Improving Precision of Clinical Trials Results in T1 Diabetes with Transferrable Prognostic Models

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BACKGROUND:

- **Assay sensitivity issues in RCTs affect statistical power** and confidence in treatment efficacy
- **Prognostic** response **contribute to this problem**.
- Machine learning models, **combining multiple covariates** into a single prognostic index, **offer a solution**
- This analysis evaluates the **transferability of the composite Placebell model**, previously tested in pain and Parkinson's disease, **to Type 1 Diabetes (T1D) trials**

METHOD:

- The **pre-trained Placebell pain model combines baseline factors** (disease severity, psychological factors, demographics) into a single covariate
- Applied to T1D using data from the **IMPACT study** and its substudy (85 and 24 patients, respectively)
- Used to adjust analysis for four endpoints**: Two C-peptide response measures, Average insulin consumption, HbA1c levels**

RESULTS

- **Improved analysis precision** across endpoints:
  - **C-peptide responses**: Improvement between **2.9% and 52.2%**
  - **Insulin and HbA1c**: Improvement between **1.6% and 20.9%**
- Precision gains can be compared to an **increase in effective sample size**

→ Equivalent to adding up to 44 patients in the main study

CONCLUSION

- The **Placebell model effectively adjusts for contextual effects** in a T1D study
- Demonstrated **strong transferability** from other conditions
- **Enhances assay sensitivity** and precision, making trials more efficient

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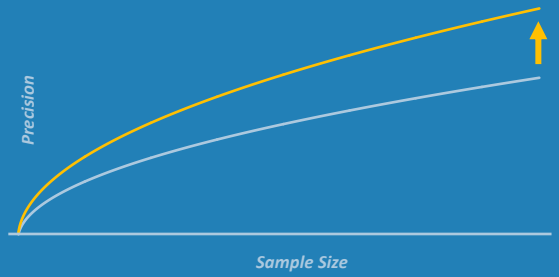
Prognostic factors remain the best solution to increase confidence in Study Results



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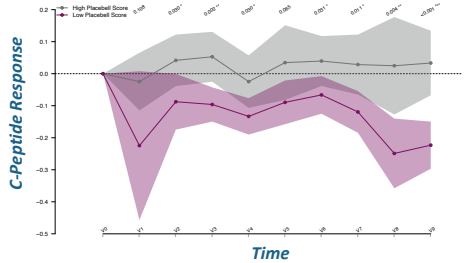
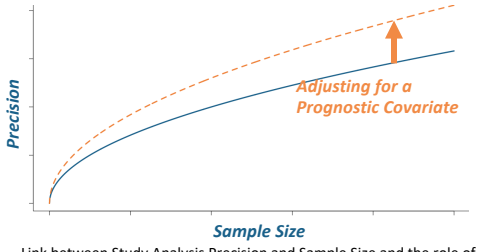
SUPPLEMENTARY MATERIAL

Outcomes	Main Study (N = 85)		Substudy (N = 24)	
	Proportion of Contextual Effects Explained	Gain in Precision/ Effective Sample Size	Proportion of Contextual Effects Explained	Gain in Precision/ Effective Sample Size
C-Peptide Response	34%	+51.5%	13.2%	+15.2%
AUC of C-Peptide Response	2.8%	+2.9%	34.3%	+52.2%
Average Insulin Consumption	17.3%	+20.9%	1.6%	+1.6%
HbA1c levels	10.5%	+11.7%	14.6%	+17.1%

Proportion of Contextual Effects explained by the prognostic model and the associated gain in precision when estimating the true treatment effect. This gain in precision is similar to a gain obtained by increasing the sample size in the same proportion



Comparison of the evolution of the C-Peptide Response in the main study between subjects with high and low Placebell score.



Link between Study Analysis Precision and Sample Size and the role of Prognostic Factors/

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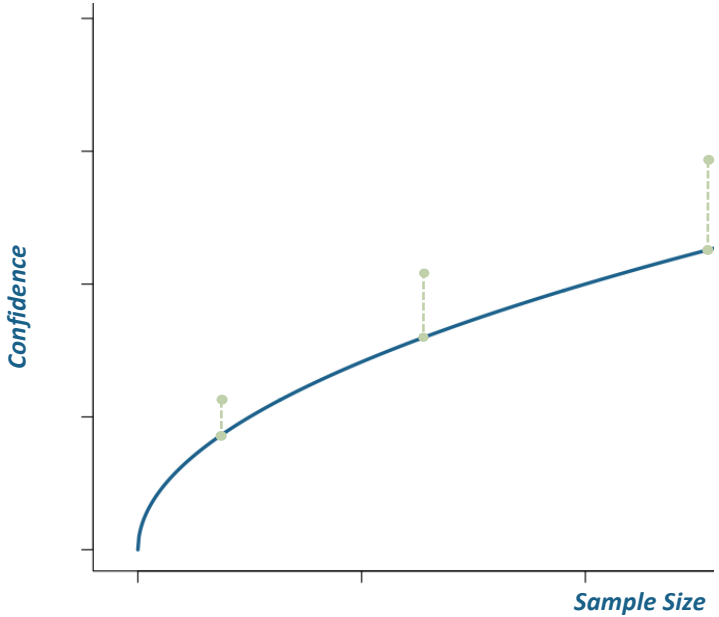
Confidence
Sample Size