Alcohol and Cancer:
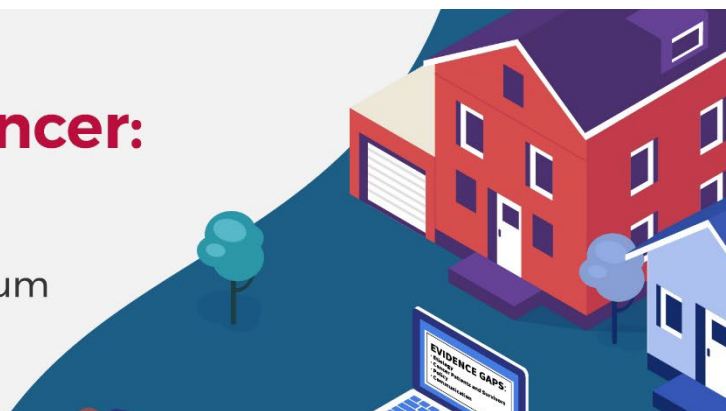Identifying Evidence Gaps
and Research Challenges
Across the Cancer Continuum

December 8–10, 2020

EXECUTIVE SUMMARY (DRAFT)

Alcoholic beverages have been widely consumed by humans worldwide for religious, cultural, and social purposes, and the health effects of alcohol consumption are of significant public health interest. The World Health Organization (WHO) estimates that globally, harmful alcohol use contributes to 5.3% of all deaths and 5.1% of the burden of disease and injury each year [1]. For cancer specifically, the WHO International Agency for Research on Cancer (IARC) classifies "alcohol consumption", "ethanol in alcoholic beverages" and "acetaldehyde associated with the consumption of alcoholic beverages" as human carcinogens [2-4]. A recent study showed that among United States (U.S.) adults aged ≥30 years, 4.8% of all cancer cases (excluding non-melanoma skin cancer) and 3.2% of all cancer deaths annually from 2013 through 2016 were attributable to alcohol drinking [5]. Despite the large scientific evidence base on which these conclusions and estimates were drawn, there remain significant evidence gaps that if filled could enhance public education to increase awareness of the cancer-related risks of alcohol consumption, reduce overall consumption and, potentially, the related cancer burden. To address these scientific evidence gaps, the U.S. National Institutes of Health National Cancer Institute organized a three-day workshop **Alcohol and Cancer: Identifying Evidence Gaps and Research Challenges Across the Cancer Continuum (December 8-10, 2020)** (Workshop Program) and a public webinar **Alcohol as a Target for Cancer Prevention and Control: Research Challenges (December 18, 2020)** (Webinar). These events brought together experts from multiple scientific disciplines with the goal of reviewing existing evidence and identifying critical gaps in four key areas: (1) the epidemiology and biology of alcohol and cancer risk; (2) the health effects of alcohol drinking during and after cancer treatment; (3) public communication efforts to address alcohol and cancer risk; and (4) effective policies relevant to reducing the health effects of alcohol consumption, with a focus on cancer. Cutting across these areas are issues of assessing alcohol consumption, social and economic disparities, and the COVID-19 pandemic. This Executive Summary briefly describes the information reviewed and examples of scientific gaps identified in each of these four areas; a more comprehensive white paper for publication in a scientific journal is in preparation by the workshop/webinar chair and session co-chairs.

The epidemiology and biology of alcohol and cancer risk: Alcohol drinking is an established preventable cause of at least seven types of cancer, i.e., oral cavity, oropharyngeal, laryngeal, esophageal (squamous cell carcinoma), colorectal, liver, and breast [4]. Moreover, the World Cancer Research Fund/American Institute for Cancer Research Continuous Update Project has concluded that, "*There is no threshold of alcohol consumption below which cancer risk does not increase, at least for some cancers*" [6]. For other types of cancer, epidemiological studies indicate there is either a probable increased risk (e.g., stomach cancer), a probable lower risk (e.g., kidney cancer), no association, or limited or inconsistent evidence [4, 6]. Numerous biological mechanisms appear to be involved in alcohol-induced carcinogenesis, including DNA, protein and lipid alterations/damage, oxidative stress, inflammation, nutritional malabsorption, immune-dysregulation, and for breast cancer, increased estrogen levels [4]. However, further epidemiological, and mechanistic research is needed to improve estimates of the burden of cancer due to alcohol intake, improve modelling and consequent recommendations of how alcohol policies can reduce the burden of cancer, and better

understand the biological factors that contribute to alcohol-induced carcinogenesis to mitigate risk. For example, there remain gaps in evidence regarding:

- The accurate assessment – both self-reported and objective – of alcohol consumption in epidemiological studies on cancer risk, including drinking volume and patterns (e.g., heavy episodic drinking) throughout life, the impact of alcohol consumption at different times of life, and alcohol consumption trajectories.
- Associations of alcohol consumption, including different patterns of alcohol consumption (i.e., heavy episodic drinking, cessation) throughout the life-course, with the risk of less common cancers, specific subtypes of cancer (e.g., those classified by molecular markers or by anatomical subsite), and cancers for which the evidence remains inconclusive.
- Disparities in alcohol-cancer associations among different subpopulations, such as those classified by socio-economic status or race/ethnicity, based on evidence from epidemiological and mechanistic studies. Community-based participatory research in this area might be particularly fruitful.
- Application of novel statistical methods to further investigate and advance our understanding of statistical control for and assessment of residual confounding (e.g., tobacco use, anthropometric factors), as well as effect modification (or synergistic effects) with other established or potential cancer risk factors, such as tobacco use, genetic mutations and other more common variants, obesity, nutritional factors, and environmental contaminants/pollutants.
- Biological mechanisms for specific types of cancer, and those mechanisms that might have more general effects, such as those that influence the immune system, metabolome, epigenome, and microbiome.

The health effects of alcohol drinking during and after cancer treatment: In the clinical setting it is recommended that cancer patients avoid or minimize alcohol consumption during treatment because of its adverse effects on chemotherapeutic clearance and toxicities[7]. However, the effects of (both pre- and post-diagnosis) alcohol consumption on long-term patient-reported outcomes (e.g., health-related quality of life) and on cancer survival is not fully understood, and most available research has focused on breast, colorectal, and head and neck cancers[8-10]. Furthermore, strategies to identify cancer patients at risk of alcohol associated harms, and ways to reduce these harms – including support for health care providers in addressing consumption – are needed. Thus, gaps in scientific evidence that could influence a cancer patient's decision to drink alcohol during and after treatment include:

- The impact of alcohol use (and cessation) among cancer patients and survivors on cancer-related outcomes such as recurrence, new primaries, co-morbidities, and mortality (keeping in mind competing risks), as well as health-related quality of life (i.e., mental and physical health, and their correlates).
- The effect of alcohol consumption on tumor biology and disease progression overall, and by cancer type, stage, treatment, and race.
- The effects of alcohol consumption and patterns of consumption on the efficacy of cancer treatments (i.e., radiation, immunotherapy, chemotherapy, surgery) among specific cancer patient populations defined by cancer type, and other factors; similarly, the effects of alcohol on drug metabolism and toxicity.
- Evaluating available (and developing new) biomarkers of alcohol exposure, assessing the efficacy of the electronic medical record to ascertain alcohol intake, and evaluating the application of these measures in the clinical setting to identify at-risk clinical populations.
- Developing and testing standard and effective communications and messaging for clinicians as well as well-defined pathways for interventions/resources to help patients reduce alcohol consumption.

Public communication efforts to address alcohol and cancer risk: Awareness among the public and health professionals about the association between alcohol and cancer risk is suboptimal[11]. In 2014 it was reported that fewer than half of the U.S. Centers for Disease Control and Prevention-funded comprehensive cancer control plans specify goals, objectives, or strategies for alcohol control[12]. Addressing important evidence gaps in health communication and health literacy about the alcohol-cancer link would guide future efforts to improve public understanding of and influence personal choices related to the link. Some of these gaps reside at the level of description and observation of societal patterns, whereas others are related to eventual implementation of interventions, and include:

- Accessible information on the prevalence of knowledge, awareness, and misperceptions about the alcohol-cancer link; and understanding about that link among the public, clinicians, policymakers, and journalists.
- Evidence about efficacy of messages regarding the association between alcohol drinking and cancer (e.g., on alcohol warning labels) or guidelines or recommendation for alcohol consumption amounts (e.g., moderate vs. up to 1 drink on days that you drink alcoholic beverages) in motivating individual alcohol consumption behaviors.
- The influence of emotion and motivation in message processing regarding the alcohol-cancer link and alcohol use (e.g., boomerang effect), to understand message reactance and individual behavior.
- Communication efforts, both at the individual-level (e.g., patient-clinician) and population-level, to address the needs of people in various socioeconomic and cultural groups, including those who are marginalized, to improve health equity.
- The role of group identity and ways to address identity, including roles of alcohol in tribalism and ideology, as well as the historical context of alcohol drinking in the U.S. in processing messages about the alcohol-cancer link.
- Issues of organizational communication, such as reaching intra- and inter-organizational consensus on messaging and language; discouraging popular fund-raising and marketing strategies involving alcohol; and optimizing strategies for campaign efforts (e.g., centralized national efforts using broadcast channels, or a coalition of efforts rooted in communities by local individuals and organizations).

Effective policies relevant to reducing the health effects of alcohol consumption: Currently, alcohol is legally produced, distributed, and consumed in most, but not all, countries or communities in the world. In some locations there have been changes in policies over time [13]. The WHO has identified a wide range of alcohol control policies targeting the reduction of harmful alcohol consumption [14], and three – increasing alcohol taxes, banning/restricting alcohol advertising, and reducing/restricting alcohol availability – were identified as "best buys", defined as interventions that cost less than $100 per disability-adjusted life-year averted. However, research on the effects of alcohol policies and their relevance to cancer is in its infancy, and there are numerous scientific gaps that if filled could inform the development and adoption of effective policies aimed at reducing consumption. These gaps in research concerning policy include, for example:
- The potential impacts of changes in alcohol-specific policies (e.g., individual policies, policy subgroups, aggregate policy environments) on total cancer incidence and mortality, as well as specific types of alcohol-associated cancer. Similarly, the impact of policies targeting other cancer risk factors (e.g., tobacco, environmental toxins) or targeting multiple behaviors (e.g., alcohol, tobacco, and diet) on cancer related outcomes.
- The effects of alcohol consumption patterns (e.g., binge drinking) and/or other modifiable cancer risk factors (e.g., smoking, overweight) as mediators or moderators of policy-cancer relationships.
- The facilitators of an integrated policy approach for reducing alcohol consumption and the burden of alcohol-associated cancers. These facilitators may include: 1) knowledge mobilization and best practices for translating research and communicating alcohol policy-cancer relationships to policy makers, non-governmental organizations (NGOs), providers, etc; 2) activation of stakeholders from multiple sectors including primary care providers, cancer-focused and other medical professionals, and NGOs; and 3) information from the public regarding their knowledge, beliefs, opinions regarding the policies that include a focus on cancer-relevant issues.
- The barriers to an integrated policy approach for reducing alcohol consumption and the subsequent burden of alcohol-associated cancers. These barriers include: 1) inconsistencies in public health and medical education curricula and the consequences of such inconsistencies for public health and clinical communication related to alcohol and cancer; and 2) the effects of misinformation campaigns and alcohol-related cause-branding and how to prevent negative consequences of these activities.
- The effects of alcohol-related digital/social media policies such as industry tactics and counter advertising on knowledge and behavior relevant to the link between alcohol and cancer across a range of demographic groups beyond youth (pre- and post-menopausal women, cancer survivors, and caregivers).

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