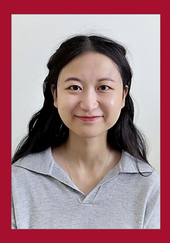
Quantification of likelihood that death certificate misclassification increases odds ratios of dose-response relationships



Xirui Liu[1], Stacey L. McComish[1], Joey Y. Zhou[2], Sergei Y. Tolmachev[1]

[1]United States Transuranium and Uranium Registries, College of Pharmacy and Pharmaceutical Sciences, Washington State University, Richland, WA, USA

[2]Office of Domestic and International Health Studies, United States Department of Energy, Washington, D.C., USA

Introduction

The causes of death on death certificates are widely used as a primary source of the health outcome information in epidemiological studies that evaluate dose-response associations. However, the autopsy report is considered the gold standard for determining underlying causes of death. In our previous research, health outcome discrepancies were observed between the underlying causes of death listed on death certificates and those on autopsy reports[1]. In epidemiology studies, the general consensus is that death certificate misclassification is more likely to reduce measures of risk, for example the odds ratio, than to increase it. In an effort to better understand how such misclassifications affect health outcome assessments and research conclusions, the study aimed to verify if the general belief is always correct and further quantify the misclassification impact by measuring the percentage of odds ratios changed compared to initial results.

Radiation Dose Data

- 5,122 cumulative colon dose records were extracted from a cohort of Rocky Flats workers

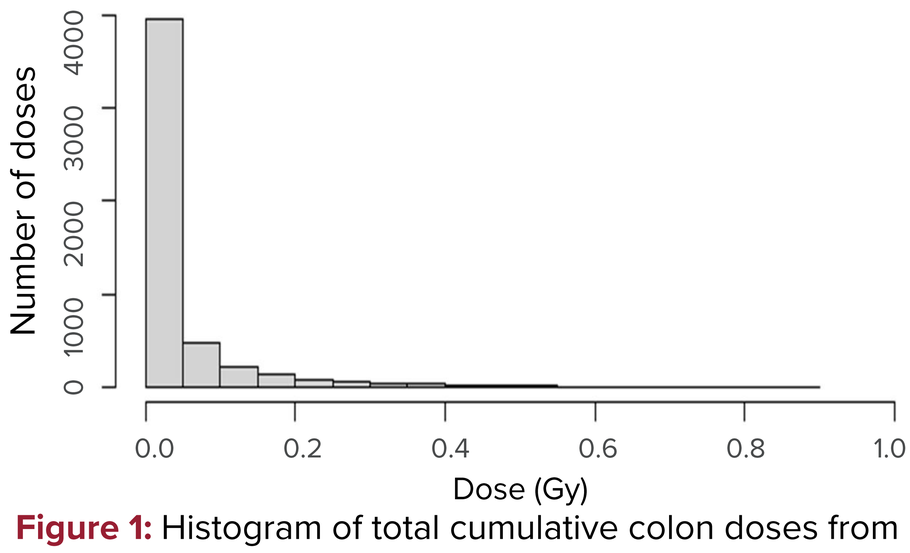


Figure 1: Histogram of total cumulative colon doses from Rocky Flats cohort

Cancer Outcome Generation

- Logistic function was used to calculate the probability of cancer outcome $p(x)$ for each dose record:

$$p(x) = \frac{1}{1 + e^{-(\beta_0 + \beta_1 x)}}$$

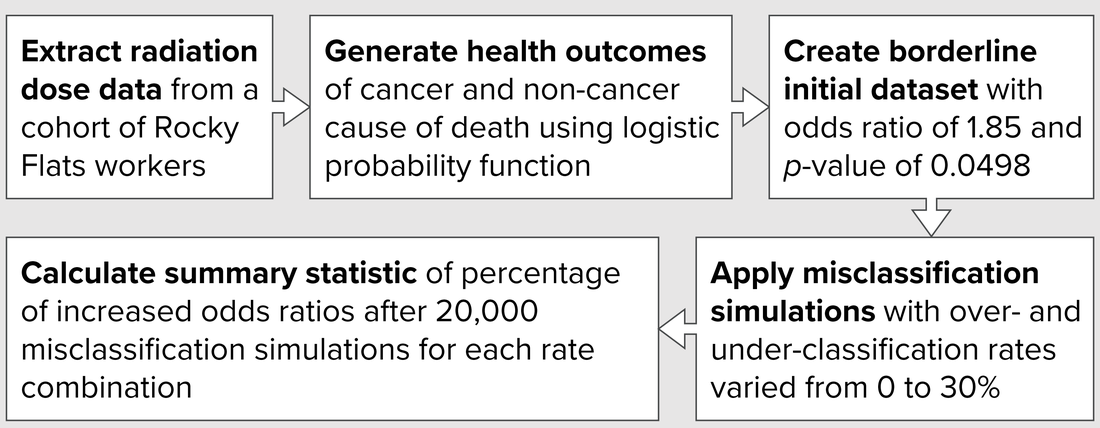
x: Dose values (Gy)

β_0: Constant derived from a baseline cancer incidence of 24%

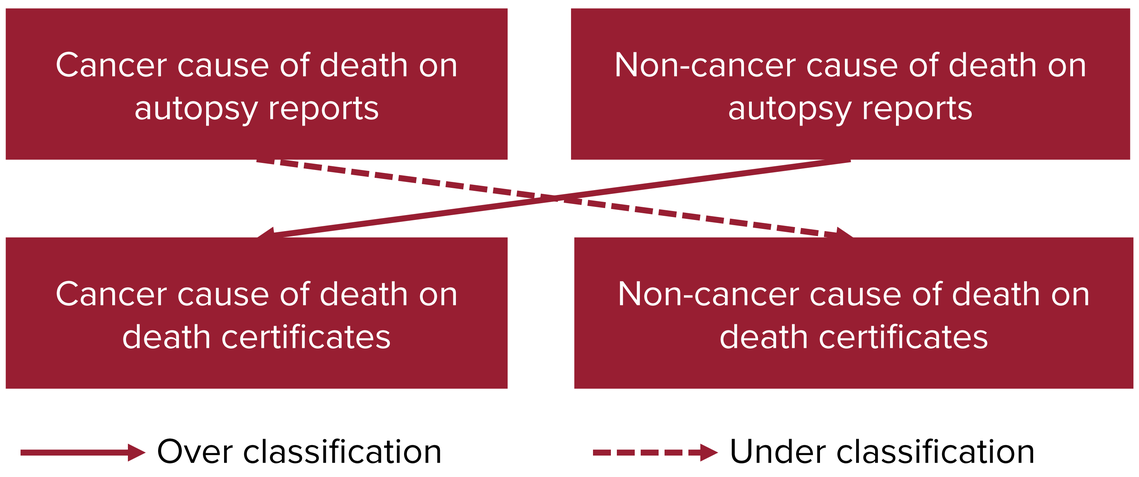
β_1: Logarithm of the predetermined initial odds ratio

- Cancer outcomes were randomly generated for each dose record using $p(x)$
- 1,000 repetitions of the outcome generation process were conducted to select an initial scenario for the misclassification simulation (a borderline scenario with p-value just below the significance threshold)

Overview of Method Workflow



Misclassification Simulation



$$\text{Over classification rate} = \frac{Number\ of\ False\ Positives}{Total\ Number\ of\ Noncancer\ on\ ARs}$$

$$\text{Under classification rate} = \frac{Number\ of\ False\ Negatives}{Total\ Number\ of\ Cancer\ on\ ARs}$$

Misclassification Rates Impact on Increased Odds Ratios

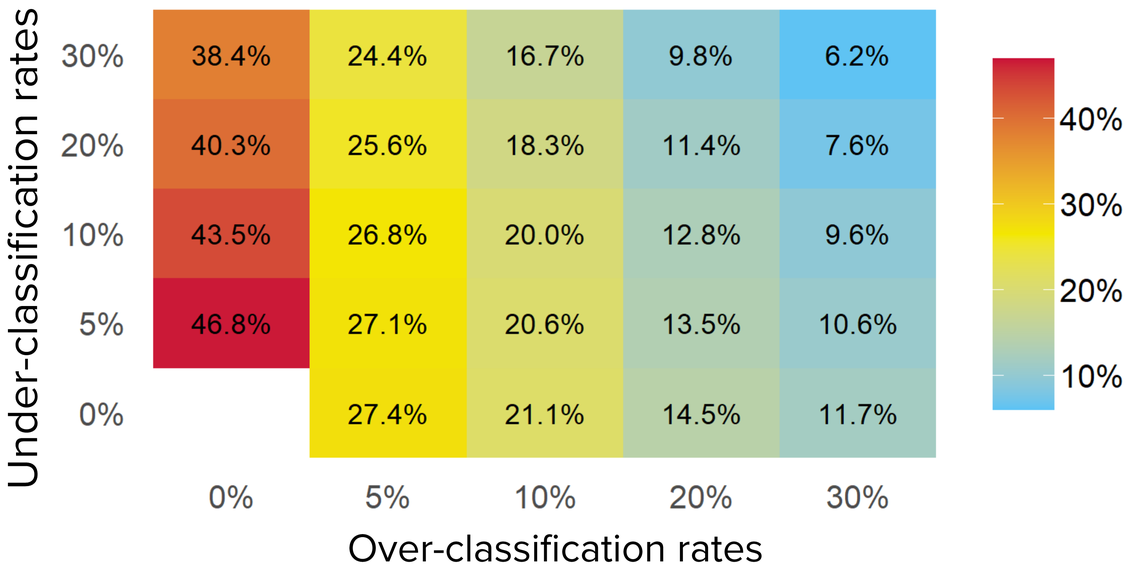


Figure 3: How different over- and under-classification rates impact on percentage of increased odds ratio after 20,000 times simulations

Conclusions

- The general consensus that death certificate misclassification is more likely to reduce the risk estimates was not always true. While the death certificate misclassification is more likely to reduce risk estimates, this study showed that the likelihood of increased risk estimates can be substantial.
- Lower misclassification rates led to a more substantial impact on the conclusion about health risks.
- Over- and under-classification effects tended to cancel each other out at higher misclassification rates.

Discussion

- While the exact percentages may vary under different assumptions, this study underscores the importance of considering the impact of death certificate misclassifications in epidemiological analyses, as the effects are more complex than generally anticipated.
- Future research will continue to explore the complex relationship between disease misclassifications and study conclusions and will simulate more representative data by altering key parameters.

Reference

1. McComish, Stacey L et al. “Misclassification of causes of death among a small all-autopsied group of former nuclear workers: Death certificates vs. autopsy reports.” PloS one vol. 19,5 e0302069. 3 May. 2024, doi:10.1371/journal.pone.0302069