Sensitivity Analysis to Quantify the Impact of Outcome Misclassification on Health Risk Models: A Simulation Approach

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

[1]United States Transuranium and Uranium Registries, Washington State University; [2]Office of Health Studies and Former Worker Programs, U.S. Department of Energy

Background: The United States Transuranium and Uranium Registries (USTUR) investigates the deposition of uranium, plutonium, and americium in humans who had documented occupational exposures to these elements. Our examination of autopsy reports from these workers revealed cause-of-death discrepancies between death certificates and autopsy reports, where death certificates are commonly used in epidemiological studies and autopsy reports are widely recognized as the diagnostic gold standard. Traditional epidemiological assumptions suggest such misclassification would bias risk estimates toward the null.

Objectives: This simulation study quantified whether cause-of-death misclassification can (1) move odds ratios away from the null, and (2) shift non-significant dose-response associations to significance. Furthermore, this study aimed to determine the likelihood of these effects in a borderline significant scenario. Methods: Simulation data included doses and outcomes, which were either derived from USTUR records or randomly generated. Initial datasets were generated with borderline statistical significance (p $\approx$ 0.05). Various over- and under-misclassification rates were used for simulation. 20,000 iterations were simulated for each combination of over- and under-classification. The logistic regression model was used to evaluate dose-outcome associations.

Results: Over- and under-misclassification rates, varying from 0 to 30%, cause-of-death misclassification moved odds ratios away from the null in 4%–47% of the simulations. In 8%–42% of cases, non-significant associations shifted to significant.

Conclusion: The traditional understanding that misclassification always biases estimates toward the null is more likely to be true when misclassification rates are high and the risk is high.

USTUR-0716-25A