Table of Contents

Table of Tables

Epidemiological Analysis of Alcohol Use and Oesophageal Cancer:

A Cohort Study Assessment

Alexander et al. (2014) define a cohort study as an analytic method used to directly calculate risk (cumulative incidence) and incidence rates (incidence density) by quantifying new occurrences of an outcome relative to the population-at-risk or person-time at risk.

1.1 Construction of 2×2 Table

A 2×2 contingency table is a fundamental tool in epidemiology. It is used to organise data from cohort studies. This table displays the relationship between exposure status and disease outcome (Setia, 2016). The table below summarises the data from the cohort study examining alcohol use and oesophageal cancer.

Exposure Status	Disease (+)	Disease (-)	Total
Alcohol Users (Exposed)	160 (a)	640 (b)	800
Non-Alcohol Users (Unexposed)	40 (c)	1,160 (d)	1,200
Total	**200**	**1,800**	**2,000**

Table 1 2×2 Contingency Table Showing the Relationship Between Alcohol Use and Oesophageal Cancer

In this table, 'a' represents exposed individuals with disease, 'b' represents exposed individuals without disease, 'c' represents unexposed individuals with disease, and 'd' represents unexposed individuals without disease. This notation follows standard epidemiological conventions (Kestenbaum, 2019).

1.2 Calculation and Interpretation of Effect Measures

1.2.1 Incidence of Oesophageal Cancer in Each Group

Incidence, also called cumulative incidence or risk, measures the proportion of new cases that develop in a population at risk over a specific time period (Centers for Disease Control and Prevention [CDC], 2012). According to Setia (2016), cumulative incidence is calculated by dividing the number of new cases by the total population at risk at the beginning of the study. This measure is appropriate for cohort studies where participants are followed over time.

Formula: Incidence = Number of new cases / Total population at risk

Incidence in Exposed Group (Alcohol Users):

$$\text{Incidence}_{\text{exposed}} = a / (a + b) = 160 / 800 = 0.20 \text{ or } 20\%$$

Incidence in Unexposed Group (Non-Alcohol Users):

$$\text{Incidence}_{\text{unexposed}} = c / (c + d) = 40 / 1{,}200 = 0.033 \text{ or } 3.33\%$$

Over the 20-year follow-up period, 20% of alcohol users developed oesophageal cancer compared to only 3.33% of non-alcohol users. This shows that the incidence of oesophageal cancer is substantially higher among individuals who consume alcohol.

1.2.2 Relative Risk (RR)

Relative risk (RR) is the ratio of the probability of disease occurrence in the exposed group to the probability in the unexposed group (StatPearls, 2023). According to Andrade (2015), relative risk tells us how much more likely exposed individuals are to develop the disease compared to unexposed individuals. The RR is a key measure of association in cohort studies because it directly compares disease risks between groups (Kestenbaum, 2019).

Formula: $\text{RR} = \text{Incidence}_{\text{exposed}} / \text{Incidence}_{\text{unexposed}}$

Calculation:

$$\text{RR} = 0.20 / 0.033 = 6.0$$

The relative risk of 6.0 indicates that alcohol users are 6 times more likely to develop oesophageal cancer compared to non-alcohol users. Since RR > 1, alcohol use is a risk factor for oesophageal cancer. As noted by the University of Nottingham (n.d.), an RR greater than 1 suggests a positive association between the exposure and disease outcome.

1.2.3 Attributable Risk (AR)

Attributable risk (AR), also known as risk difference, is an absolute measure of association (StatsDirect, n.d.). It represents the portion of disease incidence in the exposed group that can be attributed to the exposure (Andrade, 2015). Unlike relative risk which is a ratio, AR provides the actual difference in disease rates between exposed and unexposed groups. This measure is particularly important for public health planning because it indicates the potential reduction in disease burden if the exposure were eliminated (Kestenbaum, 2019).

Formula: $AR = Incidence_{exposed} - Incidence_{unexposed}$

Calculation:

$AR = 0.20 - 0.033 = 0.167$ or 16.7%

The attributable risk of 0.167 (16.7%) means that 16.7 additional cases of oesophageal cancer per 100 alcohol users can be attributed to alcohol consumption. In other words, if alcohol use were eliminated from this population, approximately 167 cases per 1,000 exposed individuals could potentially be prevented over the 20-year period.

1.2.4 Attributable Risk Percent (ARP)

Attributable risk percent (ARP), also called attributable fraction among the exposed, expresses the proportion of disease in the exposed group that is specifically due to the exposure (Andrade, 2015). According to StatsDirect (n.d.), this measure indicates what percentage of disease cases among exposed individuals would be eliminated if the exposure were removed, assuming a causal relationship exists.

Formula: $ARP = (Incidence_{exposed} - Incidence_{unexposed}) / Incidence_{exposed} \times 100\%$

Alternative Formula: $ARP = (RR - 1) / RR \times 100\%$

Calculation:

$ARP = (0.20 - 0.033) / 0.20 \times 100\% = 0.167 / 0.20 \times 100\% = 83.5\%$

Or using alternative formula: $ARP = (6.0 - 1) / 6.0 \times 100\% = 83.3\%$

The attributable risk percent of approximately 83.5% indicates that among alcohol users who developed oesophageal cancer, about 83.5% of those cases can be attributed to their alcohol consumption. This means that if we could eliminate alcohol use, we could potentially prevent 83.5% of oesophageal cancer cases among the exposed group, assuming alcohol use is a causal factor.

Summary of Effect Measures

Measure	Value	Interpretation
Incidence (Exposed)	20.0%	20% of alcohol users developed cancer
Incidence (Unexposed)	3.33%	3.33% of non-users developed cancer

Measure	Value	Interpretation
Relative Risk (RR)	6.0	6 times higher risk in alcohol users
Attributable Risk (AR)	16.7%	Additional 167 cases per 1,000 exposed
Attributable Risk Percent	83.5%	83.5% of cases in exposed are due to alcohol

Table 2 Summary of Calculated Effect Measures

1.3 Discussion of Confounding

Definition of Confounding

Confounding is a major threat to the internal validity of epidemiological studies. It occurs when a third variable, called a confounder, distorts the observed relationship between the exposure and outcome (Howards, 2018). According to Catalog of Bias (n.d.), confounding happens when the confounder is associated with both the exposure and the outcome, but is not on the causal pathway between them. Health Knowledge (n.d.) explains that confounding provides an alternative explanation for an observed association, making it appear that a relationship exists when it does not, or masking a true relationship.

For a variable to be considered a confounder, it must meet three criteria: (1) it must be associated with the exposure, (2) it must be an independent risk factor for the outcome, and (3) it must not be an intermediate step in the causal pathway between exposure and outcome (Oregon State University, 2020). When confounding is present, the crude estimate of association may be biased either towards or away from the null value.

Potential Confounders in This Study

In this cohort study examining the relationship between alcohol use and oesophageal cancer, several potential confounders could influence the results:

Tobacco Smoking: Smoking is strongly associated with both alcohol consumption and oesophageal cancer. People who drink alcohol are more likely to smoke, and smoking is a well-established risk factor for oesophageal cancer. If smoking rates differ between alcohol users and non-users, the observed association between alcohol and cancer may be partially or entirely due to smoking rather than alcohol itself.

Age: Older individuals may have different alcohol consumption patterns and are at higher risk for cancer. If the age distribution differs between exposed and unexposed groups, age could confound the results.

Socioeconomic Status: Lower socioeconomic status is associated with both higher alcohol consumption in some populations and poorer health outcomes including cancer. According to Catalog of Bias (n.d.), socioeconomic factors have been shown to confound associations in many epidemiological studies.

Dietary Factors: Poor nutrition and low intake of fruits and vegetables are associated with both alcohol consumption and increased cancer risk. Dietary habits may differ systematically between alcohol users and non-users.

Occupation: Certain occupations may expose workers to carcinogens while also being associated with higher alcohol consumption patterns.

How Confounding Could Influence the Results

If confounding is present in this study, the calculated relative risk of 6.0 may not represent the true causal effect of alcohol on oesophageal cancer. Penn State University (n.d.) notes that if the adjusted estimator differs importantly (often by 10% or more) from the crude estimator, confounding is present. The confounding could work in two directions:

Positive Confounding: If confounders like smoking are more common among alcohol users and also increase cancer risk, the observed RR of 6.0 may overestimate the true effect of alcohol. The crude estimate would be biased away from the null value of 1.0.

Negative Confounding: If certain protective factors are more common among alcohol users, the observed RR may underestimate the true effect. This is less likely in this scenario but theoretically possible.

Methods to Control Confounding

According to Lash et al. (2022), confounding can be addressed at two stages: during study design and during data analysis.

Design Stage Methods:

Restriction: Limiting the study to individuals with similar characteristics, such as including only non-smokers, eliminates confounding by that factor.

Matching: Selecting unexposed participants who are similar to exposed participants on potential confounders ensures comparability between groups (Howards, 2018).

Randomisation: While not applicable to observational cohort studies, randomisation in experimental designs helps balance both known and unknown confounders between groups.

Analysis Stage Methods:

Stratification: Analysing the association separately within strata of the confounder allows calculation of stratum-specific estimates and assessment of whether confounding is present.

Multivariable Regression: Statistical models can adjust for multiple confounders simultaneously, providing an adjusted estimate of the association (Penn State University, n.d.).

Propensity Score Methods: These methods create a summary score representing the probability of exposure given measured confounders, which can then be used for matching or weighting (Lash et al., 2022).

Limitations and Residual Confounding

It is important to note that while these methods can control for known and measured confounders, there may always be unmeasured or unknown confounders that cannot be accounted for. This is called residual confounding. Catalog of Bias (n.d.) emphasises that observational studies, unlike randomised trials, cannot eliminate the possibility of unknown confounders affecting the results. Therefore, even after controlling for confounding, caution is needed when interpreting findings from observational studies as evidence of causal relationships.

Conclusion

This cohort study demonstrates a strong association between alcohol use and oesophageal cancer. The calculated effect measures show that alcohol users have a six-fold increased risk of developing the disease, with approximately 83.5% of cancer cases among alcohol users attributable to their alcohol consumption. However, the validity of these findings depends on adequate control of confounding factors such as smoking, age, socioeconomic status, and dietary habits. Future studies should employ appropriate methods to address confounding during both the design and analysis stages to provide more reliable estimates of the causal effect of alcohol on oesophageal cancer risk.

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