Using Win Ratios as combined endpoints In trials in Oncology

Context

The win ratio (WR) and generalized pairwise comparison (GPC) have recently emerged as innovative methods for analyzing composite endpoints in clinical trials, particularly in oncology. Unlike conventional time-to-event approaches, WR compares patients in pairs across hierarchically ordered outcomes, ensuring that the most clinically meaningful events (e.g., overall survival) are prioritized over secondary outcomes (e.g., quality of life or toxicity). This framework allows for the joint assessment of mortality and non-fatal outcomes, providing a richer picture of treatment benefit or risk.

Such properties are especially attractive in the setting of non-inferiority (NI) trials. In this context, demonstrating that a new therapy is not unacceptably worse than a standard treatment often requires integrating efficacy with safety considerations. For example, in oncology, a treatment with similar survival but reduced toxicity may be judged acceptable through WR or GPC, which explicitly combine these endpoints. In addition, NI trials frequently demand very large sample sizes to ensure sufficient power under conventional statistical methods; a challenge in rare diseases or resource-limited settings.

By leveraging hierarchical comparisons, WR and related methods may increase efficiency and sensitivity, making them promising candidates for oncology trials. Yet, their use in this context remains underexplored, raising important methodological questions about margin definition, sample size, and the handling of ties that deserve systematic investigation.

Objectives of the internship

The student will explore the methodological framework of using the win ratio in oncology trials. The work will involve:

- *Literature review:* Comprehensive synthesis of existing methods for the win ratio, GPC and related statistics in the context of combined frequent oncological endpoints (survival, toxicity, quality of life)
- *Methodological analysis:* Determine suitable settings for the win ratio in oncology trials, including (but not limited to) the handling of ties, the choice between win ratio and win odds, and the adaptation of the

survival margin to the WR/WO scale.

- *Simulation study:* Implement Monte Carlo simulations to assess operating characteristics (type I error, power) of the test and investigate situations where the sample size may be reduced.
- *Practical application:* Application of the WR and GPC to a trial analyzed by the Gustave Roussy statistical team (HYPOG1 non-inferiority trial on hypofractioned radiotherapy in breast cancer) using survival, toxicity and potentially quality of life in the hierarchical endpoint definition

Required skills

- Solid background in biostatistics and survival analysis.
- Knowledge of clinical trial methodology.
- Proficiency in R for simulations.
- Interest in methodological and regulatory aspects of clinical research.

Internship location

Equipe ONCOSTAT (INSERM)
Institut Gustave Roussy
Batiment de Médecine Molléculaire (B2M)
Rue Edouard Vaillant, Villejuif

Internship duration

6 months

To apply

If you are interested, please send an email to sarah.jonas@gustaveroussy.fr or stefan.michiels@gustaveroussy.fr with your CV and cover letter with the "stage2025-WR" as object.

References:

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