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A novel approach to evaluate excess of mesothelioma deaths in a small population of former nuclear workers

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It has been noted for years that there is an excess of mesothelioma deaths among the Registrants of the U.S. Transuranium and Uranium Registries (USTUR). The latest statistics shows that there are 9 mesothelioma cases among 341 (2.6%) deceased USTUR Registrants, compared with less than 1 expected mesothelioma death (0.16%) for the U.S. general population adjusted for age, gender, race, and calendar year. A matched case control analysis was used to evaluate the cluster of mesothelioma cases in association with cumulative external radiation exposures. First, all causes of USTUR Registrants' deaths were classified into 4 groups: mesothelioma (Meso), lung cancers (LC), other cancers (OC), and non-cancers (NC). Second, for each case of mesothelioma, controls were identified in the LC (2 ~ 3 controls per case), OC (2 ~ 5 controls per case), and NC (2 ~ 5 controls per case) groups matching gender (male), race (white), years of employment (± 2.5 years), first hire (± 5 years), birth year (± 5), and age at death (± 5 years). Third, a paired t-test (one sided) was used to examine whether there were statistically significant differences in cumulative external radiation doses between cases and respective controls in LC, OC, and NC groups. In practice, a permutation paired t-test (PPTT) was developed to run the significance tests based on a large number of paired t-tests. For each paired t-test, one control for each case was randomly selected from multiple (2 ~ 5 controls per case) matching controls for the case. This procedure was repeated many times, and the percentage of statistically significant ($p \leq 0.05$) paired t-tests were counted. Inference was reached based on whether or not 5% or more of PPTTs were statistically significant. PPTTs were not significant for Meso vs. LC and Meso vs. OC; PPTTs were significant, however, for Meso vs. NC with larger than 9.0% of significant paired t-tests. A follow up conditional logistic regression for the Meso and NC groups showed a non-statistically significant odd ratio (OR) of 1.001 (95% CI: 0.997 ~ 1.006) between cumulative external radiation doses and mesothelioma. The matched case control analysis suggested that the excess of mesothelioma deaths among USTUR Registrants was not associated with cumulative external radiation exposures.

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