Name: Hang Zhou Email: hang.zhou@yale.edu

Mendelian Randomization Analysis of the Effects of Alcohol Use on Cancer Risk

Hang Zhou[1,2], Bao-Zhu Yang[1,2], Henry R. Kranzler[3,4], Joel Gelernter[1,2]

[1]Department of Psychiatry, Yale University, New Haven, CT; [2] VA Connecticut Healthcare System, West Haven, CT; [3]Department of Psychiatry, University of Pennsylvania, Philadelphia, PA; [4]Veterans Integrated Service Network 4, Crescenz Veterans Affairs Medical Center, Philadelphia, PA

Background/significance/hypothesis:
Cumulative epidemiological evidence shows that an estimated 5.5% of all cancers are attributable to alcohol use, totaling 770,000 cases annually. Alcohol consumption is associated with the development of cancer of the oral, breast, liver, and colon. GWASs have identified risk genes for alcohol-related traits and cancers. However, the relationship between alcohol use and different kinds of cancer remains unclear.

Methods:
To provide adequate power to investigate the causal relations between two alcohol-related phenotypes and different cancers, we used the GWAS summary statistics for problematic alcohol use (PAU, Zhou et al., under review, N=903,147) and drinks per week (DPW, Liu et al., N=941,280). We used Mendelian Randomization (MR) and summary statistics from GWAS of several cancers, including breast, colorectal, esophageal and oral/pharyngeal cancers. Inverse-variance weighting (IVW), weighted median, MR Egger, and MR PRESSO were implemented for MR inference.

Results:
We observed nominally significant causal effects of PAU on esophageal cancer (IVW p=0.01) and significant effects (correcting for 8 tests) on breast (IVW p=2.6×10-3) and oral cancer risks (IVW p=4.4×10-6). We found no causal effects of DPW on cancers.

Conclusions:
There are few MR studies on this topic in the literature, mainly due to underpowered GWAS of alcohol-related traits and cancers. This study finds evidence of the causal effects of PAU on the risk of specific cancer types. These results are limited to European ancestry; further studies in underrepresented, understudied, and underreported populations are needed.