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CORR Insights®: Kaplan-Meier Survival Analysis Overestimates the Risk of Revision Arthroplasty: A Meta-analysis

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Where Are We Now?

It is well known that the Kaplan-Meier estimator overestimates the probability of events of interest in the presence of competing risks [1, 8]. For example, if a study seeks to

examine the durability of a particular arthroplasty implant (so the event of interest is revision), and a substantial proportion of the patients die, the Kaplan-Meier approach will overestimate the frequency of revision, since patients who have died cannot subsequently undergo revision. As such, death is considered a competing event to the event of interest (implant revision). The more frequent the competing events, the more Kaplan-Meier-based estimates will depart from the true probability of occurrence of the event of interest. In light of this, alternative analytic approaches that account for the occurrence of such competing events have been developed to estimate the cumulative incidence [1, 8]. While these issues are mathematically demonstrated and have been illustrated in various medical domains [2, 3, 6], they have received

less attention in orthopaedic research until recently [7, 8]. But while some work has been done in individual datasets [8], to my knowledge, no study has taken a broader look at the influence of the phenomenon of competing risks on Kaplan-Meier survivorship estimates across orthopaedics more generally.

In their study, Lacny et al. [4] adopted a meta-epidemiological approach to quantify the overestimation of the probability of revision by Kaplan-Meier estimator. They performed a systematic review and included studies that presented the probability of revision after hip or knee arthroplasty using both Kaplan-Meier and competing risks methods. Results showed that using Kaplan-Meier estimator overestimated the probability of revision by 7% in the strata with highest number of revision, and by 55% in those with highest proportion of patients who died during followup, which is a substantial difference indeed. While the study failed to demonstrate the effect of a higher proportion of competing events (deaths) on the overestimation, the data still

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indicated that the overestimation increases with the ratio of competing events to revisions in both analyses.

Where Do We Need To Go?

Even if based on a small number of studies, the results of Lacny et al. [4] illustrate that using the Kaplan-Meier estimator results in a real overestimation of the probability of implant revision. Since adequate methods exist to prevent this, they should be used preferentially in this circumstance. Another issue—beyond the scope of their study—concerns how treatment effects, such as when comparing different implants or the association between patient covariates and revision, should be analyzed and reported with competing risks. Studies illustrating the extent of the overestimation of implant revision by inappropriate methods [4, 7] may help researchers become more aware of this issue and promote the use of better methods to handle competing risks.

Going a step further, *CORR*® has announced that it will begin asking authors to consider using cumulative incidence analyses instead of Kaplan-Meier survivorship estimates in studies where the frequency of competing risks is high enough to matter [8]. Such initiative is also likely to impact both research and practice, and I suspect

that such competing risks analyses will become the standard approach in the field, as it has in other domains such as hematology, for instance.

How Do We Get There?

How researchers analyze competing-risk data when estimating the effect of a covariate (such as the type of implant) on the risk of revision is even more complex. Two types of analyses can be carried out, both being methodologically correct, but with different aims and sometimes different results. Indeed, one could assess whether the cumulative incidence of revision is higher with one type of implant as compared to another, or whether the cause-specific hazard of revision—the instantaneous rate of revision among the patients still alive with their implant—is higher with the first type of implant as compared to the other [3]. In the classical survival setting where patients can only fail from one cause (overall survival analysis), both analyses are equivalent, and are commonly carried out using a Cox proportional hazards model. In a competing risks setting, the cumulative incidence depends on the cause-specific hazards of all competing events—implant failure and death without implant failure. As a consequence, the effect of a covariate on the

cumulative incidence and the cause-specific hazard of revision may be different, especially if the covariate is also associated with the cause-specific hazard of death without implant failure. This issue is now well-studied in the methodological literature [5], but its implications in the orthopaedic literature still requires further investigation and reflection, particularly on how we should summarize the effect of a covariate.

Questions like those will need to be answered by methodologists. In the meantime, though, readers of clinical research—including practicing surgeons—should be mindful that Kaplan-Meier survivorship estimates are sensitive to the presence of competing events, and are likely to overestimate revision frequency in that setting. Clinical researchers should choose the correct survivorship estimator—such as a cumulative-incidence method—based on the presence or absence of such competing events. And journals should follow *CORR*®'s lead [8], and ask authors to choose the most-correct approach for analyzing survivorship in clinical research studies.

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