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Association between Alcohol Consumption and Gastric Cancer: A Meta-Analysis

**Mahjub H. Ph.D, **Sadri Gh.H. Ph.D*

**Dept. of Biostatistics & Epidemiology, Hamadan University of Medical Sciences, Iran*
***Dept. of Biostatistics & Epidemiology, Hamadan University of Medical Sciences, Iran*

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Abstract

Background: Gastric cancer is the second most common cause of death from cancer. As conflicting studies have recently been published, we aimed to evaluate the magnitude of the epidemiological evidence for an association between alcohol consumption and gastric cancer.

Methods: This study is a meta-analysis of case-control studies which have been performed during 1989 to 2007. We systematically reviewed the literature on the association between alcohol consumption and gastric cancer. Published case-control studies were identified in Pub Med and reference lists. Random effects meta-analysis was used to pool effects from twenty studies.

Results: The odds ratio (OR) for the overall association between alcohol and gastric cancer was 1.77 (95%CI: 1.46-2.15). The pooled OR for alcohol consumption related to gastric cancer for men was 2.17 (95%CI: 1.67-2.83). The odds ratio of beer or liquor was 1.16 which is not statistically related to gastric cancer risk ($P> 0.05$). Whereas, the odds ratio of vodka, wine and other types of alcohol intake related to gastric cancer were respectively 3.26, 1.69, and 1.77 ($P< 0.01$).

Conclusion: Overall, based on the results of pooled analysis, it is reassuring that this meta-analysis shows a direct effect of alcohol associated with gastric cancer. Knowledge on the level of exposure to different alcohol constituents provides a deeper understanding of the real role of alcohol on cancer risk and ultimately allows the design of safer beverages.

Keywords: *Alcohol, Case-control, Gastric cancer, Meta-analysis*

Introduction

In the past decades gastric cancer was the most commonly diagnosed cancer worldwide, but falls in incidence in the West. After then stomach cancer was the fourth most common cancer worldwide, accounting for approximately 876 000 new cases or 9% of the global cancer burden. In addition, gastric cancer is the second most common cause of death from cancer accounting 10% of all deaths from cancer (1-6).

Epidemiological studies have indicated that while the exact cause for stomach cancer has not been identified, having poor nutritional habits, eating a lot of cured, pickled or smoked foods, eating foods high in starch and low in fiber, smoking, drinking alcohol, and vitamin A deficiency are believed to be risk factors for gastric cancer (7-9). The risk of cancer rises with increasing level of consumption of alcoholic beverages (10, 11). Alcohol consumption, particularly vodka consumption, was found to increase the risk of gastric cancer (12).

Some authors have concluded an inverse association with wine consumption and these authors suggested that it was antioxidants and/or phytoestrogens in wine, rather than the alcohol itself causing a protective effect (13-15).

Previous studies have provided conflicting information on the role of alcohol in gastric carcinogenesis. The association between alcohol

Corresponding author: Dr H Mahjub, Fax: +98 811 825 5301, E-mail:mahjub@umsha.ac.ir

consumption and risk of gastric cancer remains controversial (16, 17).

Given the results from the previous studies, the aims of this study were: 1) to evaluate the epidemiological evidence for an association between alcohol consumption and gastric cancer; and 2) how much is the magnitude of alcohol consumption related to gastric cancer risk?

Material and Methods

The search strategy involved the electronic databases of PubMed. We used PubMed to identify studies published from 1989 to 2007, under the searching expression "(stomach cancer OR gastric cancer) in the title AND "(alcohol AND (case-control OR case-referent))" in the abstract. The reference lists provided by the identified papers was additionally hand-searched. Additional manual searches were made using the reference lists from the selected articles to retrieve other papers relevant to the topic. If results of the same studies were presented more than once, the most recent publication was used, because of the possible impact of duplicate publication (18). We evaluated papers published in English.

Primary inclusion criteria for the selection of all relevant articles were: 1) the exposure variable must be alcohol consumption; 2) the disease of interest must be gastric cancer or gastric carcinoma; and 3) studies must be case-control study and published after 1989.

Secondary inclusion criteria were developed to identify studies with a case-control design, which were: 1) there were two defined groups of subjects; 2) cases had to be identified as having gastric carcinoma; 3) controls must be free of gastric carcinoma; and 4) statistical results should be in the form of an odds ratio.

We classified the alcohol consumption as follows: wine and red wine as "wine"; bear, liquor and hard liquor as "bear or liquor"; vodka as "vodka"; other types of alcohol as "other types". Also, based on what was in the original papers, we considered the gender of exposed persons as men vs. men & women.

Over the period of eighteen years, 157 articles were found which twelve articles were relevant to the defined criteria (12, 19-29).

Two reviewers extracted information from each study following a previously defined data collection procedure. Discrepancies in the evaluation of the articles were resolved by consensus. The protocol for data extraction covered: study design (case-control, population-based or hospital-based and number of subjects); and risk estimates for the association between alcohol consumption and gastric cancer, considering exposure levels; precision estimates (confidence intervals, *P* values, and number of participants in each exposure category); control of confounding factors; and country of origin. When a study provided more than one estimate, we selected the one adjusted for the largest set of variables.

We performed a meta-analysis of case-control evaluating the association between alcohol consumption and gastric cancer. The analysis sought to identify the combined odds ratio (OR) of alcohol consumption on gastric cancer. Combined estimate of the odds ratio for alcohol consumption on gastric cancer was performed. Random effects estimates are reported rather than fixed effects because of marked inter-study variation. Cochran's Q test was used for evaluating effect equality. This tests the null hypothesis that all effects are equal or homogeneous versus the alternative that at least one effect had a different effect or heterogeneous. Also, this test is used to choose between the use of a fixed effect model and a random effects model.

Combined risk estimates and 95% confidence intervals were computed using the random effects method, and statistical tests for homogeneity were performed. Heterogeneity was investigated by subgroup analysis, looking at the magnitude of the combined risk estimates in each stratum as well as to the respective tests of heterogeneity. The software NCSS

and PASS 2000 Released December 2005 was used for analysis.

Results

This meta-analysis consists of 5452 subjects with gastric cancer as the case group and 8463 subjects as the control group. Table 1 shows the characteristic of case-control studies of alcohol consumption on gastric cancer from published studies.

Table 2 shows the odds ratio and effect equality test for gastric cancer risk based on gender of alcohol consumers. Although, the odds ratio for the "males" is higher than the "males & females" but there is not any significant difference between the two groups (P= 0.21). The Table shows the combined odds ratio for alcohol consumption related to gastric cancer is 1.77 (95%CI, 1.46-2.15). Moreover, the Table shows the results of the effect equality test. This test shows that using random effect model is appropriate.

Table 3 shows odds ratio and effect equality test for different type of alcohol related to gastric cancer. This Table shows that different types of alcohol are statistically related to gastric cancer except beer or liquor. As the Table shows, the odds ratio of beer or liquor is not related to gastric cancer risk statistically significance (P> 0.05). Whereas, the odds ratio of vodka, wine and other types of alcohol intake related to gastric cancer were respectively 3.26, 1.69, and 1.77 (P< 0.01).

Fig. 1 and 2 show the forest plot of odds ratio for the selected reports based on sex and alcohol type, respectively.

Table 1: Characteristic of case-control studies of alcohol consumption on gastric cancer from published studies

Study	Country	Sex	OR (95% CI)	Type of alcohol	Study characteristics	Amount of consumption	Confounding Variables considered
Agudo A, 1992	Spain	M	1.54 (1.03-2.31)	Alcohol intake	Case-control Hospital based	Usual consumption	Sex, Age, Area of residence
Zaridze D, 2000	Russia	M	3.4 (1.2-10.2)	Vodka	Case-control Hospital based	Usual consumption	Age, Sex, area of residence, Smoking
Chen M, 2000	Taiwan	M/F	1.5 (0.9-3.2)	Alcoholic beverage	Case-control Hospital based	3 to 4 per week	Sex, Age, Socio-economic Status, Smoking
D'Avanzo B, 1994	Italy	M/F	1.6 (1.1-2.4)	Wine	Case-control Hospital based	6 drink per week	Sex, Age, Smoking
Falcao J, 1994	Portugal	M/F	2.61 (1.04-6.37)	Red Wine	Case-control Hospital based	One bottle per day for more than 20 years	Smoking, Socio-economic, Education
Jedrychowski W, 1993	Poland	M	3.06 (1.9-4.95)	Vodka	Case-control Hospital based	Those drunk at least once a weak	Socio-demographic, Dietary, Smoking cigarette
Jedrychowski W, 1993	Poland	M	2.98 (1.6-5.53)	Vodka	Case-control Hospital based	Those drunk before breakfast	Socio-demographic, Dietary, Smoking cigarette
Jedrychowski W, 1992	Poland	M/F	4.45 (2.26-8.75)	Vodka	Case-control Hospital based	At least once a week	Sex, Age, Smoking
Jedrychowski W, 1992	Poland	M/F	3.28 (1.33-8.13)	Vodka	Case-control Hospital based	Those drink vodka on an empty stomach	Sex, Age, Smoking
Ji B, 1998	China	M	1.55 (1.07-2.26)	Alcohol intake	Case-control Population based	Heavy alcohol drinking	Smoking

Table 1 : Continued...

Kabat G, 1993	USA	M	2.3 (1.3-4.3)	Whiskey	Case-control Hospital based	Four or more ounces of whiskey	Smoking
Vaughan T, 1995	USA	M/F	1.1 (0.7-1.8)	Alcohol intake	Case-control Population based	7 to 13 alcohol drink per week	Cigarette use, BMI, Age, Gender, Race, Education
Vaughan T, 1995	USA	M/F	1.2 (0.6-2.3)	Alcohol intake	Case-control Population based	14 to 20 alcohol drink per week	Cigarette use, BMI, Age, Gender, Race, Education
Vaughan T, 1995	USA	M/F	1.8 (1.1-3.1)	Alcohol intake	Case-control Population based	more than 21alcohol drink per week	Cigarette use, BMI, Age, Gender, Race, Education
Gammon M, 1997	USA	M/F	0.7 (0.5-1.1)	Beer or liquor	Case-control Population based	more than five alcohol drink per week	Cigarette use, Age, Sex, Race, BMI, Region
Gammon M, 1997	USA	M/F	0.6 (0.4-1.0)	Beer or liquor	Case-control Population based	less than 5 drink per week	Cigarette use, Age, Sex, Race, BMI, Region
Gammon M, 1997	USA	M/F	0.8 (0.5-1.3)	Beer or liquor	Case-control Population based	5 to 11 drink per week	Cigarette use, Age, Sex, Race, BMI, Region
Gammon M, 1997	USA	M/F	0.7 (0.4-1.1)	Beer or liquor	Case-control Population based	12 to 30 drink per week	Cigarette use, Age, Sex, Race, BMI, Region
Gammon M, 1997	USA	M/F	0.7 (0.4-1.2)	Beer or liquor	Case-control Population based	more than 30 drink per week	Cigarette use, Age, Sex, Race, BMI, Region
De Stefani E, 1998	Uruguay	M	2.4 (1.5-3.9)	Beer and hard liquor	Case-control Hospital based	Usual consumption	smoking, Age, Sex, Region other types of alcohol beverages

Table 2: Odds ratio and effect equality test for gastric cancer risk based on sex of alcohol consumers

Sex	**OR and 95% CI**			**Effect Equality Test**		
	OR	**Lower**	**Upper**	**Cochran's Q**	**df**	***P*-value**
Male	2.18	1.678	2.84	13.38	6	0.037
Male & Female	1.58	1.23	2.02	43.01	12	<0.001
Combined	1.77	1.46	2.15	65.91	19	<0.001

Table 3: Odds ratio and effect equality test for different types of alcohol related to gastric cancer

Alcohol type	**OR and 95% CI**			**Effect Equality Test**		
	OR	**Lower**	**Upper**	**Cochran's Q**	**df**	***P*-value**
Beer or Liquor	1.16	0.89	1.53	12.21	5	0.032
Vodka	3.267	2.50	4.25	0.92	4	0.922
Wine	1.69	1.16	2.46	1.04	1	0.308
Other types	1.77	1.47	2.12	8.34	6	0.214
Combined	1.77	1.46	2.15	65.91	19	<0.001

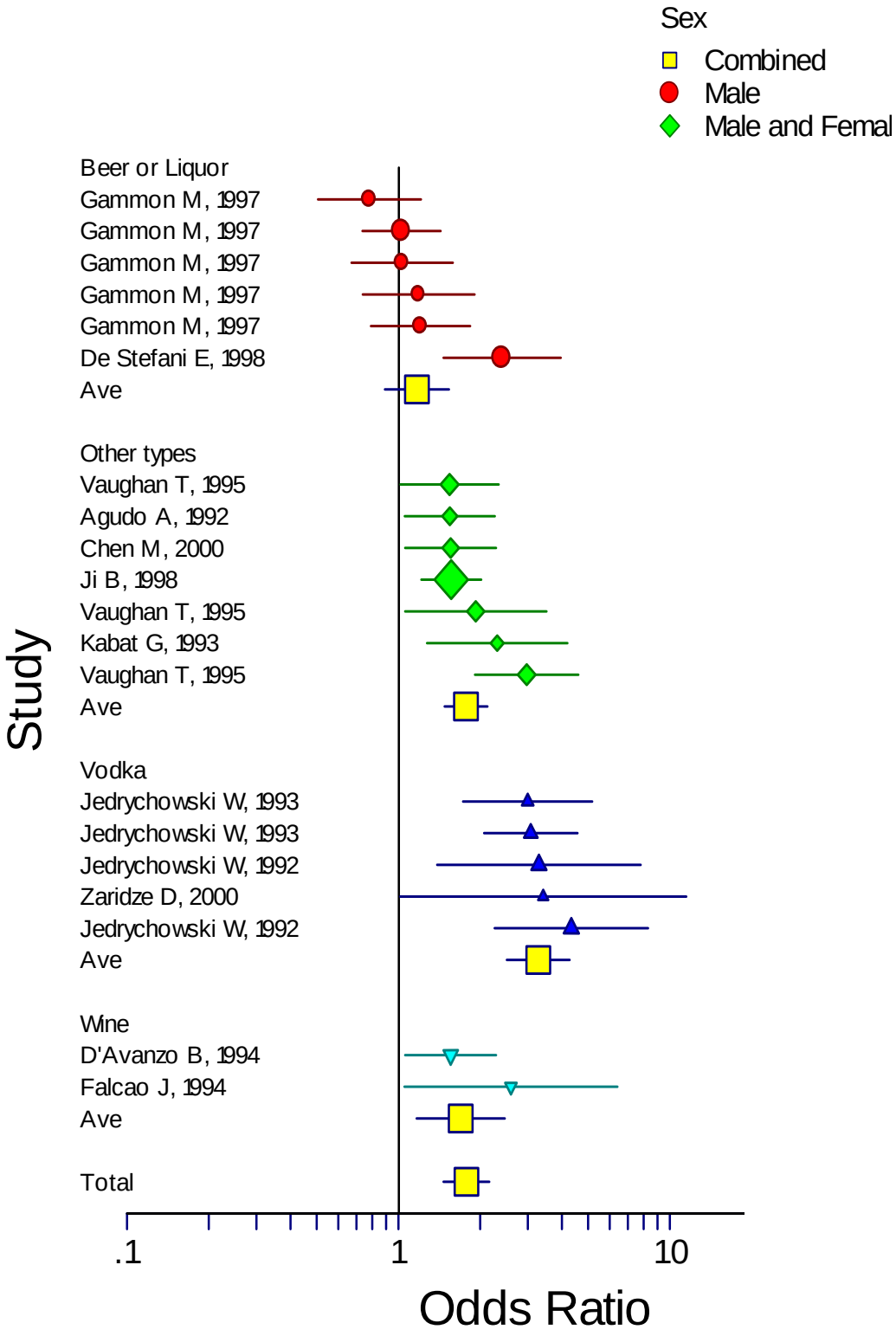

Fig. 1: Forest plot of odds ratio for alcohol consumption related to gastric cancer based on sex

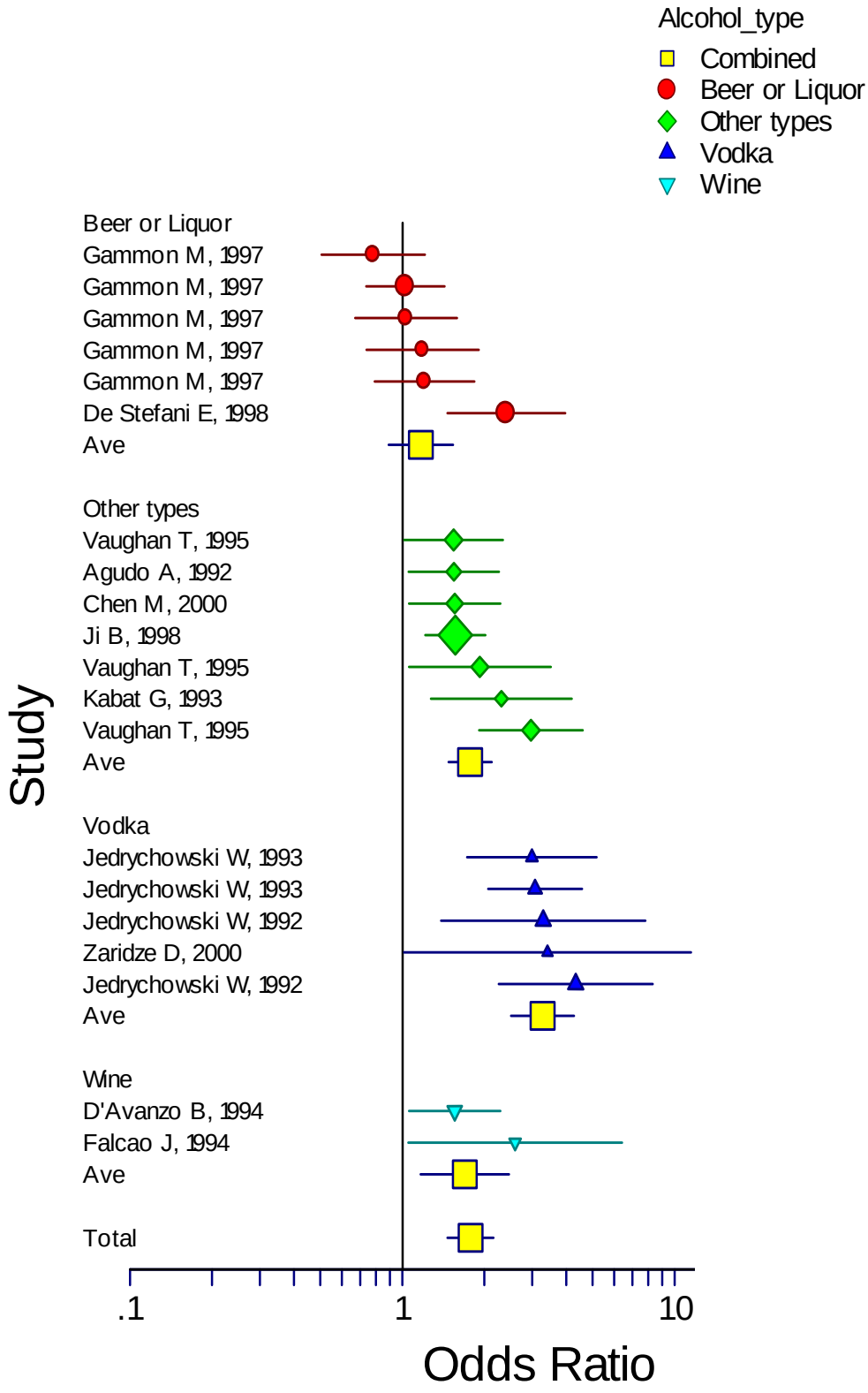

Fig. 2: Forest plot of odds ratio for alcohol consumption related to gastric cancer based on alcohol type

Discussion

This meta-analysis of studies published during the last two decades showed an overall effect of alcohol consumption on gastric cancer risk.

Meta-analysis is a statistical analysis that combines or integrates the results of several studies to provide increased power for the combined studies (30). Numerous case-control studies were launched to assess the risks for different types of cancer (31-33).

The present study provides detailed estimates of the risk of gastric cancer for different type of alcohol beverage after adjusting for major confounders of the disease including sex, age, area of residence, smoking, BMI, dietary and socio-economic status. The results are consistent with the existence of an alcohol effect on the risk of gastric cancer, contributed mainly by consumption of wine, vodka, hard liquor and beer. The study suggests a moderate difference in the risk of gastric cancer with different type of alcoholic beverage.

Several case-control studies showed an increase in gastric cancer risk among alcohol consumers, with odds ratio ranging from 1.54 to 4.45 (12, 19, 21-23, 25, 26, 28, 29, 34). On the other hand, at least two other studies have failed to show association between gastric cancer and alcohol consumption (20, 27). A number of studies have reported a higher risk for vodka consumption, compared with other types of alcohol (12, 23, 24).

In this meta-analysis, we observed substantial methodological differences between studies that have potential effect on the risk estimates. In this analysis, several sources of heterogeneity are likely, even if most risk estimates from individual reports were not significantly different as assessed by statistical tests. In case-control studies, alcohol consumption among controls may not represent the target population, and bias is even more probable with hospital controls. However, considering the results from hospital and population-based studies, this appears unlikely.

The classification of exposure differs considerably across the reviewed studies, and the results were shown to be significantly different according to the type of consumption. In this meta-analysis, we opted for individual risk estimates based on exposure categories with different type of alcohol.

Alcohol consumption tends to be associated with tobacco smoking (12), but we account this potential confounding in the data analysis. Moreover, other factors may be influencing the estimates for the association between alcohol and gastric cancer, since non-alcohol drinkers may differ from the general population of alcohol drinkers, concerning other exposures such as tea, coffee, or fruit and vegetable intake (35, 36). The studies included in our review rarely considered confounding or interaction from these variables.

Since, the classification of exposure based on women's gender on the selected studies rarely have been performed, we could not combined the risk ratio for women, separately. So, we classified the gender in two groups of "men" and "men and women". In this case, our study presents no different risk estimates across strata of gender.

Alcohol is one dietary factor where there is "conflict" between risks and benefits for different diseases. It is worth mentioning that the content of non-ethanol compounds varies among the different types of alcoholic beverages as well as among countries, and these facts could partly explain the differences observed in the studies published so far. On the other hand, a limitation of our study was the inability to distinguish among different kinds of alcohol in details.

Light to moderate alcohol consumption has been associated with an increase of up to 33 percent in the risk of gastric cancer (16). The study noted that previous research on the association between gastric cancer and alcohol consumption yielded "inconsistent results," with some studies finding a link between alcohol and gastric cancer and others not; the authors

felt that their further research was necessary because alcohol is consumed in many forms worldwide and stomach cancer is the second most common form of cancer deaths globally. The results of our study point to the need for carrying out further research on the issue of alcohol consumption and the incidence of gastric cancer, even among populations with moderate to low levels of exposure.

We observed differences in risk estimates according to the geographical origin of the study. The underlying risk of gastric cancer in each population, international differences in the typical amount of alcohol consumed, alcohol type, may contribute to these differences.

Since alcohol drinking carries a strong social stigma in many populations, it is likely that individuals underestimate and under-report their intake of alcohol, particularly in the case of heavy consumption. This could result in an underestimation of the actual carcinogenic effect of the habit and therefore alcohol is possibly a stronger risk factor than perceived. The complexity of alcohol composition and the multiple social contexts underlying consumption make the evaluation of the effect of alcohol on gastric cancer very difficult. Human experimental studies on such associations are unlikely, making observational studies the best available source of evidence on risk.

Overall, it is reassuring that this meta-analysis showed a direct effect of alcohol associated with gastric cancer. Knowledge on the level of exposure to different alcohol constituents provide a deeper understanding of the real role of alcohol on cancer risk and ultimately allow the design of safer beverages.

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