N$. The E_n represent “exposures” to drinking “ n ” drinks on “ E_n ” days. For example, E_3 represents the number of days on which three drinks were consumed. The accumulated number of problems over one month, R , is then assumed to be proportional to quantities of alcohol used on each day:

$$R = \alpha_1 E_1 + \alpha_2 E_2 + \alpha_3 E_3 + \dots + \alpha_N E_N \quad A.6$$

The α_n are in units of problems per drinking event. If $\alpha = \alpha_1 = \alpha_2 = \alpha_3 = \dots = \alpha_N$, then:

$$R = \alpha (E_1 + E_2 + E_3 + \dots + E_N) = \alpha F \quad A.7$$

This equation clarifies what is being estimated when problem measures are regressed over measures of drinking frequency in epidemiologic studies. If the α_n are linear increasing with slope β , then $\alpha_n = n\beta$ so that $\alpha_1 = \beta$, $\alpha_2 = 2\beta$, $\alpha_3 = 3\beta$, etc., and:

$$R = \beta E_1 + 2\beta E_2 + 3\beta E_3 + \dots + N\beta E_N \quad A.8$$

where β is the increase in numbers of problems with each increase in quantity consumed, dose-response. Note that $E_1 + 2E_2 + 3E_3 + \dots + NE_N = V$ is the volume of alcohol consumed, and now $R = \beta V$; this provides a definition of volume effects observed in epidemiologic studies.

As a matter of practice, since drinking frequencies are conflated with problems related to other aspects of drinking contexts (e.g., unique risks related to the presence of other drinkers in those contexts, (11, 12)), it is important to distinguish risks related to the first drink

consumed on each occasion, α , from risks related to greater quantities consumed (dose-response, β). This requires a reformulation of equation A.6 as:

$$R = (\alpha)E_1 + (\alpha + \beta)E_2 + (\alpha + 2\beta)E_3 + \dots + [\alpha + (N-1)\beta]E_N \quad A.9$$

where all drinking events E_n have a component of risk related to the first drink consumed, α , and each subsequent drink adds β units of additional risk. Equation A.9 can be rearranged as:

$$R = \alpha(E_1 + E_2 + E_3 + \dots + E_N) + \beta[E_2 + 2E_3 + \dots + (N-1)E_N] \quad A.10$$

Remembering that $F = E_1 + E_2 + E_3 + \dots + E_N$ and $V = E_1 + 2E_2 + 3E_3 + \dots + NE_N$ then $V - F = E_2 + 2E_3 + 3E_4 + \dots + (N-1)E_N$ and equation A.10 can be reduced to:

$$R = \mu + \alpha F + \beta(V - F) \quad A.11$$

where $V - F$ is the continued volume of alcohol consumed, the volume consumed beyond the first drink. Notice that α refers to the number of problems per drinking occasion that arise in correspondence to the first drink consumed and β refers to the increase in the number of problems that arise in correspondence to each increase in quantity beyond that point. This measure of β is our empirical estimate of dose-response. The nonlinear role of average drinking quantities becomes evident by noting that $V = QF$ and therefore:

$$R = \mu + \alpha F + \beta F(Q - 1) \quad A.12$$

Thus, one can think of drinking quantities as moderating frequency effects, increasing the impacts of F on R for each unit increase in Q .

As shown in previous studies, β is an increasing decelerating function of drinking levels such that $\beta_i = \delta(i-1)^\zeta$ where $i = 1, 2, 3, \dots, n$ drinks consumed on any drinking occasion and $\zeta < 1.0$. Both parameters δ and ζ can be estimated using a simplex search algorithm suited to a variant of equation A.8 with β suitably redefined (8). Importantly, this nonlinear model fits data on problems related to drinking better than the linear model expressed in equation A.11. However, this observation also suggests that any function which expresses β as an increasing decelerating function of drinking levels will capture much the same information. This is the case expressed by equation A.5 where dose-response, β , is a reciprocal function of drinking quantities, Q^* :

$$\beta = a + b(1/Q^*) \quad A.13$$

leading to the reduced form equation used to estimate heterogeneous dose-response in the current study:

$$R = \mu + \alpha F + [a + b(1/Q)](V - F) \quad A.14$$

where $Q = 1, 2, 3, \dots N$ average drinks, $\beta = a + b$ when $Q = 1$, and $\beta \rightarrow a$ when $Q \rightarrow \infty$. “Heterogeneity” in dose-response refers to the different β s that arise as a function of Q ; estimates of β should be large when Q is small and small when Q is large.

Finally, assuming errors in equations A.13 and A.14, e and ε respectively, the estimable reduced form becomes:

$$\begin{aligned} R &= \mu + \alpha F + [a + b(1/Q^*) + e](V - F) + \varepsilon \\ R &= \mu + \alpha F + a(V - F) + b(1/Q^*)(V - F) + [e(V - F) + \varepsilon] \end{aligned} \quad A.15$$

showing that errors in parameter estimates will be heteroskedastic over V and F . While there may be other sources of heteroskedastic measurement error in statistical analyses of linear dose-response models, it is clear that controls for heteroskedasticity related to V and F are crucial to minimize bias in parameter estimates.

Figure 1. Distributions of average number of drinking days by drinking quantities for (a) all drinkers, (b) drinkers grouped by average number of drinks consumed, and (c) weighted by subgroup population size per 1000 college drinkers.

Figure 2. Linear, nonlinear, and heterogeneous (a) dose-response functions and (b) population risk distributions per 28 days

Figure 3. Heterogeneous dose-response disaggregated by subgroup (a) dose-response functions, (b) risk distributions, and (c) population weighted risk distributions

Figure 4.
Heterogeneous dose-response functions, drinking and risk distributions by gender and age group

Table 1

Descriptive Statistics (n=37,762)

Drinking measures		Mean (SD)
Mean quantity (Q)	Overall	3.211 (2.044)
	Men	3.705 (2.282)
	Women	2.865 (1.780)
	Underage	3.556 (2.142)
	Of-Age	2.904 (1.901)
Frequency (F) *	Overall	5.904 (5.664)
	Men	6.885 (6.281)
	Women	5.216 (5.075)
	Underage	5.010 (4.841)
	Of-Age	6.700 (6.199)
Continued volumes (V-F) *	Overall	16.911 (26.910)
	Men	23.066 (32.763)
	Women	12.595 (20.835)
	Underage	17.044 (26.086)
	Of-Age	16.792 (27.623)
Number of physiological problems *	Overall	1.233 (1.966)
Other measures		n (%)
Sex	Male	15,564 (41.22%)
Age	Of-age drinker	19,970 (52.88%)
Currently employed	Yes	20,535 (54.38%)
Fraternity/sorority member	Yes	4,356 (11.54%)
Married	Yes	1,614 (4.27%)
Access to a car for personal use	Yes	26,489 (70.15%)
Where are you living?	Off campus	30,046 (79.57%)
	Residence hall/dorm	6,507 (17.23%)
	Student co-op	248 (0.66%)
	Fraternity/sorority	718 (1.90%)
	Other	243 (0.64%)
Campus intervention?	Yes	19,205 (50.86%)
Race	White	21,274 (56.34%)
Academic year	Freshman	5,652 (14.97%)
	Sophomore	6,288 (16.65%)
	Junior	11,300 (29.92%)
	Senior	14,522 (38.46%)

*
In the past 28 days

Table 2
Tobit coefficients of linear, non-linear, and heterogeneous dose-response models (n=37,762)

Linear Dose-Response		B	Z	95% CI
Dose-response effects	Drinking Risks (α)	0.0617	21.56	(0.0561, 0.0673)*
	Dose-Response function slope (β)	0.0591	70.52	(0.0575, 0.0608)*
Covariates	Currently employed	0.0854	4.55	(0.0487, 0.1221)*
	Fraternity/sorority member	0.3845	13.5	(0.3287, 0.4403)*
	Married	-0.6965	-14.56	(-0.7902, -0.6028)*
	Access to a car	-0.0801	-3.49	(-0.1250, -0.0352)*
	Living off campus	0.0948	3.23	(0.0373, 0.1523)*
	Sophomore	0.0920	2.65	(0.0238, 0.1602)*
	Junior	0.0323	0.88	(-0.0393, 0.1038)
	Senior	0.0981	2.27	(0.0132, 0.1829)*
	Campus intervention	-0.0329	-1.81	(-0.0686, 0.0028)
	White	0.0929	4.97	(0.0562, 0.1295)*
	Of-age drinker	-0.1262	-4.34	(-0.1831, -0.0692)*
	Male	-0.3379	-18.56	(-0.3735, -0.3022)*
Constant		-0.4775	-7.60	(-0.6007, -0.3543)*
Sigma		1.2354	121.25	(1.2154, 1.2554)*
Pseudo-R ²	0.0912			
AIC	109602.3			
Nonlinear Dose-Response				
Dose-response effects	Drinking Risks (α)	0.0120	3.54	(0.0054, 0.0186)*
	Dose-Response function slope (β)	0.1393	72.75	(0.1356, 0.1431)*
	Dose-response function exponent (ρ)	0.6117	26.50	(0.5679, 0.6584)*
Covariates	Currently employed	0.0861	4.59	(0.0493, 0.1228)*

	B	Z	95% CI
Fraternity/sorority member	0.3644	12.79	(0.3086, 0.4202)*
Married	-0.6686	-13.92	(-0.7627, -0.5744)*
Access to a car	-0.0749	-3.27	(-0.1198, -0.0300)*
Living off campus	0.1060	3.62	(0.0485, 0.1634)*
Sophomore	0.0864	2.49	(0.0184, 0.1544)*
Junior	0.0348	0.95	(-0.0366, 0.1062)
Senior	0.0956	2.21	(0.0108, 0.1804)*
Campus intervention	-0.0332	-1.82	(-0.0689, 0.0026)
White	0.0896	4.80	(0.0530, 0.1262)*
Of-age drinker	-0.1160	-3.99	(-0.1729, -0.0590)*
Male	-0.3088	-17.03	(-0.3444, -0.2733)*
Constant	-0.5288	-8.42	(-0.6519, -0.4058)*
Sigma	1.2218	121.85	(1.2022, 1.2415)*
Pseudo-R ²	0.0931		
AIC	109363.9		
Heterogeneous Dose-Response			
Dose-response effects			
Drinking Risks (α)	-0.0478	-8.01	(-0.0595, -0.0361)*
Dose-response, slope (a)	0.0297	19.62	(0.0268, 0.0327)*
Dose-response, heterogeneity (b)	0.2947	21.92	(0.2683, 0.3210)*
Covariates			
Currently employed	0.0822	4.4	(0.0456, 0.1188)*
Fraternity/sorority member	0.3599	12.68	(0.3043, 0.4155)*
Married	-0.6341	-13.21	(-0.7281, -0.5400)*
Access to a car	-0.0758	-3.32	(-0.1205, -0.0311)*
Living off campus	0.1026	3.52	(0.0454, 0.1598)*
Sophomore	0.0812	2.35	(0.0135, 0.1488)*
Junior	0.0289	0.8	(-0.0421, 0.1000)
Senior	0.0864	2	(0.0019, 0.1708)*

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	B	Z	95% CI
Campus intervention	−0.0334	−1.84	(−0.0690, 0.0022)
White	0.0811	4.36	(0.0446, 0.1176)*
Of-age drinker	−0.1144	−3.95	(−0.1711, −0.0577)*
Male	−0.3242	−17.88	(−0.3597, −0.2887)*
Constant	−.04664	−7.46	(−0.5890, −0.3439)*
Sigma	1.2108	121.59	(1.1913, 1.2303)*
Pseudo-R ²	0.0955		
AIC	109079.3		

* p<0.05

Pseudo-R² calculated using McFadden's vs. a null model with no dose-response covariates