INTERNSHIP IN STATISTIC AND CLINICAL RESEARCH

Sample size for difference in restricted mean survival time in cluster randomized trials

Mission

Context: Cluster randomized trials (CRTs) are trials in which intact social units, such as medical practices, hospitals, or communities, are randomised to intervention or control conditions while outcomes are assessed on individuals within clusters. This study design is a natural choice to evaluate the impact of public health or health system interventions delivered at the cluster level and their use is rapidly increasing. In CRTs, outcomes assessed on individuals from a given cluster tend to be more similar than outcomes of individuals from different clusters. This clustering must be accounted for in the sample size calculation and in statistical analysis.

Although methods for analyzing binary and continuous outcomes are well established, those relating to time-to-event outcomes remain more limited. Such outcomes, including death or the occurrence of a major clinical event, are subject to censoring, which complicates both sample size calculation and statistical analysis.

In CRTs with a time-to-event outcome, the intervention effect is usually quantified by a hazard ratio, relying on the proportional hazards assumption. Alternative measures could be more relevant, such as the difference in restricted mean survival time (ΔRMST) between the intervention and control groups up to time t^*. The intervention effect measured by the ΔRMST is not relying on the proportional hazards assumption and is easily interpretable as the expected survival duration gain due to intervention over t^*.

Methods estimating RMST differences in CRTs has been developed, such as the integration of Kaplan-Meier survival curves and pseudo-value regression methods. These findings represent an important advance for the analysis of time-to-event outcomes in CRTs. However, several major barriers still limit the practical use of these methods:

1. To date, no formula is available for calculating the required sample size to detect an RMST difference in a CRT.
2. Researchers still have limited operational tools to support the design of such trials in practice.

Objective: The objectives of this internship are therefore to:

1) Develop a sample size formula based on the RMST difference for CRTs (either using an analytical formula or by simulation)
2) Begin implementing an R Shiny application to facilitate its adoption and implementation in practice.

Profile

Level: Bac +5 in statistics (Master 2 University, ENSAI,…)

Required skills:

- Knowledge in survival models and in methods for correlated data (e.g. mixed-effect models, etc)
- Knowledge in clinical trials, simulation study and R shiny would be appreciated
- Proficient in R programming
- Writing and communication skills

Work environment

Place: Inserm Unit SPHERE 1246 in Tours (37), France.

Duration: 6 months

Beginning: between January and April 2027

Renumeration: The internship will be paid according to the applicable rate.

PhD: Opportunity to continue after the internship with a PhD (funding already available)

Supervisors:

- Floriane Le Vilain--Abraham, Biostatistician, Inserm Unit SPHERE 1246
- Agnès Caille, Biostatistician, Inserm Unit SPHERE 1246
- Virginie Rondeau, Biostatistician, Inserm U1219 Bordeaux Population Health

If you are interested, please apply directly to the following mail:

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Reference

Vilain-Abraham FL, Tavernier E, Dantan E, Desmée S, Caille A. Restricted mean survival time to estimate an intervention effect in a cluster randomized trial. Stat Methods Med Res. Published online August 9, 2023:9622802231192960.

Vilain-Abraham FL, Desmée S, Thompson JA, et al. Restricted mean survival time in cluster randomized trials with a small number of clusters: Improving variance estimation of the intervention effect from the pseudo-values regression. Stat Methods Med Res. 2026;35(2):426-455.