Placebo Response Propensity Scale (PRPS) Scores and Probability of Placebo Response by Disease Severity

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Background

- Placebo (PBO) response can make the demonstration of efficacy difficult. An assessment administered at screening can serve as a measure of potential PBO response providing important information when assessing the true therapeutic impact of a novel treatment.
- The Placebo Response Probability Scale (PRPS) is a measure of the propensity for PBO response that can be used to retrospectively assess or prospectively to minimize PBO response increasing confidence in the therapeutic value of compounds in development.
- Previous studies have demonstrated the ability of the initial version of the PRPS to identify PBO responders.[1]

Objectives

- Using established PRPS thresholds identify the proportion of potential PBO responders by disease severity.
- Identify individual items most predictive of PBO response within the PRPS.

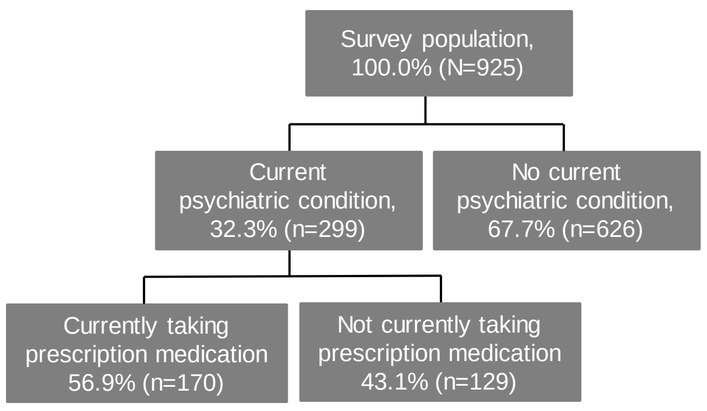
Methods

- A 2021 cross-sectional health survey of United States (US) adults was carried out.
- Participants, ≥18 years old, were recruited using a random stratified sampling framework.
- Participants completed a depression screener (PHQ9[2]), an anxiety screener (GAD7[3]), and self-reported current psychiatric conditions.
- Participants currently taking an Rx for their psychiatric condition also completed the PRPS.
- The proportion of likely PBO responders by severity of depression and anxiety is summarized using descriptive statistics.
- The NetraAI Artificial Intelligence (AI) identified groups of items within disease severity clusters most likely to predict PBO response.[4,5,6]

Results

- 925 participants completed the survey (response rate: 83.9%).
- 32.3% (n=299) participants reported having a psychiatric condition and of those, 56.9% (n=170) reported currently taking a medication. (Figure 1)

Figure 1. Study Populations



- Most participants who reported a psychiatric condition (n=299) were male (58.9%), White (90.3%), with a mean age of 41.35 years. (Table 1)
- Most participants who reported a psychiatric condition and currently taking a prescription medication (n=170) were male (49.4%), White (92.9%), with a mean age of 45.03 years. (Table 1)

Table 1. Participant Characteristics

	Current psychiatric condition n=299	Current psychiatric condition and taking a prescription medication n=170
Gender		
Male	58.9%	49.4%
Mean age		
Age, mean (SD)	41.35 (14.04)	45.03 (14.87)
Ethnicity		
African American or Black	4.0%	2.9%
White	90.3%	92.9%
Other	5.7%	4.1%
Region		
Northeast	12.7%	14.7%
Midwest	12.0%	15.9%
South	45.5%	42.9%
West	29.8%	26.5%
Charlson Comorbidity Index[7,8] (CCI) score		
CCI score, mean (SD)	0.53 (1.02)	0.66 (1.18)
Body mass index (BMI, lbs./in^2)		
BMI, mean (SD)	27.81 (7.34)	29.11 (7.80)
Median household income (Census data derived from zip code)		
Income, mean (SD)	67,875 (28,447)	66,756 (26,374)
Education		
More than high school	76.9%	78.2%
Employed		
≥ 32 hours per week	41.1%	36.5%

Results

Probability of Placebo Response Decreases as Disease Severity Increases

Green – lower probability of being a PBO responder

Red – higher probability of being a PBO responder

Figure 2. No/Minimal Depression (PHQ-9 score, 0-4)

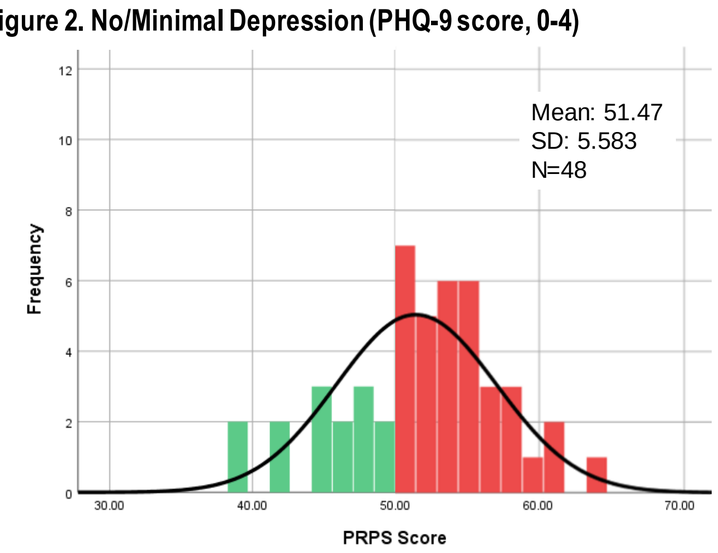
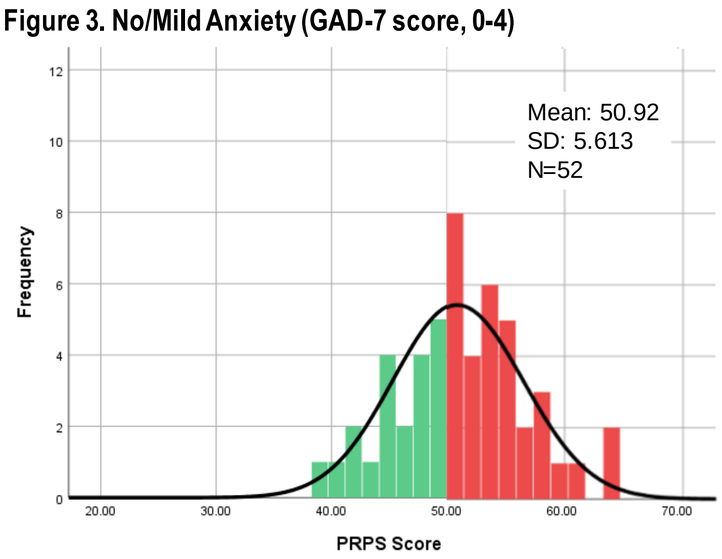


Figure 3. No/Mild Anxiety (GAD-7 score, 0-4)



Highest Probability of PBO Response with the lowest disease severity

Figure 4. Mild/Moderate Depression (PHQ-9 score, 5-14)

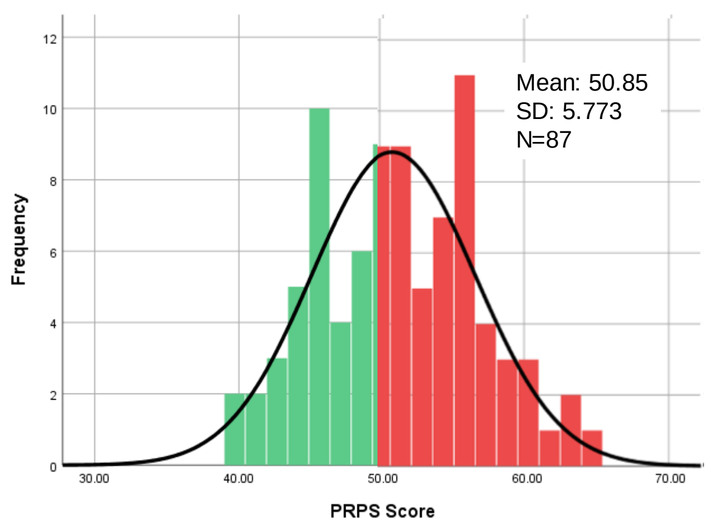


Figure 5. Moderate/Moderately Severe Anxiety (GAD-7 score, 5 to 14)

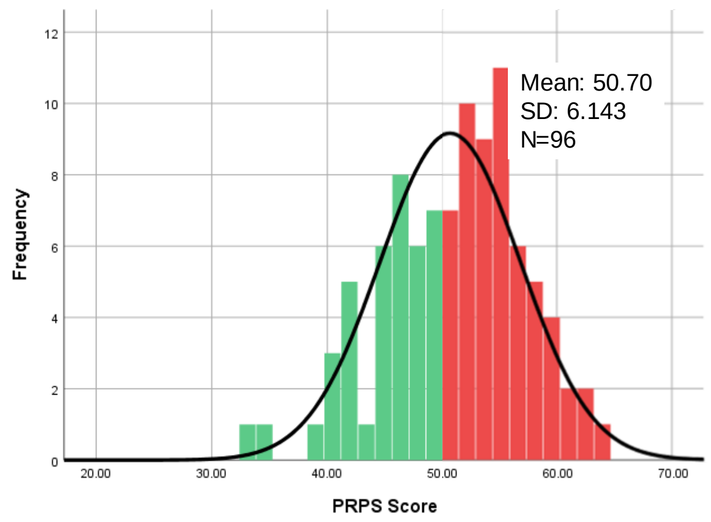


Figure 6. Moderately Severe/Severe Depression (PHQ-9 score ≥ 15)

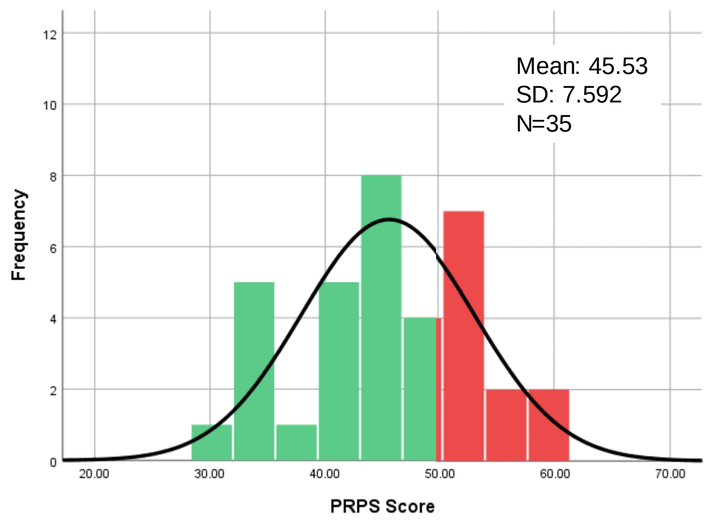
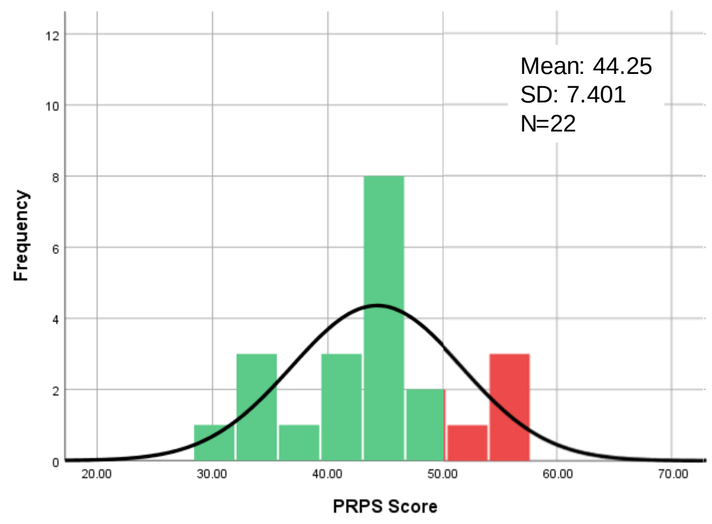


Figure 7. Severe Anxiety (GAD-7 score ≥ 15)



Lowest Probability of PBO Response with the highest disease severity

Artificial Intelligence

- NetraPharma's machine intelligence platform was employed to view patient populations from multiple perspectives using a fusion of random matrix theory, contraction mappings, reinforcement learning and other methods, which allowed us to merge insights from several different machine learning algorithms. The particular algorithm utilized here is called NetraAI and it was designed to work with complex patient populations where precise labels are impossible, such as in placebo response. The unique specialized mathematical methods allow the algorithm to create hypotheses that transcend the labels. Smaller samples sizes are optimized by NetraAI, as well. The approach identified 3 items as most predictive of having a PRPS score above 50: time with the condition; expectations about medications controlling symptoms and the belief they were taking an active medication.

Limitations

- The PRPS was developed and validated for use in a generalized anxiety trial and the concepts identified as well as threshold scores may be different for depression and other psychiatric conditions.
- The small sample size of self-reported data may limit generalizability.

Conclusion/Discussion

The PRPS was able to identify a greater proportion of potential PBO responder in those with lower levels of disease severity. Although PBO response is likely to decrease with higher levels of disease severity required for trial entry, a significant number of potential PBO responders exist even in those with highest disease severity. Including measures of potential PBO response within trials allows assessment of results with and without those with a high propensity for PBO response allowing for more confidence when trying to establish a true signal of efficacy,

Conflicts of Interest

NetraMark Corp holds the IP for the NetraAI technology and YourCareChoice holds the copyright for the PRPS.

References

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