



Published in final edited form as:

*Drug Alcohol Depend.* 2018 September 01; 190: 159–165. doi:10.1016/j.drugalcdep.2017.12.035.

## Male-Female Differences in the Onset of Heavy Drinking Episode Soon after First Full Drink in Contemporary United States: From Early Adolescence to Young Adulthood

Hui G. Cheng and James C. Anthony

Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, 48824, USA

### Abstract

**Background**—Globally, there is a male excess in the occurrence of heavy drinking once alcoholic beverages are consumed, with some new evidence that this ‘gender gap’ might be null among underage drinkers. Here, we estimate age-specific male-female differences in heavy drinking episode (HDE) incidence across the first eight calendar-quarters after first full drink.

**Methods**—Study population is non-institutionalized civilians in the United States (2006-2014). Standardized audio computer-assisted self-interviews were used to assess the date of first full drink and the date of first HDE (i.e., 5+ drinks on one occasion) among ~33,000 12-to-21-year-old newly incident drinkers (all with 1<sup>st</sup> full drink and HDE evaluated within 24 months of drinking onset). Time-to-HDE survival analyses are used to estimate age-specific male-female ratios in the hazard of HDE onset.

**Results**—We found that among early adolescent new drinkers (drinking onset at age 11-14), the newly incident drinking females progress to HDE more quickly than males (HR=1.3, 95% CI=1.1, 1.6). In contrast, male excess risk is observed when drinking starts at or after age 15 years. For underage drinkers, age-specific hazard ratios (HR) depend upon age at first full drink.

**Conclusions**—Based on recent survey data from the US, this study's survival analyses support early adolescent female excess in the onset of HDE. When drinking starts at or after age 15 years, a male excess becomes apparent within two years since first full drink. Future studies may probe any sex-specific mechanisms toward the rapid onset of HDE at different age groups.

### 1. Introduction

Heavy drinking causes substantial health and socioeconomic burden in the United States (US) and other countries, especially among adolescents and young adults (Rehm et al., 2010; Spear and Swartzwelder, 2014). Adolescents are especially vulnerable to alcohol-induced neurocognitive deficits compared to adults, due to the developmental nature of this period (Crego et al., 2009; Crews et al., 2007). In addition, early onset of heavy drinking is a predictor of later alcohol-related problems (Kuntsche et al., 2016, 2013).

\* Address correspondence to: James C. Anthony, Ph.D., Professor, Department of Epidemiology and Biostatistics, Michigan State University, East Lansing, MI 48823, janthony@msu.edu.

**Conflict of Interest:** None

A consistent male excess in heavy drinking, a traditional ‘masculine’ behavior, has been reported around the world (Holmila and Raitasalo, 2005; Keyes and Miech, 2013; Slade et al., 2016; Wilsnack et al., 2009). In the US, adult males are two to five times more likely to experience a recent heavy drinking episode (HDE) compared to females (Kerr et al., 2009; Wilsnack et al., 2009). Some studies in the adult population in the US and many other countries have found evidence supporting a narrowing of the ‘gender gap’ in heavy drinking, with smaller male-female ratios in younger cohorts compared to older cohorts (Johnson and Gerstein, 1998; Keyes et al., 2011; Keyes and Miech, 2013; Slade et al., 2016). Compared to adults, smaller male-female differences have been reported for adolescents for the prevalence of heavy drinking (Johnston et al., 2016; White et al., 2015). For example, estimates from the US National Surveys on Drug Use and Health (NSDUH) show a 1-2% male excess in heavy drinking during the past 30 days among 12-17 year olds as an aggregate and a ~15% male excess in young adults (White et al., 2015). Grade-specific point estimates from the US Monitoring the Future study suggest a slightly higher prevalence of HDE among girls in 8<sup>th</sup> grade, a slightly higher prevalence among boys in 10<sup>th</sup> grade, and a larger male excess in 12<sup>th</sup> graders (Johnston et al., 2016).

Although HDE prevalence provides insights about the extent of the problem, few studies have focused on the ‘risk’ of becoming a case of HDE once drinking starts. That is, prevalence estimates are affected by two different processes, namely the risk of onset and persistence (Kramer, 1957; Lapouse, 1967). Causes and mechanisms for these two processes can differ. In addition, the occurrence of HDE is composed of two processes, namely, the onset of drinking and the transition from drinking to HDE. With a focus on the onset of drinking, we recently discovered an early-adolescent female excess in drinking onset (Cheng et al., 2016b). In this context, it is not clear whether the slightly higher prevalence of HDE documented in the Monitoring the Future study is due to drinking onset, or due to the transition from drinking to HDE, or both. A sole focus on HDE ‘risk’ estimates provides important information about rapid escalation of drinking soon after drinking onset, the key period for prevention and intervention strategies (McBride and Cheng, 2011), especially for adolescent underage drinking. In a previous study of newly incident drinkers who had their first full drink during the 12 months prior to the survey, we found an early-adolescent male-female parity in the risk of transition from 1<sup>st</sup> drink to 1<sup>st</sup> HDE by the time of assessment; among older new drinkers, a male excess is seen (Cheng and Anthony, 2016). Nonetheless, in this study new drinkers had a window varying from one month to 12 months since their 1<sup>st</sup> full drink. Therefore, there is uncertainty about the timing of onset of HDE once drinking had started. For example, HDE might emerge immediately after drinking onset, or might be delayed until later after the drinking onset. There are questions about the natural history of HDE onset, or “mechanisms” through which being a male or a female might be linked to greater risk of HDE onset. Built upon previous investigations, we seek to estimate the male-female differences in the *onset* of HDE using time-to-event information among newly incident drinkers 12-21 years of age in the US in relation to four age groups spanning from early adolescence to young adulthood. Specification of these four groups is grounded in recent empirical evidence on incidence rates for newly incident drinking in the US (Cheng et al., 2016a, 2016b). Specifically, we categorized newly incident drinkers into four groups based on their age at first drink: 11-14 (early-adolescence-onset new drinkers), 15-17 (mid-

adolescence-onset new drinkers), 18-20 (early-adult-onset underage drinkers), and 21 (early-adult ‘postponers’). This categorization is guided by a previously described pattern of drinking incidence, characterized by a sharp increase among 12-15 year olds, a more gradual increase from 16 to 18, a dip at 19 and 20, and a high peak at 21 (Cheng et al., 2016a). This specification is generally in line with the US school system: age 11-14 is middle school; age 15-17 is high school; age 18-20 is the transition to college or working; age 21 is the legal drinking age.

Guided by previous studies, our hypothesis is a consistent male excess in the occurrence of HDE onset among 12-to-21-year-old newly incident drinkers with a smaller male-female ratio among early adolescents. An alternative is that the male-female difference might have become null among early adolescents. Compared to studies with multiple assessments over time or with long-term recall, this study's tight focus on recent experiences no more than 24 months prior to the assessment helps restrain response reactivity and recall bias (i.e., “forward telescoping”) (Shillington et al., 2012; Shillington and Clapp, 2000). Estimates are from nine successive cross-sectional national surveys (2006-2014). Compared to the data pooling approach, our use of meta-analysis to summarize single-year estimates helps assess the consistency of estimates year by year.

## 2. Materials and Methods

### 2.1 Study population and sample

The study population consisted of non-institutionalized civilians in the US, with nine independently drawn nationally representative samples of 12-to-21-year-olds from NSDUH, with oversampling of 12-17 year olds, using a multi-stage sampling method after Institutional-Review-Board-approved parent consent and child assent (United States, 2015, 2012). Participation level ranges were 72%-76%, yielding over 240,000 12-to-21 year olds. In contrast to school or household surveys of adolescents, the NSDUH sample includes young people irrespective of school attendance, and its sampling frame includes non-household group quarters such as homeless shelters. More details about the NSDUH methodology is provided in previous publications (United States, 2012; United States Substance Abuse and Mental Health Services Administration, 2014).

### 2.2 Assessments

NSDUH confidential assessments were audio computer assisted self-interviews (ACASI), each with standardized multi-item modules on health and drugs, including alcohol use. A full drink was defined as “a can or bottle of beer, a glass of wine or a wine cooler, a shot of liquor, or a mixed drink with liquor in it” (United States, 2015). In this study, HDE is defined as 5+ drinks on one occasion. Among individuals who had their first full drink at the current age or a year younger (current age minus one), ACASI items assessed month, year, and age at first full drink. This approach identified 33,908 12-to-21-year-olds who had their first full drink within 24 months prior to the assessment. A similar approach is used for the assessment of first HDE onset. Information about the date of first HDE is available from 2006 to 2014.

Information about sex and age are from survey items in the Demographics module. When these items are missing, information from the household roster is used.

### 2.3 Analysis approach

The outcome for this study is the time from first drink to first HDE. For newly incident drinkers who had a HDE onset within two years of drinking onset, the analysis time is the interval between the first drink and the first HDE (i.e., subtracting the date of first full drink from the date of first HDE using the month and year of first use and the month and year of first HDE variables). For newly incident drinkers who did not have HDE within two years of drinking onset, the analysis time is the interval between the first full drink and the interview (i.e., subtracting the date of first full drink from the date of assessment using the quarter and year of first use and the quarter and year of assessment variables; right-censored). Because only the quarter of the year when the interview was conducted is available in the publicly downloadable NSDUH data sets, the unit of analysis is person-quarter-year in this study's analyses.

Kaplan–Meier estimators were used to describe sex-specific time to first HDE among newly incident drinkers for each of the four pre-defined age-of-onset groups. Next, we used Cox proportional hazard regression models to estimate year-specific female-male hazard ratios (HR) for the onset of HDE for these four age-of-onset groups, with HR estimates from each year, 2006-2014 (Yan, 2004). Variations in female-male HRs were evaluated using sex-by-age product terms. Log-log plots were used to examine the proportional hazard assumption. Our final analysis steps involved meta-analysis to summarize year-specific estimates. Random-effects estimators were used when heterogeneity was detected (DerSimonian and Laird, 1986; Higgins et al., 2003). Results are presented in forest plots to aid the assessment of consistency. Age-specific estimates are presented in the supplementary material as a post-hoc check for possible heterogeneity within each age-of-onset stratum. The rationale to use meta-analysis is to take into account potential heterogeneities and to assess consistencies across years. More details about the use of meta-analysis in this context is provided in a previous publication (Cheng et al., 2016a).

In this research, we followed previous studies and specified HDE onsets within 24 months after first full drink with phrases and terms such as 'HDE soon after first drink' and 'rapid HDE onset' (O'Brien and Anthony, 2009; Reboussin et al., 2006). We provide an exploratory sub-study to empirically assess the median induction interval using survival analysis. In order to explore potential influence of memory errors, we constrained the analysis to those who consumed their first full drink within the six months prior to the assessment (Engels et al., 1997; Kuntsche et al., 2016; Shillington et al., 2012). Details of these sub-studies are presented in the online supplementary material.

Analysis weights were used to adjust for selection probability, and post-stratification factors were used to bring the sample into balance with the source population. The NSDUH methodological summary provides details about the calculation of weights and post-stratification factors (United States., 2014). Standard errors and 95% confidence intervals (CI) are from complex survey delta methods. Analyses were conducted using the Stata statistical software version 14.2 (StataCorp, College Station, Texas, USA).

### 3. Results

To reiterate, this project's survival analysis results are focused on the first Heavy Drinking Episode (HDE) as experienced during the first eight calendar-months after the first full drink (i.e., 'rapid-onset' HDE), whereas prior reports have been focused on estimation of "30-day prevalence proportions" and "cumulative incidence estimates." Table 1 offers a description of the study sample. The mean interval from the 1<sup>st</sup> full drink to 1<sup>st</sup> HDE decreases with age. No male-female difference is seen for 11-20 year olds. For 21 year olds, males have a shorter mean interval compared to females.

Figure 1 presents sex-specific HDE onset for the four age-of-onset groups. (Supplementary Figure S1 presents age-specific hazard functions.) For early-adolescence-onset new drinkers (i.e., age of onset between 11 and 14), HDE tends to occur sooner in females than in males, whereas the opposite is true for the three older groups. Log-log plots show generally parallel lines for males and females for all age groups (supplementary Figure S2); tests based on Schoenfeld residuals reveal no evidence for violation of the proportional hazard assumption ( $p=0.67, 0.59, 0.22, \text{ and } 0.60$  for the four age-of-onset groups) (Schoenfeld, 1982). Therefore, we turned to the Cox regression modeling approach. The sex-by-age product terms indicate smaller female-male HRs in the three older age-of-onset groups compared to the youngest group (i.e., drinking onset at 11-14 years of age). No variations in female-male HRs are found across the three older groups.

Figure 2 presents estimated female-male ratio for the onset of HDE for each of the drinking-onset age groups. For early-adolescence-onset new drinkers, the point estimates for female-male hazard ratios are greater than one for each survey year, except for 2013. The meta-analytic summary estimate reveals a robust female excess for the rapid progression from 1<sup>st</sup> drink to 1<sup>st</sup> HDE (estimated HR=1.3, 95% CI=1.1, 1.6). In the other age subgroups, newly incident drinking females have a lower hazard for the onset of HDE compared to male new drinkers who started drinking at the same age (15-17 year olds: HR= 0.7, 95% CI=0.7, 0.8; 18-20 year olds: HR= 0.6, 95% CI=0.5, 0.7; 21 year olds: HR= 0.7, 95% CI=0.5, 0.9). For those with first full drink at 15-20 years of age, the estimates are consistent across years, but when drinking was postponed to the legal minimum drinking age at 21, there is a wider variation in estimates across years. Nonetheless, for these 'postponers', the meta-analysis summary estimate for the female-male contrast is inverse, as shown in the final panel of Figure 2.

Exploratory analyses to probe age-specific estimates disclosed congruent patterns with the one described above: estimates showing female excess risk among those who started drinking between 11 and 14, and a male excess among those who started later (Figure 3).

We also provide forest plots of sex-specific hazard ratios comparing age groups in supplementary Figure S3 for interested readers. Among males, positive hazard ratios are seen for rapid-onset HDE when comparing the three older age groups with early adolescent underage drinkers. A similar pattern is observed for females except that no appreciable difference is seen when comparing 21-year-onset and early-adolescent-onset new drinkers (meta-analysis summary= 0.8, 95% CI=0.6, 1.1, Figure S3 Panel 9).

In the post-estimation exploratory analyses which focused on the subsample of newly incident drinkers who had their first full drink during the six-month interval before assessment, the just-described pattern is observed (e.g., early female excess risk of HDE; supplementary Table S1).

## 4. Discussion

Against a historical background of a consistently documented male excess in prevalence of HDE, as well as a recently described male-female parity in early adolescents in the US, the especially noteworthy finding of this study is a *female excess* risk for a fairly rapid onset of the first HDE not long after consumption of the first full drink, when drinking starts in early adolescence (i.e., at age 11-14 years). The evidence from basic Kaplan-Meier survival analyses is strengthened by this study's multiple yearly replications and meta-analysis. In contrast, when drinking starts at or after age 15 years, a clear male excess risk is observed. These results on a female excess risk of HDE among early adolescent drinkers are congruent with recently reported US estimates showing what now is a *female excess* in the risk of becoming a new drinker during early adolescence, as well as evidence suggesting a female excess risk of making a rapid transition from the first full drink to alcohol dependence, also observed during early adolescence (Cheng et al., 2016b; Cheng and Anthony, 2016). Some differences are noted as well. The male excess in the risk of HDE in older adolescents and young adults is not observed for drinking onset or rapid transition to alcohol dependence (Cheng et al., 2016b, 2016c). In addition, the female excess was not seen in a previous analysis on cumulative incidence of HDE among newly incident drinkers as an aggregate (Cheng and Anthony, 2016).

### 4.1 Limitations and Strengths

This study's findings should be interpreted with the following important limitations in mind. Of central concern to us is the lack of fine-grained information about the exact dates of the first drink and the first HDE. Moreover, due to the lack of the exact dates of the ACASI assessment, we had to specify our unit of analysis as person-quarter-year instead of person-month or person-day.

In this study, our definition of HDE deviates from the US National Institute of Alcoholism and Alcohol Abuse definition of binge drinking, which is “a pattern of drinking that brings blood alcohol concentration (BAC) levels to 0.08 g/dL. This typically occurs after 4 drinks for adult women and 5 drinks for adult men—in about 2 hours.”(National Institute on Alcohol Abuse and Alcoholism, 2004). We did not use different metrics for males and females for two reasons. First, we held the metric constant in order to provide initial evidence for a measurable behavior. Second, the validity of the 5/4 drinks threshold to reach a BAC of 0.08 g/dL is less clear for adolescents. That is, if we had used a 5+ drinks HDE case definition for males and a 4+ drinks HDE case definition for females, any observed female-male difference might be due to this sex-related variation in the case definition (Cheng and Anthony, 2016). To be sure, BAC variations are crucial in research on alcohol toxicity and physiological changes after alcohol intake.

Nonetheless, in this research on first occurrence of HDE, it is not necessary to conduct any analysis in order to check whether our main finding about the early adolescent female excess is contradicted when sex-specific HDE case definitions are used. By reducing to a 4+ drink case definition for females and by leaving the male case definition at 5+ drinks, the female excess in early adolescence would become even larger than we now estimate with the case definition held constant. After early adolescence, the male excess would become smaller or null.

Some readers may be concerned about our study of newly incident drinkers in a cross-sectional sample versus the hypothetical alternative of studying newly incident drinkers in a prospectively conducted follow-up study. With respect to these issues, there is no ambiguity about the order of events: first drink precedes first HDE (when it occurs), and the assessment comes next. With respect to the cross-sectional approach, any prospectively designed study approach will confront similar issues with respect to newly incident drinkers unless the approach includes elements such as continuous time monitoring of the first full drink and the first HDE. Readers will appreciate that the cross-sectional approach used in this investigation does not suffer from the almost certain attrition from the sample and response reactivity that must be faced during prospective studies of adolescents (Anthony, 2010). In addition, prospective studies of nationally representative samples are not always feasible.

Several other study strengths deserve attention. First, our tight focus on newly incident drinkers restricts the recall period to a relatively short interval prior to the survey assessment, which should help constrain memory errors (i.e., telescoping) (Engels et al., 1997; Shillington et al., 2012). Few HDE studies with samples of adults or older adolescents have had recall intervals as short as the intervals specified in this investigation. Second, with respect to the hazard ratio estimates from Cox regressions, our meta-analysis approach provides an assessment of the consistency of estimates from independently drawn nationally representative samples taken in each survey year. In addition, the use of ACASI assessments with a nationally representative probability sample should enhance validity of the survey estimates, relative to available alternatives. Last but not the least, our study population is not restricted to school-attending individuals, which enhances the external validity of this study. In sum, the novelty of this study is the focus on incidence estimates based on nationally representative samples of all non-institutionalized residents in our specified age range.

## 4.2 Interpretation of findings

We do not interpret this study's estimates in terms of causal relationships linking age of first drink and the development of rapid-onset HDE because age of first drink clearly is not assigned at random; it apparently depends upon uncontrolled background susceptibility traits such as gestational age, tendencies to engage in socially maladaptive behavior and norm violations, as well as one's chances to try an alcoholic beverage precociously (Do et al., 2016; Kuntsche et al., 2016). Rather, our new discovery shows age-varying male-female differences in HDE occurrence during a relatively short time after the first full drink.

At present we cannot offer a solid theory or a definitive answer as to why or how it happens that we are observing this *female excess* in HDE onset during the early adolescent years, but some speculations are possible. Social norms and stigma-laden views about female drinking

often have been cited as major contributors to the widely documented male excess in HDE around the globe; changes in these social norms have been noted (e.g., reduced stigma toward female drinking and heavy drinking) (Rahav et al., 2006; Wilsnack et al., 2009; Wilsnack and Wilsnack, 1992), and it is possible that within the US, especially during early adolescence, there is an incomplete expression of stigma-laden views about female drinking practices. We also can note maturational changes that occur throughout adolescence, with implications for physiological processes, acquisition of social skills, and configuration of sex- and gender-related social roles and identities (Casey et al., 2008; Schulte et al., 2009). Of special importance might be maturational acceleration with girls entering puberty earlier than boys, with concomitant increases in novelty-seeking and risk-taking (Casey et al., 2008).

### 4.3 Implications and Future Directions

Despite the lack of a complete understanding of the *female excess* in HDE onset during early adolescence, HDE is an established cause for injuries and death from injury (Borges et al., 2013; Taylor et al., 2010). In addition, early onset HDE predicts later alcohol-related problems, and it has been associated with an array of adverse outcomes including use of other drugs, teen pregnancies, and dropping out of school (Kuntsche et al., 2013; Rehm et al., 2010; Salas-Wright et al., 2015). Previous prevention and intervention strategies have focused on males because of the consistently documented male excess (Kuhn, 2015; Schulte et al., 2009). Our finding of a *female excess* in rapid-onset HDE among very young new drinkers provides additional evidence that these strategies must encompass early female drinking as well, at least within the US.

We are confident that future research can build from findings such as these in order to understand the underlying mechanisms that account for observed age-dependent patterns of male-female differences in HDE onset soon after drinking initiation. In order to be definitive, these future studies must be based upon a comprehensive conceptual model that can bridge multiple scientific disciplines, given the likely importance of genetics and birth influences, physical growth and developmental maturation, peer influences, parenting practices, neighborhood and school environments, and gender role expectations (Ahern et al., 2008).

### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

### Acknowledgments

The authors are grateful to the United States Substance Abuse and Mental Health Services Administration Office of Applied Studies (now the Center for Behavioral Health Statistics and Quality) for completion of its annual nationally representative surveys on drug use and health, as well as its direction and supervision of the annual data gathering and preparation of public use datasets. We wish to thank the National Institute of Drug Abuse (NIDA T32 DA021129 [HGC] and K05DA015799 [JCA]) and Michigan State University to fund the current analysis. We also wish to thank Dr. Cora Lee Wetherington for her helpful comments and careful review of the manuscript as well as Dr. Brian Fairman for valuable insights about the assessment procedure.

**Funding:** The study is supported by funds from the National Institute on Drug Abuse grants K05DA015799 (to JCA), and T32DA021129 (to HGC), as well as Michigan State University. The opinions expressed in this paper are



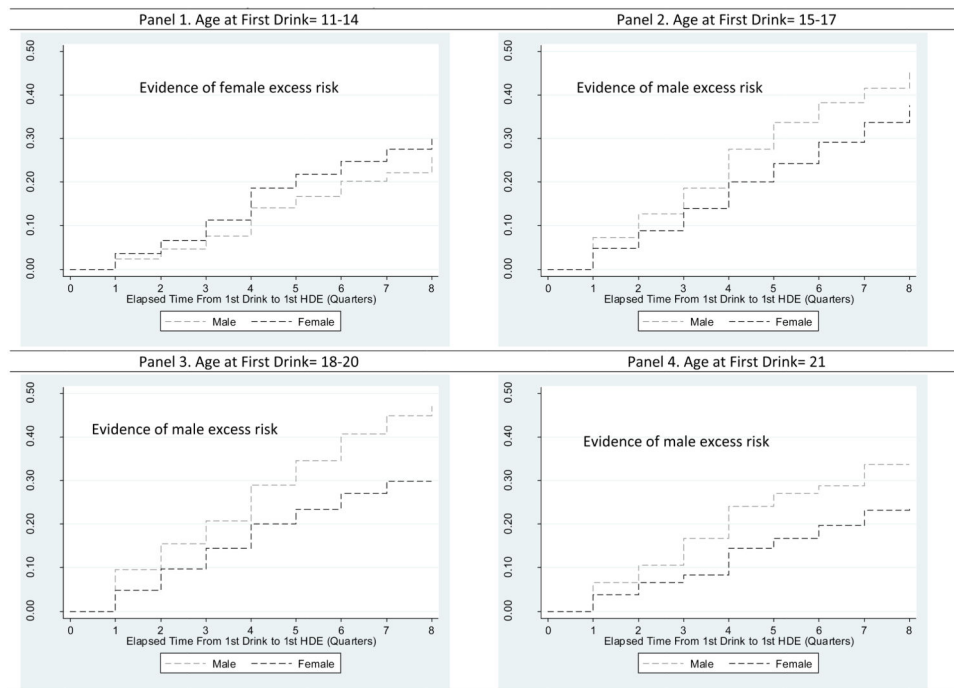
solely those of the authors and do not reflect those of the sponsoring agencies, which included the National Institute of Drug Abuse, the National Institutes of Health, and Michigan State University.

## References

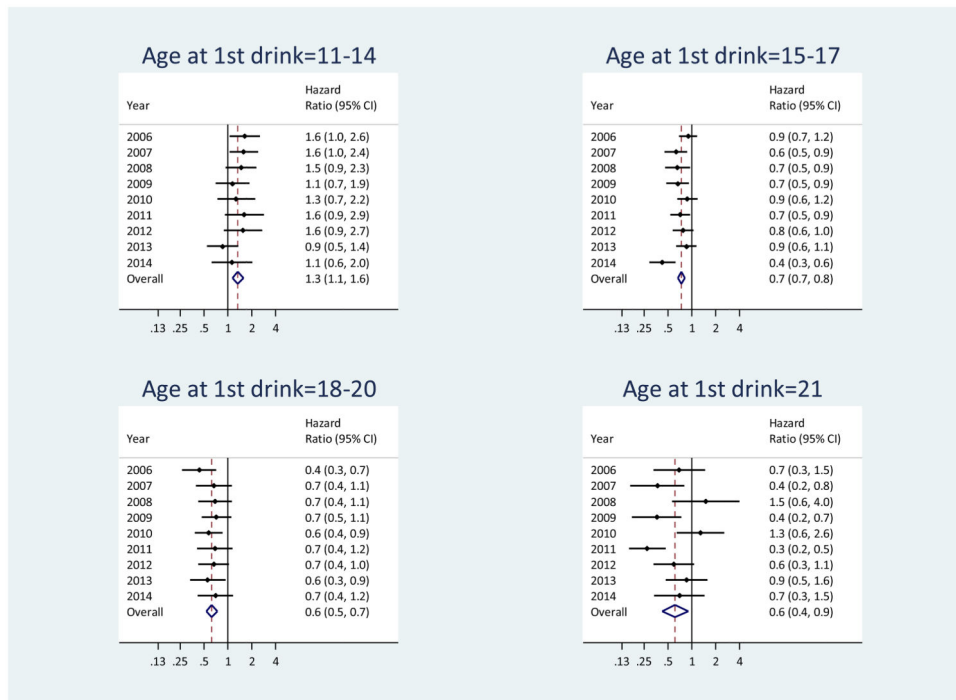
- Ahern J, Galea S, Hubbard A, Midanik L, Syme SL. "Culture of drinking" and individual problems with alcohol use. *Am J Epidemiol*. 2008; 167:1041–1049. DOI: 10.1093/aje/kwn022 [PubMed: 18310621]
- Anthony JC. Novel phenotype issues raised in cross-national epidemiological research on drug dependence. *Ann N Y Acad Sci*. 2010; 1187:353–369. DOI: 10.1111/j.1749-6632.2009.05419.x [PubMed: 20201862]
- Borges G, Orozco R, Monteiro M, Cherpitel C, Then EP, López VA, Bassier-Paltoo M, Weil DA, M de Bradshaw A. Risk of injury after alcohol consumption from case-crossover studies in five countries from the Americas. *Addiction*. 2013; 108:97–103. DOI: 10.1111/j.1360-0443.2012.04018.x [PubMed: 22775508]
- Casey BJ, Jones RM, Hare TA. The adolescent brain. *Ann N Y Acad Sci*. 2008; doi: 10.1196/annals.1440.010
- Cheng HG, Anthony JC. Does our legal minimum drinking age modulate risk of first heavy drinking episode soon after drinking onset? Epidemiological evidence for the United States, 2006–2014. *PeerJ*. 2016; 4:e2153.doi: 10.7717/peerj.2153 [PubMed: 27366651]
- Cheng HG, Cantave MD, Anthony JC. Taking the First Full Drink: Epidemiological Evidence on Male-Female Differences in the United States. *Alcohol Clin Exp Res*. 2016b; 40:816–25. DOI: 10.1111/acer.13028 [PubMed: 27038595]
- Cheng HG, Cantave MD, Anthony JC. Alcohol experiences viewed microscopically: Newly incident drinking of twelve- to twenty-five-year-olds in the United States, 2002–2013. *J Stud Alcohol Drugs*. 2016a; 77:405–412. DOI: 10.15288/jsad.2016.77.405 [PubMed: 27172572]
- Cheng HG, Chandra M, Alcover KC, Anthony JC. Rapid transition from drinking to alcohol dependence among adolescent and young-adult newly incident drinkers in the United States, 2002–2013. *Drug Alcohol Depend*. 2016c; 168:61–68. DOI: 10.1016/j.drugalcdep.2016.08.015 [PubMed: 27620346]
- Crego A, Holguin SR, Parada M, Mota N, Corral M, Cadaveira F. Binge drinking affects attentional and visual working memory processing in young university students. *Alcohol Clin Exp Res*. 2009; 33:1870–1879. DOI: 10.1111/j.1530-0277.2009.01025.x [PubMed: 19673739]
- Crews F, He J, Hodge C. Adolescent cortical development: a critical period of vulnerability for addiction. *Pharmacol Biochem Behav*. 2007; 86:189–199. DOI: 10.1016/j.pbb.2006.12.001 [PubMed: 17222895]
- DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986; 7:177–188. DOI: 10.1016/0197-2456(86)90046-2 [PubMed: 3802833]
- Do EK, Latendresse SJ, Edwards AC, Kendler KS, Dick DM, York TP. Associations Between Gestational Age at Birth and Alcohol Use in the Avon Longitudinal Study of Parents and Children. *Alcohol Clin Exp Res*. 2016; 40:1328–1338. [PubMed: 27155784]
- Engels RCME, Knibbe RA, Drop MJ. Inconsistencies in adolescents' self-reports of initiation of alcohol and tobacco use. *Addict Behav*. 1997; 22:613–623. DOI: 10.1016/S0306-4603(96)00067-6 [PubMed: 9347063]
- Higgins JPT, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ*. 2003; 327:557–560. DOI: 10.1136/bmj.327.7414.557 [PubMed: 12958120]
- Holmila M, Raitasalo K. Gender differences in drinking: Why do they still exist? *Addiction*. 2005; : 1763–1769. DOI: 10.1111/j.1360-0443.2005.01249.x [PubMed: 16367976]
- Johnson RA, Gerstein DR. Initiation of use of alcohol, cigarettes, marijuana, cocaine, and other substances in US birth cohorts since 1919. *Am J Public Heal*. 1998; 88:27–33.
- Johnston LD, O'Malley PM, Miech RA, Bachman JG, Schulenberg JE. Monitoring the Future results on drug use: 1975–2015: Overview, Key Findings on Adolescent Drug Use, 2015. *Ann Arbor Inst Soc Res Univ; Michigan*: 2016.

- Kerr WC, Greenfield TK, Bond J, Ye Y, Rehm J. Age-period-cohort modelling of alcohol volume and heavy drinking days in the US National Alcohol Surveys: divergence in younger and older adult trends. *Addiction*. 2009; 104:27–37. DOI: 10.1111/j.1360-0443.2008.02391.x
- Keyes KM, Li G, Hasin DS. Birth cohort effects and gender differences in alcohol epidemiology: a review and synthesis. *Alcohol Clin Exp Res*. 2011; 35:2101–2112. DOI: 10.1111/j.1530-0277.2011.01562.x [PubMed: 21919918]
- Keyes KM, Miech R. Age, period, and cohort effects in heavy episodic drinking in the US from 1985 to 2009. *Drug Alcohol Depend*. 2013; 132:140–148. DOI: 10.1016/j.drugalcdep.2013.01.019 [PubMed: 23433898]
- Kramer M. A discussion of the concepts of incidence and prevalence as related to epidemiologic studies of mental disorders. *Am J Public Heal Nations Heal*. 1957; 47:826–840.
- Kuhn C. Emergence of sex differences in the development of substance use and abuse during adolescence. *Pharmacol Ther*. 2015; 153:55–78. DOI: 10.1016/j.pharmthera.2015.06.003 [PubMed: 26049025]
- Kuntsche E, Rossow I, Engels R, Kuntsche S. Is “age at first drink” a useful concept in alcohol research and prevention? We doubt that *Addiction*. 2016; 111:957–965. DOI: 10.1111/add.12980 [PubMed: 26147610]
- Kuntsche E, Rossow I, Simons-Morton B, Bogt TT, Kokkevi A, Godeau E. Not early drinking but early drunkenness is a risk factor for problem behaviors among adolescents from 38 European and North American countries. *Alcohol Clin Exp Res*. 2013; 37:308–314. DOI: 10.1111/j.1530-0277.2012.01895.x [PubMed: 23240610]
- Lapouse R. Problems in studying the prevalence of psychiatric disorder. *Am J Public Heal Nations Heal*. 1967; 57:947–954.
- McBride O, Cheng HG. Exploring the emergence of alcohol use disorder symptoms in the two years after onset of drinking: Findings from the National Surveys on Drug Use and Health. *Addiction*. 2011; 106:555–563. DOI: 10.1111/j.1360-0443.2010.03242.x [PubMed: 21182549]
- National Institute on Alcohol Abuse and Alcoholism. NIAAA Council Approves Definition of Binge Drinking. *NIAAA Newsl*. 2004; 3:3.
- O'Brien MS, Anthony JC. Extra-medical stimulant dependence among recent initiates. *Drug Alcohol Depend*. 2009; 104:147–155. DOI: 10.1016/j.drugalcdep.2009.04.016 [PubMed: 19515516]
- Rahav G, Wilsnack R, Bloomfield K, Gmel G, Kuntsche S. The influence of societal level factors on men's and women's alcohol consumption and alcohol problems. *Alcohol Alcohol Suppl*. 2006; 41:i47–55. DOI: 10.1093/alcalc/agl075 [PubMed: 17030503]
- Reboussin BA, Song EY, Shrestha A, Lohman KK, Wolfson M. A latent class analysis of underage problem drinking: evidence from a community sample of 16-20 year olds. *Drug Alcohol Depend*. 2006; 83:199–209. DOI: 10.1016/j.drugalcdep.2005.11.013 [PubMed: 16359829]
- Rehm J, Baliunas D, Borges GL, Graham K, Irving H, Kehoe T, Parry CD, Patra J, Popova S, Poznyak V, Roerecke M, Room R, Samokhvalov AV, Taylor B. The relation between different dimensions of alcohol consumption and burden of disease: an overview. *Addiction*. 2010; 105:817–843. DOI: 10.1111/j.1360-0443.2010.02899.x [PubMed: 20331573]
- Salas-Wright CP, Vaughn MG, Ugalde J, Todic J. Substance use and teen pregnancy in the United States: evidence from the NSDUH 2002-2012. *Addict Behav*. 2015; 45:218–225. DOI: 10.1016/j.addbeh.2015.01.039 [PubMed: 25706068]
- Schoenfeld D. Partial residuals for the proportional hazards regression model. *Biometrika*. 1982; 69:239–241. DOI: 10.1093/biomet/69.1.239
- Schulte MT, Ramo D, Brown SA. Gender differences in factors influencing alcohol use and drinking progression among adolescents. *Clin Psychol Rev*. 2009; doi: 10.1016/j.cpr.2009.06.003
- Shillington AM, Clapp JD. Self-report stability of adolescent substance use: are there differences for gender, ethnicity and age? *Drug Alcohol Depend*. 2000; 60:19–27. [PubMed: 10821986]
- Shillington AM, Woodruff SI, Clapp JD, Reed MB, Lemus H. Self-Reported Age of Onset and Telescoping for Cigarettes, Alcohol, and Marijuana Across Eight Years of the National Longitudinal Survey of Youth. *J Child Adolesc Subst Abus*. 2012; 21:333–348. DOI: 10.1080/1067828X.2012.710026

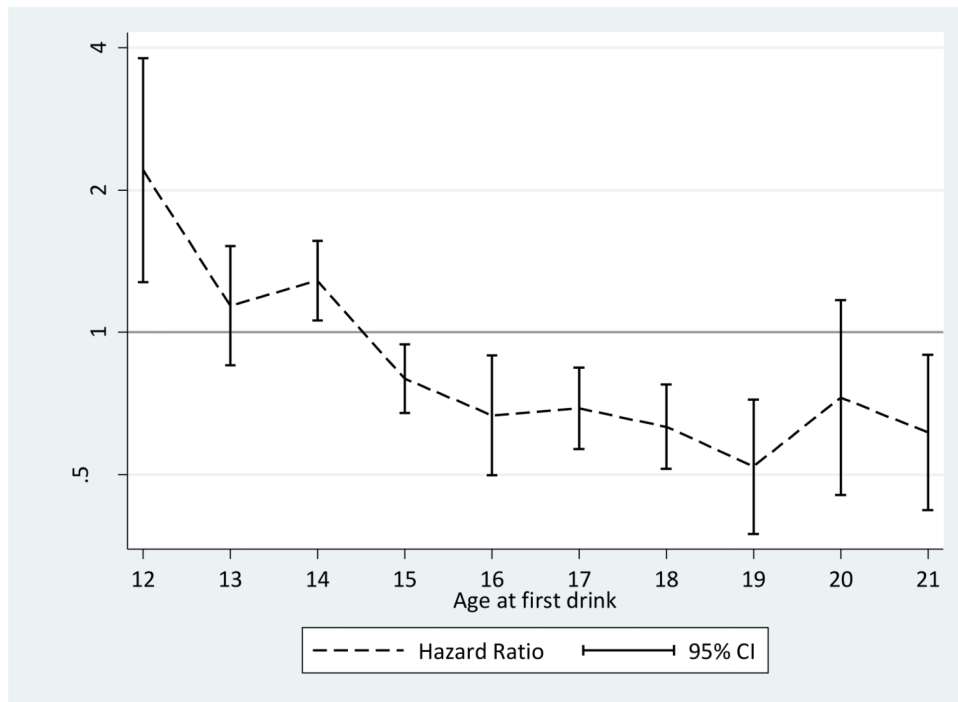
- Slade T, Chapman C, Swift W, Keyes K, Tonks Z, Teesson M. Birth cohort trends in the global epidemiology of alcohol use and alcohol-related harms in men and women: systematic review and metaregression. *BMJ Open*. 2016; 6:e011827.doi: 10.1136/bmjopen-2016-011827
- Spear LP, Swartzwelder HS. Adolescent alcohol exposure and persistence of adolescent-typical phenotypes into adulthood: a mini-review. *Neurosci Biobehav Rev*. 2014; 45:1–8. DOI: 10.1016/j.neubiorev.2014.04.012 [PubMed: 24813805]
- Taylor B, Irving HM, Kanteres F, Room R, Borges G, Cherpitel C, Greenfield T, Rehm J. The more you drink, the harder you fall: a systematic review and meta-analysis of how acute alcohol consumption and injury or collision risk increase together. *Drug Alcohol Depend*. 2010; 110:108–116. DOI: 10.1016/j.drugalcdep.2010.02.011 [PubMed: 20236774]
- United States. Department of Health and Human Services. Substance Abuse and Mental Health Services Administration Center for Behavioral Health Statistics and Quality National Survey on Drug Use and Health: 2-Year R-DAS (2002 to 2003, 2004 to 2005, 2006 to 2007, 2008 t. ICPSR34482-v3. 2015.
- United States. Substance Abuse and Mental Health Services Administration. Center for Behavioral Health Statistics and Quality. Comparing and evaluating youth substance use estimates from the National Survey on Drug Use and Health and other surveys. 2012
- United States., S.A. and M.H.S.A.C. for B.H.S. and Q. National Survey on Drug Use and Health: summary of methodological studies, 1971-2014. Substance Abuse and Mental Health Services Administration; Rockville, MD: 2014.
- United States Substance Abuse and Mental Health Services Administration. Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings, NSDUH Series H-48, SMA 14-4863.
- White A, Castle IJ, Chen CM, Shirley M, Roach D, Hingson R. 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. DOI: 10.1111/acer.12815 [PubMed: 26331879]
- Wilsnack RW, Wilsnack SC. Women, work, and alcohol: failures of simple theories. *Alcohol Clin Exp Res*. 1992; 16:172–179. [PubMed: 1590537]
- Wilsnack RW, Wilsnack SC, Kristjanson AF, Vogeltanz-Holm ND, Gmel G. Gender and alcohol consumption: patterns from the multinational GENACIS project. *Addiction*. 2009; 104:1487–1500. DOI: 10.1111/j.1360-0443.2009.02696.x [PubMed: 19686518]
- Yan J. Survival Analysis: Techniques for Censored and Truncated Data. *J Am Stat Assoc*. 2004; 99:900–901. DOI: 10.1198/jasa.2004.s348



**Figure 1.** Sex-Specific Cumulative Probability of First Onset of Heavy Drinking Episode (HDE) within the First Eight Quarters After Drinking Onset for Four Age-of-Drinking-Onset Groups. Data From United States National Surveys on Drug Use and Health, 2006-2014. (Unweighted  $n=33,908$  12-to-21-Year-Old Newly Incident Drinkers).<sup>1</sup>



**Figure 2.** Estimated Year-Specific Female-Male Hazard Ratios for First Heavy Drinking Episode Occurrence Within the First Eight Quarters After Drinking Onset for Four Age-of-Drinking-Onset groups, with Meta-Analytic Summary Estimate for the Hazard Ratio Showing Statistically Robust Female Excess Risk in Early Adolescence, Followed by Male Excess Risk. Data from United States National Surveys on Drug Use and Health, 2006-2014. (Unweighted n=33,908 12-to-21-Year-Old Newly Incident Drinkers). Note: For 21 year olds, heterogeneity across replications motivated use of the random effects variance estimation approach.



**Figure 3.**

Estimated Age-Specific Meta-Analytic Summary Estimates for Female-Male Hazard Ratios of First Heavy Drinking Episode Occurrence Within the First Eight Quarters After Drinking Onset. Data from United States National Surveys on Drug Use and Health, 2006-2014. (Unweighted  $n=33,908$  12-to-21-Year-Old Newly Incident Drinkers).

Note: For 12, 16, 20, and 21 year olds, heterogeneity across replications motivated use of the random effects variance estimation approach. Estimate for 11 year olds in 2014 is not shown due to imprecision.

Table 1

Sample Description and Estimated Mean Interval (in Months) from First Full Drink to First Occasion of Heavy Drinking Episode (HDE) Among 12-to-21-Year-Olds in the United States. Data from National Surveys on Drug Use and Health, 2006-2014. (Unweighted n=33,908 12-to-21-Year-Old Newly Incident Drinkers).

Age at 1 <sup>st</sup> drink	Unweighted Number (Weighted %) of HDE cases Among Newly Incident Drinkers <sup>1</sup>		Estimated Mean Interval (in Months) From 1 <sup>st</sup> Full Drink to 1 <sup>st</sup> HDE Among Newly Incident HDE Cases (95% CI) <sup>2,3</sup>		p
	Female	Male	Female	Male	
11-14	1050 (23.0)	739 (19.4)	5.1 (4.7, 5.6)	5.2 (4.6, 5.7)	0.917
15-17	2179 (27.8)	2721 (37.0)	4.3 (4.0, 4.6)	4.2 (3.9, 4.4)	0.430
18-20	1038 (28.0)	1313 (40.2)	4.2 (3.8, 4.7)	3.7 (3.4, 4.1)	0.091
21	606 (27.4)	691 (42.8)	3.6 (2.9, 4.2)	2.6 (2.2, 3.0)	0.014

<sup>1</sup> Weighted proportion (%).

<sup>2</sup> HDE, heavy drinking episode. Weighted means (x) and 95% confidence intervals (CI). The p-values are from two sample t-tests.

<sup>3</sup> Converted to months, based on subtraction of mid-month of first full drink from mid-month of HDE onset.