Highlighting the Multidimensional Benefits of a Treatment Using Generalized Pairwise Comparisons

#CO30

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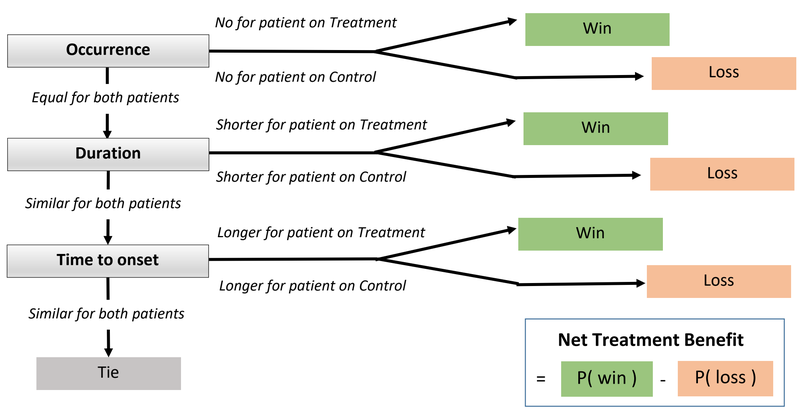
Generalized Pairwise Comparisons (GPC)

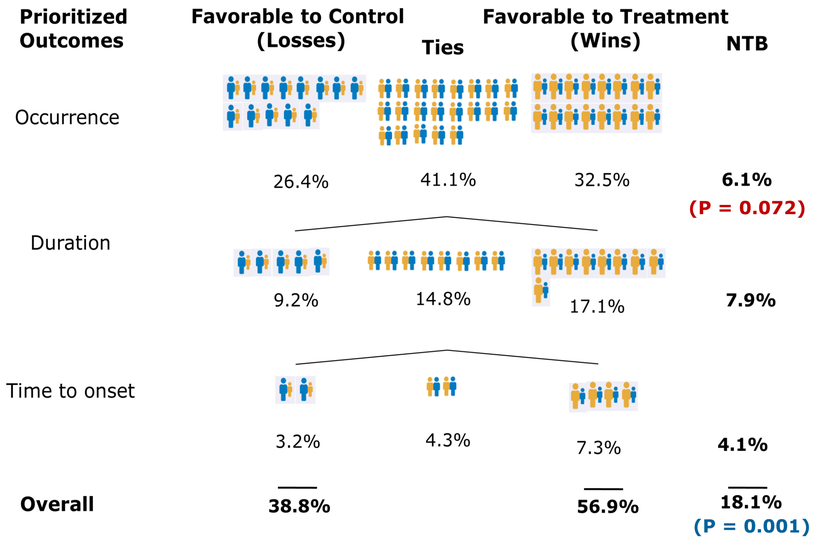
GPC is a statistical method to analyze simultaneously **multiple outcomes** when comparing a treatment group to a control group (*e.g.*, in a randomized trial). The method classifies each possible pair of patients from both groups as a:

- ***Win*** : if patient on Treatment has a ***better*** outcome than patient on Control
- ***Loss*** : if patient on Treatment has a ***worse*** outcome than patient on Control
- ***Tie*** : if patient on Treatment has a ***similar*** outcome as patient on Control

GPC estimates the **Net Treatment Benefit,** which is the net probability $\in[-1,1]$ that a randomly chosen patient on Treatment group has a better outcome than a randomly chosen patient on Control.

The main advantage of the method is that it is possible to **include and prioritize any number of outcomes** from the most important to the least important, by performing pairwise comparisons on outcomes of successively lower priority until the pair can be classified as a win or a loss.





Case Study Background

A randomized phase III clinical trial was conducted to show that a drug could **prevent Severe Adverse Events** (SAEs) from a cancer therapy.

Univariate analyses of the primary endpoint, which focused on the incidence of SAEs, did not take into account the effect of the drug on the duration of these AEs or the time to their onset.

GPC was used to **capture the multidimensional benefit** of the drug, which was expected to reduce the occurrence of SAEs, shorten their duration and delay their time to onset.

Results

The primary GPC analysis on the occurrence of SAEs **did not reach significance** with a Net Treatment Benefit of **6.1%** (**P = 0.072**, 95% CI: -4.9%, 17.1%). Further analyses of the overall effect of the drug in a multivariate GPC led to a **significant Net Treatment Benefit** of **18.5%** (**P = 0.001**, 95% CI: 10.4%, 26.6%).

The data presented here were anonymized for confidentiality reasons, but the case study is real. This drug is currently under review for potential approval by FDA.

Conclusions

GPC can highlight the multidimensional benefits of a treatment, enhancing the **clinical relevance** of the analysis **for clinicians and patients**, and making optimal use of **all** available data.

By analyzing several outcomes in a single analysis, GPC has the potential of increasing statistical power as well as clinical relevance of the analysis.

GPC leads to a **personalized** and more exhaustive **benefit-risk assessment** of new therapies, as all outcomes reflecting benefit from treatment can be combined with all outcomes reflecting harm. The order of priorities can be changed according to individual patient or health care provider preferences.

More information on GPC:

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References :

[1] Buyse M. *Statistics in Medicine* 2010, 29, 3245–57.
[2] Buyse M, Saad ED, Péron J, et al. *Journal of Clinical Epidemiology* 2021, 137, 148-58.