MSR107

Assessment of the Power of ITCs to Detect Minimally Important Treatment Effects in Subsequent Head-to-Head Trials

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Introduction

- NMAs and other anchored ITCs leverage randomization via comparison of relative effects compared to placebo. In most cases, trials included in ITCs are powered to detect large differences compared to placebo.
- Differences between any two active therapies are expected to be smaller, and thus this combined with the increased variance of treatment differences estimated via an anchor may mean that ITCs are under-powered.
- We use a recent Cochrane NMA in Psoriasis to explore the power of ITCs compared to the same comparisons in subsequent head-to-head trials.

Objective

- Assess the ability of estimates from an NMA to detect a difference of the magnitude of those used for sample size calculations in subsequent head-to-head trials.

Methods

- We used PASI 90 data from a recently conducted Cochrane review in Psoriasis[1] to fit a fixed effect meta-analysis on the log odds ratio scale. Data consisted of 12 to 16 weeks, with efforts to harmonize timepoints across studies when possible.
- Clinical trial registries, statistical analysis plans, and publications of open-access head-to-head comparisons were searched for details regarding assumptions used for sample size planning. If a trial listed PASI 90 at 12/16 weeks as the primary or co-primary outcome, the effect sizes used for these calculations were extracted.
- For each head-to-head trial, we conducted an NMA of the publications available on the year that trial was initiated, extracted the standard error of the effect estimate and combined that with the lower and upper ends of the range of odds ratios used for sample size estimation to estimate relevant design characteristics:
  - Power: The probability that a statistically significant claim will be made given the estimate of standard error and true effect estimate.
  - Type-M error: The degree of inflation of the estimated effect to the true value when results are statistically significant.
  - Type-S error: The probability that statistically significant claim is in the wrong direction.

Results

- In most cases, NMAs showed poor to very poor power to detect small (OR = 1.3) or large (OR = 3) effects.
- Comparisons involve therapies with multiple existing trials in the network may have the same or better power as the subsequent head-to-head trials.

Comparison	True OR = 1.6			True OR = 3.1		
	Power	Type-M	Type-S	Power	Type-M	Type-S
adalimumab vs bimekizumab	0.06	7.24	0.18	0.12	3.161	0.03
brodalumab vs ustekinumab	0.06	7.19	0.18	0.12	3.172	0.03
ixekizumab vs etanercept	0.06	7.2	0.18	0.12	3.141	0.03
etanercept vs ustekinumab	0.07	5.46	0.12	0.18	2.434	0
certolizumab vs etanercept	0.08	5.15	0.1	0.19	2.322	0
secukinumab vs guselkumab	0.23	2.06	0	0.82	1.113	0
guselkumab vs ixekizumab	0.23	2.07	0	0.82	1.114	0
secukinumab vs risankizumab	0.52	1.38	0	1	1.001	0
ustekinumab vs secukinumab	0.67	1.22	0	1	1.001	0
ustekinumab vs ixekizumab	0.88	1.07	0	1	0.999	0

Conclusions

Most comparisons in this network were underpowered to detect even large effects, suggesting that point estimates should be interpreted cautiously. In these cases, the lack of significant effects should not be used to claim therapies are “similar” or “no different” and more sophisticated methods should be used if these claims are to be made. In some cases, NMAs provide a similar level of power as subsequent head-to-head studies suggesting that they may be a valuable tool for trial planning or decision making. A simple design analysis may help to guide which comparisons are sufficiently powered for this purpose.

References

1. Sbidian, Emilie, et al. "Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis." *Cochrane Database of Systematic Reviews* 5 (2022).
2. Gelman, Andrew, and John Carlin. "Beyond power calculations: Assessing type S (sign) and type M (magnitude) errors." *Perspectives on Psychological Science* 9.6 (2014): 641-651.

Disclosures

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