IN THE INTRODUCTION to this supplemental issue to the Journal of Studies on Alcohol and Drugs, we described how?Most of the studies suffered from attrition bias, but all demonstrated "significant effects across a range of different exposure variables and outcome mea- sures" (p. 7). Reviews such as these speak to consistency of effect across a heterogeneous group of studies, an important Bradford Hill criterion. The authors concluded the data from these studies suggested a modest association between expo- sure and subsequent alcohol consumption in young persons. Jernigan et al. (2017) conducted a systematic review of longitudinal studies published after the Smith and Foxcroft (2009) review that examined exposure to advertising and drinking among underage persons. All 12 studies found a positive association between marketing exposure and one or more alcohol consumption outcomes. For initiation of alcohol use the odds ratios for different marketing exposures ranged from 1.00 to 1.69, and for subsequent hazardous or binge drinking, the range was somewhat higher: 1.38 to 2.15. Thus, a review of longitudinal studies published after 2009 offered the same conclusion--evidence of a modest effect of alcohol marketing, with consistency across heterogeneous measures of marketing exposure and drinking. The review of cross-sectional studies by Finan et al. (2020) presents mixed results. In general, the authors report more evidence for a positive relationship between alcohol marketing exposure and alcohol use behavior among adoles- cents and young adults than negative or null evidence. For example, of the 38 studies reviewed comprising 32 differ- 116 JOURNAL OF STUDIES ON ALCOHOL AND DRUGS / SUPPLEMENT NO. 19, 2020 TaBLe 2. Bradford Hill criteria addressed mainly and secondarily in 11 review articles Author/review topic Number of studies or (references) Number of countries Number of subjects Bradford Hill criterion Strength of association Jernigan & Ross/ alcohol marketing landscape (70) n.a. Weitzman & Lee/ alcohol and tobacco similarities (97) n.a. M+ Jackson & Bartholow/ psychological processes (120) n.a. M+ Courtney et al./ neuro- biological studies (133) n.a. M+ Henehan et al./ youth cognitive responses 22 6 M+ M+ Finan et al./ cross- sectional studies 38 15 M+ Noel et al./ digital alcohol marketing 25 8 M+ Saffer/ econometric studies 17 OECD countries M+ Smith & Foxcroft (2009)/ longitudinal studies 7 3 13,255 M+ Jernigan et al. (2017)/ longitudinal studies 12 6 35,219 M+ Stautz et al. (2016)/ experimental studies 24 5 M+ Dose-response relationship S+ Temporal precedence S+ Consistency S- Specificity of association S+ Plausibility M+ Experimental S+S+ S+ evidence Coherence S- Analogy M+M+M+ S+ S+ S+ S+ M+ M+ M+ S+ M+ M+ M+ M+ M+ S+ S+ S- M+ M+ M+ S- S+ Notes: Supported (+); not supported (-). M refers to the main conclusion of a systematic review that supports (+) or does not support (-) one of the Bradford Hill principles; S refers to a secondary conclusion of the review that is supported by citations and the description of evidence from other scientific research that supports (+) or does not support (-) one of the Bradford Hill principles. n.a. = not applicable; OECD = Organisation for Economic Co-Operation and Development. This review used statistical significance and whether the association was positive or negative. For most drinking outcomes, the association, if significant was positive. In only two studies was it negative; but in one third, it was null. ent associations between marketing exposures and lifetime drinking outcomes, the authors found 21 positive relation- ships compared with 11 null association relationships and only a handful of negative relationships--more evidence for a modest association. They also found that relationships for alcohol promotion and owning alcohol-related merchandise exposures were more consistently positive

than for other advertising exposures. As the authors note, methodological issues make it difficult to review, evaluate, and summarize cross-sectional findings. Similarly, in Noel et al.'s (2020) review of the litera- ture on digital marketing, which comprises studies using cross-sectional, longitudinal, and experimental designs, the strength of associations across the 25 studies was mixed. Nevertheless, the findings support the conclusion of a mod- est positive association between engagement with digital alcohol marketing and increased alcohol consumption as well as increased binge or hazardous drinking behavior. In addition, their review showed that liking or sharing an ad- vertisement on social media or downloading alcohol-branded content was positively associated with alcohol use, whereas the effects of simple exposure to digital alcohol advertising were inconclusive. Based on the cumulative evidence, we conclude that the strength of association, temporal precedence, and consis- tency criteria have been met but that more research is needed to establish dose-response relationships. Specificity and independence Even when an association is moderately strong and sta- tistically significant, the ability to draw causal inferences is limited if the study does not adjust for confounding, which occurs when exposure and drinking behavior are both in- fluenced by an unmeasured third variable that accounts for the association. It is important to distinguish between con- founders and mediators, which are statistically identical. A confounder is a variable associated with both the exposure and the outcome but independent of the causal pathway from exposure to behavior. A mediator is on the causal pathway-- a variable that is set in motion by the exposure and contrib- utes indirectly to the effect of the exposure on behavior. Psychological constructs that lie on the theoretical pathway between advertising exposure and drinking (e.g., alcohol expectancies) should not generally be modeled as covariates but as mediators in order to test theoretical models that shed light on mechanisms. Parenting styles, peer and family drinking, and personal- ity traits such as sensation seeking have all been found to increase the risk of underage drinking. To the extent that they also increase exposure to advertising, not accounting for them could cause us to reach a spurious conclusion. For- tunately, alcohol advertising has also been shown to be inde- pendent of many of these confounders in the cross-sectional and longitudinal studies cited above. For example, one study (Stoolmiller et al., 2012) found a longitudinal association be- tween ownership of alcohol-branded merchandise (marketing receptivity) and drinking onset as well as binge drinking af- ter accounting for age, sex, race/ethnicity, parental education, family income, alcohol use by parents and peers, poor school performance, sensation seeking, rebelliousness, parenting ef- fectiveness, weekly spending allowance, television viewing, and exposure to alcohol in movies. Jackson and Bartholow (2020) note that much of the sup- port for an association between alcohol-related marketing and youth drinking is based on prospective cohort studies that adjust for potential interpersonal-level (parent, peer in- fluence) and individual-level (sociodemographics, sensation seeking) confounders. These studies lend credence to the argument that marketing exposure is a causal factor in drink- ing behavior. Not only does this review make a strong case for independence of association, but it also supports several plausible psychological mechanisms that could be responsible for causal associations between alcohol-related marketing and youth drinking. The fact that modest associations are found across multiple studies, each of which adjusts for a somewhat different set of covariates, is a very strong indicator of the robustness and consistency of the association. The review of

econometric studies by Saffer (2020) points out the limitations of older research (Nelson, 1999) that could not adequately rule out a third unmeasured causal variable, with a focus on minimizing the possibility of a third variable effect. In econometric language, endogeneity is the unmeasured third factor. Endogeneity could involve reverse causality (demand for alcohol can prompt more advertising) or factors that work at the individual level. Endogeneity is a concern with any marketing assessment that goes in the direction from product consumption to heightened awareness of advertising for the product. For example, engagement in online marketing is not only a measure of "exposure" to such advertising, but it also is often a measure of the degree to which an individual is engaged in the consumption.In Hill's words, "No formal tests of significance can answer those questions" (p. 299). Neither can one study, regardless of how compelling it might be, answer the ques- tion. Moreover, a judgment of causality is always subject to revision as the science underlying the judgment progresses. In this concluding article, we provide our own scientific judgment of findings presented in this supplement and be- yond, along with suggesting implications for public health policy and further action. The articles, commissioned as part of a larger Cochrane review that will address longitudinal and experimental stud- ies of alcohol marketing, cover a broad variety of approaches that have been taken to answer the causality question. The approaches comprise different research designs (cross-sec- tional, longitudinal, experimental), measurement techniques (survey studies, econometric research, randomized trials, laboratory studies), national contexts of exposure (high-, middle-, and low-income countries), and media/communica- tion channels (e.g., print, television, digital, films). Received: December 13, 2019. *Correspondence may be sent to James D. Sargent at the C. Everett Koop Institute, Geisel School of Medicine at Dartmouth, One Medical Center Drive, Lebanon, NH 03756, or via email at: james.d.sargent@dartmouth.edu. ogy. Results: Evidence of causality for all nine of the Bradford Hill criteria was found across the review articles commissioned for this supplement and in other previously published reviews. In some reviews, multiple Bradford Hill criteria were met. The reviews document that a substantial amount of empirical research has been conducted in a variety of countries using dif- ferent but complementary research designs. Conclusions: The research literature available today is consistent with the judgment that the association between alcohol marketing and drinking among young persons is causal. (J. Stud. Alcohol Drugs, Supplement 19, 113–124, 2020) Alcohol marketing research has matured since the days when exposures were measured across a collection of high- income countries in terms of aggregate amounts of industry spending on traditional advertising and when effects were measured in terms of cross- sectional association with per capita alcohol consumption at the national level (Saffer, 2020). With the addition of more sophisticated longitudinal designs, new ways to address confounding, and more repre- sentative samples responding over time to better measures of exposure to different types of advertising, confidence in the directionality of the associations and the validity of the findings has increased. For example, a recent systematic review of research on the association between alcohol marketing and youth drink- ing (Jernigan et al., 2017), based on studies published since 2009, using sophisticated longitudinal designs with more than 35,000 persons, reported a significant association be- tween youth exposure to alcohol marketing and subsequent drinking behavior. One deficiency with this method of sum- marizing the literature, which the present supplement was designed to correct, is that the research

literature had never been organized to address multiple causal criteria in a way that would satisfy both the scientist and the policy maker. The articles in this supplement go beyond the evidence from prior reviews of the alcohol marketing literature and attempt at integration (e.g., Babor et al., 2017) by critically evaluat- ing a variety of observational and experimental research of putative mechanisms that covers laboratory-based neurobio- logical studies (Courtney et al., 2020), psychological studies (Jackson & Bartholow, 2020), and econometric studies (Saf- fer, 2020). In the remainder of this article, we explain how the re- search findings assembled in this project provide clear an- 113 114 JOURNAL OF STUDIES ON ALCOHOL AND DRUGS / SUPPLEMENT NO. 19, 2020 swers to the questions posed at the beginning: Does exposure to alcohol marketing have a causal influence, and, if so, what are the implications for alcohol policy and public health? Does exposure to alcohol marketing have a causal influence on youth drinking? Sir Austin Bradford Hill (1965) was an environmental ep- idemiologist who focused on workplace hazards. He is well known for his contributions to our understanding of the rela- tion between smoking and disease. The basis for the widely held notion that smoking is one cause of cancer and other conditions is purely observational science--science that has been periodically summarized by panels of experts using a Hill causality framework. That is the process whereby causal statements about smoking and disease came to be. In 1965, Hill identified a set of criteria used to assess cau- sality for associations between environment and disease. The Bradford Hill criteria have been widely used in establishing consensus judgments about causality in medicine and public health, playing an important role in justifying evidence-based public health regulations (Doll, 2002; Hill, 1965; McDonald & Strang, 2016). These criteria may also be applied to re- search involving behavioral outcomes. For example, a causal statement on tobacco marketing and adolescent smoking was made by the U.S. Department of Health and Human Services (National Center for Chronic Disease Prevention and Health Promotion Office on Smoking and Health, 2012) by applying Bradford Hill criteria to that literature. Causality is most convincingly demonstrated by random- ized clinical trials, and there are some examples in the al- cohol marketing literature of the use of this "gold-standard" research design to evaluate short-term relationships at the psychological, neurobiological, and behavioral levels of analysis (e.g., Jackson & Bartholow, 2020; Courtney et al., 2020; Noel et al., 2020).Their re- view suggests how the mechanisms of action work and helps explain the different strategies used by the alcohol industry either intentionally or indirectly in the complex world of alcohol marketing, such as frequent exposure to promote familiarity and evaluative conditioning, a tactic that pairs a more familiar object with a less familiar product to influence the perception of the new product.Bradford Hill criteria: Definitions and application to alcohol marketing researcha SARGENT AND BABOR 115 Criterion Definition Application to alcohol marketing exposures Strength of association The stronger the association between the exposure and the clinical outcome, the less likely it is influenced by an exter- nal variable or confounded by a variable associated with the exposure and outcome of interest.Hill's causality criteria comprised the following: (a) strength of association, (b) consistency, (c) specificity of association, (d) temporality, (e) biological gradient (dose- response relationship), (f) biological plausibility (to this we would add plausibility regarding psychological theory), (g) coherence, (h) experimental evidence (e.g., reproducibility in animal models; experiments involving randomization), and (i) analogy.However, most of

the Bradford Hill criteria apply to results from multiple observational studies, especially when randomized clinical trials are difficult to conduct for practical or ethical reasons (e.g., it would be unethical to assign persons to smoke cigarettes as a test of the smoking–lung cancer association).In the following analysis of the findings presented in available literature reviews, along with those presented in this supplement, we have adapted the Bradford Hill criteria to the hypothesized causal association between alcohol marketing exposures and adolescent drinking.Strength of the association, dose–response, temporal precedence, and consistency One of the most important Bradford Hill criteria is the strength of the association, which can be measured statisti- cally in terms of relative risk (for dichotomous outcomes) or Cohen's d (for continuous ones).Longitudinal observational studies typically assess marketing exposure in a cohort of adolescents, starting with never drinkers during childhood or early adolescence who are followed over time to evaluate the association between exposure at baseline and onset of drinking.In addition, most of the studies conducted on the alcohol marketing–drinking association were based on nonexperimental observational studies in which the independent variable (exposure/recep- tivity to alcohol marketing) was not under the control of the researcher because of ethical or logistical constraints.As noted in the introductory article to this supplement (Sargent et al., 2020, Figure 1), the Cochrane review proj- ect contributing to these reviews screened 18,997 articles, finding 11,126 of them to be relevant to alcohol marketing research.Because the recent reviews of longitudinal and experimental studies are highly relevant to the criteria of strength of association, temporal precedence, and consistency, they are included here in our concluding causality assessment.Saffer highlights several recent econometric studies (e.g., Molloy, 2016) that used instrumental variables analysis to ensure the exogeneity of the marketing exposure measure and found a modest association.eight manuscripts were commissioned to address dif- ferent Bradford Hill criteria (Hill, 1965) to assess whether the association between alcohol marketing and the onset and severity alcohol consumption by youth is causal.For example, Morgenstern et al. (2011) showed that alcohol marketing receptivity was associ- ated with drinking independent of receptivity to marketing for other products (e.g., candy and mobile phones), and Tanski et al. (2015) showed that the association between receptivity to television alcohol advertising and onset of drinking and binge drinking was independent of receptivity to fast food advertising.Plausibility One indicator of the maturity of an area of research (e.g., marketing research) is its ability to articulate plausible conceptual models and theoretical explanations based on cu- mulative findings.In contrast to the p value, in which there is general agreement on the .05 cutoff level, there are no widely agreed–upon categories for strength of relative risk; most scientists would agree that the association between smoking and lung cancer is strong (adjusted relative risk10; i.e., smokers are at more than 10 times greater risk for lung cancer than nonsmokers) and the association with breast cancer (adjusted relative risk = 1.3) is modest or weak.In recent years, psychologists have developed and tested theoretical models in which marketing exposures are hypoth- esized to affect psychological mediators relating to thoughts, cognitions and attitudes.The table also adds ratings of the evidence from three recent reviews not included (Smith & Foxcroft, 2009; Jernigan et al., 2017; Stautz et al., 2016) because of their focus on longitudinal and experimental studies.Have there been multiple observations of alcohol market- ing effects across multiple media, in multiple countries, as reported by different investigators using a variety

of exposure measures and covariate controls?Hill empha- sized that many exposures cause multiple diseases, such that this type of specificity should not be seen as an absolute prerequisite to causality, and the same is probably also true with marketing effects on risk behaviors.Henehan et al. (2020) review research on youth cognitive responses to advertising to evaluate underlying theories that might explain the association between marketing exposures and alcohol use by youth.Jackson and Bartholow (2020) provide a narrative summary of psychological plausibility using an integrated conceptual model that depicts relevant psychological processes as they work together in a complex chain of influence.Table 2 summarizes the evidence for each Bradford Hill criterion as described in the narrative and systematic reviews presented in this supplement.How strong is the association between exposure to alcohol marketing and changes in alcohol consumption compared to other neurobiological, psychological, and behavioral cor- relates of drinking behavior?Is there experimental evidence that relies on randomization of marketing exposure or instrumental variables to rule out third variable explanations?Coherence Causality between an exposure and a health outcome is sup- ported when the association is coherent with current knowl- edge of the health condition.This criterion places a premium on longitudinal research in which marketing exposures are measured before the onset of alco- hol use.Plausibility refers to whether an associa- tion has a credible empirical or theoretical basis in terms of biological, psychological, or social mechanisms.Plausibility was explored directly in two of the reviews in this supple- ment, and indirectly in several others, on the psychological and the biological levels of analysis.The evidence suggests that perceptions of others' behaviors and attitudes in relation to alcohol (social norms) may be a more potent driver of youth drinking than evaluations of drinking outcomes (expectancies).Causality is not a conclusion that derives from any one scientific study: It is a judgment call--a summary statement that describes how a scientist (or group of scientists) views the evidence as a whole.Dose–response relationship If a dose–response relationship can be observed for the cause–and–effect hypothesis, increased exposure will proportionally impact the clinical outcome.Consistency The credibility of a finding increases if different investiga- tors can replicate it across different locations, with different populations, and under different circumstances.Plausibility There is stronger support for causality if there is a likely bio- logical and/or psychological mechanism that can explain the association between exposure and the outcome.Experimental evidence If experimental manipulation of the exposure–outcome as- sociation impacts the outcome, this represents very strong support for causation.Analogy If an exposure factor similar to A leads to a clinical outcome similar to B, then this analogy counts as evidence in support of our hypothesis that A causes B. Are the effects of exposure to alcohol marketing similar the results of research on exposure to tobacco marketing?Smith and Foxcroft (2009) published a review of seven longitudinal studies that followed 13,000 young people ages 10–26 years and evaluated a range of alcohol advertising and marketing exposures.Cognitive responses to alcohol advertising were found to be complex, with many factors modifying the association, including differences by age, experience with alcohol, and alcohol advertising content.Of these, 1,736 were eligible for consideration of causality, and 163 of these studies were included in the quantitative synthesis.Hill also considered it helpful when there was a dose–re- sponse association, such that higher doses of the exposure could be demonstrated to result in progressively higher risk TaBLe 1.Is it biologically plausible

that changes in neurobiological responses and psychological processes can account for the association?Are there documented examples of youth alcohol use increas- ing without marketing exposures or decreasing with them?Some studies begin with adolescents who have not engaged in hazardous drinking but who may be experimenting with alcohol and examine the transition to hazardous or binge drinking.These marketing-induced changes are hypothesized to predict whether an individual will en- gage in drinking behavior.The extent of this literature indicates that a significant amount of empirical research has been conducted on this topic.The table also shows that these review articles are based on substantial empirical research that has been con- ducted in a variety of countries.For continuous outcomes, Cohen recommended a rule of thumb: .2 was considered modest, .5 moderate, and .8 strong.Does risk of alcohol consumption increase monotonically with higher levels of exposure to marketing or marketing receptivity?Did the exposure to alcohol marketing precede early onset of drinking and progression to binge drinking?Another important aspect of causality is to demonstrate that the exposure precedes the outcome.These studies go a long way to assure us that the modest strength associations for cross-sectional and longitudinal studies listed above are real.This would be demonstrated if alcohol marketing exposure predicted binge drinking but not other risk behaviors, such as smoking.However, it has been possible to show that alcohol mar- keting is associated with drinking, independent of exposure to other marketing inputs.Is the asso- ciation between exposure to alcohol marketing and drinking reciprocal?Specificity Causality can be established when one type of exposure leads to one specific outcome.Is the association between alcohol marketing exposure and substance use confined only to drinking, or does it also include other behaviors like smoking?Temporal association Is there evidence that the presumed cause precedes the effect in time?Is exposure to other marketing inputs (e.g., food) associated with higher risk of drinking?Few of the studies tested explicitly for specificity of the marketing message.To the extent risk behaviors cluster, this could be difficult to demonstrate.For example, younger populations tend to be less skeptical of advertising claims than are older adolescents.In addition, youth who reported prior alcohol use liked alcohol advertisements more than their peers with less or no alcoholThe criteria, their definitions and their application to alcohol marketing research are shown in Table 1.A review of these studies will also be covered in the forthcoming Cochrane review.The table gives evidence of causality for all nine of the Bradford Hill criteria.In some reviews, multiple criteria have been met.We would consider a relative risk that is less than 2.0 to be modest and a relative risk of 2 to less than 10 to be moderately strong.Do mediational analyses confirm psychological theory?Conflicting or lack of supporting evidence would count against coherence.If so, does this empirical evidence conflict with a causal interpretation?aAdapted from McDonald and Strang (2016).This explains the need for segmentation and specification of different types .of alcohol advertising.These authors also point out developmental consider- ations.for the outcome