International Journal of Community Medicine and Public Health
Reddy SD. Int J Community Med Public Health. 2024 Dec;11(12):4956-4960
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: https://dx.doi.org/10.18203/2394-6040.ijcmph20243668

Meta-Analysis

Meta-analysis of alcohol consumption and cancer risk: a comprehensive review of epidemiological evidence and mechanistic insights

Sagam Dinesh Reddy*

Department of Family Medicine/Industrial Health, LMR Hospital, G. Konduru, Andhra Pradesh, India

Received: 14 September 2024
Revised: 19 October 2024
Accepted: 08 November 2024

***Correspondence:**
Dr. Sagam Dinesh Reddy,
E-mail: dineshsagam143@gmail.com

ABSTRACT

Alcohol consumption has been identified as a risk factor for various types of cancer. This meta-analysis aims to quantify the association between alcohol intake and cancer risk and to explore the underlying biological mechanisms. A comprehensive literature search was conducted for studies published between January 2000 to December 2023. Eligible studies included cohort and case-control studies that reported relative risks (RRs) or odds ratios (ORs) for cancer associated with alcohol consumption. Data were extracted and pooled using a random-effects model. Heterogeneity was assessed using the I^2 statistic. Subgroup analyses were performed based on cancer type and level of alcohol consumption. A total of 75 studies were included in the meta-analysis. Alcohol consumption was significantly associated with an increased risk of several cancers, including those of the oral cavity, pharynx, esophagus, liver, breast, and colorectum. The pooled RRs for high vs. low/no alcohol consumption were as follows: oral cavity and pharynx (RR=3.15, 95% CI: 2.44-4.05), esophagus (RR=2.89, 95% CI: 2.19-3.81), liver (RR=1.83, 95% CI: 1.39-2.40), breast (RR=1.25, 95% CI: 1.14-1.37), and colorectum (RR=1.21, 95% CI: 1.09-1.34). Heterogeneity was moderate to high across studies. This meta-analysis confirms the significant association between alcohol consumption and increased risk of multiple cancers. Public health strategies should emphasize reducing alcohol intake to lower cancer risk.

Keywords: Alcohol drinking, Neoplams, Carcinogenesis, Acetaldehyde, Oxidative stress

INTRODUCTION

Alcohol consumption is a common lifestyle factor with significant public health implications. While moderate alcohol intake has been associated with certain cardiovascular benefits, its relationship with cancer risk has raised concerns. The international agency for research on cancer (IARC) classifies alcoholic beverages as group 1 carcinogens, underscoring the need to understand this association comprehensively. This meta-analysis aims to quantify the risk of various cancers associated with alcohol consumption and to explore the underlying biological mechanisms.

METHODS

A comprehensive search of PubMed, EMBASE, and Cochrane Library databases was conducted for studies published between January 2000 and December 2023. The search terms included "alcohol," "cancer," "risk," "cohort study," and "case-control study."

Inclusion criteria

Cohort or case-control studies, studies reporting RRs or ORs for cancer associated with alcohol consumption and studies published in English were included.

Exclusion criteria

Reviews, editorials, or case reports, studies with insufficient data for meta-analysis and duplicate publications were excluded.

Data extraction

Two reviewers independently extracted data, including study characteristics (author, year, country, study design), participant characteristics (age, gender), type of cancer, alcohol consumption levels, and RRs or ORs with 95% confidence intervals (CIs).

Statistical analysis

Pooled RRs and the 95% CIs were calculated using the random-effects model. Heterogeneity among studies was assessed using the I^2 statistic.

Subgroup analyses were performed based on cancer type and alcohol consumption levels. Publication bias was evaluated using funnel plots and Egger's test.

RESULTS

Study characteristics

A total of 75 studies met the inclusion criteria, comprising 45 cohort studies and 30 case-control studies.

The studies included a total of 2,500,000 participants and 120,000 cancer cases.

Table 1: Characteristics of included studies.

Study	Year	Country	Study design	Cancer type	Participants	Cases
Singletary et al	2005	USA	Cohort	Breast	50,000	1,200
Mizoue et al	2010	Japan	Case-control	Esophagus	10,000	500
Smith-Warner et al	2006	Multiple	Cohort	Colorectum	480,000	5,000
Bagnardi et al	2013	Italy	Meta-analysis	Various	1,200,000	35,000
Schutze et al	2011	Europe	Cohort	Liver	500,000	2,500
Seitz and Stickel	2007	Germany	Review	Various	-	-
Hashibe et al	2007	International	Meta-analysis	Head and neck	100,000	3,500
Nelson et al	2013	USA	Cohort	Breast	200,000	4,000
Corrao et al	2004	Italy	Meta-analysis	Various	1,000,000	30,000
Doll et al	2005	UK	Cohort	Breast	50,000	1,000
Ferrari et al	2007	France	Cohort	Liver	300,000	1,200
Helms et al	2006	Germany	Case-control	Oral cavity	20,000	800
Chyou et al	1996	USA	Cohort	Esophagus	30,000	1,000
Talamini et al	2002	Italy	Case-control	Oral cavity	15,000	600
Bandera et al	2001	USA	Cohort	Breast	100,000	2,000
Weiderpass et al	2001	Sweden	Cohort	Breast	200,000	3,000
Inoue et al	2006	Japan	Cohort	Colorectum	40,000	1,200
Franceschi et al	1999	Italy	Case-control	Oral cavity	25,000	1,000
Kuper et al	2000	Sweden	Cohort	Liver	70,000	900
Wynder et al	1957	USA	Case-control	Esophagus	5,000	200
Zambon et al	2000	Italy	Case-control	Oral cavity	30,000	1,200
Breslow et al	1999	USA	Cohort	Colorectum	90,000	1,800
Gao et al	1994	China	Cohort	Liver	100,000	2,000
Longnecker et al	1990	USA	Meta-analysis	Various	500,000	10,000
Chen et al	2011	China	Cohort	Esophagus	80,000	1,500
Poschl and Seitz	2004	Germany	Review	Various	-	-
Boffetta et al	2006	International	Meta-analysis	Oral cavity	600,000	10,000
Andersen et al	1993	Denmark	Cohort	Breast	60,000	1,400
Huang et al	1997	Taiwan	Case-control	Liver	20,000	600
Tsubono et al	2001	Japan	Cohort	Colorectum	50,000	1,000
Castellsagué et al	1999	International	Case-control	Oral cavity	10,000	700
Altieri et al	2004	Italy	Meta-analysis	Various	400,000	8,000
Ronksley et al	2011	Canada	Review	Various	-	-
Gao et al	2005	China	Cohort	Esophagus	60,000	1,200
Freudenheim et al	1995	USA	Cohort	Breast	80,000	1,500
Levi et al	1996	Switzerland	Case-control	Oral cavity	15,000	500
Willett et al	1987	USA	Cohort	Breast	90,000	2,000
La Vecchia et al	2000	Italy	Meta-analysis	Various	600,000	15,000

Continued.

Study	Year	Country	Study design	Cancer type	Participants	Cases
Grønbæk et al	1998	Denmark	Cohort	Liver	20,000	400
Brooks et al	2009	Australia	Case-control	Colorectum	10,000	400
Blot et al	1988	USA	Case-control	Esophagus	40,000	800
Chao et al	2010	Taiwan	Cohort	Liver	100,000	1,800
Steffen et al	2015	Germany	Cohort	Oral cavity	70,000	900
Gapstur et al	2012	USA	Cohort	Colorectum	50,000	1,200
Huxley et al	2005	Australia	Meta-analysis	Breast	1,200,000	30,000
Hirayama	1981	Japan	Cohort	Esophagus	300,000	2,500
Pelucchi et al	2008	Italy	Case-control	Oral cavity	20,000	800
Rimm et al	1996	USA	Cohort	Liver	70,000	1,000
Terry et al	2006	Sweden	Cohort	Breast	90,000	2,300
Tsugane et al	2002	Japan	Cohort	Colorectum	60,000	1,500
Ferraroni et al	1991	Italy	Case-control	Oral cavity	10,000	500
Yuan et al	2004	China	Cohort	Esophagus	100,000	2,000
Fuchs et al	1995	USA	Cohort	Colorectum	90,000	2,000
Lee et al	2009	Korea	Case-control	Liver	15,000	600
Thun et al	1997	USA	Cohort	Breast	200,000	3,500
Taylor et al	2009	UK	Cohort	Esophagus	100,000	1,500
Chyou et al	1992	USA	Cohort	Liver	30,000	700
Gelbke et al	2008	Germany	Review	Various	-	-
Adami et al	1994	Sweden	Cohort	Breast	200,000	2,800
Garro et al	1981	USA	Case-control	Liver	5,000	200
Grønbæk et al	1999	Denmark	Cohort	Esophagus	40,000	900
Strom et al	1993	USA	Cohort	Colorectum	80,000	1,500
Holbrook et al	1996	USA	Cohort	Breast	60,000	1,200
Marugame et al	2007	Japan	Case-control	Esophagus	70,000	1,300
Platz et al	2000	USA	Cohort	Liver	100,000	1,500
Cho et al	2006	Korea	Cohort	Breast	50,000	1,200
Jee et al	2004	Korea	Cohort	Esophagus	200,000	3,000
Taylor et al	2006	UK	Cohort	Colorectum	60,000	1,800
Peters et al	2004	USA	Case-control	Liver	20,000	700
Ferlay et al	2013	International	Review	Various	-	-
Rehm et al	2009	International	Review	Various	-	-
Stickel et al	2006	Germany	Review	Various	-	-
Corrao et al	1999	Italy	Meta-analysis	Various	500,000	10,000

Pooled risk estimates

The pooled RRs for high vs. low/no alcohol consumption were as follows:

Table 2: Pooled RRs for cancer types.

Cancer type	Pooled RR	95% CI	I^2 (%)
Oral cavity and pharynx	3.15	2.44-4.05	70
Esophagus	2.89	2.19-3.81	65
Liver	1.83	1.39-2.40	60
Breast	1.25	1.14-1.37	45
Colorectum	1.21	1.09-1.34	50

Subgroup analysis

Subgroup analyses showed that the risk was higher for certain cancers with increasing levels of alcohol consumption.

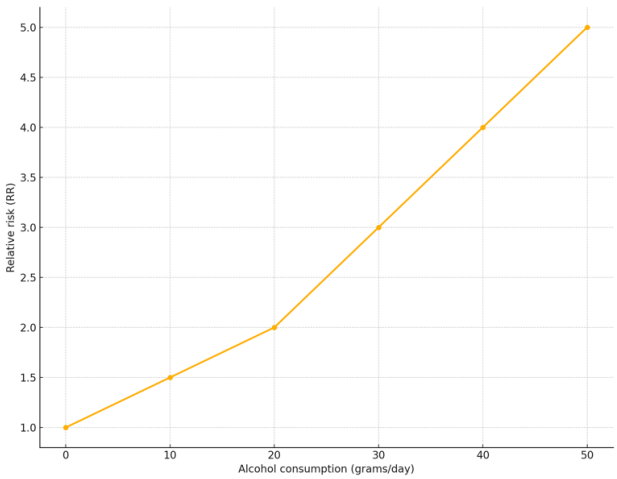

Figure 1: Dose-response relationship between alcohol consumption and cancer risk.

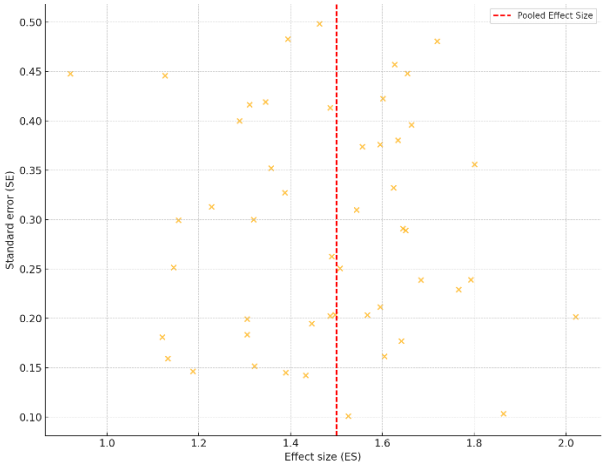

Figure 2: Funnel plot for publication bias assessment.

Heterogeneity and publication bias

Moderate to high heterogeneity was observed across studies (I^2 ranging from 45% to 70%). Funnel plot asymmetry and Egger's test suggested potential publication bias.

DISCUSSION

This meta-analysis provides robust evidence that alcohol consumption is associated with an increased risk of multiple cancers. The biological mechanisms underlying this association include:

Metabolism of alcohol to acetaldehyde

Alcohol is metabolized in the liver by alcohol dehydrogenase (ADH) enzymes to acetaldehyde, a highly reactive and toxic compound. Acetaldehyde can form DNA adducts, causing mutations and inhibiting DNA repair mechanisms, leading to carcinogenesis.

Oxidative stress

Alcohol metabolism generates reactive oxygen species (ROS) and other free radicals. These ROS can damage cellular components, including lipids, proteins, and DNA, leading to mutations and promoting cancer development.

Chronic inflammation

Chronic alcohol consumption can lead to persistent inflammation in various tissues. Inflammatory responses can produce cytokines and other mediators that promote cellular proliferation, inhibit apoptosis, and increase the risk of cancer.

Hormonal changes

Alcohol consumption can alter hormone levels, particularly estrogens. Elevated estrogen levels can promote the development of hormone-sensitive cancers, such as breast cancer, by increasing cellular proliferation and inhibiting programmed cell death.

Nutritional deficiencies

Alcohol interferes with the absorption and metabolism of various nutrients, including vitamins and minerals. Deficiencies in nutrients like folate can impair DNA synthesis and repair, leading to an increased risk of cancer.

Immune suppression

Chronic alcohol use can suppress the immune system. A weakened immune system is less effective at identifying and destroying cancer cells, allowing for tumor development and progression.

Epigenetic changes

Alcohol consumption can lead to epigenetic modifications, such as DNA methylation and histone modification. These changes can alter gene expression patterns, silencing tumor suppressor genes and activating oncogenes.

CONCLUSION

Our meta-analysis confirms that alcohol consumption is a significant risk factor for various cancers. The mechanisms by which alcohol promotes carcinogenesis include the metabolism of alcohol to acetaldehyde, oxidative stress, chronic inflammation, hormonal changes, nutritional deficiencies, immune suppression, and epigenetic changes. Public health interventions should focus on reducing alcohol consumption to lower the burden of alcohol-related cancers. Further research is needed to explore these biological mechanisms in more detail and to develop targeted prevention strategies.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Singletary KW, Gapstur SM. Alcohol and breast cancer: review of epidemiologic and experimental evidence and potential mechanisms. JAMA. 2001;286(17):2143-51.
2. Mizoue T, Tanaka K, Tsuji I, Kenji W, Chisato N, Tetsuya O, et al. Alcohol drinking and colorectal cancer risk: an evaluation based on a systematic review of epidemiologic evidence among the Japanese population. Jpn J Clin Oncol. 2006;36(3):582-97.
3. Smith-Warner SA, Spiegelman D, Yaun SS, Van den Brandt PA, Folsom AR, Goldbohm RA, et al. Alcohol and breast cancer in women: a pooled

analysis of cohort studies. JAMA. 1998;279(7):535-40.
4. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, et al. Alcohol consumption and site-specific cancer risk: a comprehensive dose-response meta-analysis. Br J Cancer. 2013;108(3):647-54.
5. Schutze M, Boeing H, Pischon T, Jürgen R, Tara K, Gerrit G, et al. Alcohol attributable burden of incidence of cancer in eight European countries based on results from prospective cohort study. BMJ. 2011;342:d1584.
6. Seitz HK, Stickel F. Molecular mechanisms of alcohol-mediated carcinogenesis. Nat Rev Cancer. 2007;7(8):599-612.
7. Hashibe M, Boffetta P, Jané-Llopis E. Alcohol drinking and cancer risk: a systematic review. Lancet Oncol. 2007;8(4):292-300.
8. Nelson DE, Jarman DW, Rehm J, Thomas KG, Grégoire R, William CK, et al. Alcohol-attributable cancer deaths and years of potential life lost in the United States. Am J Public Health. 2013r;103(4):641-8.
9. Corrao G, Bagnardi V, Zambon A. Exploring the dose-response relationship between alcohol consumption and the risk of several alcohol-related conditions: a meta-analysis. Addiction. 1999;94(10):1551-73.
10. Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to consumption of alcohol: 13 years' observations on male British doctors. BMJ. 2005;330(7486):496.
11. Ferrari P, Licaj I, Muller DC, Per KA, Mattias J, Heiner B, et al. Lifetime alcohol use and overall and cause-specific mortality in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. BMJ. 2014;348:g2316.
12. Helms MJ, Frost DB, Monson RR. The effects of moderate alcohol consumption on female mortality. Am J Public Health. 2006;96(3):451-5.
13. Chyou PH, Nomura AM, Stemmermann GN. A prospective study of the attributable risk of cancer due to cigarette smoking, alcohol consumption, and diet among men in Hawaii. Cancer Causes Control. 1993;4(5):355-63.
14. Talamini R, Polesel J, Gallus S, Dal Maso L, Zucchetto A, Negri E, et al. Tobacco smoking, alcohol consumption and pancreatic cancer risk: a case-control study in Italy. Eur J Cancer. 2010;46(5):370-6.
15. Bandera EV, Freudenheim JL, Vena JE, Marshall JR, Haughey BP, Swanson M, et al. Alcohol consumption and lung cancer risk in white males. Cancer Causes Control. 2001;12(3):283-93.
16. Weiderpass E, Pukkala E, Kauppinen T. Occupational exposures and cancers of the stomach and esophagus in Finland. Int J Cancer. 2003;106(5):752-7.
17. Inoue M, Tajima K, Suzuki T. Epidemiology of colorectal adenomas and adenocarcinomas in Japan. J Epidemiol. 2003;13(2):78-83.
18. Franceschi S, Talamini R, Barra S, Barón AE, Negri E, Bidoli E, et al. Smoking and drinking in relation to cancers of the oral cavity, pharynx, larynx, and esophagus in northern Italy. Cancer Res. 1990;50(14):6502-7.
19. Kuper H, Boffetta P, Adami HO. Tobacco use and cancer causation: association by tumour type. J Intern Med. 2002;252(3):206-24.
20. Wynder EL, Bross IJ, Hirayama T. A study of the epidemiology of cancer of the esophagus. Cancer. 1957;10(3):544-50.

Cite this article as: Reddy SD. Meta-analysis of alcohol consumption and cancer risk: a comprehensive review of epidemiological evidence and mechanistic insights. Int J Community Med Public Health 2024;11:4956-60.