From Chronic to Acute Pain: Evaluating the baseline prognostic covariates in Severe Acute Lower Back Pain

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INTRODUCTION

- The FDA's 2023 guidance on baseline covariate adjustment highlights the importance of incorporating prognostic covariates into randomized clinical trials (RCTs) efficacy analyses.
- The variability of the prognostic response contribute to this problem.
- Placebell baseline prognostic covariates were developed for chronic pain indications to integrate baseline factors such as disease severity, psychological traits, and demographics.
- This analysis evaluates the transferability of the Placebell prognostic covariates in Acute Lower Back Pain.

METHOD

- Phase II trial (NCT05096494) on severe acute lower back pain (N = 72).
- Primary Endpoint:
  APS_SPID: Average LBP NPRS Summed Pain Intensity Difference (D1-D7)
- Secondary Endpoint:
  APS_SPID_V5: Average LBP NPRS Summed Pain Intensity Difference (D1-D28)
  CMPS_SPID_V5: Current on movement pain LBP NPRS SPID (D1-D28)
  CRPS_SPID_V5: Current at rest pain LBP NPRS SPID (D1-D28)
  WPS_SPID_V5: Worst pain LBP NPRS SPID (D1-D28)
- The Placebell covariates were build on chronic pain patients to account for the impact of the baseline efficacy, expectations and other psychological traits on the response.

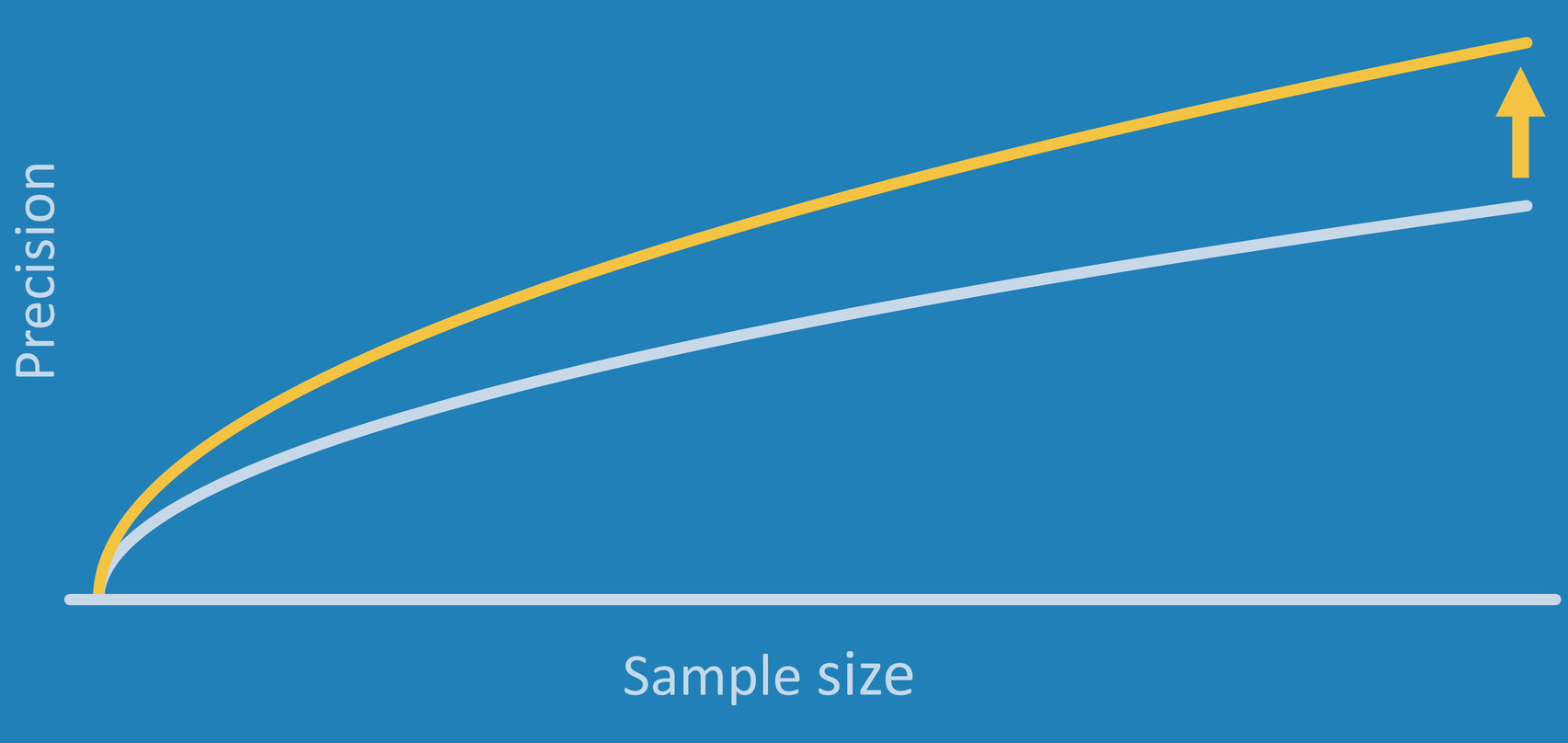
RESULTS

- The Placebell covariates significantly improves the estimation of the treatment effect for the primary and secondary endpoints.
- For the primary endpoint (APS_SPID), using the Placebell covariates increased the precision of the estimated treatment effect by 34.75% ($p<0.001$).
- Having the same precision on the primary endpoint would have required adding 25 patients to the 72 per protocol from the study.
- Furthermore, the Placebell covariates were able to differentiate between Low and High placebo responders.
- No treatment effect was observed across primary and secondary endpoints.

CONCLUSION

- The Placebell chronic pain prognostic covariates were highly prognostic in this acute pain trial on LBP.
- These results confirms the robustness of the Placebell prognostic covariates across pain diseases chronic as well as acute pain.
- By significantly enhancing assay sensitivity, Placebell covariates offer a practical approach to improving precision equivalent to a larger sample size in acute pain RCTs.

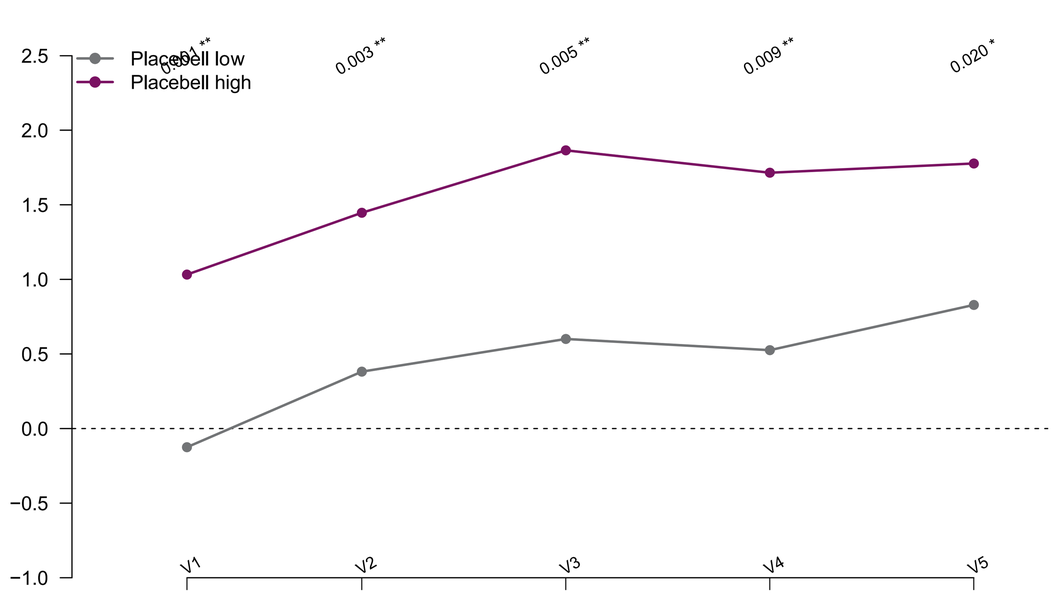
Covariate Adjustment Is Important!



SUPPLEMENTARY MATERIAL

Endpoint	Gain in Precision
APS SPID (D1-D7)	34.8%***
APS SPID (D1-D28)	27.9%**
CMPS SPID (D1-D28)	21.1%**
CRPS SPID (D1-D28)	14.8%*
WPS SPID (D1-D28)	43.1%***

Variance of the Expectations explained by each group of features.
(*: $p<0.05$, **:$p<0.01$, ***:$p<0.001$)



Evolution of APS_SPID for the **Placebell low** and the **Placebell high** in PPP.

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