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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, James C. Anthony*

Department of Epidemiology and Biostatistics, Michigan State University, 909 Fee Road, East Lansing, 48824, USA

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<i>Keywords:</i> Heavy episodic drinking Male- f emale differences Age differences United States	<i>Background:</i> Globally, there is a male excess in the occurrence of heavy drinking once alcoholic beverages are consumed and 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. <i>Methods:</i> 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 $\sim 33,000$ 12-to-21-year-old newly incident drinkers (all with 1st 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. <i>Results:</i> 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. <i>Conclusions:</i> 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).

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 malefemale 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 in 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 8th grade, a slightly higher prevalence among boys in 10th grade, and a larger male excess in 12th graders (Johnston et al., 2016).

Although HDE prevalence provides insights about the extent of the

* Corresponding author.

E-mail address: janthony@msu.edu (J.C. Anthony).

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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: 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 earlyadolescent 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, 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 1st drink to 1st 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 1st 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, i.e., "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 timeto-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,b). 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 and a smaller male-female ratio among early adolescents. An alternative is that the male-female differences 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. Nine independent, nationally representative samples of 12-to-21-year-olds were drawn 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, 2014).

2.2. Assessments

NSDUH confidential assessments were audio computer assisted selfinterviews (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 ageof-onset stratum. The rationale for using 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 substudy to empirically assess the median induction interval using survival analysis. In order to explore potential influence of memory errors, we

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