Predicting the remaining time to achieve the required number of needed patients or events in an ongoing clinical trial

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Background: When a randomized clinical trial is designed, the number of patients to be included is determined to achieve an adequate statistical power to detect relevant differences in the assessed outcome, basing these calculations on strong assumptions held on literature results or other evidences. Subsequently, additional assumptions on the patient inclusion rate must also be undertaken to estimate the duration of the clinical and to assess its feasibility. However, during the clinical trial, some lack in the accuracy of the assumptions as well as other practical issues may appear, which could lead to a decrease on the observed inclusion rates. In these cases, a new estimation of the expected time to achieve the required number of patients is required. In addition, when the main outcome is the occurrence of an event during the follow-up time, the total number of events can also be determined, using this as a second condition for ending the clinical trial. In this case, the lack of accuracy in the assumptions or other practical issues could also lead to a lower rate of events than the expected one, being of interest to provide an estimation of the remaining time. The aim of the work presented here is to provide a solution to this problem and, particularly, to apply this approach to the currently ongoing ISAACC clinical trial (NCT01335087, ClinicalTrials.gov)

Methods: Different strategies were used for modelling, in each calendar time period (considering weeks, months, trimesters or semesters), the number of included patients, based on Poisson and Negative Binomial distributions. Kaplan-Meier method and parametric Weibull model were used to estimate the survival curve.

Results: Predictions for the expected number of new patients to be included were obtained from the estimated models for count data, and were used to calculate the remaining time to achieve the required number of patients to end the clinical trial. These predictions were then considered to predict the number of events in the future time periods, using the estimated survival curves, including predictions for larger follow-up times. Several functions were implemented in R.

Discussion: The results obtained in the application of the proposed approach in ISAACC suggested that it might be a useful solution for similar studies. However, the choice of models for counting and survival data may be data-dependent, providing our R functions facilities for assessing different scenarios.

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