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Alcohol intake and gastric cancer: Meta-analyses of published data versus individual participant data pooled analyses (StoP Project)

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ABSTRACT

Background: Individual participant data pooled analyses allow access to non-published data and statistical re-analyses based on more homogeneous criteria than meta-analyses based on systematic reviews. We quantified the impact of publication-related biases and heterogeneity in data analysis and presentation in summary estimates of the association between alcohol drinking and gastric cancer.

Methods: We compared estimates obtained from conventional meta-analyses, using only data available in published reports from studies that take part in the Stomach Cancer Pooling (StoP) Project, with individual participant data pooled analyses including the same studies.

Results: A total of 22 studies from the StoP Project assessed the relation between alcohol intake and gastric cancer, 19 had specific data for levels of consumption and 18 according to cancer location; published reports addressing these associations were available from 18, 5 and 5 studies, respectively. The summary odds ratios [OR, (95%CI)] estimate obtained with published data for drinkers vs. non-drinkers was 10% higher than the one obtained with individual StoP data [18 vs. 22 studies: 1.21 (1.07–1.36) vs. 1.10 (0.99–1.23)] and more heterogeneous (I^2: 63.6% vs 54.4%). In general, published data yielded less precise summary estimates (standard errors up to 2.6 times higher). Funnel plot analysis suggested publication bias.

Conclusion: Meta-analyses of the association between alcohol drinking and gastric cancer tended to overestimate the magnitude of the effects, possibly due to publication bias. Additionally, individual participant data pooled analyses yielded more precise estimates for different levels of exposure or cancer subtypes.

1. Introduction

Systematic reviews have the potential to settle controversies arising from apparently conflicting findings and to answer questions not directly addressed by single studies, as well as to enhance the precision of effect measures [1–4]. Individual participant data pooled analyses are considered more capable of overcoming some of the limitations of systematic reviews and meta-analyses of published data [5], since they allow access to data not previously published and statistical reanalysis based on more homogeneous criteria [3]. However, individual participant data pooled analyses require much more complex and costly management of data, as well as coordination of the underlying consortium of research groups, and the gains in terms of precision and validity of the results may be expected to vary with the topic being addressed. Comparisons of individual participant data pooled analyses with meta-analyses based on the published data from the same studies contribute to understand the extent to which conventional meta-analyses may be biased or lack statistical power, and different results may be expected for distinct research questions.

The World Cancer Research Fund reported evidence of a probable association between alcohol drinking and gastric cancer in April 2016. There were no individual participant pooled analyses for this exposure in that update [6]. The Stomach Cancer Pooling (StoP) Project [7] has recently published a pooled analysis assessing the association between alcohol intake and gastric cancer, based on information from more than 10,000 cases and 26,000 controls evaluated in 20 studies conducted in 10 countries. Heavy drinkers, defined as those drinking more than six drinks per day, had a significant excess risk of gastric cancer of approximately 50%, compared to never drinkers [8]. That study includes results from studies that never addressed this topic before and was based on more homogeneous methodological approaches, namely regarding the definition of alcohol intake and control of confounding. Therefore, it adds to previous evidence supporting a potential role of alcohol as a probable risk factor for gastric cancer [9–14], specifically for three or more drinks per day [6].

In the present study, we provide quantitative estimates of the impact of publication biases and heterogeneity in data analysis and presentation, in the summary estimates of the association between alcohol drinking and gastric cancer obtained from conventional meta-analyses. We used data available in previously published reports from studies that take part in the Stomach Cancer Pooling (StoP) Project, for comparison with individual participant data pooled analyses including the same studies.

2. Methods

2.1. Individual participant data meta-analysis

The StoP Project is a consortium of case-control studies (including nested case-control within cohort studies), including at least 80 incident, histologically confirmed, gastric cancer cases [7]. The StoP Project received ethical approval from the University of Milan Review Board.

The first release of the StoP Project dataset included 23 case-control studies, comprising 10,290 cases (6,804 men, 3,486 women) and 26,145 controls (15,600 men, 10,545 women) from Greece [15], Italy (four studies) [16–19], Portugal [20], Russia [21], Spain (two studies) [22,23], Sweden (three studies, two of which were nested in cohort studies) [24,25], China (four studies) [26–29], Iran (three studies) [30–32], Japan [33], Canada [34] and the United States of America (USA) (two studies, one of them unpublished) [35].

The association between alcohol drinking and gastric cancer was estimated through a two-stage modeling approach [8]. Briefly, in the first stage, the association between alcohol drinking and gastric cancer for each study was assessed through multivariable logistic regression models that included, whenever available, terms for age, sex, education/social class, smoking, fruit and vegetable consumption, study center (for multicenter studies), as well as terms for the matching variables, when applicable. In the second stage, the pooled effects estimates were computed using a random-effect models, through the DerSimonian and Laird method [36]. This was performed for the comparison of the following levels of exposure: 1) drinkers vs. non-drinkers; 2) drinkers of less than one drink per day vs. non-drinkers; 3) drinkers of one to four drinks per day vs. non-drinkers; 4) drinkers of over four drinks per day vs. non-drinkers. Heterogeneity was quantified using the I^2 statistic [37].

2.2. Meta-analysis of published data

2.2.1. Search strategy

The strategy to identify all published reports from the 23 studies included in the first version of the StoP Project database is depicted in Supplementary Fig. 1.

We searched PubMed, from inception to December 31, 2016, and conducted forward citation tracking of the reference provided in the StoP Project presentation paper to identify papers based on the same dataset, through Google Scholar and Web of Science™. The responsible investigators for each study were then asked to confirm if all published reports of results from their study had been included, and no additional