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"Effect of follow-up period on minimal-significant dose in the atomic-bomb survivor studies"

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Study Findings

This study demonstrated that longer follow-up of the Life Span Study (LSS) cohort of atomic-bomb survivors provides more reliable estimates of radiation risk. In particular, we refuted a counter-intuitive claim recently made by others that earlier RERF reports based on the LSS cohort might provide estimates of the risk of radiation at low doses that are better than risk estimates provided in more recent RERF reports.

Explanation

To obtain estimates of radiation risk that are accurate (unbiased) and precise (estimated with a high level of confidence) requires that we be able to estimate well the parameters of statistical models for the background rates of disease or death (according to attained age, birth cohort, sex, etc.) and modification of risk by attained age and age at exposure. Continued follow-up of the LSS cohort of atomic bomb survivors is therefore deemed to be important because it is expected that longer follow-up—and the resulting accumulation of data—should permit more precise estimation of these parameters and therefore allow us to obtain better estimates of radiation risk.

1. Study purpose

The notion that longer follow-up should lead to better estimates of radiation risk was challenged by two researchers in an article published last year in the same journal. We suspected that the analytical method used by those authors might be flawed, because it ignored the most recent information about the background-rate and effect-modification parameters that are needed to accurately and precisely estimate radiation risk. We therefore undertook an analysis to ascertain how risk estimates depend on length of follow-up by using a method not suffering from this shortcoming.

2. Study methods

We analyzed solid cancer incidence and mortality in the LSS cohort using the most recent data from LSS mortality report 14, published in 2014, and the third LSS solid cancer incidence report, published earlier this year. Complete follow-up data were used to estimate background-rate and effect-modification parameters, but the radiation dose response (the excess relative risk, or ERR*) was estimated separately for each of the follow-up periods employed in previous mortality and incidence reports. We also estimated the ERR over shorter and shorter intervals of dose from zero up to pre-specified cutpoints and estimated likelihood-based confidence intervals for those dose ranges. By doing so, we could ascertain the lowest dose level below which estimated ERR is not consistently significant statistically (what we call "minimal-significant dose").

*excess relative risk is the relative risk minus 1; it reflects the mortality or incidence that can be attributed to the radiation exposure (as a proportion times the background rate)

3. Study results

The minimal-significant dose tended to be lower with longer follow-up. In other words, longer follow-up permits substantiation of a significant radiation effect at progressively lower dose levels. Furthermore, attained age and age at exposure were shown to be highly correlated in the earlier follow-up periods, so effect modification by these two factors could not be estimated precisely in earlier periods due to their collinearity (lack of independent information about each factor).

Study Significance

Our results underscore the need for continued follow-up of the LSS cohort.

The Radiation Effects Research Foundation has studied A-bomb survivors and their offspring in Hiroshima and Nagasaki for around 70 years. RERF's research achievements are considered the principal scientific basis for radiation risk assessment by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and for recommendations regarding radiation protection standards by the International Commission on Radiological Protection (ICRP). RERF expresses its profound gratitude to the A-bomb survivors and survivors' offspring for their cooperation in our studies.

[§]***Radiation and Environmental Biophysics,*** is a quarterly peer-reviewed scientific journal, first published in 1974, covering research in biophysics and radiation biology. (Impact factor in 2016/2017: 2.398)