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# Moderate alcohol and cancer

Ned Calonge, Chair and Ian Saldanha Committee on Review of Evidence on Alcohol and Health NATIONAL Sciences Engineering Medicine

Review of Evidence on Alcohol and Health

Consensus Study Report

## Committee, consultants and staff

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## The Committee's Task and Approach

Congress asked the USDA to contract with the National Academies to convene an expert committee to undertake a review of the current scientific evidence on the relationship between consumption of alcohol and health outcomes—including "certain cancers"

The committee focused on moderate alcohol consumption, defined as consuming alcoholic beverages up to the limit defined by the *Dietary Guidelines* for *Americans*, meaning two drinks or 28 grams of alcohol in a day for men and one drink or 14 grams of alcohol in a day for women

The Committee developed a list of inclusion and exclusion criteria to identify published literature published in English since 2010 and contracted with the Academy of Nutrition and Dietetics to conduct systematic reviews (SR)

## **Levels of Certainty**

The committee based its framework for assigning certainty to conclusions on methods from the U.S. Preventive Services Task Force:

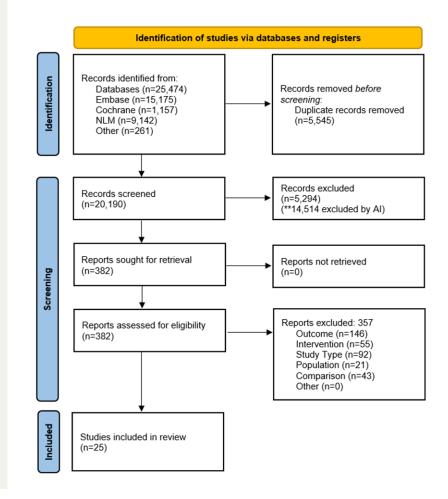
- High certainty: Evidence includes consistent results from good quality studies in relevant populations assessing effects on health outcomes; the conclusion is unlikely to be affected by future studies. High certainty is unlikely to be assigned without a randomized controlled trial (No conclusions were issued with high certainty)
- Moderate certainty: Evidence is sufficient to determine effects on health outcomes but is constrained by issues raised in the quality assessment of the evidence.
- Low certainty: Evidence is insufficient to assess effects on health outcomes;
   additional information from future studies may allow for assessment.

## **Abstainer Bias**

- A key criteria for studies included in the review was that the comparison group did not combine former drinkers with never drinkers
- This avoids "abstainer bias"—former drinkers can include individuals
  who stopped drinking due to health reasons and this can bias results,
  such as overestimating potential benefits of moderate drinking
- Therefore, results in this report are not directly comparable to past evidence and reviews that did not address abstainer bias

## Cancer (Chapter 5)

- Includes
  - Breast (female)
  - Oral, pharyngeal, laryngeal, esophageal
  - Colon, rectal
- Excludes
  - Studies that exclusively examine cancerrelated mortality, prevalence, survivorship, or recurrence of cancer
- 25 eligible studies screened from 20,190



## **Breast Cancer (Female)**

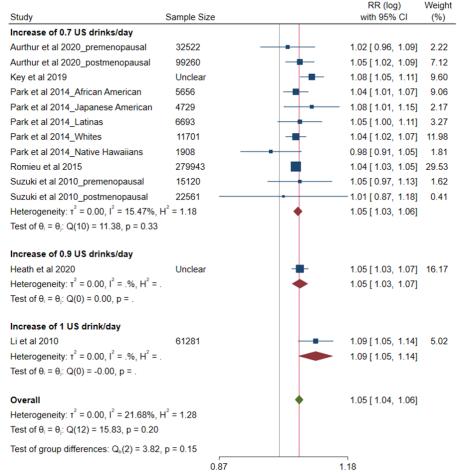
FIGURE 5-2 Associations between moderate alcohol consumption and breast cancer compared to never consuming alcohol

Oh. d.	0	LIO deimber/des		RR (log)	Weight
Study	Sample Size	US drinks/day		with 95% CI	(%)
Kawai et al 2011	14406	≥0.4 - <1.1		- 1.21 [ 0.71,  2.07]	2.11
Klatsky et al 2015	86531	<1	-	1.10 [ 1.00, 1.20]	73.28
Li et al 2010	Unclear	0.6-0.99		1.12 [ 0.92, 1.37]	15.09
White et al 2017	Unclear	<1	<del></del>	1.06 [ 0.82, 1.37]	9.52
Overall			•	1.10 [ 1.02, 1.19]	
Heterogeneity: τ <sup>2</sup> =	$0.00$ , $I^2 = 0.00\%$	$_{0}$ , $H^{2} = 1.00$			
Test of $\theta_i = \theta_j$ : Q(3)	= 0.23, p = 0.97				
Test of $\theta = 0$ : $z = 2$ .	42, p = 0.02			_	
			1	<sup>—</sup> 2	

Random-effects REML model

## **Breast Cancer** (Female)

FIGURE 5-3 Meta-analysis of relationship between increasing alcohol consumption by 10–14 grams (0.7-1.0 U.S. drinks/day) and breast cancer





## **Breast Cancer (Female)**

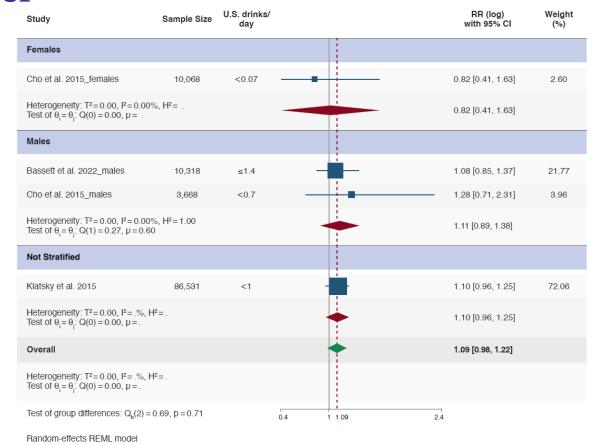
FIGURE 5-4 Meta-analysis on association between higher and lower moderate alcohol consumption and breast cancer

Study	Sample Size	U.S. drinks/ day (exposure)	U.S. drinks/ day (reference)		RR (log) with 95% Cl	Weight (%)
Key et al. 2019	Unclear	0.6–1.1	0.2-0.5		1.05 [1.02, 1.09]	66.49
Romieu et al. 2015	225,293	0.4-1.1	≤0.4		1.06 [1.01, 1.11]	33.51
Overall					1.05 [1.02, 1.08]	
Heterogeneity: $T^2 = 0.00$ , $I^2 = 0.00$ ,	= 0.75	1.00				
Random-effects REML mod	iel		1	1.05	1.2	



## **Colorectal Cancer**

FIGURE 5-5 Meta-analysis on associations between moderate alcohol consumption and colorectal cancer compared to never consuming alcohol





## **Cancer Conclusions**

**Conclusion 5-1**: The committee concludes that compared with never consuming alcohol, consuming a moderate amount of alcohol was associated with a higher risk of **breast cancer** (*moderate certainty*).

**Conclusion 5-2**: The committee concluded that among moderate alcohol consumers, higher versus lower amounts of moderate alcohol consumption were associated with a higher risk of **breast cancer** (*low certainty*).

**Conclusion 5-3**: The committee determined that no conclusion could be drawn regarding the association between moderate alcohol consumption compared with lifetime non-consumers and risk of **colorectal cancer**.

## **Research Gaps – Methodological Challenges**

- Exposure (alcohol) measurement
  - Standard drink sizes 14 grams is a "standard drink" in the U.S.
  - Alcoholic beverage type predominantly wine/predominantly beer/predominantly spirits
  - Drinking patterns number/timing/frequency/amount (e.g., 1 per day vs. 7 on a night)
  - Intake reporting self-reporting (often underreported) vs. biochemical markers (expensive for large-scale studies) vs. sales/taxation records
- Comparison groups
  - Inclusion of former drinkers in nondrinker groups (abstainer bias)

## **Research Gaps – Methodological Challenges**

- Analysis issues
  - Confounders & effect modifiers e.g., age, sex, genetic ancestry, SES, education, diet
  - Mediators avoidance of adjustment for mediators (may mask/lessen true effects)
- Causal inference study designs
  - Challenges with randomized trials costs, long duration, blinding, ethical issues
  - Mendelian randomization no known genes adequately capture differences in alcohol intake

## Research Gaps – Cancer-specific gaps

Outcome	Research Gaps (Future studies should )	
Cancer	Breast: Stratify by menopausal status	
	Colorectal: Include larger sample sizes for greater statistical power	
	<ul> <li>Other sites: Evaluate oral, pharyngeal, laryngeal, esophageal, liver, gastric, pancreas, prostate, urinary bladder, renal (kidney), and endometrial cancer</li> </ul>	