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Alcohol availability and onset and recurrence of alcohol use disorder: Examination in a longitudinal cohort with co-sibling analysis

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Abstract

Background—Recent reviews of associations of alcohol availability with alcohol outcomes suggest findings are highly inconsistent and highlight a lack of longitudinal and causal evidence. Effect modification (moderation or statistical interaction), which could contribute to the inconsistent picture in the existing literature, has not been systematically assessed. We examined associations of alcohol availability with onset and recurrence of alcohol use disorder (AUD) using multi-level, longitudinal population data from Sweden and test hypothesized effect modifiers to identify groups for whom increased alcohol availability may be particularly risky. We also employed co-sibling models to assess potential causality for AUD onset by accounting for genetic and shared-environment confounders.

Methods—Data come from all individuals born in Sweden between 1950 and 1975 who were registered in a residential neighborhood at the end of 2005 (N=2,633,922). We used Cox proportional hazards models to investigate time to AUD onset and logistic regression to assess odds of AUD recurrence over an 8-year period.

Results—Living in a neighborhood with at least one alcohol outlet of any type was associated with a small increase in the likelihood of developing AUD, with an adjusted hazard ratio (aHR) of 1.16 (95% CI: 1.13–1.19). Among people with a prior AUD registration, alcohol availability was not significantly associated with recurrence of AUD, with an adjusted odds ratio (aOR) of 1.02 (95% CI: 1.00–1.05). Associations of alcohol availability with AUD onset varied according to sex,

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age, education, neighborhood deprivation and urbanicity. Hazard ratios from the sibling models were similar to those in the general population models, with aHR=1.19 (95% CI: 1.15–1.24).

Conclusions—Effects varied among neighborhood residents, but greater alcohol availability was a risk factor for AUD onset (but not relapse) in all groups examined except women. Co-sibling models suggest there may be a causal relationship of greater alcohol availability with adult-onset AUD.

Keywords

alcohol outlets; alcohol use disorder; longitudinal; causal analysis; co-sibling models

Introduction

Recent reviews (Gmel et al., 2016; Holmes et al., 2014; Kearns et al., 2015; Popova et al., 2009) have described associations of increased availability of alcohol for on-premise (in bars and restaurants) and off-premise (in locations such as liquor, convenience, and grocery stores) consumption with a variety of alcohol outcomes such as risky drinking (e.g., heavy drinking and drunkenness), driving under the influence of alcohol, motor vehicle crashes and other injury outcomes, as well as violence (assaults), suicides, and child abuse. Despite studies suggesting there are associations between alcohol availability and greater alcohol consumption and related harms, findings are quite inconsistent and there is little evidence of causal relationships (Gmel et al., 2016; Popova et al., 2009). Overcoming these study limitations is essential for informing effective population-level prevention interventions that may have wide-ranging health benefits.

One principal shortcoming in the extant literature is the paucity of longitudinal studies of the impacts of alcohol availability on individuals living in the community. Exceptions typically are longitudinal ecological studies involving time series analysis (see, for example, Livingston, 2011) or using natural experiments to examine policy changes, such as the impact of returning to government monopolization of sales of medium-strength beer in state-run liquor stores in Sweden on alcohol-related hospitalization rates over time (Ramstedt, 2002). Rigorous longitudinal studies are critical for understanding the temporality of effects of limiting (or expanding) alcohol availability on alcohol consumption and related outcomes (Ahern et al., 2009).

In addition to a lack of longitudinal analysis of the relationships between alcohol availability and individual-level alcohol outcomes, another key limitation of the existing literature is that effect modification (also called moderation or statistical interaction) has not been consistently examined, and this could contribute to the wide variation in results seen across —and even within—studies. By identifying effect modifiers, we will be better positioned to target our interventions to reach the population subgroups that are most likely to benefit from their effects.

Another unanswered question is whether any observed associations of alcohol availability with drinking and alcohol-related problems are due to causal area-level influences or due to confounding by genetic or other factors. Evidence from longitudinal studies of

interrelationships between socioeconomic disadvantage and alcohol problems indicates that selection effects and confounding each are likely to be relevant (Buu et al., 2007; Kendler et al.). A final consideration is that relatively little attention has been paid to the role that alcohol availability may play in the development or relapse of alcohol use disorders (AUD). These questions can be effectively addressed using longitudinal within-person designs, which typically are costly and time-intensive.

To start to address some of these limitations, we examined associations of alcohol availability with both the onset and recurrence of AUD using multi-level, longitudinal population data from Sweden. We examined a set of hypothesized effect modifiers to identify groups for whom increased alcohol availability may be particularly risky. We also employed co-sibling models to assess potential causal relationships between alcohol availability and AUD onset by controlling for genetic confounding.

Alcohol availability and AUD

Studies from the 1970s and 1980s on the relationships between alcohol availability and AUD took an ecological approach, assessing availability with area-based densities of outlets and measuring AUD with population-level rates (Harford et al., 1979; Parker et al., 1983; Parker and Wolz, 1979; Smart, 1977), and recent ecological studies have confirmed associations between alcohol outlet density and population-level rates of hospitalization for alcohol-related conditions (Livingston, 2011). Multi-level studies considering individual-level AUD as an outcome of greater alcohol availability are relatively rare, but this approach is important for eliminating ecological biases (Gmel et al., 2016).

A small number of studies have examined the relationship between alcohol availability and alcohol problems without considering AUD per se. For example, one study considered “at-risk drinking” as an outcome, defined based on an Alcohol Use Disorders Identification Test (AUDIT) score greater than seven (Theall et al., 2011); in this relatively small sample of 321 African Americans living in the US state of Louisiana, greater liquor store densities were associated with more at-risk drinking. Another study operationalized alcohol-related problems as having at least one of 25 alcohol-related social problems or dependence symptoms, but they did not see a significant association of this outcome with alcohol outlet density in a US national sample of couples (McKinney et al., 2012). When considering the lifecourse, the environmental context may be particularly relevant for the initiation and maintenance of heavy drinking that leads to AUD onset, but environmental cues also may trigger relapse of AUD and make recovery more difficult.

Effects on AUD onset and relapse also may vary by the type of outlet, as some research has found that greater densities of on- and off-premise alcohol outlets are associated with different outcomes in the same sample (Freisthler et al., 2004; Livingston, 2011). In their conceptual model delineating pathways from limiting alcohol outlet density to alcohol use and associated problems, Campbell and colleagues (2009) suggest that limiting on-premise outlet density may have larger effects on injuries and outcomes related to drinking and driving, while limiting off-premise outlet density may be most beneficial for long-term health outcomes. It is not clear whether this distinction would extend to relapse to AUD, or whether it would apply in a national context where off-premise alcohol outlet density is

strictly regulated, however. In the current study, we separately examined relationships between different types of alcohol outlets with both onset and recurrence of AUD using 8 years of longitudinal population registry data from Sweden.

Modifiers of effects of alcohol availability on AUD

Inconsistency in prior studies indicates there may be unidentified effect modifiers that interact with alcohol availability to increase negative outcomes for select sub-populations. In terms of age, younger people may be more likely than their older counterparts to drink in on-premise establishments, which thereby could increase the relevance of increased bar density for younger neighborhood residents. In terms of possible sex differences, although drinking norms vary for men and women, it is unclear whether greater alcohol availability would be riskier for men or women. Men may be particularly encouraged to drink more in areas with a greater density of bars or other on-premise settings, but women also may drink more in areas perceived to be “wetter” due to a higher density of alcohol outlets. Some studies have assessed effect modification by demographic characteristics such as age and sex, and findings suggest that younger residents and women may be especially susceptible to environmental risk from increased availability of alcohol (see, for example, Theall et al., 2011; Treno et al., 2003). Ascertaining whether there may be differential benefits for younger neighborhood residents or for women of limiting alcohol availability has implications for prevention of onset of AUD as well as for prevention of alcohol-related harm to children, including fetal alcohol spectrum disorder caused by women’s drinking during pregnancy.

In addition to possible age and sex differences, socioeconomic status also may modify effects of increased alcohol availability on the development and recurrence of AUD. At the individual level, personal socioeconomic status (SES) may modify availability effects, although the nature of this modification is not immediately apparent. Because alcohol is relatively expensive in Sweden, higher-income residents may be more likely than their lower-income counterparts to respond to a greater availability of alcohol in their neighborhoods, but lower SES may cause stress-related drinking in areas of greater alcohol availability. In Finland, reductions in alcohol prices have widened socioeconomic disparities, as lower-SES groups have suffered more adverse consequences than their higher SES counterparts with the availability of less expensive alcohol (Mäkelä et al., 2015). At the neighborhood level, neighborhood deprivation may be accompanied by stressors that trigger drinking in a high-availability context; conversely, social norms in more affluent areas may promote social drinking (which this study is not designed to detect). Additionally, the type of municipality may be important, as longer distances to travel to procure alcohol in rural or suburban areas may discourage heavy drinking and thereby reduce risk of AUD. Better understanding of these potential effect modifiers could guide specific prevention initiatives to reduce alcohol-related disparities by reaching high-risk people in high-risk places.

With the goal of advancing the science on relationships between alcohol availability with AUD, our specific research questions were as follows:

1. Is the onset of AUD predicted by neighborhood alcohol availability? Is AUD relapse predicted by neighborhood alcohol availability? Are effects specific to on- or off-premise outlets?
2. Are effects of greater exposure to alcohol outlets on AUD modified by individual or area-level characteristics, such as age, sex, socioeconomic status (individual SES and neighborhood deprivation) and type of municipality (based on urbanicity)?
3. Are these neighborhood influences likely to be causal or are they confounded by genetics and shared family environment?

Materials and Methods

We analyzed information on individuals from Swedish population-based registers with national coverage. These registers were linked using each person's unique identification number, which had been replaced by a serial number to preserve confidentiality. We secured ethical approval for this study from the Regional Ethical Review Board of Lund University.

Measures

The primary outcome, ***alcohol use disorder (AUD)***, was ascertained using three sources. The first used ICD codes for main and secondary diagnoses from Swedish medical registries (the Swedish Hospital Discharge Register, containing all hospitalizations for all Swedish inhabitants from 1973–2012; the Outpatient Care Register, containing information from all outpatient clinics from 2001 to 2012; and the Swedish Cause of Death Register, containing information on all deaths in Sweden from 1963 to 2012) for the following diagnoses: ICD8 and ICD9 codes for alcohol-related psychiatric disorders (291), alcohol dependence (303), alcohol abuse (305A), alcohol-related polyneuropathy (357F), alcohol-related cardiomyopathy (425F), alcohol-related gastritis (535D), alcoholic fatty liver, alcohol hepatitis, alcoholic cirrhosis, unspecified liver damage caused by alcohol (571A-D), toxic effects of alcohol (980), alcoholism (V79B); ICD10: alcohol-related psychiatric and behavioral disorders (F10, excluding acute alcohol intoxication: F10.0), rehabilitation of a person with alcohol abuse (Z50.2), guidance and medical advice to a person with alcohol abuse (Z71.4), alcohol-related pseudo-Cushing syndrome (E24.4), alcohol-related degeneration of the nervous system and brain (G31.2), alcohol-related polyneuropathy (G62.1), alcohol-related myopathy (G72.1), alcohol-related cardiomyopathy (I42.6), alcohol-related gastritis (K29.2), liver diseases caused by alcohol (K70.0-K70.9), acute pancreatitis caused by alcohol (K85.2), chronic pancreatitis caused by alcohol (K86.0), treatment of pregnant alcoholic woman (O35.4), and toxic effects of alcohol (T51.0-T51.9). The second used Anatomical Therapeutic Chemical (ATC) codes in the Prescribed Drug Register (containing all prescriptions in Sweden picked up by patients from July 2005 to 2012) for disulfiram (N07BB01), acamprosate (N07BB03), or naltrexone (N07BB04). The third used registrations of individuals in the Swedish Crime Registers (the Swedish Crime Register included national complete data on all convictions from 1973–2013 and the Swedish suspicion register included national complete data on all individuals strongly suspected of crime from 1998–2013) with at least two convictions of drunk driving

(suspicion code 3005, law 1951:649 (paragraph 4 and 4A)) or being drunk in charge of a maritime vessel (suspicion code 3201, law 1994:1009 (chapter 20, paragraph 4 and 5)). We did not count arrests in the suspicion register that described any events also contained in the conviction register. The validity of our definition of AUD is supported by the high rates of concordance for registration across our different ascertainment methods during the follow-up period (see Supplemental table S2).

The principal exposure variable, ***neighborhood alcohol outlets***, was defined based on the number of licensed restaurants, bars, nightclubs and governmental outlets within a neighborhood in 2005. In our study, neighborhoods (as defined by Statistics Sweden, the Swedish government-owned statistics bureau) are based on Small Areas for Market Statistics (SAMS). There are approximately 9,200 SAMS throughout Sweden, with an average population of 1,000 each. These SAMS units were initially created by the Swedish authorities for administrative and marketing purposes. They are often characterized by homogeneous types of buildings and are limited by "natural" boundaries, such as highways, rivers or hills. The governmental outlets are the only off-premise retail stores in Sweden allowed to sell alcoholic beverages that contain more than 3.5% alcohol by volume; beer is not available at grocery stores or other neighborhood stores. The minimum purchase age is 20 for the government outlets. Alcohol also can be sold in restaurants, bars and nightclubs for on-premise consumption, but these establishments need permission from the municipality to sell alcohol. The minimum purchase age is 18 in these venues, and alcohol may be served only between 11 AM–1 AM, although municipalities can permit a later venue closing time, sometimes as late as 5 AM. All alcohol purchased must be for immediate consumption, and guests are not allowed to bring alcoholic beverages into or out of a restaurant, bar or nightclub. Additionally, outdoor areas in restaurants must be clearly separated from the street, and consumption is limited to these cordoned areas. There are 1,459 licensed alcohol outlets in Sweden: 365 are off-premise government outlets and the remainder are on-premise restaurants, bars and nightclubs. In our sample, 65% of individuals lived in the same neighborhood in 2005 as in 2013, and 79% lived in a neighborhood with the same number of outlets in 2005 as in 2013. Preliminary analyses showed the rates of AUD onset and AUD recurrence did not vary substantially between neighborhoods with 1–3 and more than 3 alcohol outlets (Table 1). Because alcohol outlets are relatively sparse, we used a dichotomous variable to indicate whether an individual's neighborhood contained one or more alcohol outlets (vs. none).

Effect modifiers were age (continuous year of birth, with ages ranging from 30 to 55 in 2005), sex, disposable income in 2005 (standardized with 0 mean and 1 standard deviation), educational status in 2005, unemployment status in 2005, neighborhood deprivation in 2005, and urbanicity. Neighborhood deprivation (see Winkleby et al. (2007)) was a composite measure including four aggregated characteristics of the neighborhood population aged 25–64: proportion with low education (<10 years), low income (defined as less than 50% of individual median income from all sources, including from interest and dividends), unemployment (not employed, excluding full-time students, those completing compulsory military service, and early retirees) and receipt of social welfare (at any time during that year). In the models, the composite was kept as a continuous variable, with the

neighborhood deprivation score ranging between −3 and 11, with higher values indicating greater levels of neighborhood deprivation. Urbanicity was defined based on Statistics Sweden's definition of municipalities; ranging from 1 (big cities) to 9 (sparsely populated municipalities). In the models, we used a categorical variable of urbanicity to contrast (a) large cities and suburbs with (b) mid-size cities and commuter zones, as well as with (c) rural areas.

Covariates in the models were marital status in 2005, criminal behavior (in criminal registers for a crime other than drunk driving; see Kendler et al. (2016) for a detailed definition of criminal behavior), drug abuse (in medical registers for drug-related conditions or care; see Kendler et al. (2016) for a detailed definition of drug abuse), and genetic risk for AUD. Genetic risk for AUD was calculated as follows. First, we calculated the morbid risk for AUD for the population in Sweden born between 1950 and 1990. We used a larger sample of the Swedish population in order to get stable estimates of genetic risk. We used the Weinberg correction (Fuchs et al., 2010) to modify the denominator to reflect whether subjects were affected or not, and among the latter, to weight the observations according to age at the end of 2013. That is, we divided the non-AUD population into three groups based on the distribution of age at first AUD registration: individuals in the first quartile (15–23 years age) were weighted 0; individuals in the second and third quartile (24–44 years) were weighted 0.5; individuals in the last quartile (45+) were weighted 1. The denominator is meant to approximate the number of lifetimes at risk. Subjects who had not entered the risk period were not counted at all. Thereafter, we performed a logistic regression analysis based on information from the same population and their relatives (monozygotic (MZ) twins, dizygotic (DZ) twins, full siblings, half-siblings, mother, father and cousins). In this regression model, the outcome variable was AUD and the predictor variables were the morbid risk of AUD among the different relative types. The results from the regression model produce one regression coefficient for each relative type that is corrected for the age in 2013; these followed quantitative genetic expectations that can be seen in Supplemental Table S3. The regression model produced a predicted probability, which we used for the genetic risk score in the analyses described below.

Analyses

In the first analysis in which we wanted to investigate the association between exposure to alcohol outlets and first registration of AUD, we selected all individuals born in Sweden between 1950 and 1975 who were registered in a neighborhood SAMS at the end of 2005. Furthermore, we required that the individual did not have an AUD registration prior to the end of 2005 (N=2,560,045). We used Cox proportional hazards models to investigate time to first AUD registration, death, emigration or end of follow-up (in 2013). In the unadjusted model, we only included alcohol outlets (by type, with separate models for off-premise governmental outlets and for on-premise restaurants and bars, and a combined measure that also included nightclubs). The second model controlled for individual demographic characteristics and neighborhood characteristics, and finally in the third model we also controlled for genetic risk. In the effect modification analyses, we examined interactions of alcohol outlets with age, sex, individual SES, neighborhood deprivation and urbanicity,

including the full set of covariates. As there were several individuals from the same families in the models, we controlled for this non-independence in all analyses.

In the next step, we sought to assess the degree to which the results from the regression models reflect confounding by familial risk factors using a co-sibling design. The use of siblings as controls will automatically account for many unmeasured factors, including cultural background, parental characteristics and child-rearing practices, as well as genetics (as siblings share 50% of their genes). Using the Swedish Multi-Generation Register to identify all full-siblings, we refit all analyses within strata of full-siblings, in which the members of the stratum differed in their exposure to alcohol outlets in 2005 (using the same dichotomous indicator of 0 versus 1 or more outlet in the residential neighborhood). Within each sibling stratum, the hazard ratio is then adjusted for the familial cluster, and, therefore, accounts for an array of unmeasured genetic and environmental factors shared among siblings from the same family. For the co-sibling analysis we used Cox proportional hazards models with a separate strata for each set of siblings to investigate time to first AUD registration, death, emigration or end of follow-up.

In the second analysis, we wanted to investigate the effect of alcohol outlets on recurrence of AUD. From the population born in Sweden between 1950 and 1975 we selected all individuals registered for AUD prior to 2005 (N=73,877). We used unadjusted and adjusted logistic regression models to investigate the association between exposure to alcohol outlets at the end of 2005 and any AUD re-registration in 2006–2013. Due to the small numbers of eligible people (sibling pairs where both have AUD but they have different exposure to neighborhood alcohol outlets), we were unable to use a co-sibling design to examine recurrence of AUD. All statistical analyses were conducted in SAS 9.4 (SAS Institute, 2012).

Results

Living in a neighborhood with at least one alcohol outlet of any type was associated with a small increased risk for AUD (Table 2), with the hazard ratio (HR) in the unadjusted model of 1.21 (95% CI: 1.18–1.24) that was only slightly attenuated in the fully-adjusted model (HR: 1.16; 1.13–1.19). In the fully adjusted models, on-premise outlets and off-premise government outlets both were associated with similar increases in AUD onset (HR=1.17 and 1.16, respectively). Among people with a prior AUD registration, living in a neighborhood with at least one alcohol outlet was not significantly associated with recurrence of AUD, with the odds ratios (OR) of 1.04 (95% CI: 1.01–1.07) in the unadjusted model and 1.02 (95% CI: 1.00–1.05) in the fully-adjusted model.

Coefficients for the sociodemographic variables can be found in supplemental Table S1. The indicators of individual SES each were associated with both AUD onset and AUD recurrence such that higher SES (whether indexed by income, level of education or employment status) was protective. At the neighborhood level, deprivation was a risk factor for AUD onset but it was not associated with AUD recurrence. Both drug abuse and criminal behavior had stronger associations with AUD onset than with AUD recurrence, while genetic risk for AUD had a stronger association with AUD recurrence than with AUD onset.

The effect modification analyses revealed that associations of living in a neighborhood with at least one alcohol outlet with AUD onset varied according to sex (p-value for interaction: p=.002), age (p=.001), level of education (p=.02), neighborhood deprivation (p=.0004) and urbanicity (p=.06 for mid-size cities and p=.0001 for rural areas vs. large cities). Specifically, the association of alcohol availability with AUD onset was stronger for men (HR=1.17 [95% CI: 1.13–1.20]) than for women (HR=1.07 [95% CI: 0.99–1.15]); for older people (HR=1.28 [95% CI: 1.22–1.34] for oldest cohort in sample) than for younger people (HR=1.11 [95% CI: 1.06–1.17] for youngest cohort); for those with higher levels of education (HR=1.25 [95% CI: 1.20–1.30]) than for those with lower levels of education (HR=1.17 [95% CI: 1.14–1.21]); for those in areas with high levels of neighborhood deprivation (HR=1.25 [95% CI: 1.21–1.29]) than for those in areas with low levels of neighborhood deprivation (HR=1.16 [95% CI: 1.13–1.20]); and for residents of large cities (HR=1.22 [95% CI: 1.18–1.27]) and mid-size cities (HR=1.16 [95% CI: 1.10–1.21]) than for residents in rural areas (HR=1.08 [95% CI: 1.02–1.13]). There were no significant effect modifiers for recurrence of AUD (p>.11 for all interactions).

The sibling analyses suggested that the association between living in a neighborhood with at least one alcohol outlet and onset of AUD was not highly confounded by unmeasured family factors (genetic and shared environment), as the HRs were similar to those seen in the general population models. The hazard ratios from both the unadjusted and adjusted sibling models (Table 2) were highly similar across the different types of alcohol outlets, with the HR for the fully-adjusted sibling model of 1.19 (95% CI: 1.15–1.24) for the combined indicator (living in a neighborhood with one or more alcohol outlet of any type versus no outlets in the neighborhood).

Discussion

In this population registry study of the onset and recurrence of AUD among adults ages 30 to 55 years of age, there was a small association of residence in an area with greater alcohol availability with onset of AUD over the 8-year study period, with similar hazard ratios for on-premise outlets and off-premise government outlets in both Cox proportional hazard models and in sibling analyses, suggesting homogeneity of effects for different types of alcohol outlets. Our results from the co-sibling models support the hypothesis that the association between alcohol availability and AUD is in part causal and unlikely to result entirely from personal attributes which both increase risk for AUD and cause selection into areas with greater alcohol availability. That is, at least part of the association between alcohol availability and AUD arises because exposure to greater alcohol availability causes an increased risk of AUD. These findings using contextual data linked with individual outcomes are consistent with those from early ecological studies examining associations of alcohol availability with population rates of AUD (Harford et al., 1979; Parker et al., 1983; Parker and Wolz, 1979; Smart, 1977) and alcohol-related hospitalizations (Livingston, 2011), and they contribute to the literature showing higher rates of heavy drinking in areas with greater availability of alcohol (Theall et al., 2011). Future analyses should examine mediators of these associations to determine how a greater availability of alcohol in someone’s residential neighborhood affects drinking, heavy drinking and subsequent development of AUD.

There was no evidence consistent with an association of greater alcohol availability on recurrence of AUD during the follow-up interval. The other neighborhood indicator, neighborhood deprivation, also showed an association with AUD onset but not with AUD recurrence. In our models, the strongest predictor of AUD recurrence was genetic risk for AUD (with an adjusted odds ratio of 2.13), which also was associated with AUD onset (with an adjusted hazard ratio of 1.05). Prior work in Sweden suggests that deprived neighborhoods have *greater* access to healthcare services than less-deprived areas (Kawakami et al., 2011), and these resources may be essential for off-setting effects of greater alcohol availability on recurrence of AUD. Environmental triggers for and buffering factors to prevent relapse to AUD among people who have received treatment deserve further study to identify possible points of intervention to support people in the recovery process.

Our effect modification analyses suggest that the impact of increased alcohol availability is not uniform across all neighborhood residents, although the associations suggested that living in a neighborhood with at least one alcohol outlet was a risk factor for AUD onset in all groups examined except women. US studies have found women to be at greater risk than men in areas with greater alcohol availability (Theall et al., 2011; Treno et al., 2003), but some evidence from Finland has shown men to be more at risk than women when prices of alcohol are reduced (Herttua et al., 2015). It may be that social norms around drinking in Sweden and other Scandinavian countries help inhibit the development of AUD by women who live in areas with greater alcohol availability. This deserves future study to identify protective factors, as these also may help men who live in high-risk neighborhoods.

We found that individual SES and neighborhood deprivation modified effects of alcohol availability in contradictory ways. The associations of increased alcohol availability with AUD onset were stronger for people with *higher* levels of education and for people living in more deprived neighborhoods. We expected income to modify the effect of living in a neighborhood with easier access to alcohol, in part because Sweden imposes high taxes on alcohol, which are passed on to consumers in the form of higher prices for both on- and off-premise consumption (World Health Organization, 2016). Although income was not an effect modifier, education did modify the effect of greater alcohol availability on AUD onset. In Sweden, there may be differences in social norms that prompt people with higher levels of education to drink more and thus develop AUD at higher rates in areas with increased availability of alcohol. The effect modification by neighborhood deprivation suggests there also may be stressors associated with living in an area with high levels of deprivation that also has easy access to alcohol. In Sweden, as in the US, deprived neighborhoods are more likely to contain alcohol outlets than higher-SES areas (Kawakami et al., 2011). Targeted interventions to reach residents of these high-risk areas may help reduce the burden of AUD. These interventions may need to take different forms, depending on whether they are intended to reduce the risk of AUD posed by greater availability of alcohol for higher-SES residents with high levels of education or for lower-SES residents in deprived areas.

Study strengths and limitations

Our study benefits from longitudinal data from a national population of adults with and without AUD at the beginning of the lengthy follow-up period. Another strength of our design is the ability to examine relationships between alcohol availability and AUD onset using co-sibling designs; these findings provide evidence that there may be a causal relationship between living in an area with at least one alcohol outlet and AUD onset between ages 30 and 55. Our study is not without limitations, however. Given the restrictions on alcohol sales in Sweden, there are relatively few alcohol outlets in the country; this limits the variety of alcohol availability measures that are meaningful for a national study such as this one. Future studies should examine whether different indicators of increased alcohol availability, such as those based on distance to the nearest outlet (Centers for Disease Control and Prevention, 2017), are associated with AUD recurrence, perhaps limiting analyses to large and mid-size cities and their suburbs where associations with AUD may be stronger. Alcohol availability, neighborhood deprivation and individual SES also were measured at the beginning of the follow-up period. Our data suggest dramatic changes in neighborhood SES are not common in Sweden, however. Another note is that, given our definition of AUD, our results represent individuals with more severe AUD who have received formal outpatient or inpatient treatment for AUD or who have developed physical health problems due to prolonged heavy drinking. The use of medical, legal, and pharmacy records will produce both false-negative (individuals with AUD who were not registered) and false-positive diagnoses (individuals detected who were not truly disordered). It is difficult to estimate these biases. Given that the population prevalence of AUD using our method is lower than estimates from most epidemiologic surveys, including one from nearby Norway (Kringlen et al., 2001), cases in our sample were likely, on average, to be more severely ill than those detected in population-based interview studies. We argue that these are the individuals who are most in need of intervention, and thus they are an essential population to include in this type of research.

Conclusion

In Sweden, there is a consistent modest association between increased alcohol availability and the onset of AUD, including evidence supporting a causal relationship between living in a neighborhood that has at least one licensed on- or off-premise sales outlet with AUD onset. Targeted population-level interventions, including limiting on- and off-premise retail alcohol outlet density, can result in beneficial reductions in AUD as well as other health and social outcomes (Campbell et al., 2009). Studies are needed to identify buffering factors that can help counteract the risk posed by exposure to alcohol to reduce the development of AUD during adulthood, as well as buffering factors that can mitigate any unintended negative consequences of limiting retail alcohol availability (such as increased drinking and driving in areas not served by public transportation). This work is particularly important given the ubiquity of alcohol outlets in other national contexts, such as the US. If we see these associations in Sweden, they may be even stronger in other countries that do not exercise such strong control over the retail alcohol environment.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Prevalence of alcohol use disorder (AUD) onset and recurrence across neighborhoods with varying levels of alcohol availability

	AUD onset during follow-up period (total # of individuals in type of SAMS area)		
	On-premise Restaurants & Bars	**Off-premise Government outlets**	**All outlets[1]**
0 alcohol outlets	1.74% (2,303,364)	1.76% (2,346,706)	1.73% (2,187,904)
1–3 alcohol outlets	2.10% (211,514)	2.02% (213,339)	2.08% (318,994)
>3 alcohol outlets[2]	2.17% (45,167)		2.14% (53,147)
	AUD recurrence during follow-up period (total # of individuals in type of SAMS area)		
	On-premise Restaurants & Bars	Off-premise Government outlets	All outlets[1]
0 alcohol outlets	45.4% (65,648)	45.5% (66,471)	45.4% (61,487)
1–3 alcohol outlets	47.2% (6,968)	46.7% (7,406)	46.7% (10,849)
>3 alcohol outlets[2]	47.4% (1,262)		47.8% (1,541)

[1] Also includes nightclubs.

[2] No neighborhood area contained more than three government stores.

Table 2

Relationships between neighborhood alcohol availability[1] and time to onset and odds of recurrence of AUD in a population of Swedish adults

	Time to AUD onset ***(N=2,560,045)***		
	On-premise Restaurants & Bars	**Off-premise Government outlets**	**All outlets[2]**
	HR (95% CI)	**HR (95% CI)**	**HR (95% CI)**
Model A	1.21 (1.18; 1.25)	1.15 (1.12; 1.19)	1.21 (1.18; 1.24)
Model B	1.17 (1.14; 1.21)	1.17 (1.13; 1.21)	1.20 (1.17; 1.23)
Model C	1.17 (1.14; 1.21)	1.16 (1.13; 1.20)	1.16 (1.13; 1.19)
	Sibling analysis for AUD onset		
	On-premise Restaurants & Bars	Off-premise Government outlets	All outlets[2]
	n = 139,287	*n = 118,884*	*n = 193,833*
	HR (95% CI)	HR (95% CI)	HR (95% CI)
Model A	1.18 (1.13; 1.22)	1.16 (1.11; 1.21)	1.19 (1.15; 1.23)
Model B	1.18 (1.13; 1.24)	1.18 (1.12; 1.24)	1.19 (1.15; 1.24)
	Time to AUD recurrence *(N=73,877)*		
	On-premise Restaurants & Bars	Off-premise Government outlets	All outlets[2]
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Model A	1.05 (1.02; 1.08)	1.04 (1.00; 1.07)	1.04 (1.01; 1.07)
Model B	1.03 (1.01; 1.06)	1.03 (1.00; 1.07)	1.04 (1.01; 1.06)
Model C	1.03 (1.00; 1.06)	1.03 (1.00; 1.07)	1.02 (1.00; 1.05)

HR, hazard ratio. CI, confidence interval. OR, odds ratio.

[1] Outlets recoded into dichotomous indicator (0 vs. 1 or more alcohol outlets).

[2] Also includes nightclubs.

Model A: unadjusted. Model B adjusted for: sex, year of birth, marital status in 2005, disposable income in 2005, educational status in 2005, criminal behavior (ever registered in the criminal register), drug abuse (ever registered for drug abuse), unemployment status in 2005 and neighborhood deprivation, urbanicity. Model C: also adjusted for genetic risk; estimates for control variables included in Supplemental Table 1.