Alcohol Exposure and Esophageal Cancer Risk in ALDH2*2 Carriers: A Systematic Review

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INTRODUCTION

Esophageal cancer remains a significant global health challenge, with high mortality rates. Particularly, the aldehyde dehydrogenase-2 (ALDH2) gene variant known as ALDH2*2 is pivotal in esophageal cancer risk. This polymorphism reduces ALDH2 enzyme activity by 60-90%, impairing acetaldehyde detoxification. Acetaldehyde is the carcinogenic metabolite of ethanol. Individuals with ALDH2*2 who consume alcohol face elevated cancer risks, including those affecting the upper aerodigestive tract, head and neck, breast, lung, oral, and gastrointestinal tract.

East Asia bears the largest global burden of alcohol-attributable cancers due to ALDH2*2's high regional prevalence ranges from 28% to 54%. While targeted endoscopic screening programs in high-risk areas demonstrated reduced incidence and mortality, the invasiveness and cost of examinations present barriers to widespread adoption. Observational studies found that risk-stratified screening using individualized risk scores could enhance compliance and optimize resource use.

To inform health policy planning and resource allocation, it is essential to evaluate the cost-effectiveness of targeted esophageal cancer screening programs for ALDH2*2 carriers in East Asia. This study aims to estimate the alcohol dose-response risk curves for esophageal cancer associated with the ALDH2*2 genotype through an updated systematic review. Furthermore, it will conduct a meta-analysis assess population health impacts and the cost-effectiveness of risk-tailored screening in Hong Kong.

OBJECTIVE

To assess the risk of esophageal cancers by alcohol exposure for ALDH2*2 carriers using an updated systematic review.

METHODS

A systematic literature search was conducted in English and Chinese databases (Web of Science, PubMed, Ovid, EBSCO, PsycINFO, Cochrane Library, and WanFang MED) to identify observational epidemiological studies published between 1900 and March 2024 reporting on the association between alcohol consumption and risk of esophageal cancer among individuals with the ALDH2*2 genotype. Keywords include "alcohol OR ethanol", "ALDH OR dehydrogenase*", "oesophageal* OR esophageal*" and "cancer OR neoplasm* OR carcinoma* OR melanoma OR Hodgkin disease OR lymphoma"

We then screened the titles and abstracts and assessed the full texts of potential articles for eligibility. Data extraction will be performed to retrieve information on study design, population characteristics, exposure assessment, and effect size.

In future stage, meta-analytic methods will be used to pool the dose-response data and generate a summary relative risk curve of esophageal cancer.

REFERENCE

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RESULTS

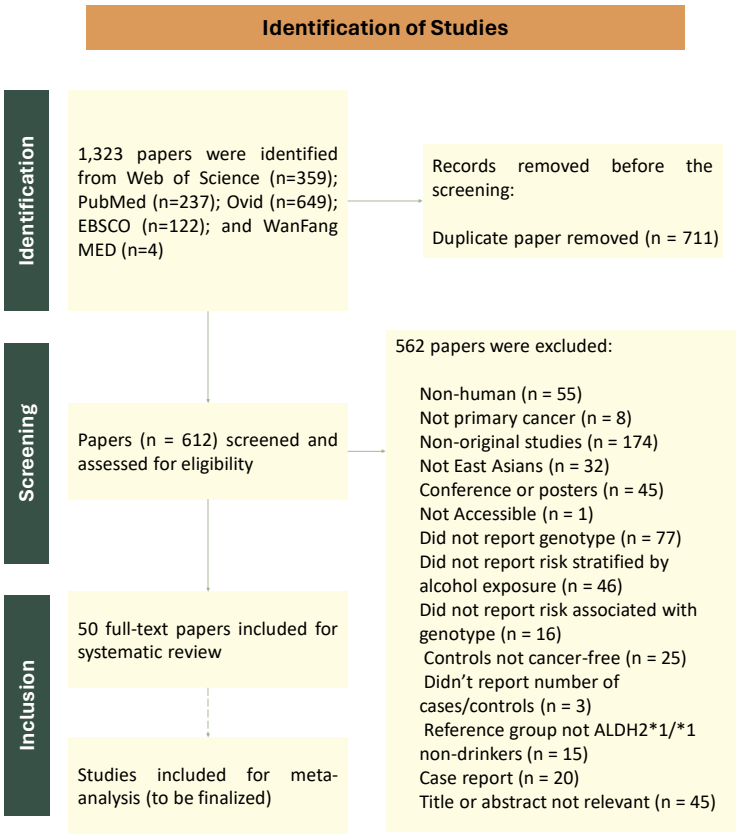

Figure 1. Flowchart for the selection of studies on esophageal cancer and alcohol consumption in East Asia

In this study, a selection of studies is completed for systematic review (Figure 1.). A meta-analysis is not yet completed but will be conducted in the later stage to generate quantitative measures evaluating cancer risk.

According to the selected studies, in China specifically:

- **21%** of the population are ALDH2*2 carriers.
- **33%** of men drank alcohol most weeks.
- Several studies found that individuals with the ALDH2*2 variant who consumed alcohol, especially heavy alcohol (>30-50 g/day), faced significantly **increased risks of esophageal cancer** compared to those who abstained or light drinkers without the variant. The odds ratios ranged from 1.28 to 11.93.
- Genetic evidence from epidemiological studies supported the conclusions that alcohol consumption causally increased risks of upper digestive tract cancers and that ALDH2*2 exacerbated these risks, particularly among heavier drinking men in China/East Asia.

CONCLUSIONS

- The review confirms that ALDH2*2 carriers face significantly **elevated risks of developing esophageal cancers** when consuming alcohol.
- **Targeted early screening programs** should be considered for ALDH2*2 carriers with a history of regular alcohol use, especially heavy long-term drinkers. Risk-stratified approaches using polygenic risk scores could optimize screening.
- Suggesting **alcohol reduction or cessation**, particularly for heavy drinkers, could lower disease incidence in genetically high-risk groups.

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