



HHS Public Access

Author manuscript

Alcohol Clin Exp Res. Author manuscript; available in PMC 2020 May 01.

Published in final edited form as:

Alcohol Clin Exp Res. 2019 May ; 43(5): 774–779. doi:10.1111/acer.13985.

Alcohol and Women: A Brief Overview

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This paper provides a brief overview of research on women and alcohol and introduces a virtual issue of *Alcoholism: Clinical and Experimental Research* devoted to this important subject. Women-focused topics include the epidemiology of alcohol use among women, health and behavioral consequences of drinking, prenatal alcohol use and interventions, and enhanced alcohol treatment services. The introduction and selected papers highlight: temporal trends that are narrowing the gender gap in alcohol use; mounting evidence of the more rapid progression and greater severity of harmful physiological and behavioral effects of alcohol in women; impact of targeted public health campaigns and public policies on prenatal drinking; and finally intervention strategies to improve detection and care of women who misuse alcohol. Finally, future research directions to address continuing knowledge gaps are identified.

There is compelling evidence that rates of alcohol use and binge drinking are increasing among women, particularly young adults¹³. We also know that many of the harmful health effects of alcohol use occur more rapidly and severely for women than men (NIAAA, 2004). Addiction pathophysiology in stress, reward and immune pathways is sex-specific. Finally, while women and men appear to have equivalent outcomes in traditional mixed-gender alcohol treatment programs, treatment in specialized, women-only settings or treatments that target women-specific issues may improve outcomes for women with alcohol use disorder. This introduction to the virtual issue of *Alcoholism: Clinical and Experimental Research (ACER)* focused on women and alcohol provides a brief overview of current knowledge and highlights ten recent ACER papers on the epidemiology, consequences and treatment of alcohol use among women.

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Conflicts of Interest: Drs. McCaul, Roach, Hasin, Weisner and Chang have no conflicts of interest to declare. Dr. Sinha is a member of the Scientific Advisory Board of Embera Neurotherapeutics, Inc.

Epidemiology of Alcohol Use Among Women

Countless studies show that males are more likely than females to be drinkers, and that among drinkers, males drink more heavily than females (Grant et al, 2015; Hasin et al, 2007). However, research suggests that this gender gap in alcohol use may be narrowing (Grant et al, 2017; Keyes et al, 2011; Slade et al, 2016). In a recent meta-analysis by Slade and colleagues (2016), temporal trends in alcohol use (any and problematic) and alcohol-related harms were analyzed by birth cohort using data derived from 68 studies (about 75% from the US or Europe). They reported a linear decrease over time in sex ratios for any and problematic alcohol use and alcohol-related problems, with ratios in younger cohorts (e.g., those born 1991–2000) being closer to equal compared to older cohorts (Slade et al, 2016). Using data derived from the 1979 and 1997 cohorts of the National Longitudinal Survey of Youth, a recent paper by Williams and colleagues (2017) included in this ACER virtual issue examined changes in heavy drinking trajectories among men and women as a function of race and ethnicity. In contrast to a decline in heavy drinking among younger men, there was an increase in heavy drinking frequency among younger White and Hispanic women. In both cohorts, heavy drinking among Black women was lower than that of White and Hispanic women. The authors attribute the increased heavy drinking frequency of younger White and Hispanic women to changes in women's social roles and norms across recent decades, including higher education attainment and rates of employment outside the home, as well as later age at first marriage and childbearing.

A recent paper by Windle and Windle (2018) included in this ACER virtual issue examined sex differences in peer selection (i.e., choosing friends similar to oneself on certain characteristics) and socialization (i.e., social processes such as perceived substance use norms, offers of alcohol, role modeling) as they relate to alcohol use patterns among young adults. Following high school participants over a 15-year period into young adulthood, they found that friend selection was more important than socialization for both sexes. Congruent with earlier findings indicating a maturing-out of substance use during the transition from adolescence to young adulthood (Chilcoat and Breslau, 1996; Lee et al, 2015), marital and parental roles were associated with decreased personal alcohol use and the percentage of friends using alcohol. Importantly these associations were more robust among women than men.

In addition to the concerning changes in drinking patterns and problems among young adult women, data from two nationally representative surveys conducted 10 years apart showed that the overall prevalence of binge drinking and alcohol use disorder increased at a strikingly higher rate in women than in men (Grant et al, 2017). Two recent ACER papers included in this virtual issue highlight new findings on patterns of increasing alcohol use among the particularly vulnerable population of older adult women. Using data from National Health Interview Surveys, 1997 – 2014, Breslow and colleagues (2017) reported sex differences in the rates of change in the prevalence of adult current drinking and binge drinking. Specifically, the prevalence of current drinking increased on average 1.6% per year among women ages 60+ compared with 0.7% per year among men ages 60+. Similarly, binge drinking increased on average 3.7% per year among women ages 60+ while remaining stable among men ages 60+. In a meta-analysis of six national survey series covering the

years 2000 through 2016, Grucza and colleagues (2018) found that rates of past-year alcohol use and binge drinking among adult women increased at more than twice the general population rate, although overall prevalence remained lower compared with men across the observation period.

The increased prevalence of heavy and binge drinking and related harmful consequences among women is also reflected in findings from other important data sources. In a 2018 study included in this virtual ACER issue, White and colleagues (2018) examined Emergency Department (ED) visits involving acute (e.g., excessive blood level) and chronic alcohol consumption (e.g., alcohol dependence, alcohol-related liver damage) as a function of age and sex. Between 2006 and 2014, they found a steep rise of 61.6% in the overall number of alcohol-related ED visits from 3,080,214 to 4,976,136, and a corresponding increase of 272% in associated costs from \$4.1 billion to \$15.3 billion. Consistent with findings of increasing rates of heavy drinking in women, the annual percentage change in rates of all alcohol-related ED visits was greater for women than men (5.3% vs. 4.0%). In line with the increase in alcohol-related ED visits, alcohol-related hospital inpatient diagnoses in US adults aged 45–64 increased 30% in men and 90% in women from 1993 to 2010 (Sacco et al, 2015). Liver disease among US persons aged 15 – 39 year old increased 90% in men and 240% in women from 1998 – 2012 (Doycheva et al, 2017). While the age-adjusted all-cause mortality rate in the US declined from 2000 to 2015, the age-adjusted death rate from alcohol-related liver cirrhosis increased from 4.3 deaths per 100,000 population in 2000 to 5.8 deaths per 100,000 population in 2015. Rates for White males and females increased by 32.4% and 85.0%, respectively, whereas rates for Black males and females declined by 27.5% and 10.7%, respectively. In line with sex differences in heavy drinking and AUD, the age-adjusted death rate from all liver cirrhosis for males was consistently about twice the rate for females, regardless of race (Yoon and Chen, 2018). Finally, in nationally representative roadside surveys conducted by the National Highway Traffic Safety Administration (Ramirez et al, 2016), overall rates of DUI have decreased sharply since 1973. In 1996, 4.8% of men versus 2.9% of women weekend nighttime drivers tested positive for DUI. In 2014, 1.4% of men versus 1.7% of women tested positive, a sharp convergence in gender rates.

Health and Behavioral Consequences of Drinking Among Women

These increased rates of alcohol misuse among women are of considerable concern since women experience the harmful health and behavioral consequences of drinking sooner and at lower levels of alcohol exposure than men (Foster et al, 2014). There are multiple reasons why this might occur. We know that there are sex-specific differences in the pharmacokinetics and pharmacodynamics of alcohol (Thomasson, 1995). Women are generally smaller than men and have relatively less total body water and more total body fat. As a result, alcohol is more concentrated in a woman's body; blood alcohol concentration rises faster and stays elevated longer in women than men. We also know that there are sex differences in brain anatomy, neurochemistry and function.

Thus, elevated levels of alcohol exposure in women give rise to a variety of negative health consequences. For example, there is more damage and inflammation in the female brain

during alcohol withdrawal (Hashimoto and Wiren, 2008). Women also are at increased risk of alcohol-related heart disease, as well as immune and infectious diseases. Even moderate drinking elevates risk of E2 positive breast cancer. In one study, there was a 12% increase in breast cancer risk per 1 drink/day increase in average alcohol consumption. We know that alcohol induces widespread alterations in estrogen receptor physiology and function that in turn affect sensitivity and risk of estrogen positive breast cancer. In a recent study of alcohol-dependent men and women admitted to a detoxification program, Kirpich and colleagues (2017) found greater elevations in liver injury markers among female compared with male patients, despite a shorter duration of heavy drinking and lower mean drinks per day. In addition, women had similar levels of inflammatory cytokines but elevated levels of liver inflammation suggesting immunological differences that may contribute to more rapid and severe progression of alcohol-related liver damage in women. Stress and immune biology are different in men and women, affecting peripheral organ physiology differently. Inflammatory responses to alcohol and traumas are highly sex specific, as are autonomic and HPA axis responses and metabolic hormones. Research is severely lacking in these areas, especially with regard to both acute but chronic adaptations.

Finally, there is growing interest not only in the effects of alcohol directly on the drinker but also on persons in relationships with the drinker. Of considerable personal and public health concern, alcohol use by women and their partners is a well-documented risk factor for trauma and violence. In a meta-analysis included in this virtual issue, Stanesby and colleagues (2018) examined data across 10 countries on the likelihood of experiencing alcohol-related harm based on the proximity of the relationship of the person's "most harmful drinker" in their life over the past year. Proximity was categorized as "close" (i.e., a partner, family member or household member) or "extended." Seven different alcohol-related outcomes were examined across a broad range of harms: physical harm; name calling or insults; feeling threatened or afraid; forced or pressured into sex; emotional hurt or neglect; having to leave home; and having less money for household expenses. Overall, women were more likely to report a close male as their "most harmful drinker," while men were more likely to report an extended male as their "most harmful drinker," demonstrating the broad, cross-cultural similarities in this public health risk. Women with a close "most harmful drinker" were more likely than women with an extended "most harmful drinker" to report experiencing one or more alcohol-related harms and each type of harm from others' drinking. In contrast, the likelihood of experiencing one or more alcohol-related harms was not increased among men having a close "most harmful drinker," although the odds of reporting some but not all harms was increased.

Prenatal Alcohol Use and Effects

Epidemiological data suggest that public health messages about the harmful effects of alcohol use during pregnancy may be having an impact, as indicated by increased prevalence of any and binge drinking among non-pregnant women of reproductive age from 2002–2014, but not in pregnant women during the same period (Hasin, Varying time trends in U.S. binge drinking, alcohol use disorders, and other adverse drinking outcomes, Symposium presentation, Research Society on Alcoholism, San Diego, CA, June 17, 2018). This contrasts sharply with findings that the prevalence of cannabis use is increasing at an equal

rate among pregnant and non-pregnant women of reproductive age, suggesting the specificity of effects of the alcohol public health messaging (Brown et al, 2017). Similarly, among pregnant women entering substance abuse treatment between 2000 – 2010, the percentage reporting alcohol use decreased from 46.6% to 34.8% while the percentage reporting drug use increased from 51.1% to 63.8% (SAMHSA, 2013). Nonetheless, rates of prenatal alcohol exposure remain high world-wide and in the US. In a recent Center for Disease Control and Prevention survey (Centers for Disease Control and Prevention, 2015), 18.2% of non-pregnant women of childbearing age and 3.1% of the pregnant women reported binge drinking in the past 30 days. Importantly, pregnant binge-drinkers reported more frequent episodes of binge drinking (4.6 vs 3.1 episodes) and more drinks during their heaviest recent binge episode (7.5 versus 6.0 standard drinks) compared with non-pregnant binge drinkers. The authors suggested that these trends might be a sign that women who binge-drink even when they are pregnant are more likely to have an alcohol use disorder than other binge-drinkers.

It is likely that self-reported drinking quantity and frequency during pregnancy underestimate the problems because of the considerable stigma and public policy sanctions associated with drinking during pregnancy. An important recent study by Subbaraman and colleagues (2018) included in this virtual ACER issue on women highlights the unintended consequences of state policies targeting alcohol use during pregnancy. Their research examined the relationship between state-level policies related to alcohol use during pregnancy and prenatal care utilization and birth outcomes (low birthweight, premature birth, APGAR score ≥ 7) drawn from the US National Center for Health Statistics Vital Statistics System birth certificates between 1972 – 2013. The study found that policies targeting alcohol use during pregnancy are associated with *increased*, not decreased, adverse birth outcomes, possibly by causing pregnant women who drink to avoid prenatal care. Importantly, there was no difference in impact between policies designated as supportive versus punitive. In contrast, policies targeting overall alcohol use in the general population were associated with improved birth outcomes. These findings underscore the importance of continued efforts to limit heavy drinking overall in the general population, rather targeting policies specifically at pregnant women regardless of their content.

Given the continued high rates of fetal alcohol exposure and the lack of benefit of state-level policies, individual-level prevention and intervention efforts aimed at reducing alcohol use among women of childbearing age and pregnant women may be potent tools to reduce rates of Fetal Alcohol Spectrum Disorders (FASD). Such findings highlight the importance of universal screening and brief intervention for alcohol use by pregnant women as recommended by the US Preventive Services Task Force (2018).

Alcohol Treatment Services for Women

Only a small percentage of persons with alcohol misuse or alcohol use disorder (AUD) ever receive treatment in a formal, specialized alcohol treatment facility (Cohen et al, 2007; Lipari et al, 2016). Gender-specific results from the 2015 National Survey on Drug Use and Health (NSDUH) suggested that among persons with AUD in the past year, only 7.4% of men and 5.4% of women received treatment (SAMHSA, 2015). Thus, women with alcohol

disorders appear to be under-represented in specialty alcohol and drug treatment facilities, despite having a shorter interval between drinking initiation and treatment entry (Alvanzo et al, 2014). In part, this may reflect that women are more likely to seek care in non-substance abuse settings, particularly primary care and mental health settings, where their drinking problems may not be recognized (Brienza and Stein, 2002). Further, compared with men, women report less social support for treatment engagement (Bendtsen et al. 2002; Grella and Joshi, 1999) and greater barriers to treatment access, including pregnancy, childcare responsibilities, threat to child custody, trauma (e.g., childhood and adult sexual and physical abuse), social stigma, and lack of economic resources (e.g., unemployment and lack of insurance)(Greenfield et al, 2010; SAMHSA, 2009). Thus, alcohol screening, brief intervention and referral for specialty treatment as needed is critical across health care settings, including primary care and mental health services, particularly for women.

Women of all ages report more medical and mental health problems than men, and women with alcohol disorders have even higher rates of co-occurring medical and mental health problems. Women usually visit their primary care physician for reasons other than their alcohol use. In primary care, unless alcohol screening is systematic, women tend to be missed (Amico, et al., 2005; Hettema et al, 2015; Weisner & Matzger, 2003); however, when screening is conducted systematically with a standardized instrument and a protocol that screens all women rather leaving it up to clinician judgement, there is no longer a difference (Ballesteros et al, 2004). Several screeners for women with alcohol use disorders have evidence of validity. Brief interventions delivered to women in health care settings show success (Chander et al, 2015; Manwell et al, 2000; Reinhardt et al, 2008), although not all studies have found significant intervention effects. Another important role for primary care is continuing care after specialty treatment. The co-occurring problems of women in addiction treatment need ongoing care in themselves, and, in addition, these problems can be associated with alcohol relapse. When they receive continuing care (i.e., annual primary care and addiction and psychiatric care when needed), women are much more likely to be remitted over 9 years, and their costs (which were due primarily to ER and inpatient care) are significantly reduced (Chi et al, 2011; Parthasarathy et al, 2012).

To improve access and address barriers to care, women's-only treatment programs have been designed to meet needs specific to or more commonly a concern for women. Currently, 46% of addiction treatment facilities provide specialized services for women (SAMHSA, 2016). Specific program components that women identify as helpful include: women's only groups, childcare services, and individual counseling (Nelson-Zlupko et al, 1996). Research suggests that women-only treatment programs are more effective for engaging subgroups of women with more complex characteristics and problems than mixed-gender programs. Specialized women's services have shown to be particularly effective for women who are pregnant, trauma-affected or experiencing comorbid psychiatric disorders (SAMSHA, 2009).

Importantly, research indicates that women and men have comparable outcomes in mixed-gender addiction treatment programs. Gender is generally not a significant predictor of treatment retention, completion, or post-treatment outcomes. But when we compare outcomes for women receiving treatment in women-only vs mixed-gender programs, it appears that women may do better in women-only residential and outpatient settings that

offer enriched wrap-around services (e.g., childcare parenting training, assertiveness training, family planning). Across studies, patients in women-only treatment averaged significantly more days in care, were more than twice as likely to complete treatment and were more than two times less likely to report substance abuse at follow-up compared with women in mixed-gender treatment (Greenfield et al, 2008; Grella, 2009, Prendergast et al, 2011). In a meta-analysis (Orwin et al, 2001), enhanced, wrap-around women's services were associated with an overall improvement in outcomes, with strongest effects seen for pregnancy outcomes, psychological well-being and HIV risk reduction. Moderate improvements were observed in psychiatric symptoms, and small effect sizes were reported for alcohol and drug use. Thus, it may be that the greatest benefits of women's-specific treatment occur in areas beyond substance use per se, including psychosocial well-being, psychiatric health, pregnancy outcomes, and health improvement. The importance of these enhanced long-term improvements associated with women's-specific services is supported by a recent paper by Kelly and colleagues (2018) included in this ACER virtual issue on women and alcohol. Specifically, the National Recovery Survey suggests that during the first 5 years of recovery, women report lower quality of life and self-esteem and greater psychological distress compared with men. This is consistent with the earlier findings that women who misuse alcohol have poorer quality of life, particularly higher rates of depression and greater sleep disturbance, compared with men (Hasin et al, 2018; Peters et al, 2003), and suggests that women may face greater long-term challenges to recovery than men.

Future Directions

Taken together, the papers included in this virtual issue on women and alcohol highlight important new knowledge on sex differences in patterns of alcohol use, consequences of alcohol misuse, and approaches to identification and treatment. They highlight the critical importance of the NIH mandate to include women in research and, more importantly, to enroll sufficient women to permit adequately powered analyses of sex differences and similarities. Importantly, they point to large gaps in information that urgently need research attention as rates of alcohol use by women increase and converge with those of men.

There are many key questions to address across the spectrum of women's-related research issues. Some research areas will be crosscutting. For example, how do the unhealthy drinking patterns that women experience vary across the lifespan? How do risk and protective factors change with age and are these changes different for women and men? How can we tailor prevention, screening and intervention approaches to more effectively address such changes in risk characteristics? How can implementation research inform integration of women-tailored services into a variety of medical and social service settings? At the community and national level, are there differential effects of social policies, the media or public education efforts on women and men?

Other questions may be more focused and drill down on specific targeted research issues. How do early experiences of trauma alter subsequent stress sensitivity and drinking patterns? None of the current screening instruments for alcohol and other substance use in pregnancy show both high specificity and sensitivity (Chang, 2014); what measurement/

interview approaches will optimize identification of women who may benefit from intervention? Is there a dose-effect for the quantity or types of women-specific treatment services that are provided? For example, are there differential effects of integrating a women's only group into a mixed-gender program (currently the most common pattern of integrated women's services) versus providing all services in a women's only setting? Do pharmacologic targets differ by sex and will sex-specific approaches to tailoring dose and duration of AUD pharmacotherapies improve treatment outcomes? We know that women with AUD experience higher rates of co-occurring physical and mental health disorders. How should care be tailored to more effectively integrate services to address these comorbid needs? Finally, does stigma remain a more potent barrier to treatment for women than men, and, if so, what screening and care engagement strategies might be useful in reducing its impact?

As evidenced by the important findings reported in the recent papers included in this ACER virtual issue on women and alcohol, the field has made substantial progress incorporating a women's focus across the full spectrum of research methodologies from preclinical to applied studies. But as rates of hazardous alcohol use by women and men converge, it is critical that we continue to frame our research questions with a focus on sex and gender similarities and differences.

Acknowledgements:

This work was supported by U24AA020801(McCaul), R01DA042094 (McCaul), R01AA025309 (Hasin), NYSPI (Hasin), R01AA025902 (Weisner), R01AA013892 (Sinha), R01AA020504(Sinha) and R21AA025277 (Sinha).

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