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## "The Influence of Alcohol Consumption on Tobacco-Associated Cancer: An All of Us Research Program Analysis"

**Background:** Alcohol consumption and tobacco use are independently recognized as major risk factors for various types of cancer. Individually, these modifiable health factors are well documented in their carcinogenic roles. However, there is a nuanced interaction, specifically the potential for alcohol consumption to moderate the association between tobacco use and the risk of tobacco-linked cancers. The NIH's All of Us Research database is a large, diverse cohort that contains extensive electronic health record (EHR) and survey data that are ideal for exploring these complex interactions. Examining alcohol and tobacco in this nuanced way is crucial for uncovering the complex health risks.

**Objectives:** The primary objective of this study was to investigate alcohol's effect on the incidence of tobacco-related cancers. Secondary objectives were to investigate if estimates of total alcohol consumption (quantity x frequency) and/or episodic heavy drinking days specifically moderate the incidence of tobacco-related cancers.

**Methods:** A retrospective analysis of data from the NIH's All of Us research program was used, which includes cross-sectional self-reported surveys and longitudinal EHR data extractions. This study looked at tobacco-linked cancers that are also not classified as alcohol-related cancers. These cancers are identified as lung cancer, pancreatic cancer, kidney cancer, bladder cancer, and cervical cancer. Cervical cancer was excluded because of the gender skew in the regression model. Using the All of Us database, a cohort was comprised of participants who were diagnosed with tobacco-linked cancer and who had available survey data detailing their alcohol and tobacco survey completion, with available data on alcohol consumption (quantified by AUDIT-C scores), tobacco use status (categorized as never, former, or current smoker), and key demographic and clinical covariates (age, sex, race, ethnicity, and BMI). A Logistic Regression Model was used to analyze how alcohol moderated tobacco-linked cancer incidence, adjusting for all specified covariates.

**Results:** Based on the Logistic Regression Model for tobacco-linked cancers, a statistically significant interaction was observed between heavy drinking frequency and tobacco status (Odds Ratio for interaction: 0.8987, P-value: 1.18e-05). This shows that the increased odds of tobacco-linked cancer associated with tobacco use become less pronounced as heavy drinking frequency increases.

**Conclusion:** This study uses the extensive All of Us dataset to explore the relationship between alcohol consumption, tobacco use, and cancer incidence. The findings contribute to a more nuanced understanding of cancer etiology