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Space and Place in Alcohol Research

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Abstract

Purpose of review: To summarize the recent literature on social and physical environments and their links to alcohol use and identify empirical research strategies that will lead to a better understanding of alcohol use in contexts.

Recent findings: Recent research has continued to describe the importance of neighborhood and regional contexts on alcohol use, while a smaller emerging scientific literature assesses the impacts of contexts on drinking.

Summary: The dynamic, longitudinal, and multiscale processes by which social and physical structures affect social interactions and substance use have not yet been uncovered or quantified. In order to understand and quantify these processes, assessments of exposures (e.g., how individuals use space) and risks within specific locations are essential. Methods to better assess these exposures and risks include model-based survey approaches, ecological momentary assessment (EMA) and other forms of ecologically- and temporally-specific analyses, affiliation network analyses, simulation models, and qualitative/multi-methods studies.

Keywords

Alcohol; social epidemiology; substance use; neighborhood effects; social environment

Introduction

Heavy drinking and the prevalence of alcohol use disorders (AUDs) are believed to be affected by both micro- and macro-ecological conditions of use [1, 2]. With 57% of adults worldwide estimated to be past-year drinkers, and 40% of those engaging in past 30-day

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heavy episodic drinking, alcohol has a tremendous impact on the health and wellbeing of global populations [3]. Critically, every drinking episode takes place at a specific time and in a specific place, and physical and social characteristics of these places can vary in ways that raise or lower risks for heavy drinking and subsequent experiences of harm. If characterized by careful social ecological research, a better understanding of the links between alcohol use and social and physical characteristics of environments can lead to the development of more effective environmental prevention interventions [4]. Effective prevention programs require not only the identification of what works but where, when, and among whom they work best. Without knowledge of the social and structural features that place individuals at risk for AUDs and problematic alcohol use, ecologically valid preventive programs cannot be developed or implemented. In this paper we summarize the recent literature on social and physical environments and their links to alcohol use and identify empirical research strategies that will lead to a better understanding of alcohol use in contexts.

Understanding the role of place in health research has been one of the key advances in the epidemiologic literature over the past twenty-five years [5]. Much of this research focuses on "neighborhoods and health", where aspects of the neighborhood area where one lives are correlated with behavioral and health outcomes [6]. A set of related studies have asked similar questions, but focused on a broader spatial scale (e.g., between countries, states, or cities). More simply, descriptive epidemiologic studies that assess one or two basic differences between neighborhoods or communities, most often rural vs. urban, fill out the bulk of the "place and health" literature. A smaller, more recent set of studies have taken advantage of recent technological and analytic advances (e.g., ecological momentary assessment (EMA)) to track the movements of individuals throughout their days to better understand in-the-moment, context-specific patterns of behaviors/states [7].

Similar concerns about the role of place in the substance abuse research field was initiated somewhat earlier in the 1990s [8–13]. This work highlighted the importance of community alcohol environments and contexts to the development of harmful use and related problems [14]. The early literature largely focused on access to alcohol in community environments (e.g., through alcohol outlets [8]) and typically found that a substantial proportion of alcohol problems was attributable to conditions assessed at the neighborhood level [15]. These population-based studies were supplemented by individual level analyses of use of outlets and their implications for community health [16]. In parallel but somewhat later developments, the social epidemiology literature continued to expand to include measures of the socioeconomic environment [17], neighborhood stressors, and social environment [18]. These studies helped establish that a range of factors, which include both physical places and social spaces, are considered important risk factors for alcohol use and problematic patterns of use. Physical neighborhood characteristics that have been linked to alcohol use include measures of alcohol access (e.g., alcohol outlet densities), physical disorder/decay, and socioeconomic environments (e.g., unemployment rate, median household income). Social environmental factors include both general measures of social environments in neighborhoods, such as social capital and social cohesion, as well as the social composition of locations at specific times of alcohol use (e.g., proportion of drinkers at a party).

While the neighborhood and regional correlates of alcohol use have been and continue to be well-explored [19, 20], the measurement and tracking of individuals through these spaces has only recently begun to emerge in the epidemiology and substance use literatures. In this article we summarize the recent (i.e., since 2015) literature on place and alcohol use and some key weaknesses, describe the challenges of assessing environmental exposures and related risks, and suggest better methods for assessing exposures and risks in environments. By better enumerating and understanding the impacts of contexts on alcohol-related risk, we can develop more precise and effective preventive interventions.

Recent Literature on Space, Place, and Alcohol Use

We conducted a review of recent literature examining contextual factors and alcohol use. Articles were identified through the PubMed database using search terms for alcohol ("alcohol", "alcohol drinking") together with terms related to contextual factors ("neighborhood factors", "community factors", "contextual factors", "residence factors", "space and place", "geospatial", "spatial", "geography"). Filters were added to the search strategy to remove articles related to drinking water and animal models and articles published in languages other than English. Lastly, the search was limited to articles published from 2015 to the time of the search (June 2019).

The search strategy identified 1,826 unique articles. All abstracts were screened and the fulltext of 283 articles were reviewed for eligibility. To be eligible for inclusion, articles must have provided quantitative empirical data; examined alcohol use as a dependent variable; examined a construct of space or place of a region, neighborhood, or drinking location as an independent variable; and included a sample with the majority being adults aged 18 or older. Reviews, commentaries, and study protocol papers were excluded. In total, 75 articles met inclusion criteria (See Supplemental Table).

Reviewed studies fell into three main categories, based on their use of contextual factors: 1) Neighborhood or regional-level factors, 2) a single geographic contextual factor (most commonly urban vs. rural residence), and 3) drinking locations and contexts [21].

Regional and Neighborhood Factors

The largest category of studies examined the relationship between neighborhood- and regional-level factors and alcohol use [21–75]. Of the 55 articles included in this category, 46 examined neighborhood-level characteristics [22–67], with 23 articles equating "neighborhoods" with Census tracts or similar administrative units. The most common neighborhood factors examined include alcohol outlet density, neighborhood deprivation and socioeconomic status, neighborhood disorder, education rates, and neighborhood violence and safety. Of the 9 studies examining alcohol outlets [22, 26, 27, 30, 35, 36, 59, 62, 63], 4 differentiated between on- and off-premise outlets [26, 27, 36, 59] and 2 focused exclusively on off-premise outlets [22, 35]. Similarly, 9 articles examined regional-level factors [21, 68–75], with 4 articles at the country level [68–70, 73], 2 at the state level [72, 75], and 4 at the county or smaller regional level [21, 71, 72, 74]. A variety of regional factors were examined, such as country GDP [68–70, 73], gender equality [68–70], regional unemployment [68–71], alcohol advertising restrictions [68–70], average regional price of

alcohol [21], education levels [71], average liberal/conservative vote share [72], country mass media exposure [73], and percent social media posts about alcohol [74, 75]. All but 6 studies [21, 50, 58, 64, 67, 73] in this category were in high-income countries (29 in the United States). Studies primarily measured alcohol use by problematic or binge drinking in the last 30 days, intoxication at the last drinking event, frequency and/or volume of consumption, and the number of drinking days in the last 30 days. A small subset of 8 studies measured alcohol use disorder (AUD) [22, 28, 41, 43, 45, 46, 50, 65] and 2 studies measured alcohol expenditures or purchases [47, 53]. Five studies used a population-level measure of alcohol use as the outcome [47, 68, 69, 74, 75]. Using group-based trajectory and latent growth-mixture modeling, two studies identified unique patterns of use and utilized these identified groups as primary outcomes [32, 55]. It is notable that "alcohol use" is not a coherent construct in this research literature; drinking patterns were measured in many different ways with each way known to have different relationships to drinking environments [76].

All studies in this category used survey data, including 30 articles that used national/state surveillance and/or census data [21, 23–27, 29, 32, 34, 38, 41, 43, 44, 47, 49, 52, 53, 56, 59– 61, 67–75] and 25 that recruited community samples [22, 28, 30, 31, 33, 35–37, 39, 40, 42, 45, 46, 48, 50, 51, 54, 55, 57, 58, 62–66]. Seventeen articles presented longitudinal analyses [23, 24, 28, 32, 33, 36, 40, 42, 45, 46, 48, 53–55, 64, 66, 70], with seven having more than 10 years of follow-up [23, 28, 32, 45, 46, 54, 55]. Three studies examined patterns of alcohol use from adolescence through young adulthood [32, 41, 55]. Of note, one study examined the impact of neighborhood factors on the effectiveness of an alcohol-related intervention [37]. Additionally, one study used geographic ecological momentary assessments (GEMA), combining EMA and GIS data [63]. Although all samples included adults, 3 studies focused exclusively on men [34, 51, 61] and six on women [30, 33, 37, 52, 58, 64]. Of the studies focused on women, 2 studies were comprised of pregnant women [37, 64] and 1 of female sex workers [58]. One study included a sample of people living with HIV [63]. Additionally, 7 studies focused on middle-aged or older adults [24, 26, 27, 60, 68– 70]. These studies also utilized a variety of analytic methods, including 22 articles with multilevel models [23-26, 31, 34, 37, 39, 40, 44, 48-50, 56, 58, 60, 64, 67-70, 73], 2 with structural equation modeling or path models [41, 65], 1 with spatial regression models [47], 1 with only latent growth mixture models [31], and 27 with generalized linear models [21, 22, 27, 29, 30, 32, 35, 36, 38, 42, 43, 45, 46, 51–55, 57, 59, 61, 62, 66, 71, 72, 74, 75]. A small subset of 2 articles utilized only bivariate analyses [33, 63].

Overall, studies in this category varied widely on their research objectives and measurements of outcomes and contextual factors. Forty-eight studies found a significant result between neighborhood/regional factors and alcohol use. Neighborhood deprivation or SES was most commonly significantly related to alcohol consumption.

Geographic Context

Fifteen articles considered associations between one simple factor of residence and alcohol use [77–91]. The vast majority of these articles (11) examined urban vs. rural residence, determined by population size or density, as a binary variable (though with different cutoff

values) [77, 78, 80, 82–88, 90], while 3 articles used three or more tiers of urbanity (e.g., urban, suburban, large rural town, isolated rural) [79, 81, 89]. Additionally, 1 article examined residence in a disaster community in the United States, defined as previously being impacted by a terrorist attack, versus non-disaster community [91]. It is noteworthy that while these articles only consider a single variable of space and place, 7 articles are focused on low and lower-middle income countries, including Cambodia [85], Ghana [77, 90], India [88], Myanmar [85], Nepal [78], Nigeria [81], and Vietnam [85, 86]. An additional five articles focus on upper-middle income countries, including Brazil [84], China [82, 83], Guatemala [87], and Namibia [80], while only three are focused on high income countries [79, 89, 91]. Twelve articles included outcomes of hazardous alcohol use, frequency, and/or volume [77-80, 82-86, 89-91], while 2 articles measured AUDs and dependence [81, 87] and 1 article included both types of outcomes [88]. Data were obtained from national or regional household surveys and surveillance programs in 12 studies [77–80, 82-84, 86-90] and surveys with community samples were used in the remaining 3 studies [81, 85, 91]. All but 3 studies in this category utilized generalized linear models [77, 78, 80– 88, 90] and the remaining articles used only bivariate analyses [79, 89, 91]. Results of these studies varied greatly by geographic context and location. Overall, 10 studies found a significant relationship between alcohol use and rural/urban residence.

Drinking Locations and Contexts

In total, a small subgroup of 6 articles examined the role of microenvironments (i.e., areas smaller than neighborhoods) on alcohol consumption [21, 92–96]. For the purposes of this review, only studies that examined characteristics or types of drinking locations were included. Studies that examined only residence and housing characteristics, such as living in a dorm vs. off-campus, or interpersonal factors were excluded. Overall, all 6 studies compared alcohol use in different drinking locations (e.g., home vs. bar), 2 additionally examined characteristics of people at the location (e.g., number of intoxicated patrons) [92, 96], and 1 examined location-specific factors (e.g., presence of a keg, enforcement of legal drinking age) [92]. One study objectively measured peak blood alcohol content (BAC) using transdermal alcohol sensors [94], while the others used survey-derived measures of alcohol use.

Three studies examining microenvironments focused on the drinking habits of university students [92–94] and 1 study sample was comprised exclusively of gay and bisexual men [96]. A variety of survey sampling designs were utilized, with 2 studies based on national and household surveys [21, 95] and two based on school-based surveys [92, 93]. No studies recruited directly from drinking venues. Further, 2 studies utilized GEMA [94, 96]. One of these studies utilized GPS-enabled devices to track individual's locations and create spatial plots of a single evening of drinking [94]. The second study tested the effectiveness of location-based GEMA within geofences, or pre-specified locations in which an individual would be asked to complete an assessment upon entering the area [96]. Analytic methods consisted of multilevel models in 2 articles [92, 96], generalized linear models in 2 articles [21, 93], and only bivariate analyses in 2 articles [94, 95]. Although these studies differed in environmental factors examined, 5 studies found significant associations between drinking locations and alcohol use.

Understanding Risks in Contexts

As summarized in the prior section, the recent literature has continued to describe the importance of neighborhood and regional contexts on alcohol use, while a smaller emerging scientific literature assesses the impacts of contexts (here defined as the places where individuals live and/or drinking-related activities take place as well as the social and physical characteristics of those places) on drinking. While these articles have made an important step forward, the dynamic, longitudinal, and multiscale processes by which social and physical structures affect social interactions and substance use have not been uncovered or quantified. In order to understand and quantify these processes, assessments of exposures (e.g., how individuals use space) and risks within specific locations are essential. In this section, we describe some of the key challenges to better understanding context-specific risks.

Assessing Exposures

The typical approach to understanding how environments and contexts impact substance use has been to assign individuals to a home location (or neighborhood), and assume that alcohol environment exposures are only relevant in that one area. In fact, 43 of the 45 neighborhood-level articles in our review of recent literature used this as their approach. While theoretical and empirical developments support the importance of this approach, a critical missing piece in understanding substance use ecology is the measurement and tracking of individuals through these spaces as they purchase and use alcohol.

Routine activities theory [97] provides the framework within which much of the recent efforts to measure social exposures that affect substance use have been developed. The emphasis of routine activities theorists is upon how the daily activity patterns of individuals are shaped by their physical and social environments, moderate exposures to neighborhood conditions, and provide opportunities for substance use and abuse. Building on these concepts, recent research has attempted to elucidate the activity spaces that underlie typical environmental exposures [98, 99]. Activity spaces are defined as that set of locations with which an individual has direct (physical) contact during their typical activities [100]. Activity spaces are most commonly operationalized using sets of "activity locations" where individuals spend time (e.g., grocery store, workplace), captured retrospectively using survey-based lists, guided interviews, geographic coordinates embedded in digital media (e.g. Twitter posts), or prospectively using travel diaries or responses to geographic ecological momentary assessments [101]. More recent work has characterized individuals' activity spaces using full activity paths that include the precise route paths that individual take to travel between activity locations captured retrospectively (e.g., using GIS-assisted interviews [102]) or prospectively using GPS tracking [103]. Despite these considerable methodological advances, there remains some uncertainty about the best way to reduce such detailed space-time data into functional measures of individuals' exposure to neighborhood conditions. For example, limits to battery life mean GPS tracking typically provides individuals' latitude and longitude coordinates at regular intervals (e.g., every 20 seconds). Researchers can then measure exposure within geographic units where GPS points are located (e.g., Census tracts), within buffers around the points, or along interpolated lines

connecting the points. The methodological decisions that researchers make can materially affect estimated associations between exposure to environmental conditions and alcohol consumption [101, 104].

Still underdeveloped is the concept of routine drinking activities and drinking activity spaces. This is the "gold standard" we would like to be able to achieve in order to best understand social and physical environmental spaces that are directly linked with specific alcohol consumption patterns. This is difficult to measure, as it involves layering information specific to drinking (where, when, with who) on top of general activity spaces assessment.

Assessing Risks

In order to understand the social ecology of alcohol use, it is necessary not just to better understand and measure exposures to social and physical environments but also how those exposures lead to risk in specific spaces at specific times. While several of the studies in our review of the literature were longitudinal [32, 42, 53, 55, 70, 94], few combined information about locations and timing of both exposure and risks, which is critical. The temporal specificity of the relationships between ecological contexts and drinking behaviors is dependent on the phenomenon of interest. It seems plausible that acute harms, such as single instances of binge drinking, are related to solitary exposures to specific contexts, such as drinking heavily at an office holiday party. In contrast, the extent to which social ecological contexts influence chronic alcohol-related harms, including AUDs, is less clear [105]. Attendance at a single event, such as our proverbial holiday party, is unlikely to lead a person to develop an AUD (though it may increase risk for an acute problem such as an alcohol-related car crash). However, continued attendance at similar events over time and continued affiliation with people who drink heavily may increase one's risks for chronic harms.

Available study designs and statistical analytic methods make it difficult to identify the location and timing of specific risky events. We typically rely on the accumulation of risks over time, with the result that analyses of different processes can look deceptively similar. The temporally-specific measurement of people within places is a critical barrier to understanding these processes and developing relevant preventive interventions. We now turn to potential solutions to these measurement issues.

Methods to Assess Exposures and Risks Related to Space and Place and Alcohol

Traditional Approaches: Individual Surveys

As detailed in the above review of the literature, recent advances have primarily focused on studying relationships between static "home" community environments and alcohol in new populations, with only a handful of studies incorporating newer methodologies to better understand spatially- and temporally-specific exposures and risks. There are important things to be learned from more traditional approaches. Survey-based approaches can be used to assess context-specific risks in large populations, and to understand risks in carefully

defined and sampled populations. When used creatively, surveys can even be used with location-based sampling, such as a portal survey of individuals entering a bar on a given night. However, while this approach is ideal conceptually, it appears to be infeasible in practice, as drinkers are hard to access before, during, and immediately after their use of contexts [106]. One alternative is to assess spatially- and temporally-specific exposures and risks retrospectively (for example, through survey-based assessments of activity spaces) [107]. This alternative approach is subject to recall bias and cannot explicate event-specific information or specific social interactions, but it at least begins to examine context-specific associations.

Model-Based Survey Approaches

Recognizing that it is difficult, and may be impossible, to assess day-to-day substance use activities and related problems in representative survey samples, one alternative is to maximize the information yield of survey data using model-based approaches. Specifying expected quantitative relationships between exposures (e.g., frequencies of going to a bar), patterns of alcohol use (e.g., heavy drinking), and problems (e.g., driving after drinking), such models guide the analysis of survey data to the elucidation of these relationships [108– 110]. These approaches assume an exposure measurement model for the behavioral processes involved in use and problems, then use that model to determine the functional form relating drinking contexts to use and problems. Using one context-specific model and survey data from over 34,000 college student drinkers, Mair and colleagues [109] found that frequent drinking in many contexts (e.g., Greek or off-campus parties) was associated with greater numbers of sexual partners and unprotected sex, whereas heavier drinking selectively increased risks at bars. In another approach, Gruenewald et al. [111, 112] elucidated the personal (e.g., impulsivity) and social (e.g., outlet density) correlates of the use of drinking contexts (e.g., drinking at bars or at home) and impaired driving across 50 cities in California. They demonstrated that while bars remained a critical point source of impaired driving events, a substantial number were associated with drinking in private residences.

Ecological Momentary Assessment (EMA) and Other Forms of Ecologically- and Temporally-Specific Analyses

Methods such as ecological momentary assessment (EMA) allow us to track individuals' routine activities in (nearly) real time and begin to measure the dynamic, evolving contexts of alcohol use [7]. By this approach, study participants are sent brief surveys, often through mobile devices, regarding their behaviors at specific times. Assessing momentary exposures and outcomes substantially limits recall bias, and enables researchers to assess relationships with high temporal specificity. Adding information about participants' physical locations, either by self-report [113] or through GPS coordinates [114], also enables researchers to assess these relationships with high spatial specificity. For example, Byrnes et al. [114] followed 170 adolescents aged 14 to 16 years for one month using EMA and GPS tracking. They identified that GPS-based measures of exposure to retail alcohol outlets at 100 meters and 200 meters around their GPS activity path was associated with increased drinking frequency over that month, whereas individuals' self reports (i.e. perceived) exposure to alcohol outlets was not associated with alcohol use. Importantly, the individual behaviors assessed using EMAs (e.g., going to a bar) are often specific instances of the same aggregate

behaviors analyzed using model-based approaches (e.g., frequencies of going to a bar); in tandem, the two approaches enable elucidation of how highly stochastic individual behaviors aggregate to support neighborhood problems.

Exponential Random Graph Models and Affiliation Networks

Model-based survey approaches have successfully identified relevant contexts for drinking and related problems, which highlights the importance of understanding what happens within specific contexts to generate excessive problems. Additionally, many studies have noted the importance of social networks in both the initiation and maintenance of drinking behaviors and the processes of treatment and recovery [115, 116]. Affiliation networks are a theoretical and analytical tool to integrate social ecological contexts with social networks and processes. They involve expanding social networks from one mode of interaction (e.g., connections between people) to two modes of interaction (e.g., connections between people in places [117]). Affiliation networks can be analyzed using bipartite graphs and exponential random graph models. These methods have been successfully employed to show, for example, that among adolescents, peer influence via shared participation in organized sports/ clubs with drinkers has a significant effect on adolescent drinking [118]. Very little work has taken advantage of these methods in substance use research. While it has been convincingly demonstrated that individual characteristics are strongly related to the assortment of individuals into different drinking contexts among adults [112] and youth [119]), it remains unclear how those assortative processes affect social network structures and related risks [120].

Simulation Models

The development of computational and mathematical models is a vital step in advancing alcohol preventive intervention research. Rather than assume independence among prevention strategies and their effects one-from-the-other, many computational and mathematical models enable us to account for system dependencies among the functional processes that underlie alcohol use. In particular, agent-based modeling approaches can be used to both elucidate specific mechanisms underlying alcohol-related problems and provide a framework for developing comprehensive preventive interventions at the community level [121, 122]. These models can account for significant heterogeneity of agent characteristics and spatially explicit agent interactions, and enable us to investigate the specific ecological circumstances of drinkers and the social mechanisms that facilitate alcohol problems in community settings. For example, Fitzpatrick and Martinez used an agent-based modeling framework to examine how the processes of drinkers assorting themselves into specific drinking venues due to spatial and social (niche) motivations impact the spatial patterns of alcohol-related problems [11]. Such models must be carefully calibrated so that the population of agents reflects the real population of interest for all dependent and independent variables of interest, and must adequately reflect the hypothesized dynamic, longitudinal, and multiscale social ecological processes that drive these context-specific associations, otherwise the resulting associations will merely reflect the input parameters.

Qualitative/Multi-Methods Studies

In order to collect ecologically- and temporally-specific data, combining multiple data collection approaches may be most effective. As described above, data collected via surveys or using more geographically- and temporally-specific measures (e.g., GEMA), provide information on the where, when, and sometimes the who, but motivations (the why) for using or drinking in those places are harder to ascertain. Qualitative interviews can provide valuable and in-depth information on why and how spaces and certain venues are used [123– 125]. Qualitative interviews that occur before embarking on surveys can also provide information on the most frequently visited contexts to include in a survey describing activity space locations [126]. In an ongoing study, we are integrating community-level, microenvironmental, and individual behavioral-level data on off-premise alcohol outlets (events) and local residents living within two blocks of these outlets (actors). These are being further boosted by including interviews with those who work at the outlets and intensive spatial secondary data sources. By examining multi-scale mechanisms with mixed-method approaches, we enable explanations of individual risk behaviors in terms of structural, local, population-level characteristics, and provide guidance to the development of effective prevention programs.

Conclusions: Prevention in Contexts

Effective prevention programs require not only the identification of what works but where, when and among whom they work best. Without knowledge of the social and structural features that place individuals at risk for AUDs and problematic alcohol use, ecologically valid preventive programs cannot be developed or implemented. The recent literature on place and alcohol use continues to illustrate the importance of context and neighborhood for alcohol-related outcomes, but largely fails to identify the mechanisms by which these associations arise. A better understanding of the social structures that occur in certain drinking environments and subsequent alcohol use-patterns can help us identify what aspects of environments might be amenable to change to decrease the occurrence of problematic drinking. If research illustrates that specific locations (or types of locations) increase risk for all social ties that form within that location, an intervention focused on eliminating or reducing access to that location would be warranted. If specific types of social ties within contexts (e.g., two impulsive people in a bar at the same time) are risky, interventions could focus on reducing interactions or conflict between impulsive people in that specific location. Finally, if social ties in specific locations are riskier at certain times (e.g., St. Patrick's Day parties; Saturdays from 11PM to 2AM), interventions could focus on reducing risk in those critical time periods. By understanding individuals' behaviors and social ties, and how drinking environments and environmental characteristics alter these, we can develop more precise and effective preventive interventions, both individual-based (e.g., a brief intervention implemented in a specific context to reduce partner conflict) and environmentally-based (e.g., a prevention message that drinking with one's partner in a bar increases risk). Epidemiologists can contribute to this important intervention work by better measuring temporally- and spatially-specific exposures and risks and using the available methodologies being developed.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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