

## **Bias in the Proportionate Mortality Ratio Analysis of Small Study Populations: a Case on Analyses of Radiation and Mesothelioma**

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**Purpose:** Quantify bias in the proportionate mortality ratio (PMR) analysis of small study populations and develop a bias correction methodology.

**Materials and Methods:** Bias in the PMR analysis of small study populations is quantified through algebraic derivation. A simulation procedure is developed to evaluate the relationship between bias and study population size. A recently published PMR analysis of radiation and mesothelioma among 329 deceased registrants in the United States Transuranium and Uranium Registries (USTUR) is used as an illustrated example.

**Results:** The proportionate mortality ratios are biased and overestimated in small population studies; the smaller the study population, the larger the overestimation. As such, the average overestimation of PMR for mesothelioma in the analyses of radiation and mesothelioma in USTUR is 7.2% (95% confidence interval = 5.1%, 9.7%); the PMR overestimation is 22.5% (95% confidence interval = 16.8%, 29.1%) when stratified by quartiles of radiation doses.

**Conclusions:** The degree of PMR small sample bias is mainly determined by the sample size ratio, which is defined as the ratio of the sample size to the number of disease categories in the reference population. Correction for the bias is recommended when the sample size ratio is less than 5. The quantification and correction algorithm of the PMR small sample bias developed in this research supplements the PMR methodology.

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