

# **Alcohol and cancer**

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# Conflicts of interest

- None

# Overview

- 1 **Cancers associated with alcohol consumption**
- 2 **Possible mechanisms of the association between alcohol consumption and cancer**
- 3 **Cancer cases and deaths attributable to alcohol consumption**
- 4 **Alcohol reduction or cessation and cancer risk**
- 5 **Evidence gaps**
- 6 **Conclusions**

# **Cancers associated with alcohol consumption**

- Standard drink in the U.S.
  - 1 Drink = 14 grams of pure ethanol

### US Standard Drink Sizes



**12 ounces**

5% ABV beer



**8 ounces**

7% ABV malt liquor



**5 ounces**

12% ABV wine



**1.5 ounces**

40% (80 proof)  
ABV distilled spirits  
(gin, rum, vodka,  
whiskey, etc.)

**ABV = Alcohol by Volume**

## Cancers associated with alcohol consumption

Cancer	International Agency for Research on Cancer	World Cancer Research Fund
Oral cavity	Sufficient evidence	Strong (convincing)
Pharynx	Sufficient evidence	Strong (convincing)
Larynx	Sufficient evidence	Strong (convincing)
Esophagus	Sufficient evidence	
Esophagus (Squamous cell carcinoma)		Strong (convincing)
Colorectum	Sufficient evidence	Strong (convincing), >30g/d
Liver		Strong (convincing), >45g/d
Hepatocellular carcinoma	Sufficient evidence	
Breast (female)	Sufficient evidence	
Premenopausal		Strong (convincing)
Postmenopausal		Strong (probable)
Stomach	—	Strong (probable), >45g/d

## Strength of evidence

- **IARC, sufficient evidence:** A causal association has been established. A positive association has been observed in the body of evidence on exposure to the agent and cancer in studies in which chance, bias, and confounding were ruled out with reasonable confidence.
- **WCRF, strong (convincing):** Evidence strong enough to support a judgement of a convincing causal relationship, which justifies goals and recommendations designed to reduce the incidence of cancer. The evidence is robust enough to be highly unlikely to be modified in the foreseeable future as new evidence accumulates.
- **WCRF, strong (probable):** Evidence strong enough to support a judgement of a probable causal relationship, which generally justifies recommendations designed to reduce the incidence of cancer.

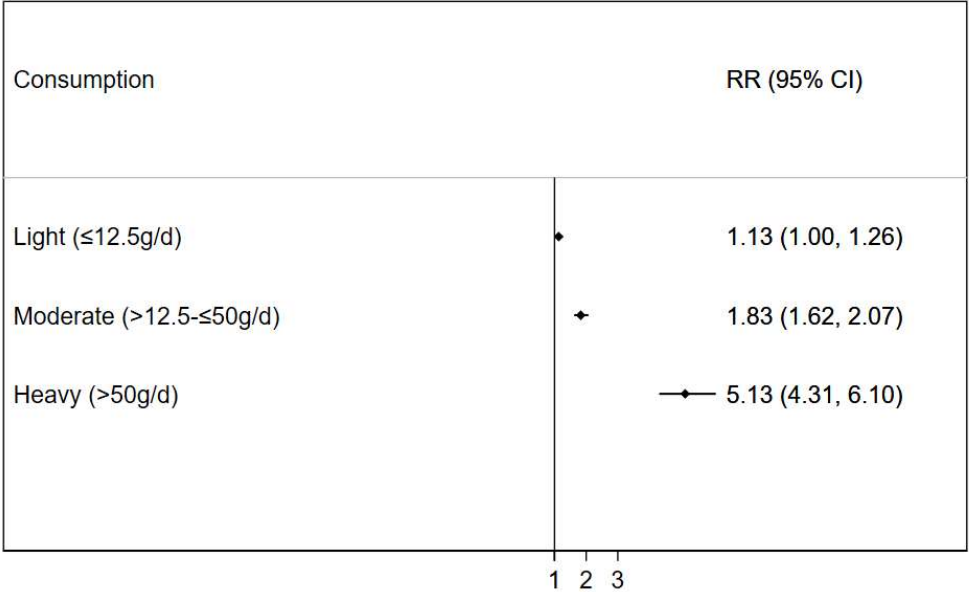
• Oral cavity

Oral cavity

Region	RR (95% CI) per 10g/d
World	1.15 (1.09, 1.22)
North America	Not reported

WCRF/AICR, 2018.

Oral cavity, pharynx



Bagnardi et al, 2015.



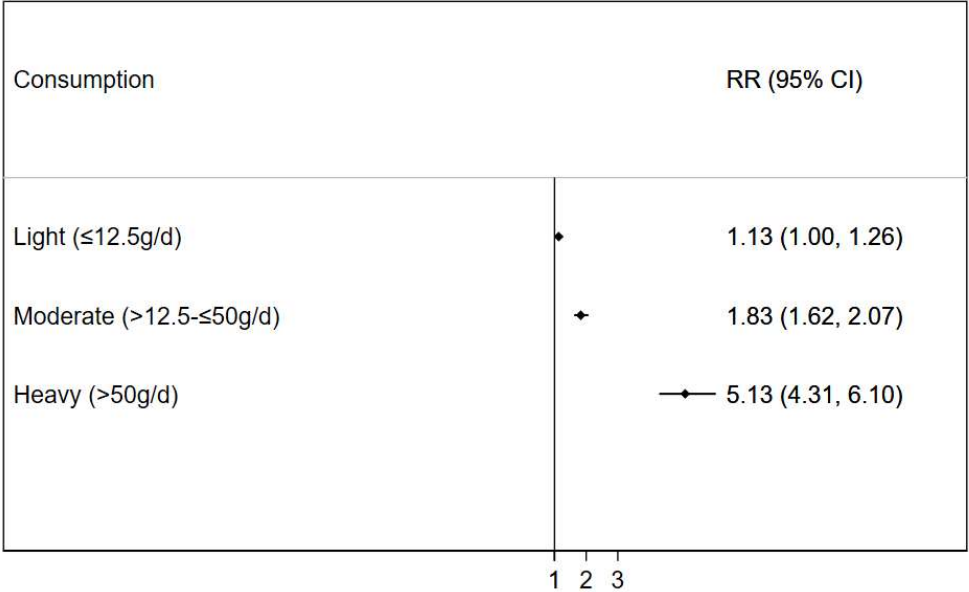
• Pharynx

Pharynx

Region	RR (95% CI) per 10g/d
World	1.13 (1.05, 1.21)
North America	Not reported

WCRF/AICR, 2018.

Oral cavity, pharynx



Bagnardi et al, 2015.

Bagnardi et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *Br J Cancer*. 2015;112(3):580-93.  
World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR). Continuous Update Project Expert Report 2018. Alcoholic drinks and cancer risk.

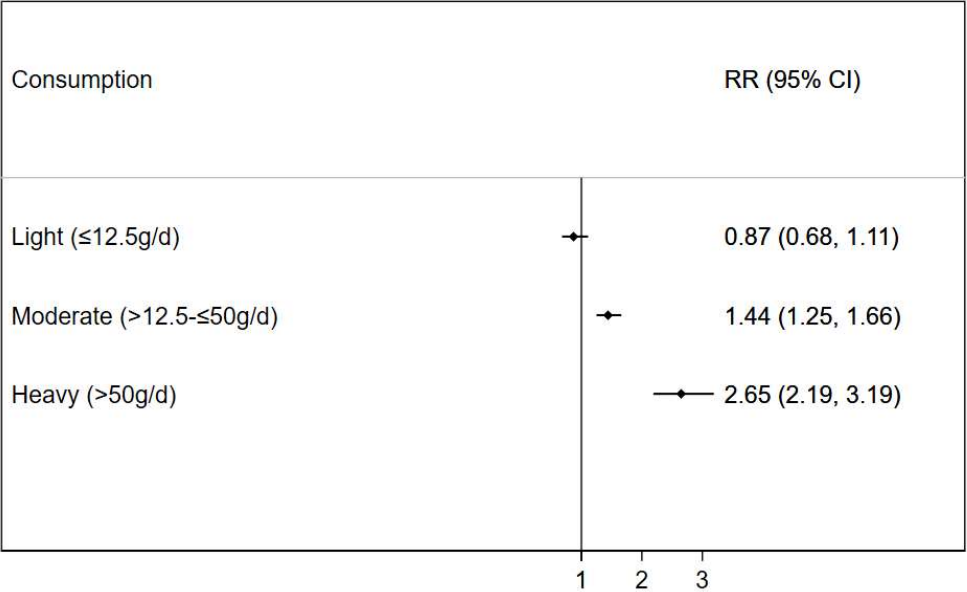
• Larynx

Larynx

Region	RR (95% CI) per 10g/d
World	1.09 (1.05, 1.13)
North America	Not reported

WCRF/AICR, 2018.

Larynx



Bagnardi et al, 2015.

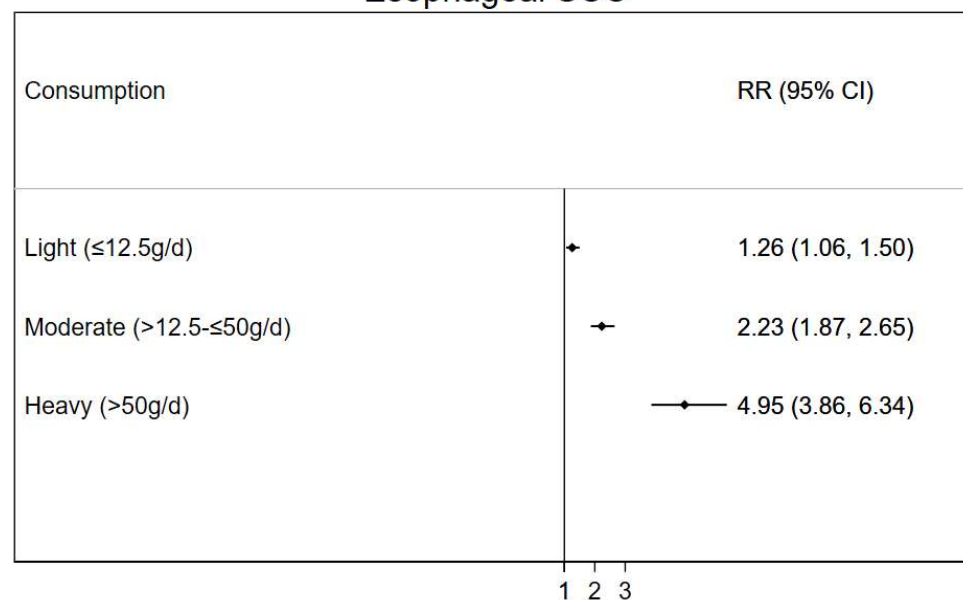
- Esophagus (squamous cell carcinoma)

## Esophagus SCC

Region	RR (95% CI) per 10g/d
World	1.25 (1.12, 1.41)
North America	1.26 (1.12, 1.41)

WCRF/AICR, 2018.

## Esophageal SCC



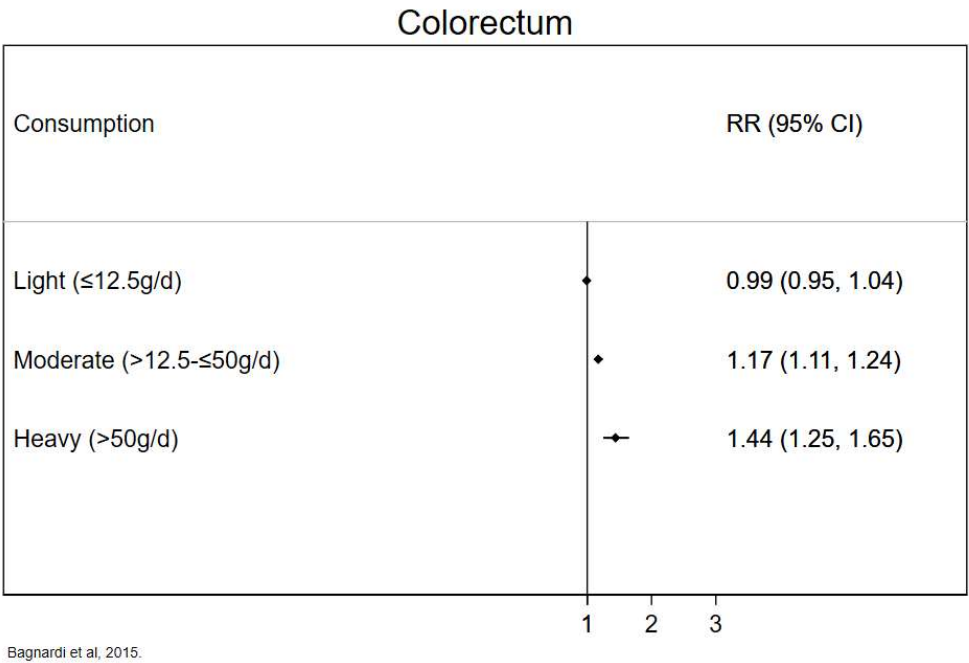
Bagnardi et al, 2015.

• Colorectum

Colorectum (for consumption >30g/d)

Region	RR (95% CI) per 10g/d
World	1.07 (1.05, 1.08)
North America	1.06 (1.01, 1.12)


WCRF/AICR, 2018.



Bagnardi et al, 2015.

- Colorectum

RR (95% CI) for the association between alcohol consumption and colorectal cancer risk in a pooled analysis of 2 U.S. cohort studies (Nurses' Health Study and Health Professionals Follow-up Study)

Consumption	Men	Women
0 g/d	Reference	Reference
0.1-4.9	0.99 (0.82, 1.20)	1.09 (0.96 to 1.24)
5-14.9	1.15 (0.96, 1.39)	1.07 (0.91 to 1.24)
15-29.9 	1.32 (1.08, 1.63)	1.08 (0.89 to 1.32)
30-44.9	1.59 (1.25, 2.03)	1.39 (1.06 to 1.83)
≥45 g/d	1.46 (1.07, 1.99)	1.46 (0.91 to 2.34)
p for trend	<0.001	<0.001

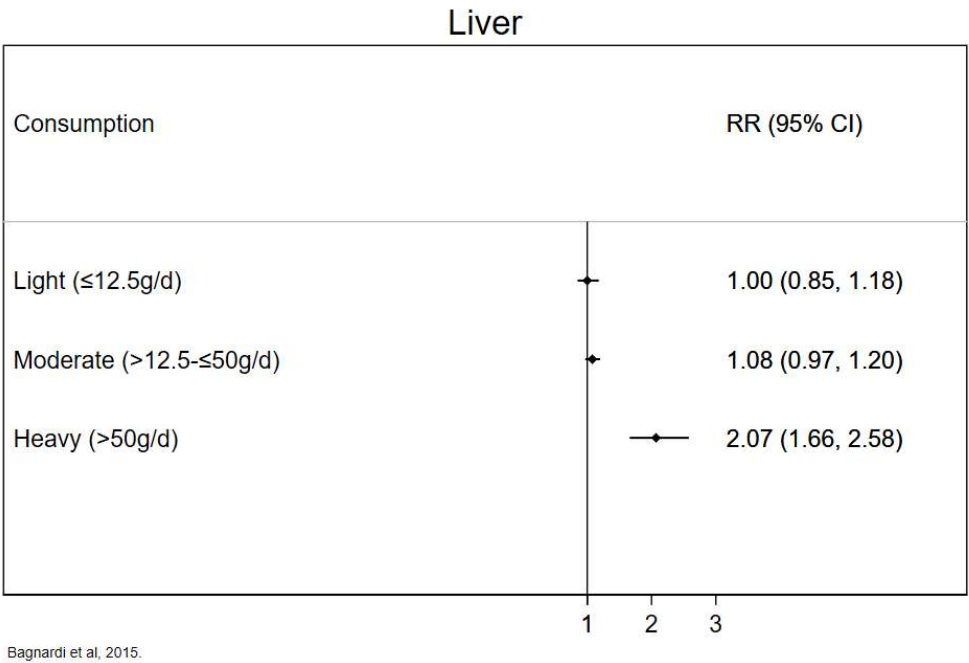
Adjusted for age, race, height, body mass index, family history of cancer, physical exam in past two years, history of colonoscopy or sigmoidoscopy, smoking in pack years, physical activity, regular aspirin use, multivitamin use, total energy intake (without alcohol), red and processed meat intake, alternate healthy eating index 2010 (without alcohol); prostate specific antigen test in past two years (men only); and menopause status, postmenopausal hormone use, and mammogram in past two years (women only).

• Liver

Liver (for consumption >45g/d)

Region	RR (95% CI) per 10g/d
World	1.04 (1.02, 1.06)
North America & Europe	1.08 (1.00, 1.16)

WCRF/AICR, 2018.



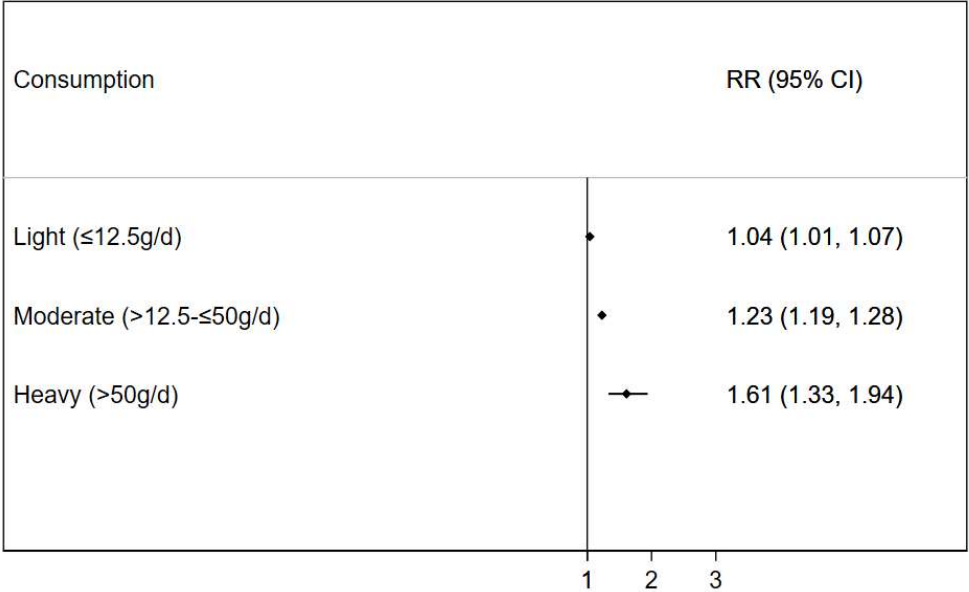
• Breast (female)

Breast (female)

Region	RR (95% CI) per 10g/d
<i>Premenopausal</i>	
World	1.05 (1.02, 1.08)
North America	1.07 (1.02, 1.12)
<i>Postmenopausal</i>	
World	1.09 (1.07, 1.12)
North America	1.11 (1.07, 1.15)

WCRF/AICR, 2018.

Breast (female)



Bagnardi et al, 2015.

Bagnardi et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. *Br J Cancer*. 2015;112(3):580-93.  
World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR). Continuous Update Project Expert Report 2018. Alcoholic drinks and cancer risk.

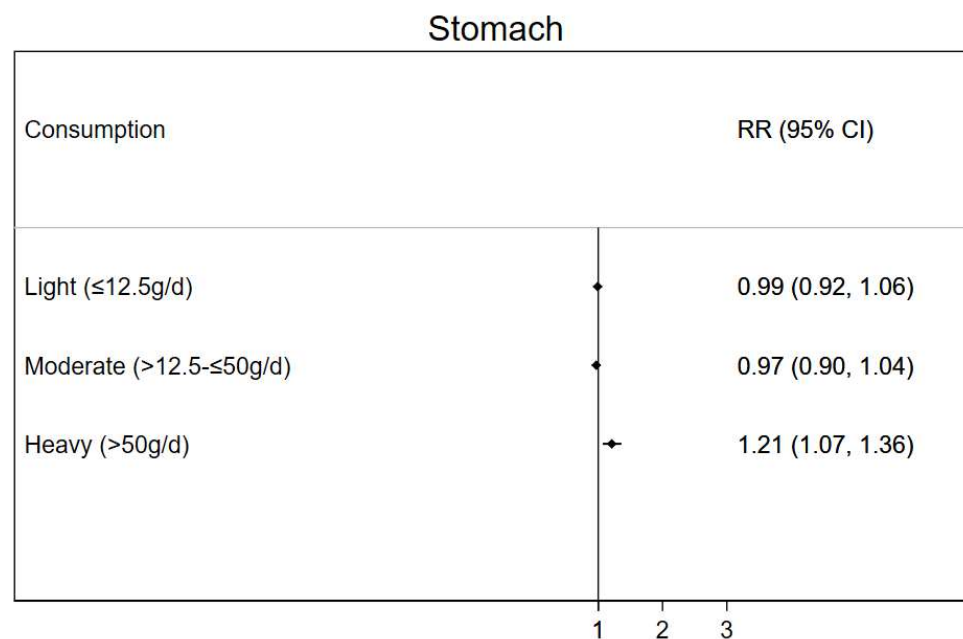
- Stomach (only based on WCRF evaluation)

Stomach (for consumption >45g/d)

Region	RR (95% CI) per 10g/d
World	1.02 (1.00, 1.04)
North America	0.82 (0.52, 1.29)

WCRF/AICR

In WCRF evaluation, not in studies from North America and Europe.



Bagnardi et al, 2015.



## The magnitude of associations, per 10g pure ethanol/day (WCRF report)

Cancer	Relative risk (95% CI)
Oral cavity	1.15 (1.09, 1.22)
Pharynx	1.13 (1.05, 1.21)
Larynx	1.09 (1.05, 1.13)
Esophagus (Squamous cell carcinoma)	1.25 (1.12, 1.41)
Colorectum (starting from ~ 2 drinks/day per WCRF)	1.07 (1.05, 1.08)
Liver (hepatocellular carcinoma) (starting from ~ 3 drinks/day per WCRF)	1.04 (1.02, 1.06)
Breast (female) Premenopausal	1.05 (1.02, 1.08)
Postmenopausal	1.09 (1.07, 1.12)
Stomach (starting from ~ 3 drinks/day per WCRF) *	1.02 (1.00, 1.04)

\* Only based on WCRF evaluation, in which the excess risk was not reported in studies from North America and Europe.

- Alcohol increases cancer risk
  - all types of alcoholic beverages can cause cancer

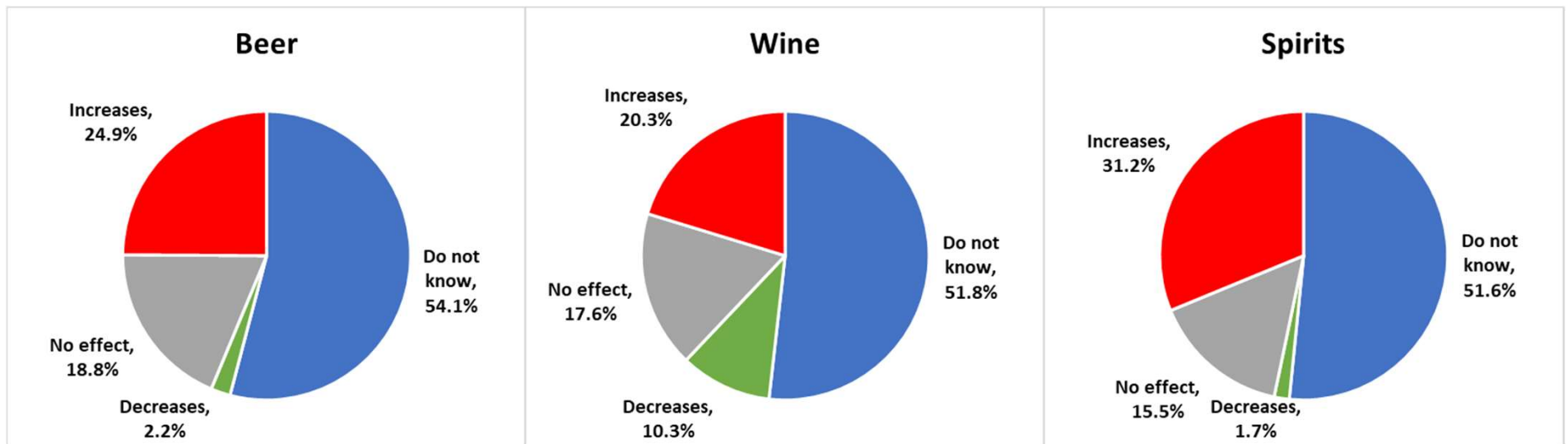
Association between alcoholic beverages and colorectal cancer risk

Alcoholic beverage	RR (95% CI) per 10g/d
Beer	1.08 (1.05, 1.11)
Wine	1.04 (1.01, 1.08)
Spirits	1.08 (1.02, 1.14)

WCRF/AICR, 2018.

- Awareness about alcohol and cancer risk

U.S. adults' beliefs about how wine, beer, and liquor consumption affect cancer risk, 2020



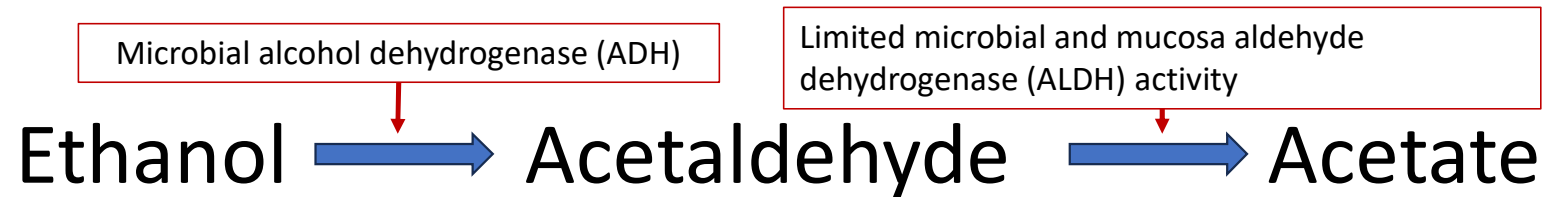
# Possible mechanisms

- International Agency for Research on Cancer:
  - consumption of alcohol is carcinogenic to humans (Group 1)
  - ethanol in alcoholic beverages is carcinogenic to humans (Group 1)
  - acetaldehyde associated with the consumption of alcoholic beverages is carcinogenic to humans (Group 1)

- Acetaldehyde: a major determinant of alcohol-related carcinogenesis
  - DNA damage
    - DNA adducts
    - mutations
    - chromosomal aberrations
    - sister chromatid exchange
    - micronucleus formation
  - Other adverse effects



## Inside the gastrointestinal tract



- Ethanol  $\rightarrow$  acetaldehyde, catalyzed by **microbial ADH** locally (high concentration up to 15–20 minutes after ingestion)

+

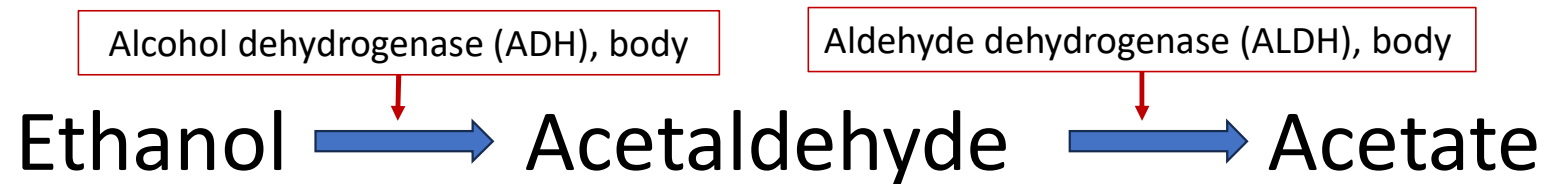
- **Low ALDH activities** of oral/gut microbiome and mucosa

$\downarrow$

**Accumulation of acetaldehyde** in saliva, gastric juice, and colonic contents



After absorption by the body



- Distribution of ethanol in body within 30 minutes after ingestion



High concentration of acetaldehyde in body until ethanol is eliminated

- Depends on amount of alcohol ingested
- Also affected by smoking and body's ALDH activity

- Interaction between alcohol and smoking
- Continuous **smoking** + heavy **alcohol** consumption → changes in oral **microbial flora**, especially in high acetaldehyde producing strains
- Other mechanisms?
- After alcohol drinking, salivary acetaldehyde levels during concomitant smoking are several times higher than levels in nonsmoking individuals

## • Interaction between alcohol and smoking

Joint effect of smoking and alcohol on head and neck cancer risk

Smoking	Alcohol	Odds ratio (95% CI)
Never	Never	Reference
1-20 cigs/day	Never	2.20 (1.57, 3.09)
>20 cigs/day	Never	4.15 (2.44, 7.07)
Never	1-2 drinks/day	1.03 (0.84, 1.25)
1-20 cigs/day	1-2 drinks/day	3.09 (2.13, 4.50)
>20 cigs/day	1-2 drinks/day	4.81 (3.21, 7.20)
Never	≥3drinks/day	1.91 (1.27, 2.87)
1-20 cigs/day	≥3drinks/day	9.92 (6.36, 15.46)
>20 cigs/day	≥3drinks/day	14.23 (8.30, 24.40)

→ **P for interaction <0.01.** A pooled analysis of 18 case-control studies with 11,211 cases and 16,152 controls. . Adjusted for age, sex, education, race/ethnicity, and study center.

Hashibe 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. *CEBP*. 2009;18(2):541-550.

- Interaction between alcohol and genetic factors



- Interaction between alcohol and genetic factors

Association between polymorphism in ALDH2 and esophageal squamous cell carcinoma risk

\*2 denotes low activity ALDH2 allele (slower metabolism of acetaldehyde)

Alcohol intake	Cases/controls	Odds ratio (95% CI)
<b>*1/*1</b>		
Non-drinker	17/191	<b>Reference</b>
0.1-30 g/d	45/103	2.2 (1.1, 4.5)
>30 g/d	49/31	7.2 (3.3, 15.9)
<b>*1/*2</b>		
Non-drinker	38/236	1.1 (0.6–2.3)
0.1-30 g/d	114/42	14.5 (7.1–29.6)
>30 g/d	129/8	102.6 (38.3–274.8)
<b>*2/*2</b>		
Non-drinker	8/44	1.2 (0.4–3.4)
0.1-30 g/d	3/1	17.3 (1.4–213.7)
>30 g/d	3/0	–

Adjusted for age, sex, study hospital, ethnicity, smoking, education, smoking, betel quid chewing, and consumption of fruits and vegetables.

# • Interaction between alcohol and genetic factors

*ADH1B\*1 & ADH1C\*2 (slow ethanol-oxidizing) & ALDH2\*2 (null) allele frequencies by population and incidence of head and neck cancer*

Prevalence of ALDH2 allele \*2 (low activity):

Higher in Asian populations (e.g., 24% in Japan).

<1% in many other populations.

~30-50% in Asian Americans.

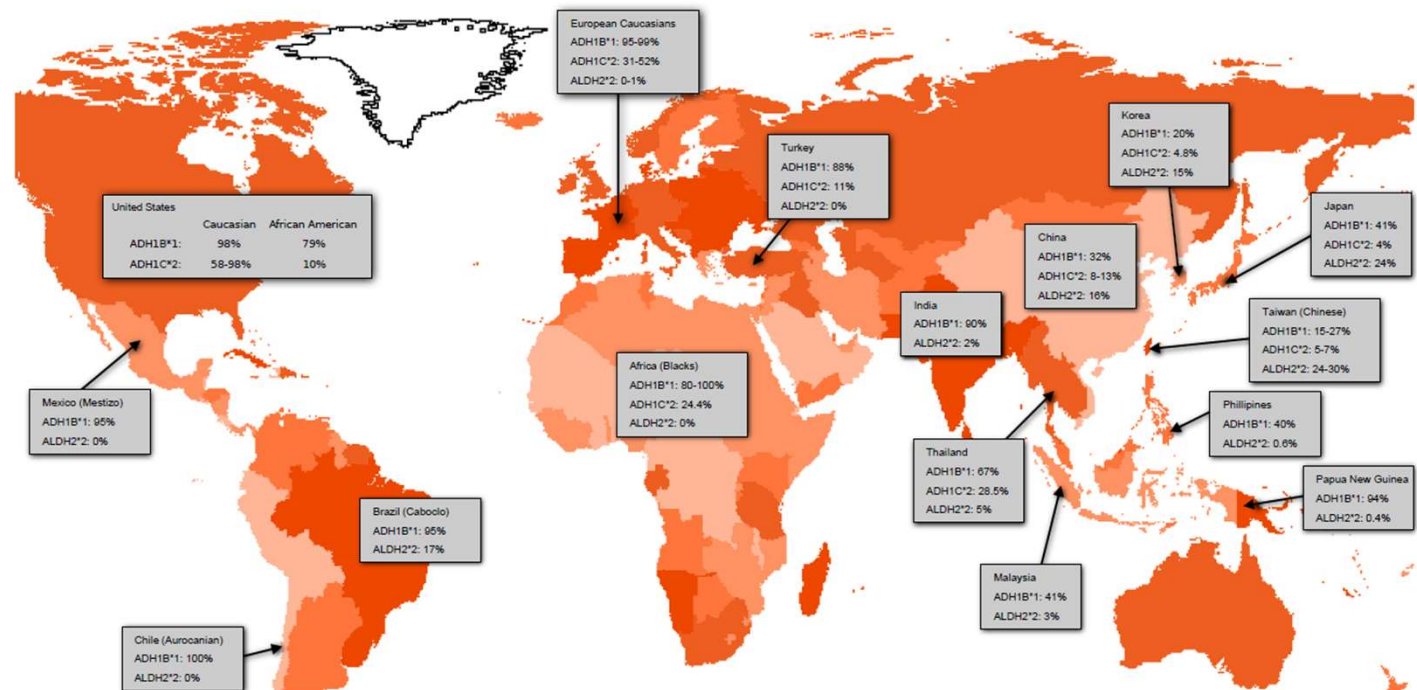




Figure from IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, vol 100. Part E: Personal habits and indoor combustions. 2012.  
Data on Asian Americans from Eng et al. ALDH2, ADH1B, and ADH1C genotypes in Asians: A literature review. *Alcohol Res Health*. 2007;30(1):22-27.

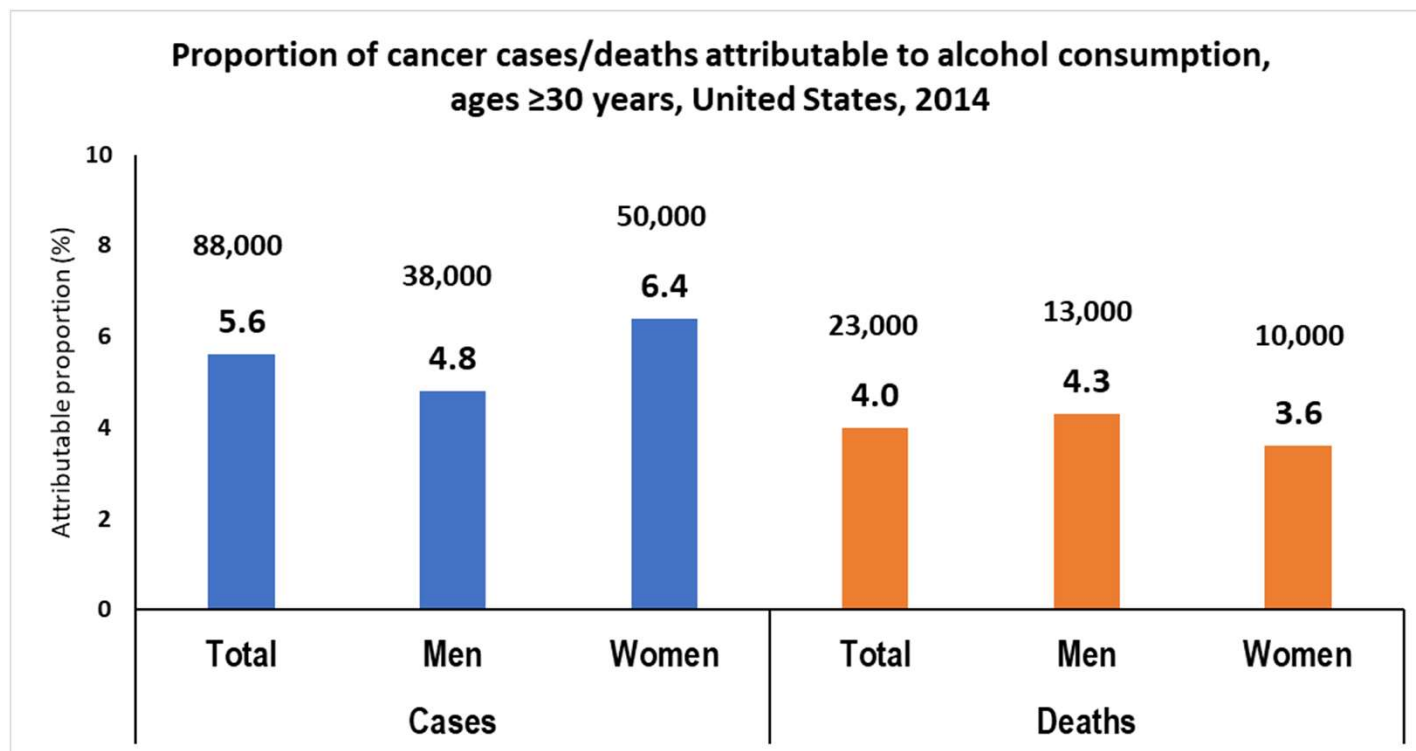
- Other possible mechanisms:
  - DNA damage by **reactive oxygen species** (induction of ethanol-inducible CYP2E1)
  - Changes in the composition of the **gut microbiota**
  - Epithelial-barrier dysfunction and **increased intestinal permeability** (inflammation)
  - Decrease in **folate absorption**
  - Increases in circulating concentrations of estradiol, testosterone, and other **sex hormones**
  - Decreases in sex hormone-binding globulin concentrations

# **Cancer burden attributable to alcohol consumption**



# Proportion and Number of Cancer Cases and Deaths Attributable to Potentially Modifiable Risk Factors in the United States

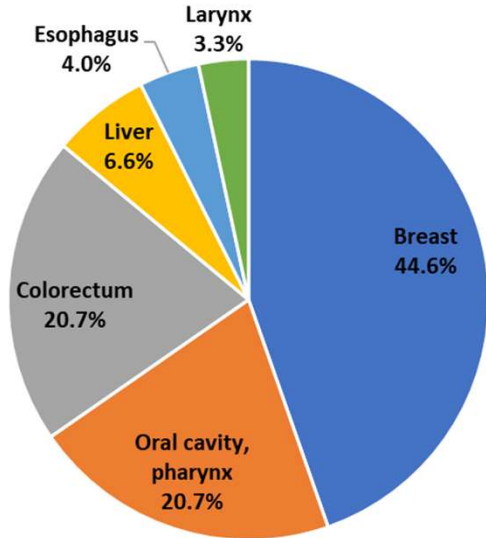
Farhad Islami, MD, PhD <sup>1</sup>; Ann Goding Sauer, MSPH<sup>2</sup>; Kimberly D. Miller, MPH<sup>2</sup>; Rebecca L. Siegel, MPH<sup>3</sup>; Stacey A. Fedewa, PhD, MPH<sup>4</sup>; Eric J. Jacobs, PhD<sup>5</sup>; Marjorie L. McCullough, ScD, RD<sup>6</sup>; Alpa V. Patel, PhD<sup>7</sup>; Jiemin Ma, PhD, MHS<sup>8</sup>; Isabelle Soerjomataram, MD, PhD, MSc<sup>9</sup>; W. Dana Flanders, MD, DSc, MPH, MA<sup>10</sup>; Otis W. Brawley, MD, MACP<sup>11</sup>; Susan M. Gapstur, PhD, MPH<sup>12</sup>; Ahmedin Jemal, DVM, PhD <sup>13</sup>



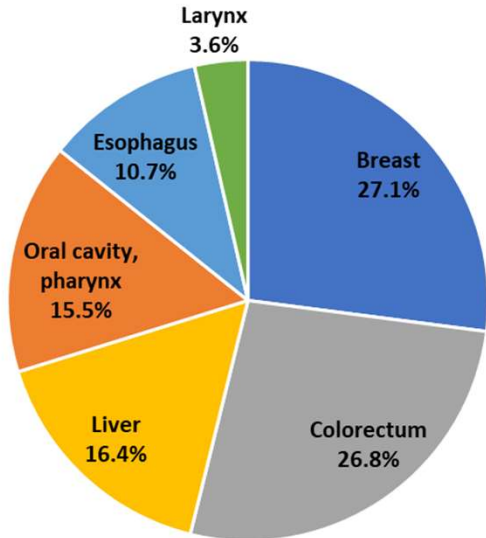
Estimated cancer cases and deaths in adults aged  $\geq 30$  years in the U.S. in 2014 attributable to alcohol consumption

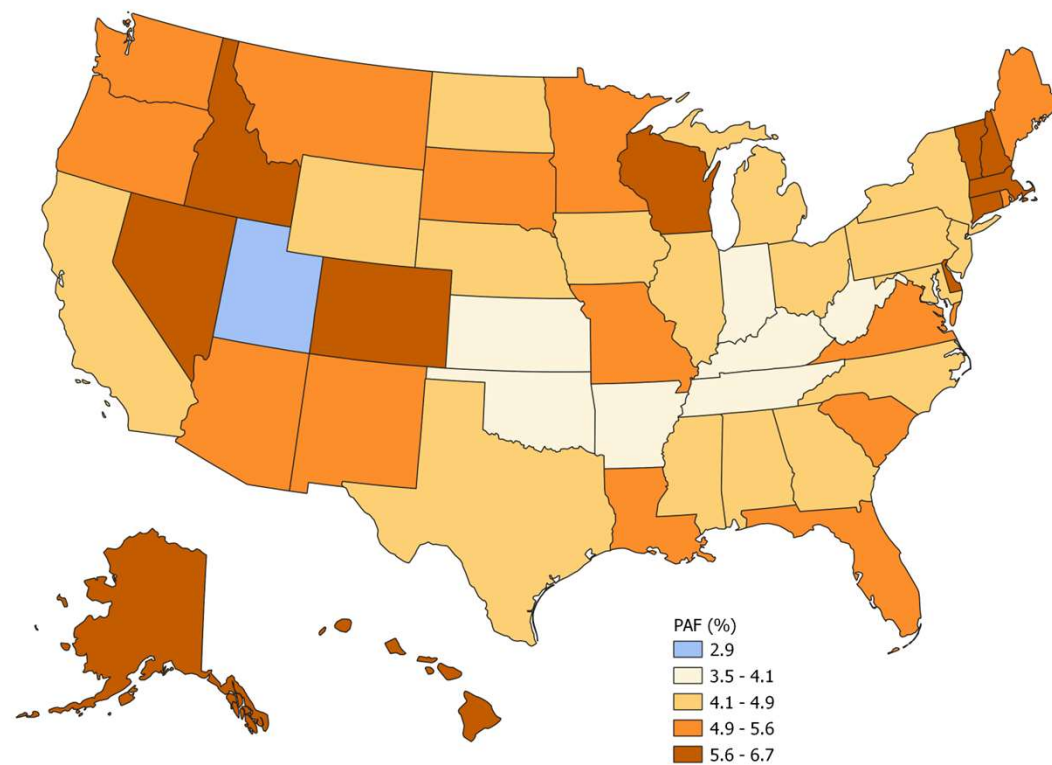
Cancer	Attributable cases, <i>N</i>	Attributable cases, %	Attributable deaths, <i>N</i>	Attributable deaths, %
Oral cavity, pharynx	18,130	40.9%	3,640	38.9%
Larynx	2,930	23.2%	840	22.3%
Liver	5,750	21.6%	3,840	20.4%
Esophagus	3,540	21.0%	2,510	16.8%
Breast	39,060	16.4%	6,350	15.4%
Colorectum	18,090	12.8%	6,290	12.0%

% of all cancer cases attributable to alcohol consumption, ages ≥30 years, United States, 2014



% of all cancer deaths attributable to alcohol consumption, ages ≥30 years, United States, 2014



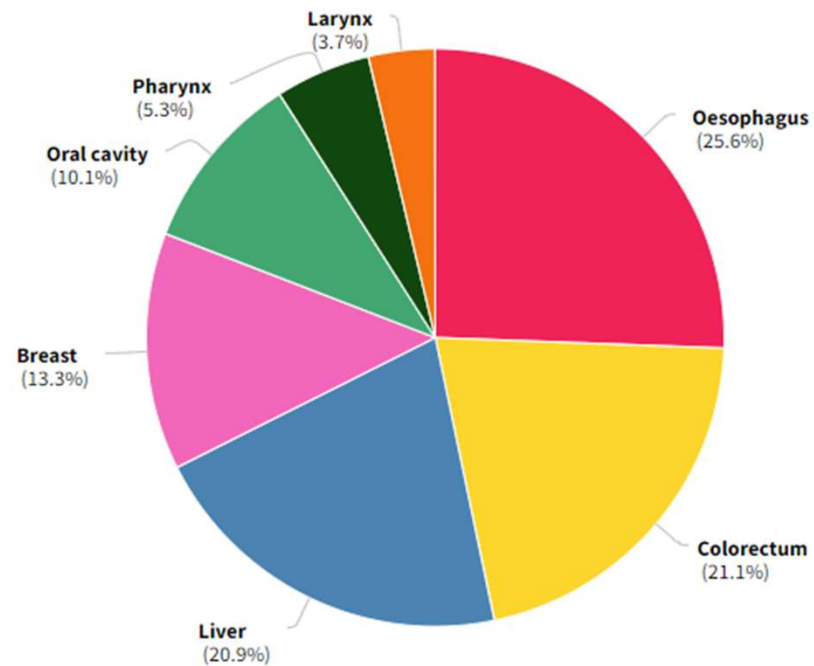
Proportion of cancer cases attributable to alcohol consumption, ages  $\geq 30$  years, 2013-2016

# Global burden of cancer in 2020 attributable to alcohol consumption: a population-based study

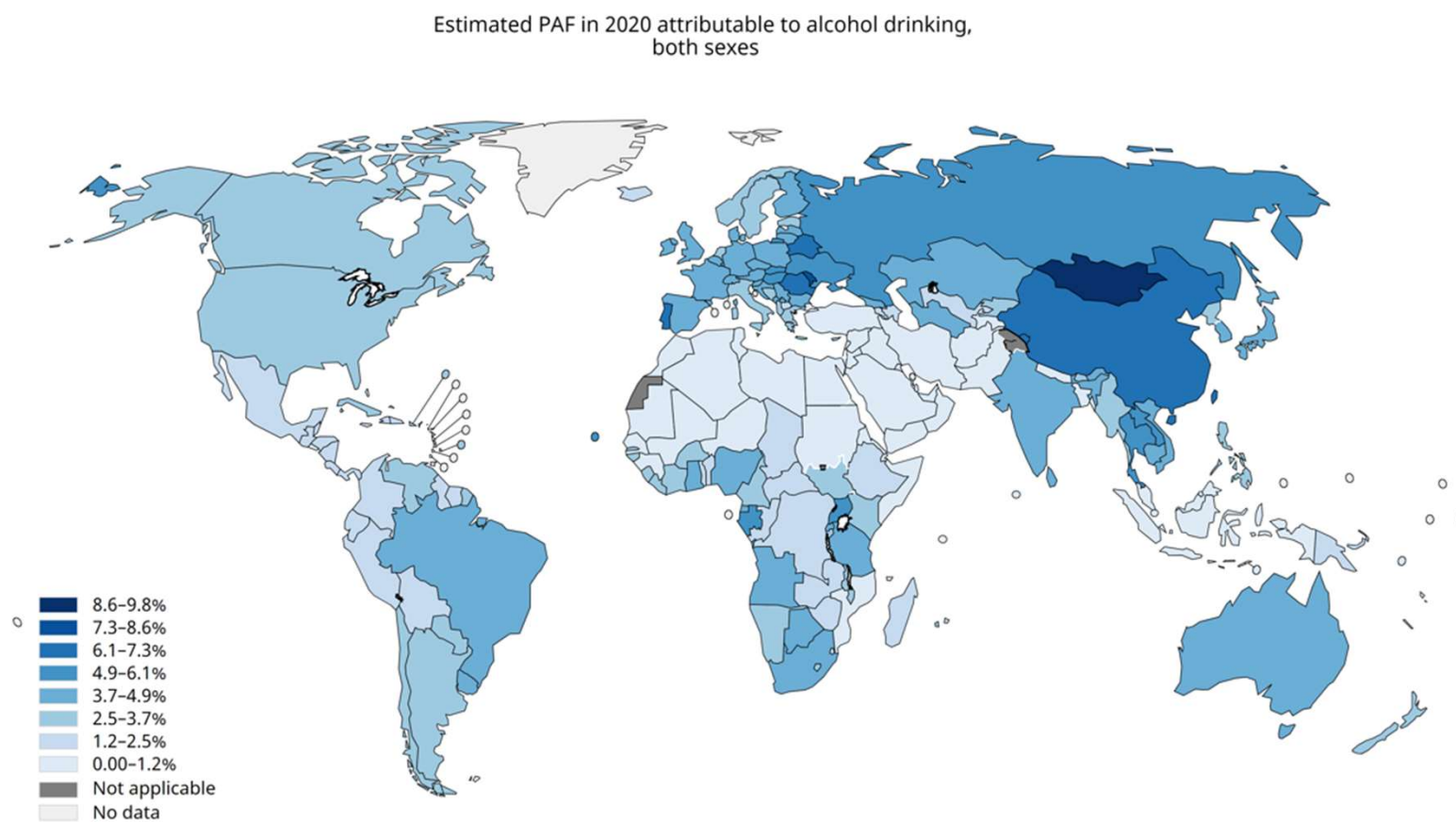
*Harriet Rumgay, Kevin Shield, Hadrien Charvat, Pietro Ferrari, Bundit Sornpaisarn, Isidore Obot, Farhad Islami, Valery E P P Lemmens, Jürgen Rehm, Isabelle Soerjomataram*

*Lancet Oncol 2021; 22: 1071–80*

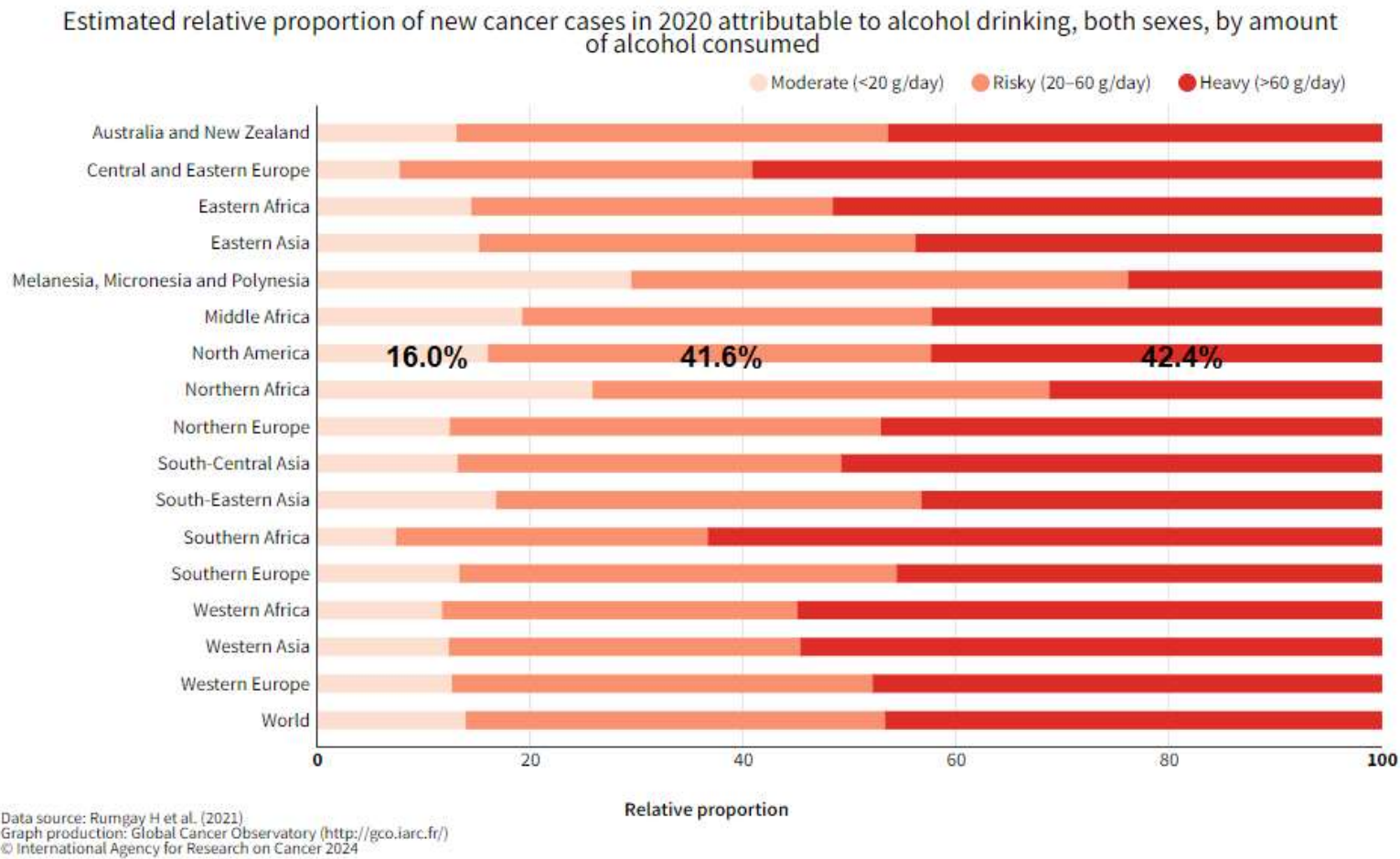
Estimated number of new cancer cases in 2020 attributable to alcohol drinking, World, both sexes



Total number of attributable cases: 740 000







# **Alcohol reduction or cessation and cancer risk**

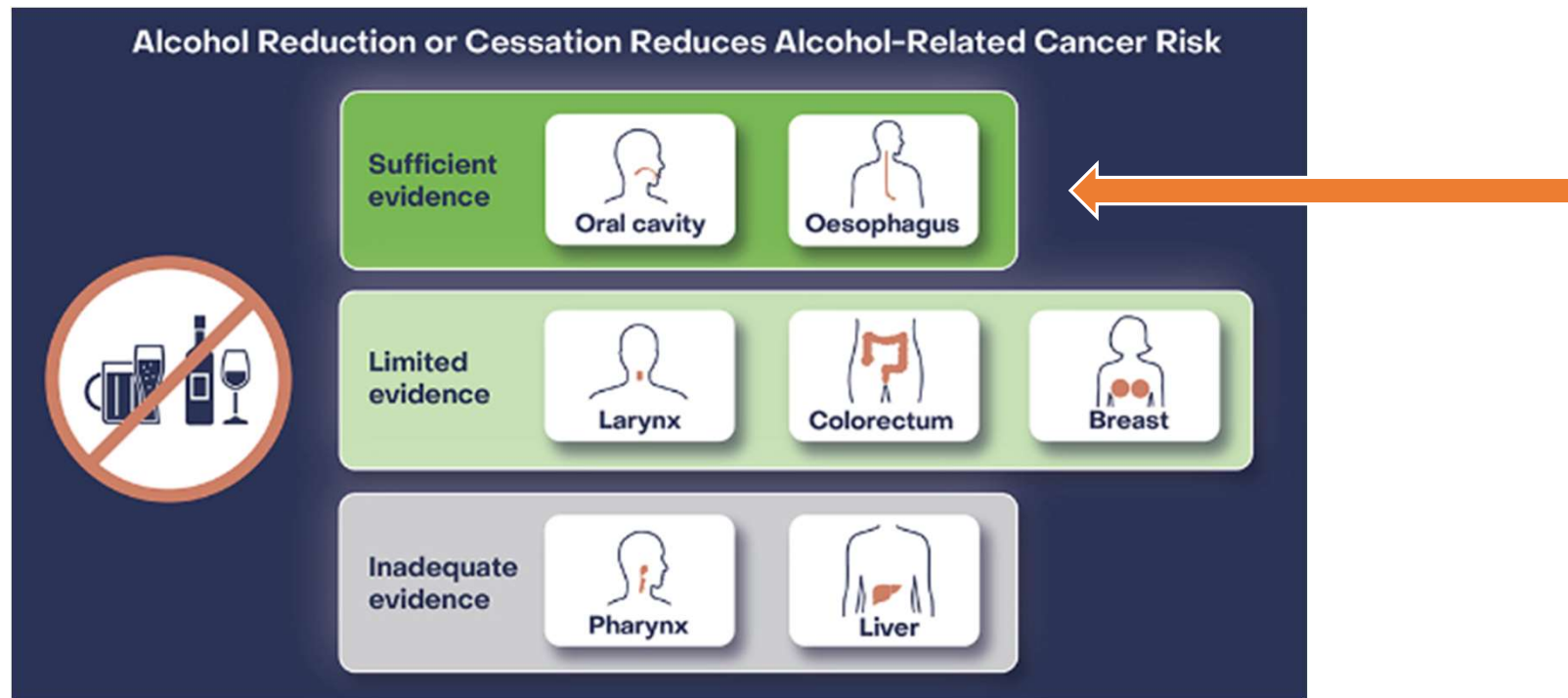
*The NEW ENGLAND JOURNAL of MEDICINE*

**SPECIAL REPORT**

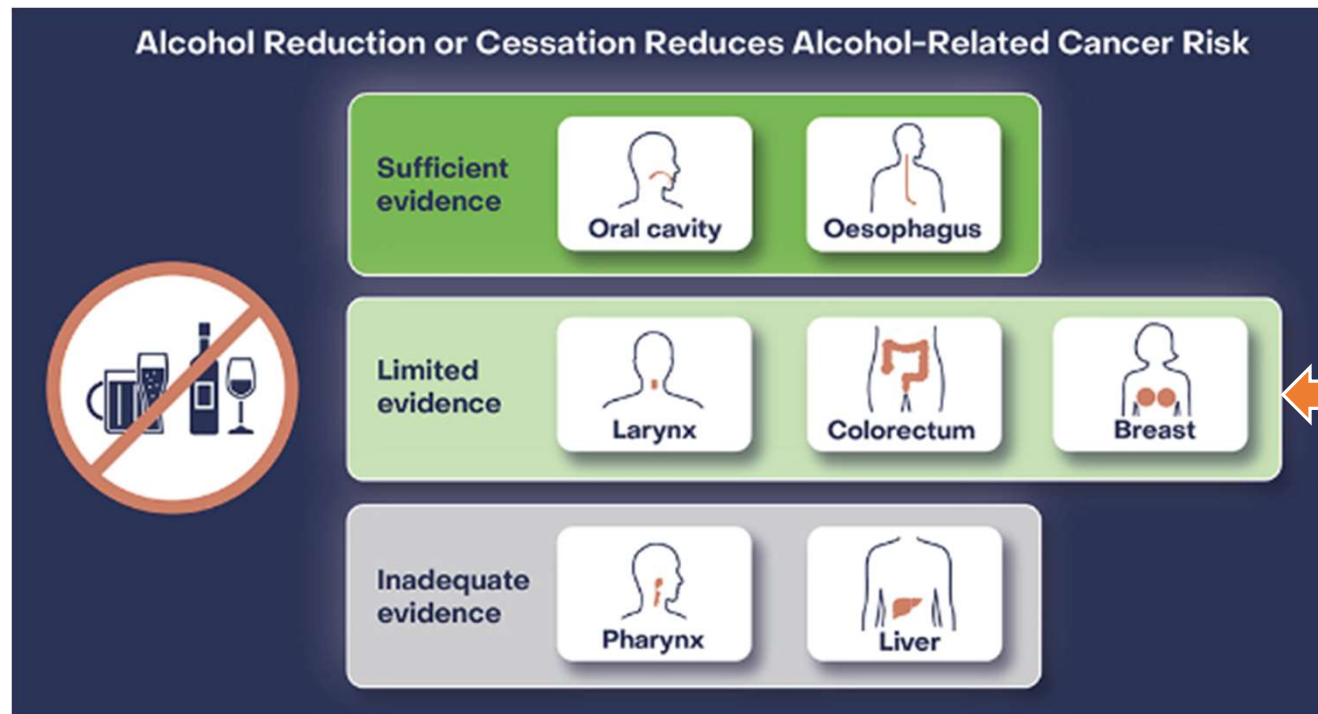
## **The IARC Perspective on Alcohol Reduction or Cessation and Cancer Risk**

Susan M. Gapstur, Ph.D., Véronique Bouvard, Ph.D., Suzanne T. Nethan, M.D.S.,  
Jo L. Freudenheim, Ph.D., Christian C. Abnet, Ph.D., Dallas R. English, Ph.D.,  
Jürgen Rehm, Ph.D., Silvia Balbo, Ph.D., Penny Buykx, Ph.D., David Crabb, M.D.,  
David I. Conway, F.D.S., Ph.D., Farhad Islami, M.D., Ph.D., Dirk W. Lachenmeier, Ph.D.,  
Katherine A. McGlynn, Ph.D., Mikko Salaspuro, M.D., Ph.D., Norie Sawada, M.D., Ph.D.,  
Mary B. Terry, Ph.D., Tatiana Toporcov, Ph.D., and Béatrice Lauby-Secretan, Ph.D.

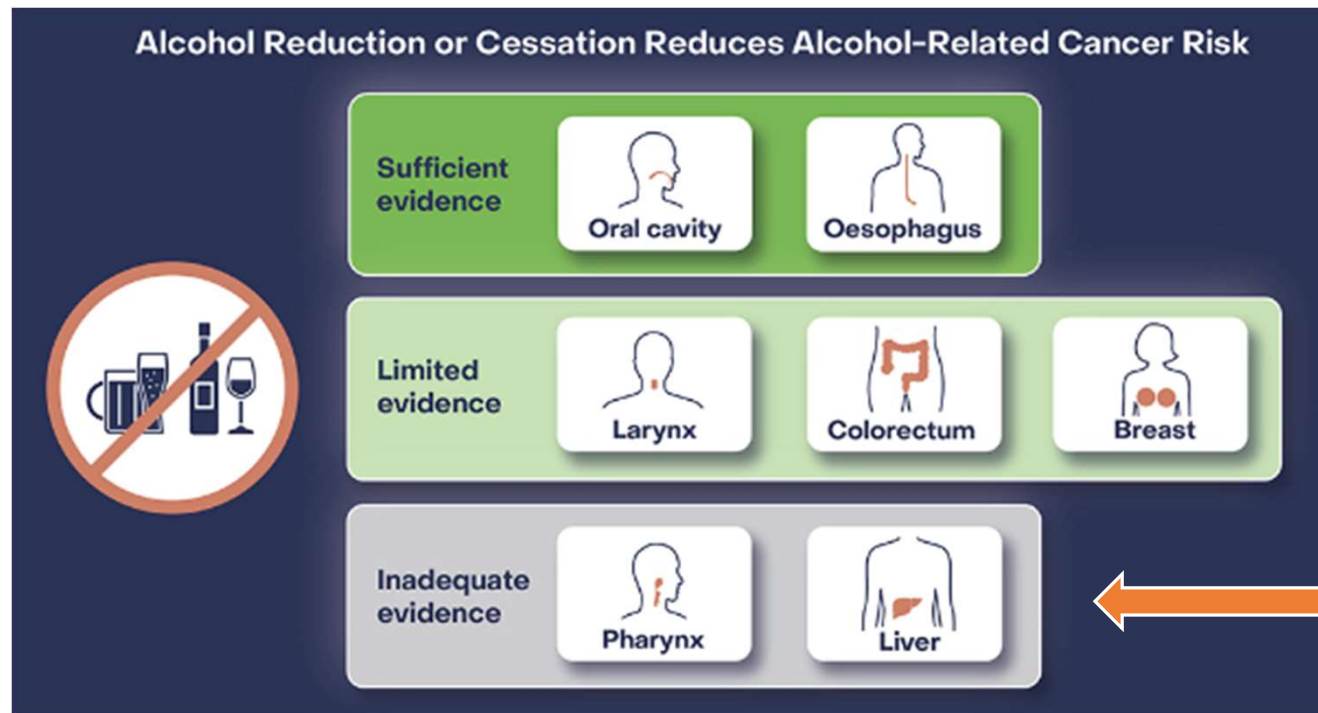
Cancer Site	Type and Number of Studies
<b>Oral cavity</b>	Cohort: $n = 2$ Case-control: $n = 5$ (all hospital-based) Pooled analysis: $n = 1$ (4 population-based and 8 hospital-based case-control studies)
<b>Esophagus</b>	Cohort: $n = 4$ Case-control: $n = 11$ (3 population-based and 8 hospital-based) Pooled analysis: $n = 1$ (2 cohort studies) Meta-analysis: $n = 1$ (4 hospital-based case-control studies)
<b>Larynx</b>	Cohort: $n = 3$ Case-control: $n = 3$ (all hospital-based) Pooled analysis: $n = 1$ (2 population-based and 7 hospital-based case-control studies)
<b>Colorectum</b>	Cohort: $n = 10$ Case-control: $n = 6$ (3 population-based and 3 hospital-based) Pooled analysis: $n = 1$ (3 cohort studies)
<b>Breast</b>	Cohort: $n = 11$ Case-control: $n = 10$ (4 population-based, 4 hospital-based, 2 both)
<b>Pharynx</b>	Cohort: $n = 2$ Case-control: $n = 6$ (4 hospital-based, 1 population-based, and 1 friend- or family-based) Pooled analysis: $n = 1$ (4 population-based and 9 hospital-based case-control studies)
<b>Liver</b>	Cohort: $n = 9$ (1 among participants with alcohol-related liver disease) Case-control: $n = 3$ (all hospital-based)



**Sufficient evidence:** A causal preventive association between the intervention and cancer in humans has been established. That is, a cancer-preventive association has been observed consistently in the body of evidence (including several high-quality studies) and chance, bias, and confounding as causes of this association were ruled out with reasonable confidence.



Limited evidence: A causal preventive association between the intervention and cancer in humans is plausible. That is, a cancer-preventive association has been observed in the body of evidence, but chance, bias, or confounding as causes of this association could not be ruled out with reasonable confidence.



**Inadequate evidence:** The current body of evidence does not enable a conclusion to be drawn about the presence or absence of a preventive association between the intervention and cancer in humans. Common situations include: (a) no data are available in humans; (b) there are studies available in humans, but of poor quality or informativeness; and (c) there are studies available in humans of sufficient quality, but their results are inconsistent or otherwise do not enable a conclusion to be drawn.

Figure from IARC Handbooks of Cancer Prevention Volume 20A: Reduction or cessation of alcohol consumption. 2023. [iarc.who.int/wp-content/uploads/2023/12/HB20A-zoom.jpg](https://iarc.who.int/wp-content/uploads/2023/12/HB20A-zoom.jpg)



Mechanisms with strong evidence

Strong mechanistic evidence: There are a substantial number of high-quality studies in humans that consistently link the intervention to a mechanistic pathway by which it could prevent cancer.



# Evidence gaps

- Patterns of **consumption over the life course**, including earlier in life, and cancer risk

**Alcohol Intake in Early Adulthood and Risk of Colorectal Cancer: Three Large Prospective Cohort Studies of Men and Women in the United States**

Hur et al. *Eur J Epidemiol.* 2021 March ; 36(3): 325–333

- Effects of heavy episodic (**binge**) **drinking**
- Alcohol consumption and risk of **additional cancer types/subtypes**
  - e.g., cancer of the pancreas

- **Confounding and modifying** effects of other factors
  - e.g., HPV and oropharyngeal cancer
  - variants of alcohol-metabolizing enzymes (e.g., ALDH2) and cancer types other than upper aerodigestive tract cancers
- Biologic **mechanisms**
- Effects of **alcohol reduction and cessation**
  - duration of cessation
  - mechanisms
- Influence of alcohol on cancer **disparities**
- Alcohol's effects on **tumor progression**
- Alcohol's effects on cancer **treatment efficacy**

# Conclusions

- Alcohol consumption →
  - increased risk of **at least 7 cancer types**
  - **About 90,000 new cancer cases and 23,000 cancer deaths** per year in the United States
  - **higher burden/risk in certain populations** (e.g., among individuals who smoke)
- **Prevention** is important
- **Alcohol cessation and reduction** can reduce the risk of cancer among individuals who drink

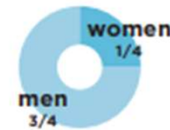
- Even **low consumption levels** are associated with several cancer types
- **No difference** between various types of alcoholic beverages and cancer risk
- **Low awareness** about alcohol and cancer risk

- Dietary Guidelines for Americans
  - **do not recommend** that individuals who do not drink alcohol **start drinking** for any reason
  - adults of legal drinking age can choose not to drink, or to drink in **moderation** by limiting intake to  $\leq 2$  drinks/day for men or  $\leq 1$  drink/day for women
- American Cancer Society
  - **it is best not to drink alcohol**
  - people who choose to drink alcohol should **limit their intake** to  $\leq 2$  drinks/day for men and  $\leq 1$  drink/day for women
- World Health Organization
  - **no level of alcohol consumption is safe for our health**

# Alcohol and health



**3 million deaths every year**  
6 deaths every minute  
from harmful use of alcohol



## Harmful use of alcohol causes

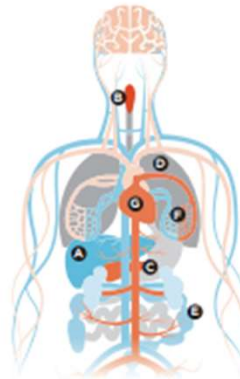
 **100%** of alcohol use disorders

 **18%** of suicides

 **18%** of interpersonal violence

 **27%** of traffic injuries

 **13%** of epilepsy



**A 48%** of liver cirrhosis

**B 26%** of mouth cancers

**C 26%** of pancreatitis

**D 20%** of tuberculosis

**E 11%** of colorectal cancer

**F 5%** of breast cancer

**G 7%** of hypertensive heart disease



***Thank You!***