ENRICHMENT BASED ON SPEECH LATENCY ENHANCES

TREATMENT EFFECTS IN A PHASE III STUDY OF BRILAROXAZINE.

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Key Findings

- Automated measurement of speech latency corresponds to clinically rated negative symptoms.
- Excluding the ~40% of individuals with normal speech latencies dramatically increases treatment effect size.
- Speech latency is a promising enrichment tool for CNS clinical trials.



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References

Siegel, J. S., Cohen, A. S., Szabo, S. T., Tomioka, S., Opler, M., Kirkpatrick, B., & Hopkins, S. (2024). Enrichment using speech latencies improves treatment effect size in a clinical trial of bipolar depression. Psychiatry Research, 116105.

Introduction

Speech latency, a measure of verbal response times, is an objective marker of cognitive, social, and motivational factors that can be assayed directly from psychiatric interviews.

We recently used speech latency to enrich participants for an antidepressant clinical trial (Siegel, Cohen, 2024), resulting in nearly double the drug-placebo effects at half the sample size.

Here we evaluate speech latencies in a clinical trial of schizophrenia.

What is a Speech Latency?

Q: How have you been doing lately?

A: Turn Latency Ok, I don't have much going on, so...

We applied a correction to account for cross-cultural variability.

Methods

Audio recordings from psychiatric interviews in a Phase 3 trial of brilaroxazine were evaluated (k = 2590 recordings for 408 participants from three countries representing eight languages).

Predicted PANSS Marder factor scores were modeled based on turn latency for post-randomization sessions and applied to the screening data for classifying individuals:

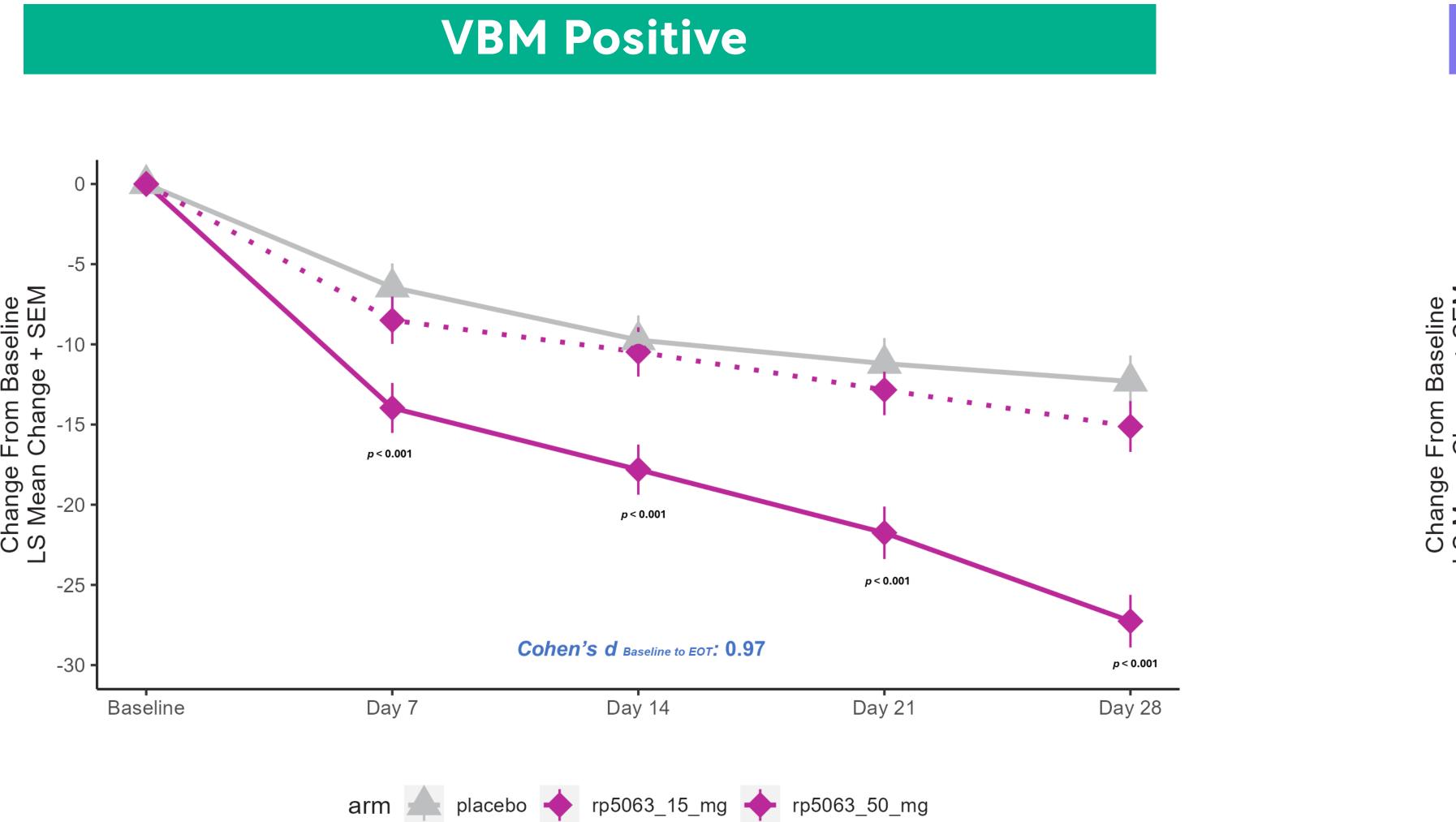
- Vocal Biomarker Positive (VBM Pos): slow latency; predicted
 Marder item average score 4+
- Vocal Biomarker Negative (VBM Neg): Fast latency; predicted
 Marder item average score 2 or below

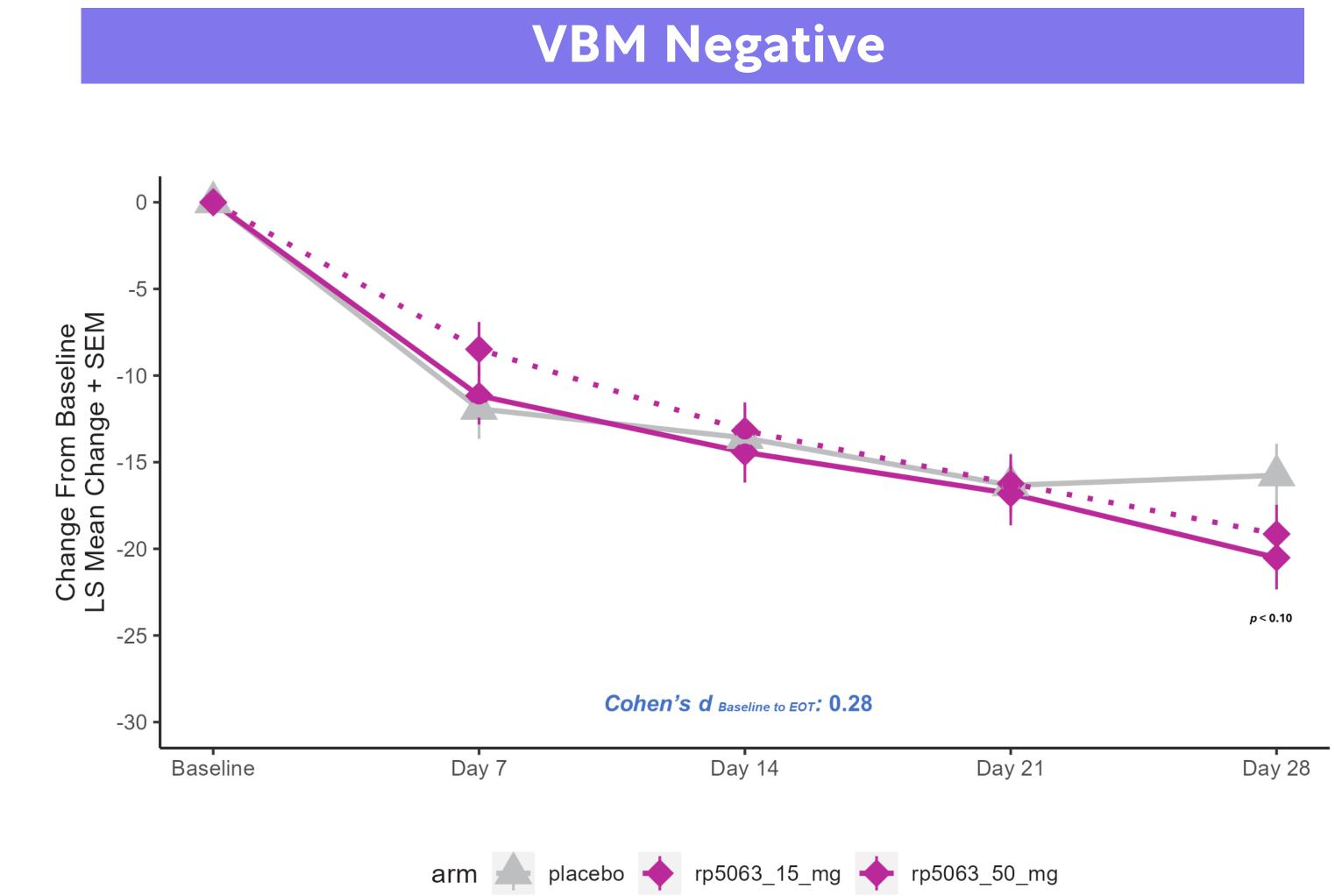
Analyses:

We evaluated treatment x time effects for VBM Pos and VBM Neg patients, in:

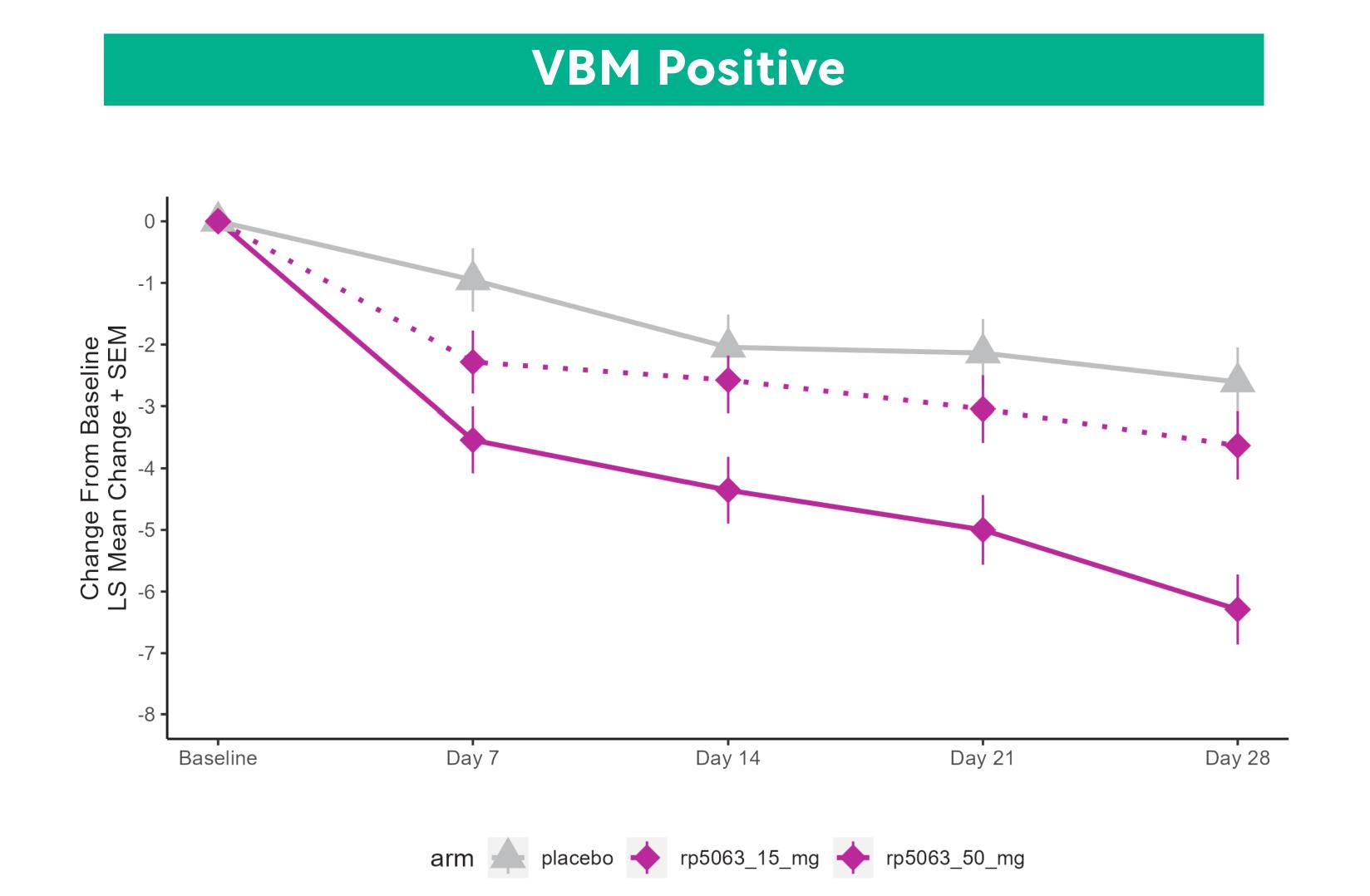
- PANSS Total scores
- PANSS Marder factor scores
- ·Clinical Global Impairseint
- Personal and Social Performance Scale

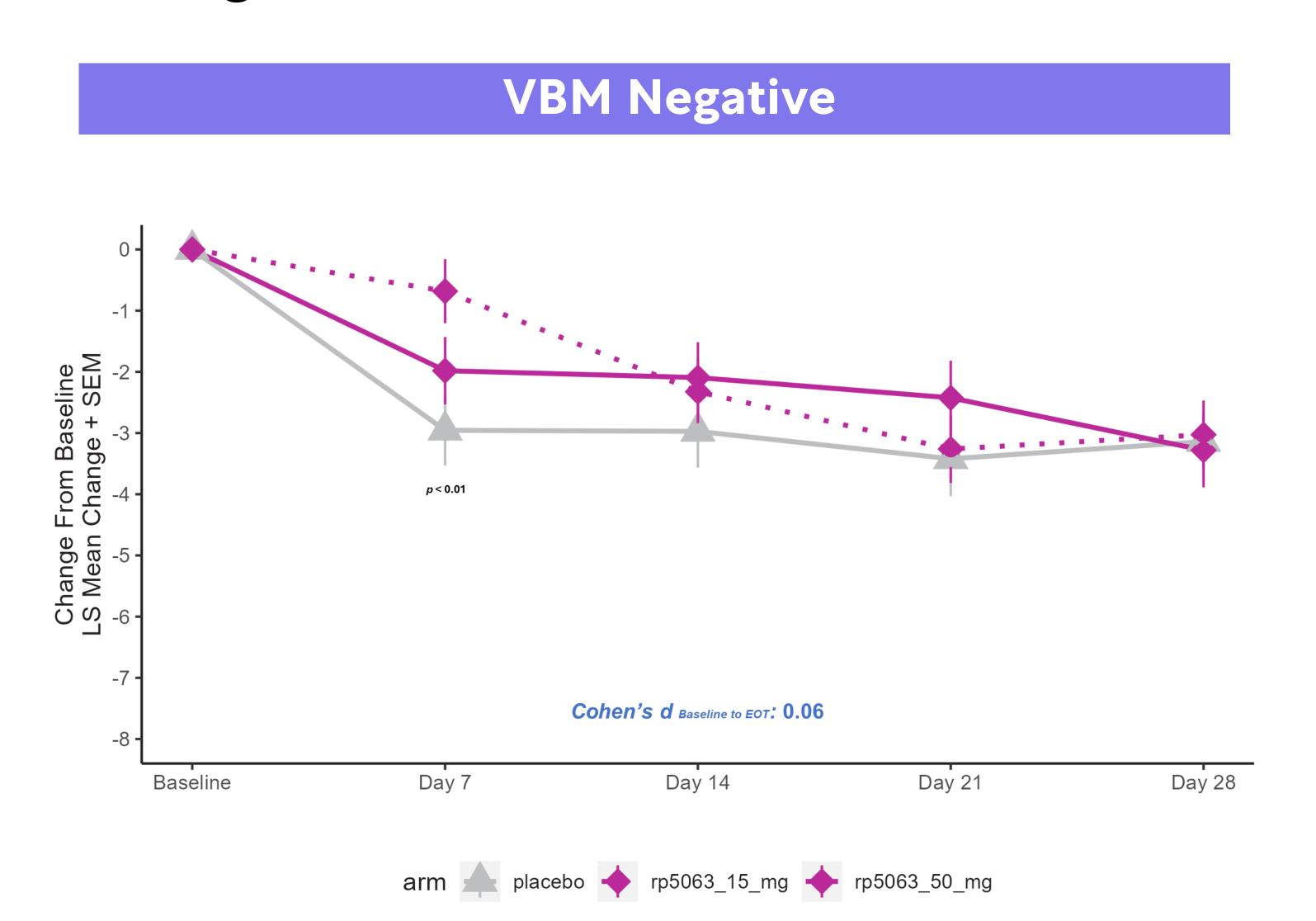
The VBM Pos Group shows fast, significant reduction in PANSS Total scores



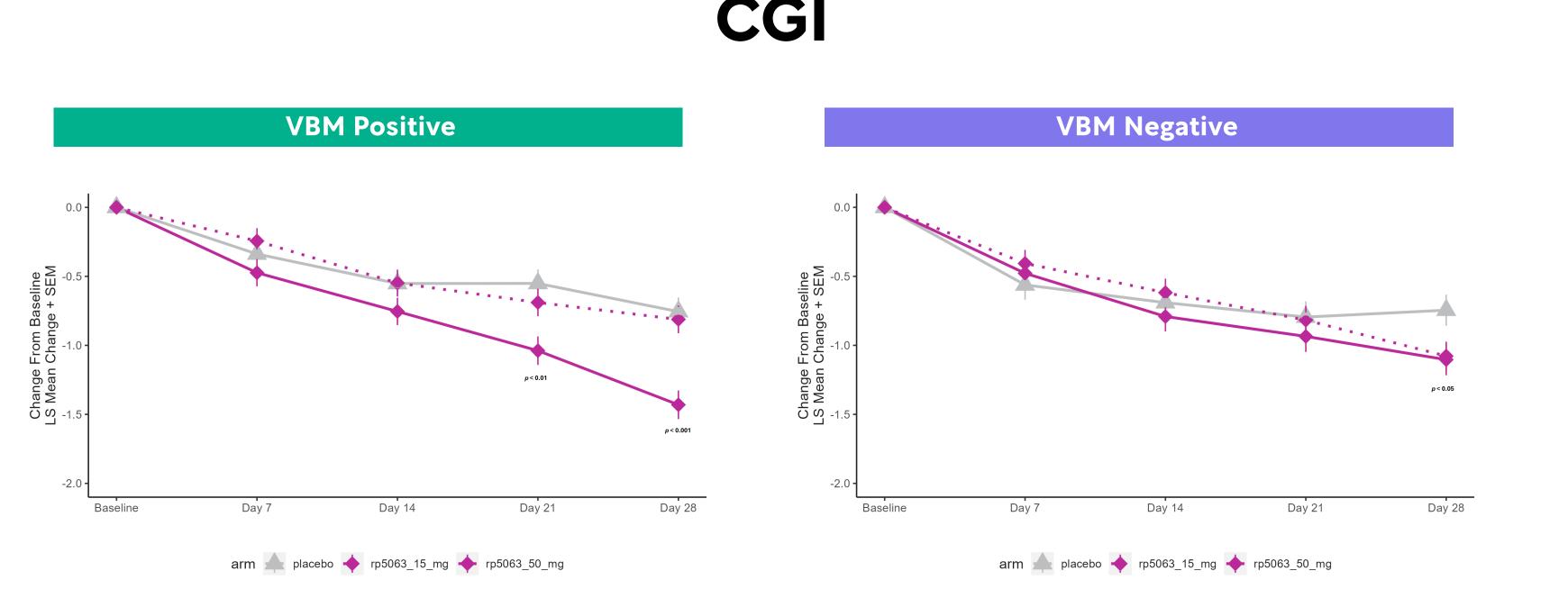


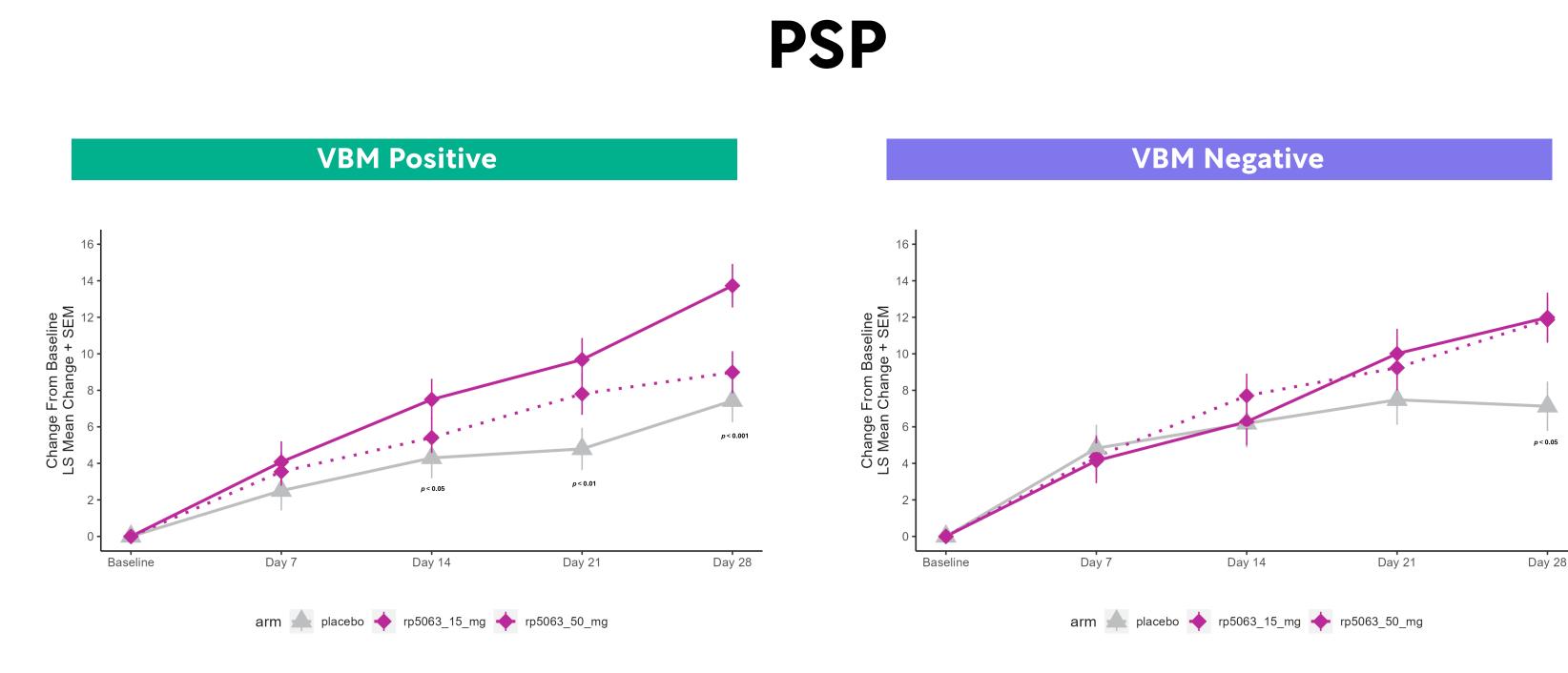
The VBM Pos Group shows fast, significant reduction in Marder Negative Factor scores





The VBM Pos Group shows similar improvement in PANSS Positive & Disorganization symptoms. And improved functioning in:





Who are the VMB Pos people?

229 people were VBM Positive based on their screening session speech.

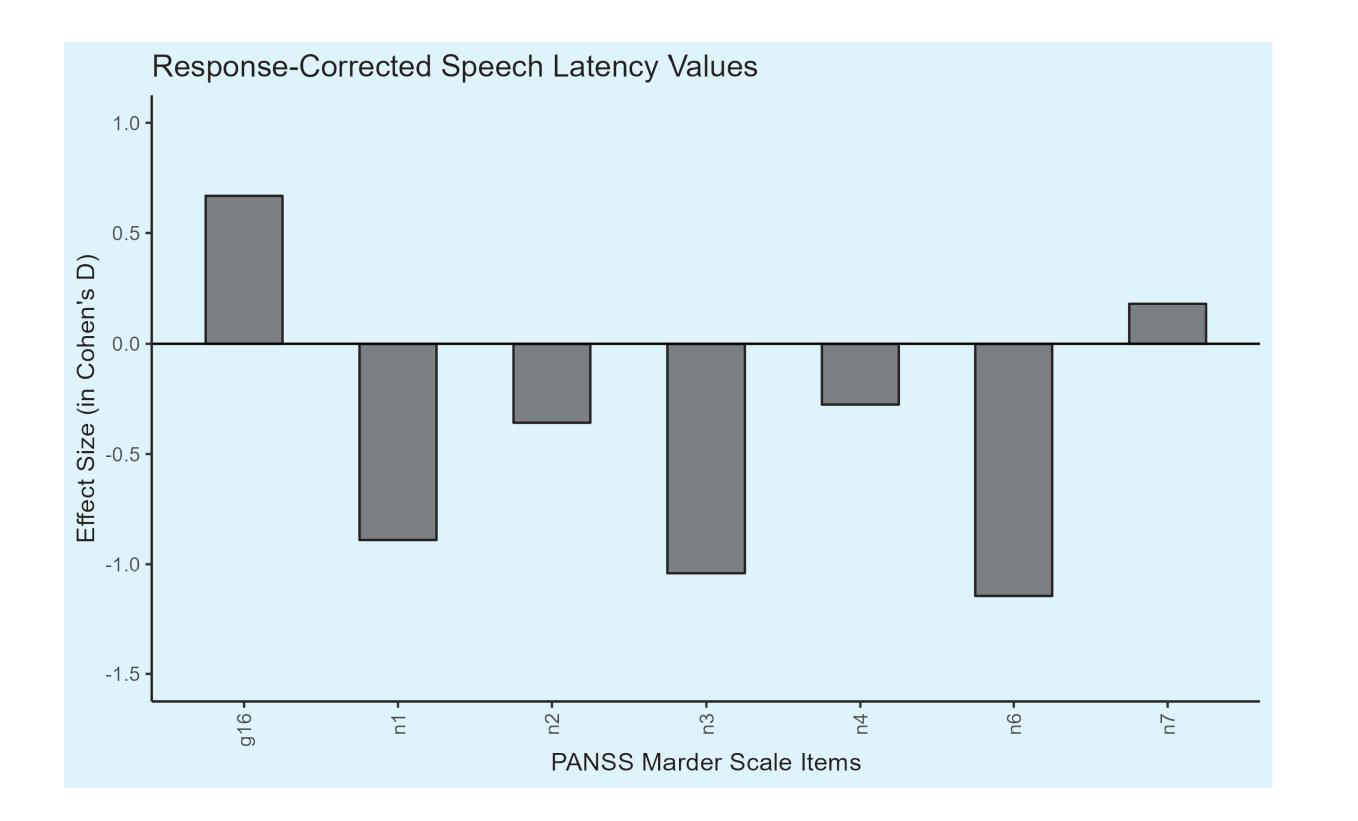
179 people were identified as VBM Negative.

VBM Positive people were younger (37 \pm 10 versus 41 \pm 11; F - 15.67, p < 0.004), but didn't differ in sex or treatment assignment.

VBM Positive people had:

- More severe negative symptoms at baseline (F = 29.43, p < 0.001, d = 0.94).
- •Slightly less severe positive and anxiety-depression symptoms at baseline (F's = 12.33 & 3.86, p's < 0.001 & < 0.05, d's = 0.40 & 0.11).

VBM Positive people showed a distinct signature in negative symptoms at baseline, characterized by more severe blunted affect, emotional withdrawal, poor rapport and alogia.



During screening, VBM Positive people took 500ms longer to respond than VBM Negative people (1.5 sec. versus 1 sec; F = 42.79, p < 0.001).

During their screening interviews, VBM Positive people talked much less, at a slower pace, and had shorter interviews with fewer turns.

VBM Positive people showed difficulty engaging in the clinical interview.