Comparison of methods for estimating the attributable risk in the context of survival analysis

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Background: The attributable risk (AR) measures the proportion of disease cases that can be attributed to an exposure in the population. Several definitions and estimation methods have been proposed for survival data.

Methods: Using simulations, we compared four methods for estimating AR defined in terms of survival functions: two nonparametric methods based on Kaplan-Meier's estimator, one semiparametric based on Cox's model, and one parametric based on the piecewise constant hazards model. We considered a fixed binary exposure with varying exposure probabilities and strengths of association, and generated event times from a proportional hazards model with constant or monotonic (decreasing or increasing) Weibull baseline hazard, as well as from a nonproportional hazards model. We simulated 1,000 independent samples of size 1,000 or 10,000. The four methods were compared in terms of mean bias, mean estimated standard error, empirical standard deviation and 95% confidence interval coverage probability at four equally spaced time points.

Results: Under proportional hazards, all four methods yielded unbiased results regardless of sample size. Nonparametric methods displayed greater variability than other approaches. All methods showed satisfactory coverage except for nonparametric methods at the end of follow-up for a sample size of 1,000 especially. With nonproportional hazards, nonparametric methods yielded similar results to those under proportional hazards, whereas semiparametric and parametric approaches that both relied on the proportional hazards assumption performed poorly. These methods were applied to estimate the AR of breast cancer due to menopausal hormone therapy (MHT) in 38,359 women of the E3N cohort.

Conclusion: In practice, our study suggests to use the semiparametric or parametric approaches to estimate AR if the proportional hazards assumption appears appropriate.

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