PLACEBO RESPONSE MODELLED BY PSYCHOLOGICAL CHARACTERISTICS IN A REMOTE OSTEOARTHRITIS TRIAL

Adjusting for **multiple psychological factors** makes treatment-effect estimates **more accurate**

Purpose
Analyze how baseline clinical and psychological factors contribute to placebo response.
- Modelled from historical data.
- Applied on ATLAS study, an online, double-blind, randomized, placebo-controlled study that assesses the efficacy and safety of an oral supplement combination in people with symptomatic knee osteoarthritis.

Methods
Model subjects' profiles using Cognivia questionnaire data:
- **Expectations**: the degree to which a patient expects improvement in their overall condition;
- **Psychological Profile**: a combination of stable dispositional traits associated with placebo responsiveness;
- **Therapeutic Alliance**: the patient's perception of relationship with study staff, and their overall view of the trial*;
- **Psychological Distress**: the level of a patient's negative psychological state.
- **Health Engagement**: the extent to which a patient actively participates in their own health care.

and classical baseline data (e.g. baseline disease intensity)
- **Disease profile**.

These **baseline covariates** were integrated into ANCOVA models already adjusted for baseline to assess their additional explanatory power.

Results
From **7% to 15% increase of explained variance** (R^2).
Main contributing covariates per endpoint:
- APS: **+14.0% R^2**, Expectations and Psy Distress.
- AQoL-8D: **+15.4% R^2**, Disease Profile and Psy Distress.
- PGA: **+11.4% R^2**, Expectations and Disease Profile.
- PGIC: **+11.1% R^2**, Expectations.
- KOOS Pain: **+7.3% R^2**, Psy Profile and Health Engagement.

Directions of associations with larger placebo response consistent across all endpoints.

* expected to be less relevant in the case of this remote study

Conclusion
- **Significant influence of psychological covariates on placebo response** in ATLAS study.
- Confirmation of important **role of Expectations**.
- Highlighted interest of **jointly adjusting for several psychological covariates to improve the precision** of the estimation of the treatment effect.

➔Leveraging models based on historical data and psychological profiling enhances analytical accuracy and supports more robust trial designs.

Supplementary Material

Endpoint	Disease Profile	Expectations	Psy Profile	Health Engagement	Psy Distress
APS	0.3%	**8.7%**	0.0%	2.0%	**7.9%**
AQOL8D	**10.2%**	0.2%	3.0%	0.7%	3.3%
KOOS PAIN	0.0%	1.7%	3.8%	2.8%	0.9%
PGA	**7.8%**	**7.4%**	0.1%	0.6%	0.6%
PGIC	3.3%	**8.1%**	0.6%	2.4%	3.0%

Type II ANOVA R^2 of individual covariates.

Relevant abbreviations and definitions
- **APS**: Average Pain Score
- **MPsQ**: Multidimensional Participant-specific Questionnaire.
- **PGA**: Patient Global Assessment.
- **PGIC**: Patient Global Impression of Change.
- **R-squared (R^2)**: proportion of variance explained by covariates in patient-reported outcomes.

www.cognivia.com
+32 71 14 02 00
info@cognivia.com

Jérôme Paul[1], Samuel Branders[1], Simone Collins[2], Karen Bracken[2], Nicolas Xaborov[1], Frédéric Clermont[1], Alvaro Pereira[1], David Hunter[2]

1. Tools4Patient S.A. d.b.a Cognivia, Mont-Saint-Guibert, Walloon Region, Belgium.
2. The University of Sydney School of Medicine, Sydney, NSW, Australia.

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