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Comparison of cancer slope factors using different statistical approaches

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Abstract

The U.S. Environmental Protection Agency's cancer guidelines (USEPA, 2005) present the default approach for the cancer slope factor (denoted here as s*) as the slope of the linear extrapolation to the origin, generally drawn from the 95% lower confidence limit on dose at the lowest prescribed risk level supported by the data. In the past, the cancer slope factor has been calculated as the upper 95% confidence limit on the coefficient (q*1) of the linear term of the multistage model for the extra cancer risk over background. To what extent do the two approaches differ in practice? We addressed this issue by calculating s* and q*1 for 102 data sets for 60 carcinogens using the constrained multistage model to fit the dose-response data. We also examined how frequently the fitted dose-response curves departed appreciably from linearity at low dose by comparing q1, the coefficient of the linear term in the multistage polynomial, with a slope factor, sc, derived from a point of departure based on the maximum likelihood estimate of the dose-response. Another question we addressed is the extent to which s* exceeded sc for various levels of extra risk. For the vast majority of chemicals, the prescribed default EPA methodology for the cancer slope factor provides values very similar to that obtained with the traditionally estimated q*1. At 10% extra risk, q*1/s* is greater than 0.3 for all except one data set; for 82% of the data sets, q*1 is within 0.9 to 1.1 of s*. At the 10% response level, the interquartile range of the ratio, s*/sc, is 1.4 to 2.0.