

Control Group Variation in the Janus Studies

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Data from historical radiobiological mega-studies is being migrated online to enable open access to the results of these studies. The availability of these large data sets offers the possibility of merging the results of multiple studies for meta-analysis. However, researchers must overcome several hurdles in order to analyze data from disparate radiobiology studies. Variations in animal treatment, autopsy methods, and nomenclature must be accounted for before developing new conclusions from merged studies.

This work focuses on differences in animal treatment between studies in the Janus radiobiology experiments. The Janus Studies data sets include coded necropsy results for more than 40,000 mice divided between 12 studies. We suspect that the incidence rates of coded pathological observations might vary within the 8465 control mice divided between the study groups.

To address this issue, we have developed models for each pathological outcome regressed against experiment number, necropsy proctor, gender, species, or date of death. We then compared Akaike Information Criterion (AIC) goodness of fit estimates for each of these models to determine which factors affected pathological incidence rates in control samples.

Our results reveal that experiment number, gender, species, date of death and most necropsy proctors have a measurable effect on the incidence rates of the majority of pathological outcomes. The date of death and participation in the JM-2 study stand out as particularly biasing. These two variables affect the average AIC value across pathologies even more than gender. One of the Janus studies, JM-10, was performed on a species of *Peromyscus* mouse. However, the effect of species on average AIC values is similar to the effect size of most study groups and some pathologists.

These findings indicate that control treatment conditions and proctor bias are important contributors to the incidence rate of observed pathological outcomes in the Janus studies. Particularly, these factors can impact pathological outcomes as much as species and gender. It is daunting to realize the extent of bias, but encouraging to think that meta-analysis might overcome these biases to reveal novel associations and dismiss artifactual findings. Future analysis will focus on methodologies to control for this between-group variation in order to extract new meaning from the Janus studies. This work is an important step towards expanding radiobiology analysis across even more data sets.