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Improving the Interpretability of Ordinal Endpoints in NMAs

Tim Disher, RN, PhD[1] | [1]EVERSANA®, Burlington, ON, Canada

Introduction

- PASI is a continuous endpoint used in psoriasis trials that is typically reported as number of patients reaching 50/75/90/100% improvement.
- In NMAs, PASI is usually analyzed as an ordinal outcome leveraging the parallel lines or proportional odds assumption.[1]
- While clinicians are familiar with % improvement thresholds, they may be more interested in summaries that not typically reported in trials:
  - The full distribution of PASI % change, mean PASI % change, or median PASI % change.
- We provide proof-of-concept for a unified framework that allows estimation of clinically relevant estimates using any PASI NMA.

Objective

- Provide a framework for generating clinically relevant summaries from NMA estimates of PASI threshold.

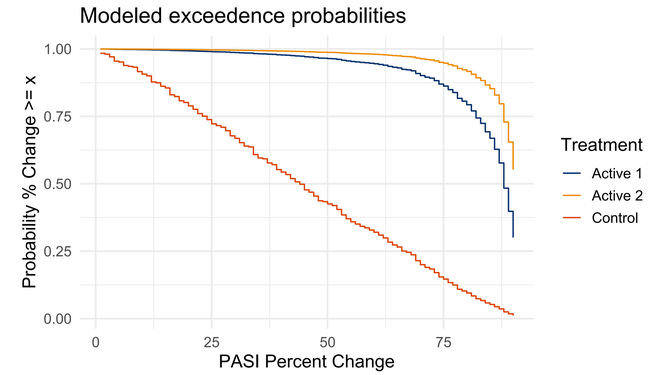
Methods

- We use simulated data to create a distribution of PASI % change that is modeled with a flexible semi-parametric proportional odds model. This is used to represent individual participant data commonly available to sponsors.
- We combine this baseline model with odds ratios output from a proportional odds ITC of PASI 75/90/100 to allow for the generation of the full PASI % change distribution in the population described by the individual participant data.

Results

- Large differences in odds ratios and achievement of PASI 100 between treatments may translate into more modest differences when assessing differences in mean and median % PASI achievement.
- Plots of exceedance probabilities allow exploration of the complete distribution of response which may be relevant for clinical decision-making.

Treatment	Mean % PASI Change	Median % PASI Change	PASI 75	PASI 90	PASI 100
Control	47.5	46	20.6%	5.2%	1%
Active 1	91.0	93	92.2%	70.4%	30.6%
Active 2	96	100	99.0%	88.7%	56.7%



Conclusions

- Combining proportional odds NMAs with a baseline model from available IPD allows for comparison of therapies on versions of PASI which are not commonly reported.
- If combined with a model on absolute PASI, this could be further extended to allow treatment effects from percent change in PASI to be translated to the absolute effect scale.
- Potential deviation from the proportional odds assumption could be explored with linear and spline terms, which can easily be incorporated in a subsequent NMA.
- Future work should assess this approach in an empirical example.

Reference

1. Armstrong, April W., et al. "Comparison of biologics and oral treatments for plaque psoriasis: a meta-analysis." *JAMA dermatology* 156.3 (2020): 258-269.

Disclosures

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