Alcohol and Cancer Risk

2025

The U.S. Surgeon General's Advisory



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About This Advisory

A Surgeon General's Advisory is a public statement that calls the American people's attention to an urgent public health issue and provides recommendations for how it should be addressed. Advisories are reserved for significant public health challenges that require the nation's immediate awareness and action.

This document is not an exhaustive review of the literature. Rather, it was developed through a substantial review of the available evidence, primarily found via research published in English and resources suggested by a wide range of subject matter experts, with priority given to, but not limited to, meta-analyses and systematic literature reviews. The scope of this advisory is specific to alcohol use and cancer risk. It does not review broader health and societal outcomes associated with alcohol use. For additional background information, and to read other Surgeon General's Advisories, visit Surgeon General.gov

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Summary

This advisory highlights alcohol use as a leading preventable cause of cancer in the United States, contributing to nearly 100,000 cancer cases and about 20,000 cancer deaths each year.^{1,2}

Alcohol use is very common—in 2019-2020, 72% of U.S. adults reported they consumed one or more drinks per week,³ but less than half of U.S. adults are aware of the relationship between alcohol consumption and cancer risk.⁴ The direct link between alcohol use and cancer was first established in the late 1980s, and evidence for this link has strengthened over time.⁵-₹ This body of scientific evidence demonstrates a causal relationship between alcohol use and increased risk for at least seven different types of cancer, including breast (in women), colorectum, esophagus, liver, mouth (oral cavity), throat (pharynx), and voice box (larynx).⁶.₹ The more alcohol consumed, the greater the risk of cancer.⁶.Ց-11 For certain cancers, like breast, mouth, and throat cancers, evidence shows that this risk may start to increase around one or fewer drinks per day.⁶.Ց-10 This Advisory describes the scientific evidence for the causal link between alcohol consumption and increased cancer risk. It also helps to better inform the public of this relationship and offers key recommendations to reduce alcohol-related cancers.

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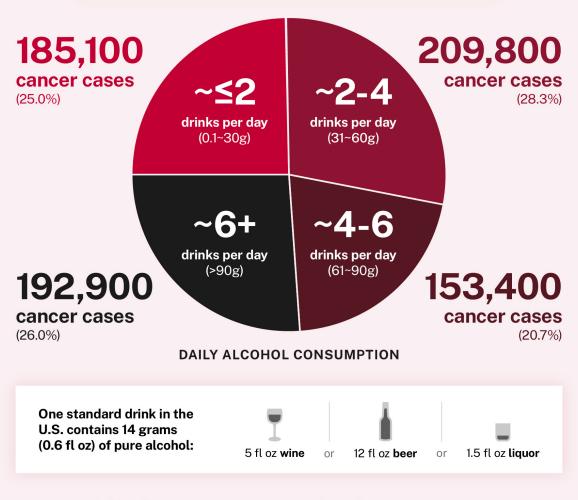
Alcohol Consumption is a Leading Preventable Cause of Cancer

Alcohol consumption is the third leading preventable cause of cancer in the United States, after tobacco and obesity.¹

In 2019, an estimated 96,730 cancer cases were related to alcohol consumption including 42,400 in men and 54,330 in women.¹ This translates to nearly 1 million preventable cancer cases over ten years in the U.S. The largest burden of alcohol-related cancer in the U.S. is for breast cancer in women with an estimated 44,180 cases in 2019, representing 16.4% of the approximately 270,000 total breast cancer cases for women.¹ Globally, 741,300 cancer cases were related to alcohol consumption in 2020; 185,100 of those cases were related to consumption of approximately two drinks daily or fewer (Figure 1).¹²

741,300 cancer cases worldwide were attributable to alcohol consumption in 2020

The risk of cancer is lower at lower levels of consumption. However, many more people consume ≤2 drinks per day, thus leading to a similar number of overall cancer cases at lower levels as higher levels of consumption.



Source: Rumgay, H., Shield, K., Charvat, H., Ferrari, P., Sornpaisarn, B., Obot, I., Islami, F., Lemmens, V. E. P. P., Rehm, J., & Soerjomataram, I. (2021). Global burden of cancer in 2020 attributable to alcohol consumption: a population-based study. *The Lancet. Oncology*, 22(8), 1071–1080. https://doi.org/10.1016/S1470-2045(21)00279-5

Drink number ranges within figure are estimates based on 14g = 1 U.S. standard drink.

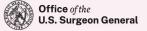


FIGURE 1: 741,300 cancer cases worldwide were attributable to alcohol consumption in 2020

In the U.S., there are about 20,000 alcohol-related cancer deaths annually.^{1,2} This is greater than the number of alcohol-associated traffic crash fatalities (about 13,500 annually) in the U.S.^{a,13} Alcohol-related cancer deaths shorten the lives of those who die by an average of 15 years.¹⁴ Annually, a total of about 305,000 years of potential life are lost due to alcohol-related cancer deaths.¹⁴ Breast cancer accounts for the majority (~60%) of alcohol-related cancer deaths in women, whereas liver cancer (~33%) together with colorectal cancer (an additional ~21%) account for the majority of alcohol-related cancer deaths in men.² About 83% of the estimated 20,000 U.S. alcohol-related cancer deaths per year occur at levels above the 2020-2025 U.S. Dietary Guidelines for Americans recommended limits of two drinks daily for men and one drink daily for women.^{2,15} Nonetheless, the remaining 17% of the estimated 20,000 U.S. alcohol-related cancer deaths per year occur at levels within those recommended limits.²

Despite clear evidence demonstrating the effect of alcohol consumption on cancer risk, there is a large gap in public understanding of the risk. In a 2019 survey, 45% of Americans recognized alcohol use as a risk factor for cancer compared to 91% of Americans who recognized the risk of radiation exposure, 89% for tobacco use, 81% for asbestos exposure, and 53% for obesity (Figure 2).^{5,4} Additionally, public awareness of alcohol consumption as a cancer risk factor has not substantially improved over nearly two decades,⁴ even as evidence documenting the link between alcohol consumption and cancer risk has increased.

^a Alcohol-associated traffic crash fatalities include impaired drivers and passengers/victims of crashes.

^b Other recent survey data demonstrate comparable alcohol consumption and cancer awareness estimates ranging from about 30-50% from the <u>National Center for Health Statistics</u> and the <u>Health Information National Trends Survey.</u>

Less than half of Americans are aware that alcohol consumption increases cancer risk

Survey of a nationally representative sample of U.S. adults ages 18 and older*

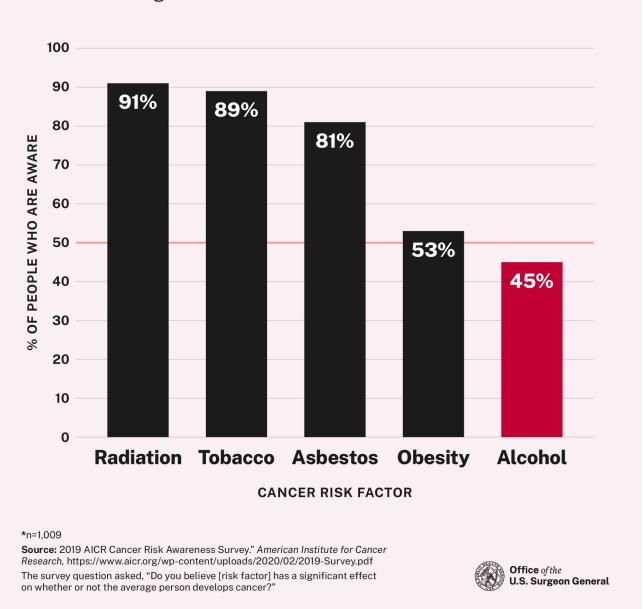


FIGURE 2: Less than half of Americans are aware that alcohol consumption increases cancer risk

2

The Causal Relationship Between Alcohol Consumption and Cancer: Summary of Evidence

Determining whether there is a causal relationship between a risk factor—a behavior, exposure, or characteristic—and a health outcome such as cancer is done through comprehensive assessments of scientific evidence and the application of well-established scientific criteria, such as the Bradford Hill criteria.¹⁶⁻²¹

This scientific approach includes assessing the relationship between the risk factor (e.g., alcohol consumption) and the subsequent occurrence of a disease outcome (e.g., cancer) in observational studies where large numbers of people are followed over time. It also includes careful review of the effect of the risk factor in animal studies and research to understand the biological and chemical pathways leading to cancer. This is the same approach that was used to conclude that cigarette smoking causes lung cancer¹⁷ and is the same approach that has established alcohol consumption as a cause of cancer.

Over the last two decades, numerous high-quality observational studies and metaanalytic reviews have assessed and observed a significant relationship between alcohol consumption and increased cancer risk.^{6-11,22} A global meta-analysis of 572 studies examining data from 486,538 cancer cases resulted in findings consistent with this conclusion.¹⁰ An additional pooled analysis of 26 studies found that the relative odds of mouth cancer increased by 40% for those who consumed about one drink daily compared to those who did not drink.^{c,9} Another pooled analysis of 20 cohorts of more than one million women found that the relative risk of breast cancer increased by 10% for women who consumed up to about one drink daily compared to those who did not drink.8 Further, a global study of 195 countries and territories involving 28 million individuals found that higher levels of alcohol consumption were associated with greater risk of cancer.11 Extensive research has demonstrated specific biological mechanisms by which alcohol causes cancer as well. For example, multiple studies have shown that giving rats and mice drinking water with ethanol (the same type of pure alcohol in alcohol-containing beverages) or its primary metabolic breakdown product, acetaldehyde, results in increased tumor numbers at multiple places in the body. At high levels such as those that occur with consumption of alcohol, acetaldehyde is highly toxic and cancer-causing.23-27

^c The odds reported occurred from alcohol consumption of 12g daily over a 5 year duration.

Further, the data in humans on alcohol and health show a strong association between drinking alcohol and increased cancer risk, regardless of the type of alcohol (e.g., beer, wine, and spirits).^{6,28} Cumulatively, rigorous research, across observational, biological, and genetic studies, has shown that alcohol consumption increases the risk of cancer for at least seven sites: breast (in women), colorectum, esophagus, liver, mouth (oral cavity), throat (pharynx), and voice box (larynx) (Figure 3).^{6,7}

The two most prominent international organizations that review evidence for carcinogenicity attribute the highest level of causal evidence to the association between alcohol consumption and the development of cancer. The International Agency for Research on Cancer (IARC), which is the specialized cancer agency of the World Health Organization (WHO), classifies alcohol as a Group 1 carcinogen—alongside tobacco, asbestos, and formaldehyde, among others—the highest level of classification by IARC for when "there is enough evidence to conclude that it can cause cancer in humans." Similarly, the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) ranks the evidence linking alcohol and cancer as "Convincing: Increases Risk," also their highest ranking. Additionally, the U.S. National Toxicology Program concluded in 2000 that "Alcoholic Beverage Consumption" is known to be a human carcinogen. Shows of cancer is also agreed upon by the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health's National Cancer Institute (NCI).

The association between alcohol use and cancer is also documented in U.S. federal reports, including the 2016 Surgeon General's Report on Alcohol, Drugs, and Health, which indicates that alcohol misuse is associated with:³¹

"... cancers of the oral cavity, esophagus, larynx, pharynx, liver, colon, and rectum. Even one drink per day may increase the risk of breast cancer."

Alcohol-related harms, including cancer, are further discussed in the 2020-2025 Dietary Guidelines for Americans, which indicates:¹⁵

"Emerging evidence suggests that even drinking within the recommended limits may increase the overall risk of death from various causes, such as from several types of cancer and some forms of cardiovascular disease. Alcohol has been found to increase risk for cancer, and for some types of cancer, the risk increases even at low levels of alcohol consumption (less than 1 drink in a day). Caution, therefore, is recommended."

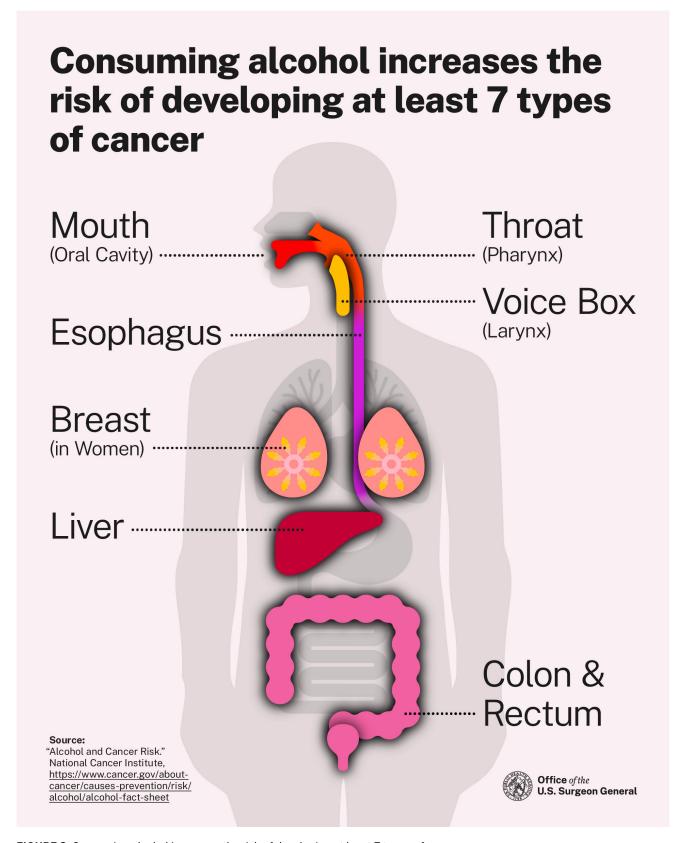


FIGURE 3: Consuming alcohol increases the risk of developing at least 7 types of cancer

While the causal relationship between alcohol consumption and cancer is firmly established, 6.7,22 further research is needed on the potential effect of alcohol consumption on increasing cancer risk at additional sites such as skin, prostate, pancreas, and stomach, 28,32,33 and decreased risk for sites such as kidney. More research is also needed to determine how specific drinking patterns (e.g., binge vs. non-binge drinking) may affect cancer risk as well as how drinking at specific ages and during certain developmental periods, such as in adolescence and older adulthood, may influence the risk of cancer. 34

How does alcohol cause cancer?

There is extensive evidence from biological studies that ethanol (the type of pure alcohol found in all alcohol-containing beverages) causes cancer in at least four distinct ways (Figure 4).^{7,23,24,29,35-38}

- First, alcohol breaks down into acetaldehyde in the body. Acetaldehyde is a
 metabolite that causes cancer by binding to DNA and damaging it. When DNA is
 damaged, a cell can begin to grow uncontrollably and create a cancerous tumor.
- Second, alcohol generates reactive oxygen species, which increase inflammation and can damage DNA, proteins, and lipids in the body through a process called oxidation.
- Third, alcohol alters hormone levels (including estrogen), which can play a role in the development of breast cancer.
- Fourth, carcinogens from other sources, especially particles of tobacco smoke, can dissolve in alcohol, making it easier for them to be absorbed into the body, increasing the risk for mouth and throat cancers.

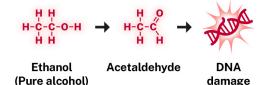
The best-established evidence is on the first two pathways of acetaldehyde and inflammation. Hormonal regulation and alcohol as a solvent are widely agreed upon to be important pathways for carcinogenesis but are not yet fully understood. Research also continues on other possible mechanisms, including folate deficiency, by which alcohol can cause cancer.

Four ways alcohol can cause cancer



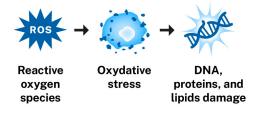
MECHANISM A

Alcohol breaks down into acetaldehyde which damages DNA in multiple ways, causing an increased risk of cancer.



MECHANISM B

Alcohol induces oxidative **stress**, increasing the risk of cancer by damaging DNA, proteins, and cells and increasing inflammation.



MECHANISM C

Alcohol alters levels of multiple hormones, including estrogen, which can increase breast cancer risk.



Source: Rumgay H, Murphy N, Ferrari P, Soerjomataram I. Alcohol and Cancer: Epidemiology and Biological Mechanisms. Nutrients. Sep 11 2021;13(9) doi:10.3390/nu13093173

MECHANISM D

Alcohol leads to greater absorption of carcinogens.



dissolve in alcohol

Carcinogens Alcohol alters cells in mouth and throat

more easily absorbed

*Rumgay et al. (2021) reviewed these four mechanisms through which alcohol can cause cancer along with several other possible pathways that appear to influence cancer risk. These include disruption of one-carbon metabolism, alteration of retinoid metabolism, and impaired immune function among others.

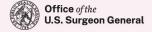


FIGURE 4: Four ways alcohol can cause cancer

How does the amount of alcohol you consume affect your risk of cancer?

The amount of alcohol a person drinks affects their risk of cancer. An important factor is the overall amount of alcohol consumed consistently over time. The risk of cancer increases as the level of consumption increases with higher risk at higher levels of consumption. For certain cancers, like breast, mouth, and throat cancers, evidence shows that this risk may start to increase around one or fewer drinks per day.^{6,8-10}

Ways of Understanding Risk

Absolute risk is the actual chance, or probability, of an outcome occurring (e.g., a new cancer diagnosis).³⁹ Relative risk is the proportional chance of an outcome occurring for one group (e.g. those who drink alcohol) as compared to another group (e.g. those who do not drink alcohol).³⁹ It is important to understand that a large change in relative risk may represent only a small change in absolute risk. For example, the absolute risk of drowning in the United States is about 1 out of 1000.⁴⁰ If a behavior increased the relative risk of drowning by 100%, this would result in an absolute risk of 2 out of 1000. This might not seem that large but is a doubling of absolute risk compared to the baseline risk of 1 out of 1000. Both absolute and relative risk estimates can be helpful in understanding risk.

One way to understand the significance of this cancer risk is to look at the *absolute risk* of developing cancer over time among those who consume alcohol in different quantities (Figures 5 and 6). For example, a study of 226,162 individuals^d reported that the absolute risk of developing any alcohol-related cancer over the lifespan of a woman increases from approximately 16.5% (about 17 out of every 100 individuals) for those who consume less than one drink per week, to 19.0% (19 out of every 100 individuals) for those who consume one drink daily on average to approximately 21.8% (about 22 out of every 100 individuals) for those who consume two drinks daily on average (Figure 5).⁴¹ That is about five more women out of 100 who would have developed cancer due to a higher level of alcohol consumption. Additionally, the absolute risk of breast cancer over the lifespan of a woman is approximately 11.3% (about 11 out of 100 individuals) for those who consume less than one drink per week compared to 13.1% (about 13 out of 100 individuals) or 15.3% (about 15 out

d Cumulative absolute risk of seven alcohol-related cancers over the lifespan up to age 80 were calculated using results from Sarich (2021). Continuous log-linear hazard ratios from Cox proportional hazard models based on the Australian 45 and Up cohort (n = 226,162) were applied to cancer rates observed for people reporting 0 to <1 drink/week, to calculate the absolute risk for consuming 7 and 14 US drinks/week (1 and 2 US drinks/day). These estimates differ in how they were calculated from the results reported in Sarich et al. because the continuous model was used rather than hazard ratios for the specific consumption categories. All hazard models were adjusted for sex, education, household income, health insurance status, partner status, country of birth, smoking status and intensity, body mass index and physical activity. Additional covariates were included for specific cancers. For these models, the reference group included very light drinkers, but not non-drinkers to avoid the sick quitter effect.

of 100 individuals) for those who consume one or two drinks per day, respectively (Figure 6).⁴¹

Over the lifespan of a man, the absolute risk of developing any alcohol-related cancer increases from approximately 10.0% (about 10 out of every 100 individuals) for those who consume less than one drink per week to about 11.4% (about 11 out of every 100 individuals) for those who consume one drink daily on average to approximately 13.1% (about 13 out of every 100 individuals) for those who consume two drinks daily on average (Figure 5).⁴¹

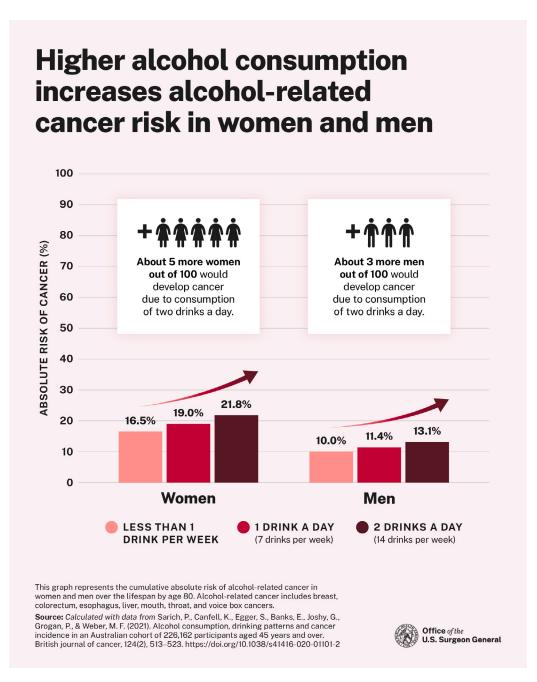


FIGURE 5: Higher alcohol consumption increases alcohol-related cancer risk in women and men

Higher alcohol consumption increases breast cancer risk in women

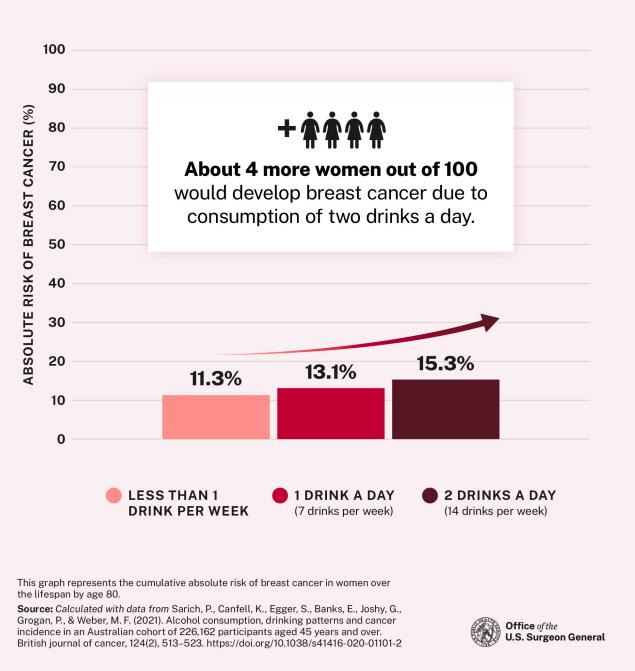


FIGURE 6: Higher alcohol consumption increases breast cancer risk in women

Another way to understand this risk is to look at the *relative risk* of developing cancer from alcohol consumption for those who drink compared to those who do not drink. One analysis found a 10% relative risk increase in breast cancer for women who consume up to about one drink per day, and a 32% relative risk increase for women who consume more than two drinks per day, compared to women who did not drink.8 Because many U.S. adults consume alcohol,3,42 and because breast cancer in particular is among the most common of cancers, 43 this constitutes a substantial number of preventable cancer cases. Another analysis in men and women found a 40% relative odds increase for mouth cancer for those drinking about one drink per day and a 97% relative odds increase for those drinking about two drinks per day, compared to those who did not drink (note: the lifetime absolute risk of developing mouth is about 0.8%).^{f,9} In other words, the absolute risk of mouth cancer for men and women who average two drinks daily is nearly twice as high as the risk for non-drinkers. Because mouth cancer is less common than breast cancer, mouth cancer cases do not account for as many alcohol-related cancer cases as breast cancer cases.

By contrast, long-term quitting or reduced drinking are associated with lower risks of some alcohol-related cancers. A recent evidence review conducted by IARC concluded that alcohol cessation or reduction decreased the risk of mouth cancer and esophageal cancer. More research is needed to determine if this risk decreases for other cancer sites and whether it decreases to the level observed in people who never consume alcohol. A4,45

Importantly, the risks presented above are average risks based on the studied populations. An individual's risk for developing cancer, including alcohol-related cancers, varies and is determined by a complex interaction of biological factors (e.g., genetics) and environmental factors (e.g., exposure to carcinogens). For example, many individuals of East Asian descent have a genetic variant that results in an alcohol flushing response and reduces their ability to metabolize acetaldehyde, which produces much higher risks for certain alcohol-related cancers. In addition, an individual's alcohol consumption level and associated cancer risk may be influenced by social and economic factors, including social norms, peer pressure, advertising, and other commercial activities. Individuals may also have different comfort levels (risk tolerances) when it comes to taking different types of risks, including alcohol consumption. 49-52

^e This study reports odds ratios (also called relative odds), a measure of risk comparable to relative risk when disease outcomes are not very common. The odds reported occurred from alcohol consumption of 12g daily over a 5 year duration.

^f Based on data from the National Cancer Institute

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We Can Take Action

There are actions we can take today to begin reducing alcohol-related cancers in the U.S. Key steps include:

- Update the existing Surgeon General's health warning label on alcohol-containing beverages to include a warning about the risk of cancer associated with alcohol consumption. [See page 17]. Pursue changes to label characteristics to make the warning label more visible, prominent, and effective in increasing awareness about cancer risks associated with alcohol consumption.
- Reassess recommended limits for alcohol consumption to account for the latest evidence on alcohol consumption and cancer risk.
- Strengthen and expand education efforts to increase general awareness that alcohol consumption causes cancer.
- Inform patients in clinical settings about the link between alcohol consumption and increased cancer risk.⁵³ Promote the use of alcohol screening and provide brief intervention and referral to treatment as needed.⁵⁴
- Highlight alcohol consumption as a leading modifiable cancer risk factor and incorporate proven alcohol reduction strategies into population-level cancer prevention initiatives and plans.
- For individuals, be aware of the relationship between alcohol consumption and increased cancer risk when considering whether or how much to drink. Cancer risk increases as you drink more alcohol.

Additional Resources:

- The National Institute on Alcohol Abuse and Alcoholism's <u>Rethinking Drinking</u> initiative offers ways to evaluate your drinking and decide whether and how to make a change. In addition, CDC offers a free, interactive tool for you to check your drinking and get personalized feedback (in <u>English</u> and <u>Spanish</u>). Additionally, there are <u>some individuals</u> who should not drink at all.
- SAMHSA's National Helpline is a free, confidential, 24/7, 365-day-a-year treatment referral and information service (in <u>English</u> and <u>Spanish</u>) for individuals and families facing mental health and/or substance use disorders.
- SAMHSA's <u>"Talk. They Hear You."</u> campaign offers tips on how to talk to children and youth about alcohol.
- Learn more about key research gaps, such as those identified in this mini-review
 in Cancer Epidemiology, Biomarkers & Prevention, to help advance the prevention of alcohol-related cancer.
- Addressing the broader population health <u>impacts</u> of alcohol consumption is beyond the scope of this Advisory. For more information on alcohol consumption and public health interventions, policies and solutions, please see information from CDC and WHO.

Updating Health Warning Labels on Alcoholic Beverages: An Important Next Step for Alcohol-Related Cancer Prevention

Health warning labels are well-established and effective approaches to increasing awareness of health hazards and fostering behavior change. Considerable evidence supports the use of health warning labels, 55,56 including promising evidence toward their role in raising awareness about alcohol-related risks. 57-60 For example, a natural experiment in Canada demonstrated that the inclusion of warning labels on alcohol beverage containers resulted in a 10% increase in knowledge about the association between alcohol and cancer after just two months of labeling.⁶¹ Additionally, scientific evidence has demonstrated that prominent, pictorial, and rotating messages, compared to less conspicuous, text-only, and static messages, are more effective for influencing awareness and behavior. 55-59,62 There are 47 countries that require alcohol warning labels related to health and safety.⁶³ South Korea requires a cancer-specific warning, 64 and spurred by existing evidence, Ireland signed into law a new requirement to display a cancer warning label on alcohol-containing beverages starting in 2026.⁶⁵ This label will state: "There is a direct link between alcohol and fatal cancers." 65

In the U.S., pursuant to 27 U.S.C. 215, every alcoholic beverage sold in the United States must currently have the following health warning label:

"GOVERNMENT WARNING: (1) According to the Surgeon General, women should not drink alcoholic beverages during pregnancy because of the risk of birth defects. (2) Consumption of alcoholic beverages impairs your ability to drive a car or operate machinery, and may cause health problems."66

This label statement has remained unchanged since its inception in 1988.⁶⁷

The power to change the label statement lies with Congress. ⁶⁶ Given the conclusive evidence on the cancer risk from alcohol consumption and the Office of the Surgeon General's responsibility to inform the American public of the best available scientific evidence, the Surgeon General recommends an update to the Surgeon General's warning label for alcohol-containing beverages to include a cancer risk warning.

Acknowledgments

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Centers for Disease Control and Prevention (CDC)

Centers for Medicaid & Medicare Services (CMS)

Food and Drug Administration (FDA)

Indian Health Service (IHS)

Office of the Assistant Secretary for Health (OASH)

Office of the General Counsel (OGC)

National Institutes of Health (NIH)

Substance Abuse and Mental Health Services Administration (SAMHSA)

References

- 1. Islami F, Marlow EC, Thomson B, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States, 2019. *CA Cancer J Clin.* Jul 11 2024;doi:10.3322/caac.21858
- **2.** Esser MB, Sherk A, Liu Y, Henley SJ, Naimi TS. Reducing Alcohol Use to Prevent Cancer Deaths: Estimated Effects Among U.S. Adults. *Am J Prev Med.* 2024 Apr;66(4):725-729. doi: 10.1016/j. amepre.2023.12.003. PMID: 38514233; PMCID: PMC10963036.
- **3.** "Updated US Drinking Norms (2020 Data)." *Alcohol Research Group*, https://arg.org/news/updated-us-drinking-norms-2020-data/. Accessed 8 November 2024.
- **4.** "2019 AICR Cancer Risk Awareness Survey." *American Institute for Cancer Research*, https://www.aicr.org/wp-content/uploads/2020/02/2019-Survey.pdf. Accessed 24 August 2024.
- **5.** IARC Working Group on the Evaluation of Carcinogenic Risks to Humans., International Agency for Research on Cancer., National Cancer Institute (U.S.). *Alcohol drinking.* IARC monographs on the evaluation of carcinogenic risks to humans,. World Health Organization, International Agency for Research on Cancer; 1988:416 p.
- **6.** WCRF/AICR. World Cancer Research Fund/American Institute for Cancer Research. Diet, nutrition, physical activity and cancer: a global perspective. Continuous Update Project Expert Report. 2018.
- **7.** Personal Habits and Indoor Combustions: IARC Monographs on the Evaluation of Carcinogenic Risks to Humans Volume 100E. IARC. 2012 https://publications.iarc.fr/122
- **8.** Jung S, Wang M, Anderson K, Baglietto L, Bergkvist L, Bernstein L, van den Brandt PA, Brinton L, Buring JE, Eliassen AH, Falk R, Gapstur SM, Giles GG, Goodman G, Hoffman-Bolton J, Horn-Ross PL, Inoue M, Kolonel LN, Krogh V, Lof M, Maas P, Miller AB, Neuhouser ML, Park Y, Robien K, Rohan TE, Scarmo S, Schouten LJ, Sieri S, Stevens VL, Tsugane S, Visvanathan K, Wilkens LR, Wolk A, Weiderpass E, Willett WC, Zeleniuch-Jacquotte A, Zhang SM, Zhang X, Ziegler RG, Smith-Warner SA. Alcohol consumption and breast cancer risk by estrogen receptor status: in a pooled analysis of 20 studies. *Int J Epidemiol*. 2016 Jun;45(3):916-28. doi: 10.1093/ije/dyv156. Epub 2015 Aug 28. PMID: 26320033; PMCID: PMC5005939.
- **9.** Di Credico G, Polesel J, Dal Maso L, Pauli F, Torelli N, Luce D, Radoï L, Matsuo K, Serraino D, Brennan P, Holcatova I, Ahrens W, Lagiou P, Canova C, Richiardi L, Healy CM, Kjaerheim K, Conway DI, Macfarlane GJ, Thomson P, Agudo A, Znaor A, Franceschi S, Herrero R, Toporcov TN, Moyses RA, Muscat J, Negri E, Vilensky M, Fernandez L, Curado MP, Menezes A, Daudt AW, Koifman R, Wunsch-Filho V, Olshan AF, Zevallos JP, Sturgis EM, Li G, Levi F, Zhang ZF, Morgenstern H, Smith E, Lazarus P, La Vecchia C, Garavello W, Chen C, Schwartz SM, Zheng T, Vaughan TL, Kelsey K, McClean M, Benhamou S, Hayes RB, Purdue MP, Gillison M, Schantz S, Yu GP, Chuang SC, Boffetta P, Hashibe M, Yuan-Chin AL, Edefonti V. Alcohol drinking and head and neck cancer risk: the joint effect of intensity and duration. *Br J Cancer.* 2020 Oct;123(9):1456-1463. doi: 10.1038/s41416-020-01031-z. Epub 2020 Aug 24. PMID: 32830199; PMCID: PMC7592048.
- **10.** Bagnardi V, Rota M, Botteri E, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *Br J Cancer*. Feb 3 2015;112(3):580-93. doi:10.1038/bjc.2014.579

- **11.** GBD. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. Sep 22 2018;392(10152):1015-1035. doi:10.1016/s0140-6736(18)31310-2
- **12.** Rumgay, H., Shield, K., Charvat, H., Ferrari, P., Sornpaisarn, B., Obot, I., Islami, F., Lemmens, V. E. P. P., Rehm, J., & Soerjomataram, I. (2021). Global burden of cancer in 2020 attributable to alcohol consumption: a population-based study. *The Lancet. Oncology*, 22(8), 1071–1080. https://doi.org/10.1016/S1470-2045(21)00279-5
- **13.** National Center for Statistics and Analysis. (2024, August, Revised). Alcohol-impaired driving: 2022 data (Traffic Safety Facts. Report No. DOT HS 813 578). National Highway Traffic Safety Administration.
- **14.** "Alcohol-Related Disease Impact (ARDI) Application." *Centers for Disease Control and Prevention*, https://nccd.cdc.gov/DPH_ARDI. Accessed 24 August 2024.
- **15.** U.S. Department of Agriculture and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025. 9th Edition. December 2020.
- **16.** HILL AB. THE ENVIRONMENT AND DISEASE: ASSOCIATION OR CAUSATION? *Proc R Soc Med.* 1965 May;58(5):295-300. PMID: 14283879; PMCID: PMC1898525.
- **17.** U.S. Surgeon General's Advisory Committee on Smoking and Health. *Smoking and Health: Report of the Advisory Committee to the Surgeon General of the Public Health Service* Washington, D.C: U.S. Department of Health, Education and Welfare, Public Health Service; 1964.
- **18.** Office of the Surgeon General (US); Office on Smoking and Health (US). The Health Consequences of Smoking: A Report of the Surgeon General. Atlanta (GA): Centers for Disease Control and Prevention (US); 2004. PMID: 20669512.
- **19.** Shimonovich M, Pearce A, Thomson H, Keyes K, Katikireddi SV. Assessing causality in epidemiology: revisiting Bradford Hill to incorporate developments in causal thinking. *Eur J Epidemiol.* 2021 Sep;36(9):873-887. doi: 10.1007/s10654-020-00703-7. Epub 2020 Dec 16. PMID: 33324996; PMCID: PMC8206235.
- **20.** Kenneth J. Rothman and Sander Greenland, 2005: <u>Causation and Causal Inference in Epidemiology</u>. *American Journal of Public Health* 95, S144_S150, https://doi.org/10.2105/AJPH.2004.059204
- **21.** Mervyn Susser, What is a Cause and How Do We Know One? A Grammar for Pragmatic Epidemiology, *American Journal of Epidemiology*, Volume 133, Issue 7, 1 April 1991, Pages 635–648, https://doi.org/10.1093/oxfordjournals.aje.a115939
- **22.** NTP (National Toxicology Program). 2021. Report on Carcinogens, Fifteenth Edition. Research Triangle Park, NC: U.S. Department of Health and Human Services, Public Health Service. DOI: https://doi.org/10.22427/NTP-OTHER-1003
- **23.** Brooks PJ, Theruvathu JA. DNA adducts from acetaldehyde: Implications for alcohol-related carcinogenesis. *Alcohol*. 2005;35:187–193. doi: 10.1016/j.alcohol.2005.03.009.
- **24.** Seitz HK, Stickel F. Molecular mechanisms of alcohol-mediated carcinogenesis. *Nat Rev Cancer.* 2007;7:599–612. doi: 10.1038/nrc2191.

- **25.** Lachenmeier DW, Monakhova YB. Short-term salivary acetaldehyde increase due to direct exposure to alcoholic beverages as an additional cancer risk factor beyond ethanol metabolism. *J Exp Clin Cancer Res.* 2011 Jan 6;30(1):3. doi: 10.1186/1756-9966-30-3. PMID: 21211027; PMCID: PMC3022748.
- **26.** Stornetta A, Guidolin V, Balbo S. Alcohol-Derived Acetaldehyde Exposure in the Oral Cavity. *Cancers*. 2018; 10(1):20. https://doi.org/10.3390/cancers10010020
- **27.** Nieminen MT, Salaspuro M. Local Acetaldehyde An Essential Role in Alcohol-Related Upper Gastrointestinal Tract Carcinogenesis. *Cancers.* 2018; 10(1):11. https://doi.org/10.3390/cancers10010011
- **28.** National Center for Chronic Disease Prevention and Health Promotion. "Alcohol and Cancer." U.S. Centers for Disease Control and Prevention, https://www.cdc.gov/cancer/risk-factors/alcohol. html#print. Accessed 19 November 2024.
- **29.** IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Personal habits and indoor combustions. IARC Monogr Eval Carcinog Risks Hum. 2012;100(Pt E):1-538. PMID: 23193840; PMCID: PMC4781577.
- **30.** "Alcohol and Cancer Risk." *National Cancer Institute*, https://www.cancer.gov/about-cancer/causes-prevention/risk/alcohol/alcohol-fact-sheet. Accessed 24 August 2024.
- **31.** SG. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016.
- **32.** World Cancer Research Fund/American Institute for Cancer Research. Continuous Update Project Expert Report 2018. <u>Diet, nutrition, physical activity and pancreatic cancer</u>. Available at dietandcancerreport.org
- **33.** World Cancer Research Fund International: Continuous Update Project . How Diet, Nutrition and Physical Activity Affect Skin Cancer Risk: Report; 2018. https://www.wcrf.org/wp-content/uploads/2024/10/skin-cancer.pdf Accessed 24 August 2024.
- **34.** Gapstur SM, Bandera EV, Jernigan DH, LoConte NK, Southwell BG, Vasiliou V, Brewster AM, Naimi TS, Scherr CL, Shield KD. Alcohol and Cancer: Existing Knowledge and Evidence Gaps across the Cancer Continuum. *Cancer Epidemiol Biomarkers Prev.* 2022 Jan;31(1):5-10. doi: 10.1158/1055-9965.EPI-21-0934. Epub 2021 Nov 2. PMID: 34728469; PMCID: PMC8755600.
- **35.** Freudenheim JL. Alcohol's Effects on Breast Cancer in Women. *Alcohol Res.* 2020;40(2):11. doi:10.35946/arcr.v40.2.11
- **36.** Rumgay H, Murphy N, Ferrari P, Soerjomataram I. Alcohol and Cancer: Epidemiology and Biological Mechanisms. *Nutrients*. Sep 11 2021;13(9) doi:10.3390/nu13093173
- **37.** Hashibe M, Brennan P, Chuang SC, et al. Interaction between tobacco and alcohol use and the risk of head and neck cancer: pooled analysis in the International Head and Neck Cancer Epidemiology Consortium. *Cancer Epidemiol Biomarkers Prev.* Feb 2009;18(2):541-50. doi:10.1158/1055-9965.Epi-08-0347
- **38.** Tóth ME, Vígh L, Sántha M. Alcohol stress, membranes, and chaperones. *Cell Stress Chaperones*. 2014 May;19(3):299-309. doi: 10.1007/s12192-013-0472-5. PMID: 24122554; PMCID: PMC3982023.
- **39.** Marlies Noordzij, Merel van Diepen, Fergus C. Caskey, Kitty J. Jager, Relative risk versus absolute risk: one cannot be interpreted without the other, *Nephrology Dialysis Transplantation*, Volume 32,

- Issue suppl_2, April 2017, Pages ii13-ii18, https://doi.org/10.1093/ ndt/gfw465
- **40.** "Odds of Dying." *National Safety Council*, https://injuryfacts.nsc.org/all-injuries/preventable-death-overview/odds-of-dying/Accessed 24 August 2024.
- **41.** Sarich, P., Canfell, K., Egger, S., Banks, E., Joshy, G., Grogan, P., & Weber, M. F. (2021). Alcohol consumption, drinking patterns and cancer incidence in an Australian cohort of 226,162 participants aged 45 years and over. *British journal of cancer*, 124(2), 513–523. https://doi.org/10.1038/s41416-020-01101-2
- **42.** "Alcohol's Effects on Health." *National Institute on Alcohol Abuse and Alcoholism*, https://www.niaaa.nih.gov/alcohols-effects-health/alcohol-topics/alcohol-facts-and-statistics/alcohol-use-united-states-age-groups-and-demographic-characteristics. Accessed 24 August 2024.
- **43.** "Cancer Stat Facts: Common Cancer Sites." *National Cancer Institute*, https://seer.cancer.gov/statfacts/html/common.html. Accessed 24 August 2024.
- **44.** Gapstur SM, Bouvard V, Nethan ST, et al. The IARC Perspective on Alcohol Reduction or Cessation and Cancer Risk. *N Engl J Med.* Dec 28 2023;389(26):2486-2494. doi:10.1056/NEJMsr2306723
- **45.** Reduction or Cessation of Alcoholic Beverage Consumption. IARC Handbooks of Cancer Prevention Volume 20A https://publications.iarc.fr/Book-And-Report-Series/larc-Handbooks-Of-Cancer-Prevention/Reduction-Or-Cessation-Of-Alcoholic-Beverage-Consumption-2024
- **46.** Sim W, Pan JT, Chua CWX, Fong KY, Wong SH, Lee B, Oon HH. Association between alcohol flushing syndrome and cancer: A systematic review and meta-analysis. *Ann Acad Med Singap.* 2024 Jul 30;53(7):420-434. doi: 10.47102/annals-acadmedsg.2023351. PMID: 39132959.
- **47.** Brooks PJ, Enoch MA, Goldman D, Li TK, Yokoyama A. The alcohol flushing response: an unrecognized risk factor for esophageal cancer from alcohol consumption. *PLoS Med.* 2009 Mar 24;6(3):e50. doi: 10.1371/journal.pmed.1000050. PMID: 19320537; PMCID: PMC2659709.
- **48.** Im PK, Yang L, Kartsonaki C, Chen Y, Guo Y, Du H, Lin K, Kerosi R, Hacker A, Liu J, Yu C, Lv J, Walters RG, Li L, Chen Z, Millwood IY; China Kadoorie Biobank (CKB) Collaborative Group. Alcohol metabolism genes and risks of site-specific cancers in Chinese adults: An 11-year prospective study. *Int J Cancer*. 2022 May 15;150(10):1627-1639. doi: 10.1002/ijc.33917. Epub 2022 Jan 20. PMID: 35048370; PMCID: PMC7612513.
- 49. Karlsson Linnér R, Biroli P, Kong E, Meddens SFW, Wedow R, Fontana MA, Lebreton M, Tino SP, Abdellaoui A, Hammerschlag AR, Nivard MG, Okbay A, Rietveld CA, Timshel PN, Trzaskowski M, Vlaming R, Zünd CL, Bao Y, Buzdugan L, Caplin AH, Chen CY, Eibich P, Fontanillas P, Gonzalez JR, Joshi PK, Karhunen V, Kleinman A, Levin RZ, Lill CM, Meddens GA, Muntané G, Sanchez-Roige S, Rooij FJV, Taskesen E, Wu Y, Zhang F; 23and Me Research Team; eQTLgen Consortium; International Cannabis Consortium; Social Science Genetic Association Consortium; Auton A, Boardman JD, Clark DW, Conlin A, Dolan CC, Fischbacher U, Groenen PJF, Harris KM, Hasler G, Hofman A, Ikram MA, Jain S, Karlsson R, Kessler RC, Kooyman M, MacKillop J, Männikkö M, Morcillo-Suarez C, McQueen MB, Schmidt KM, Smart MC, Sutter M, Thurik AR, Uitterlinden AG, White J, Wit H, Yang J, Bertram L, Boomsma DI, Esko T, Fehr E, Hinds DA, Johannesson M, Kumari M, Laibson D, Magnusson PKE, Meyer MN, Navarro A, Palmer AA, Pers TH, Posthuma D, Schunk

- D, Stein MB, Svento R, Tiemeier H, Timmers PRHJ, Turley P, Ursano RJ, Wagner GG, Wilson JF, Gratten J, Lee JJ, Cesarini D, Benjamin DJ, Koellinger PD, Beauchamp JP. Genome-wide association analyses of risk tolerance and risky behaviors in over 1 million individuals identify hundreds of loci and shared genetic influences. *Nat Genet*. 2019 Feb;51(2):245-257. doi: 10.1038/s41588-018-0309-3. Epub 2019 Jan 14. PMID: 30643258; PMCID: PMC6713272.
- **50.** Dave D, Saffer H. Alcohol demand and risk preference. *J Econ Psychol.* 2008 Dec;29(6):810-831. doi: 10.1016/j.joep.2008.03.006. PMID: 19956353; PMCID: PMC2636710.
- **51.** Umberson D, Crosnoe R, Reczek C. Social Relationships and Health Behavior Across Life Course. *Annu Rev Sociol.* 2010 Aug 1;36:139-157. doi: 10.1146/annurev-soc-070308-120011. PMID: 21921974; PMCID: PMC3171805.
- **52.** John Cawley, Christopher J. Ruhm, Chapter Three The Economics of Risky Health Behaviors. Editor(s): Mark V. Pauly, Thomas G. Mcguire, Pedro P. Barros, *Handbook of Health Economics, Elsevier*, Volume 2, 2011, Pages 95-199. ISSN 1574-0064, ISBN 9780444535924. https://doi.org/10.1016/B978-0-444-53592-4.00003-7.
- **53.** Wiseman, K.P., Seidenberg, A.B. & Klein, W.M.P. Clinician Role in Patient Awareness Regarding Carcinogenic Nature of Alcohol Consumption in the US: a Nationally Representative Survey. *J GEN INTERN MED* 37, 2116–2119 (2022). https://doi.org/10.1007/s11606-021-07113-9.
- **54.** "Unhealthy Alcohol Use in Adolescents and Adults: Screening and Behavioral Counseling Interventions." U.S. Preventive Services Task Force, https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/unhealthy-alcohol-use-in-adolescents-and-adults-screening-and-behavioral-counseling-interventions#toc. Accessed 24 August 2024.
- **55.** Hammond D. Health warning messages on tobacco products: a review. *Tob Control*. Sep 2011;20(5):327-37. doi:10.1136/tc.2010.037630
- **56.** U.S. Department of Health and Human Services. Smoking Cessation. A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2020.
- **57.** Zuckermann AME, Morissette K, Boland L, et al. The effects of alcohol container labels on consumption behaviour, knowledge, and support for labelling: a systematic review. *Lancet Public Health*. Jul 2024;9(7):e481-e494. doi:10.1016/s2468-2667(24)00097-5
- **58.** Giesbrecht N, Reisdorfer E, Rios I. Alcohol Health Warning Labels: A Rapid Review with Action Recommendations. *Int J Environ Res Public Health*. Sep 16 2022;19(18) doi:10.3390/ijerph191811676
- **59.** Joyce KM, Davidson M, Manly E, Stewart SH, Al-Hamdani M. A systematic review on the impact of alcohol warning labels. *J Addict Dis.* Jul-Sep 2024;42(3):170-193. doi:10.1080/10550887.2023.2210020
- **60.** Kokole D, Anderson P, Jané-Llopis E. Nature and Potential Impact of Alcohol Health Warning Labels: A Scoping Review. *Nutrients*. 2021 Aug 31;13(9):3065. doi: 10.3390/nu13093065. PMID: 34578942; PMCID: PMC8469468.
- **61.** Hobin E, Weerasinghe A, Vallance K, et al. Testing Alcohol Labels as a Tool to Communicate Cancer Risk to Drinkers: A Real-World Quasi-Experimental Study. *J Stud Alcohol Drugs*. Mar 2020;81(2):249-261. doi:10.15288/jsad.2020.81.249

- **62.** Noar, S. M., Francis, D. B., Bridges, C., Sontag, J. M., Brewer, N. T., & Ribisl, K. M. (2017). Effects of Strengthening Cigarette Pack Warnings on Attention and Message Processing: A Systematic Review. *Journalism & Mass Communication Quarterly*, 94(2), 416-442. https://doi.org/10.1177/1077699016674188
- **63.** Global status report on alcohol and health 2018. Geneva: World Health Organization; 2018. Licence: CC BY-NC-SA 3.0 IGO
- **64.** Stockwell T, Solomon R, O'Brien P, Vallance K, Hobin E. Cancer Warning Labels on Alcohol Containers: A Consumer's Right to Know, a Government's Responsibility to Inform, and an Industry's Power to Thwart. *J Stud Alcohol Drugs*. 2020 Mar;81(2):284-292. PMID: 32359059.
- **65.** "Health warning labels on alcoholic beverages in the WHO European Region in 2024." World Health Organization, who.int/docs/librariesprovider2/default-document-library/24-05-21_factsheet_labels.pdf. Accessed 21 November 2024.
- **66.** Office of the Law Revision Counsel. "Subchapter II Alcoholic Beverage Labeling." *United States Code*, https://uscode.house.gov/view.xhtml?path=/prelim@title27/chapter8/subchapter2&edition=prelim. Accessed 21 November 2024.
- **67.** "H.R.5210 Anti-Drug Abuse Act of 1988." *Congress.gov*, https://www.congress.gov/bill/100th-congress/house-bill/5210. Accessed 21 November 2024.

