

# Association of Single-Nucleotide Polymorphisms of C-Reactive Protein Gene with C-Reactive Protein Blood Levels and Outcomes in Treatment-Resistant Bipolar Depression Treated with Escitalopram and Celecoxib

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## BACKGROUND

- Inflammatory biomarkers are reportedly elevated in bipolar depression; anti-inflammatory combination therapy may enhance response to treatment and reverse treatment resistance.<sup>1,2</sup>
- This study investigated the impact of polymorphisms within the C-reactive protein (CRP) gene on CRP blood levels, Hamilton Depression Rating Scale, 17-item (HAMD-17) scores, and Perceived Stress Scale (PSS-14) score in treatment-resistant bipolar depressed (TRBDD) patients receiving celecoxib and escitalopram relative to those receiving escitalopram and placebo.

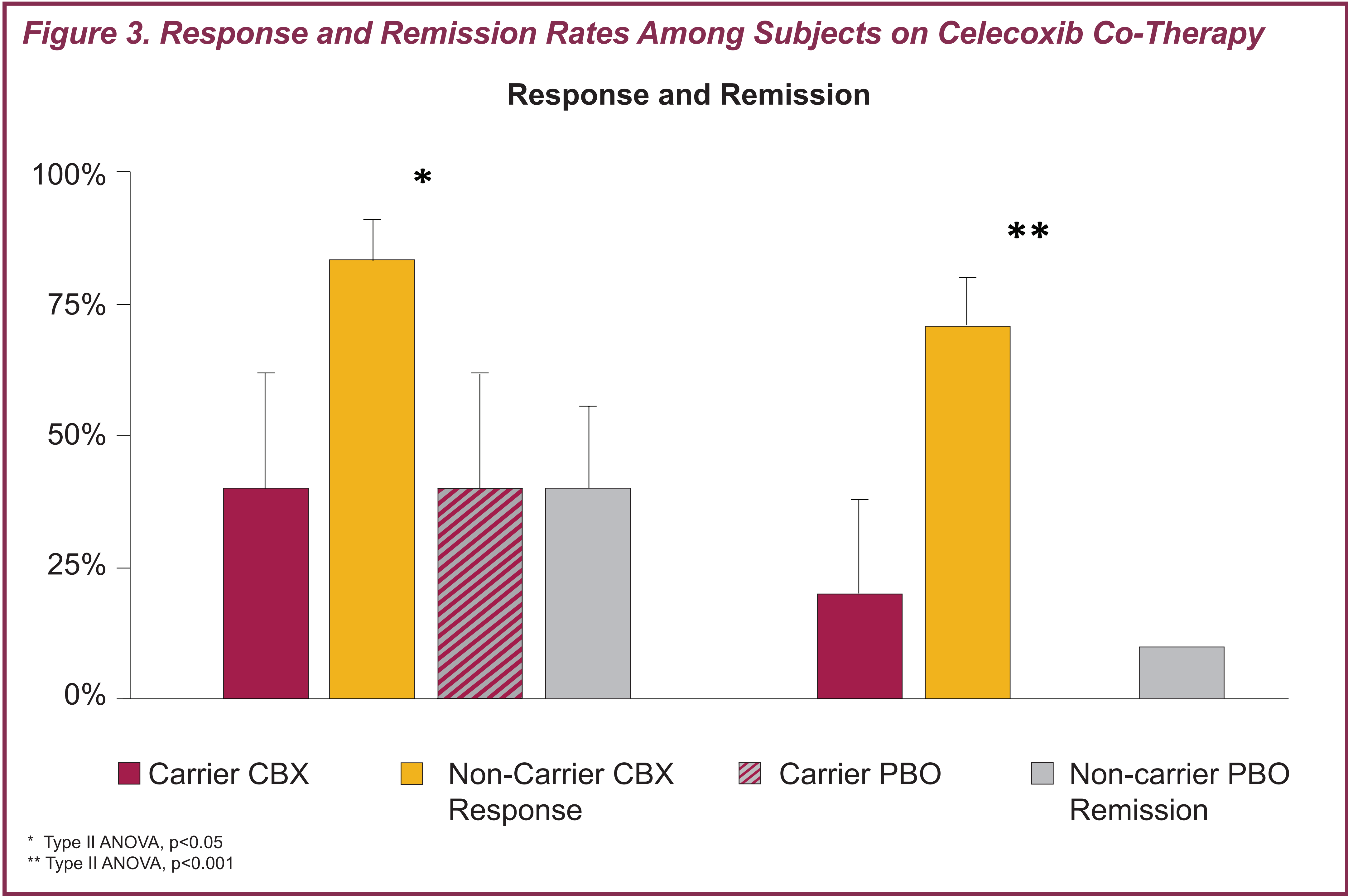
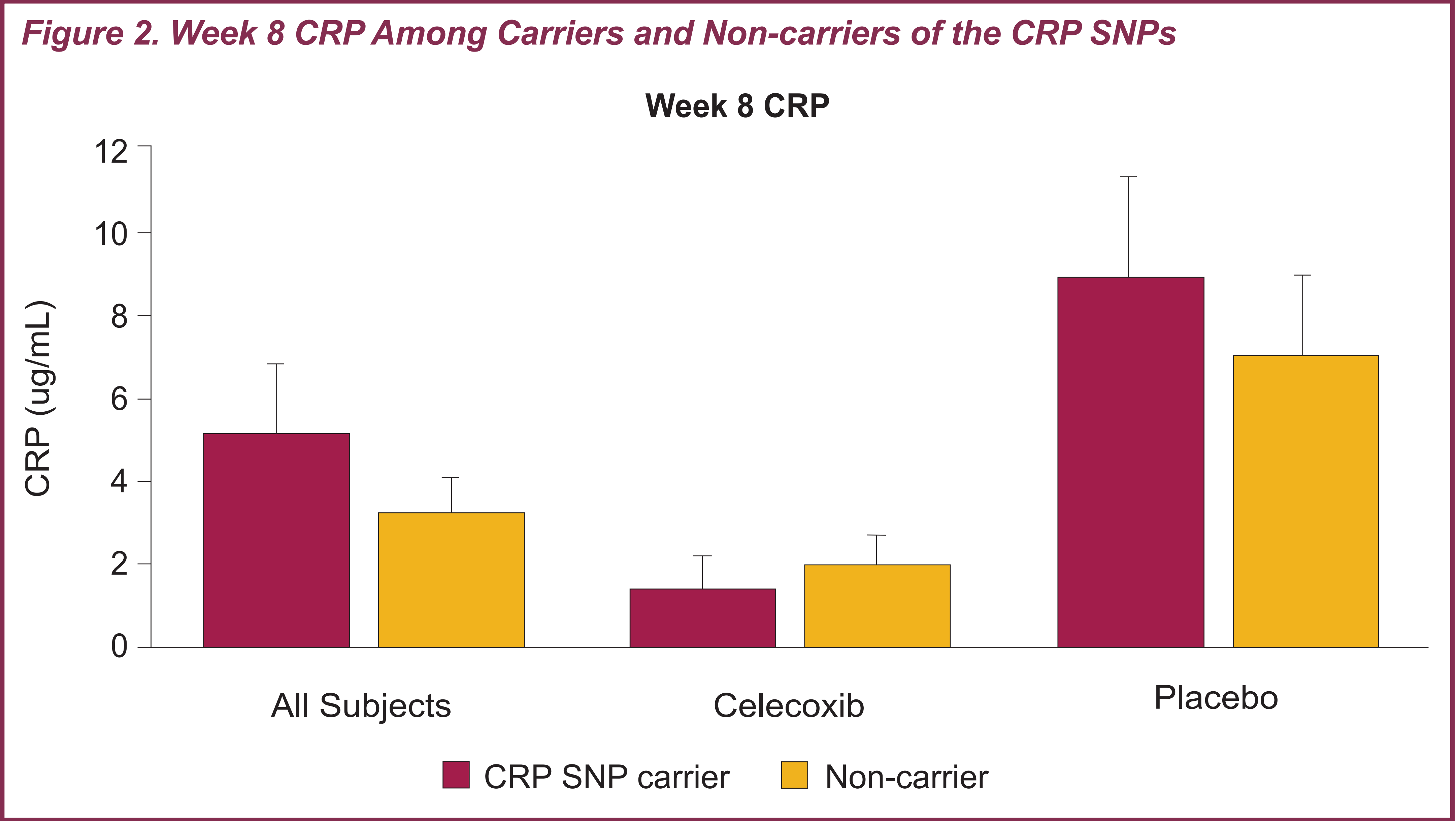
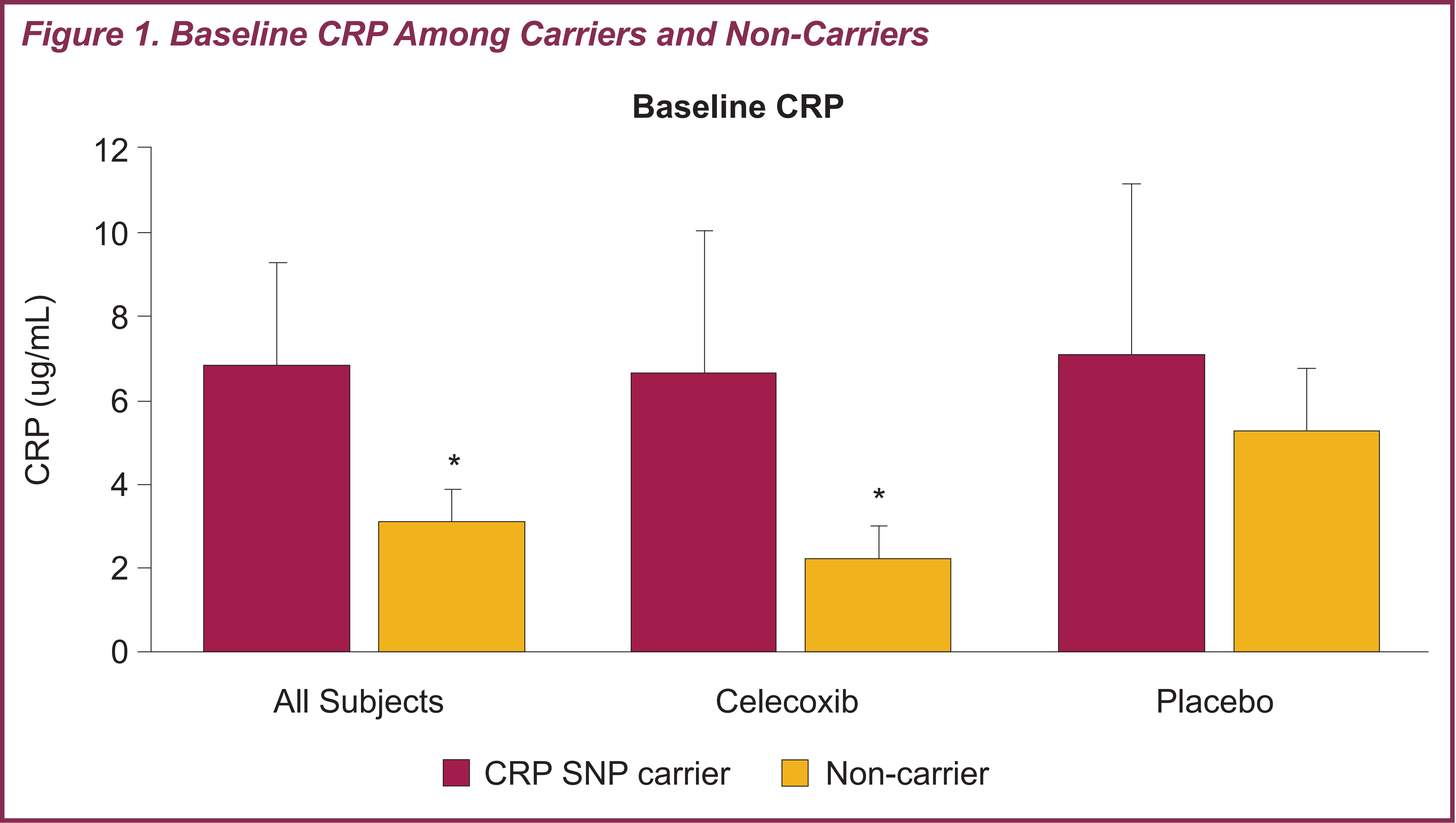
## METHODS

- 43 patients (baseline HAMD-17  $\geq 18$ ) were randomized to a treatment arm and received combination therapy or escitalopram and placebo for 8 weeks.
- Baseline and week 8 CRP blood levels were collected. Rating scales were administered at baseline and weeks 1, 2, 4, and 8.
- Response was defined as  $\geq 50\%$  reduction in HAMD-17 from baseline to week 8. Remission was defined as week 8 HAMD-17 score  $< 7$ .

## RESULTS

- CRP single nucleotide polymorphism (SNPs), rs3093077 and rs3093059, were in complete linkage disequilibrium, with 5 carriers in each treatment arm.
- Figure 1 shows the baseline CRP blood levels in all subjects, those receiving celecoxib, and those receiving placebo split by CRP SNP carrier status.

- Among all patients, non-carriers had significantly lower baseline CRP blood levels ( $p < 0.05$ ).
- Analysis of variance revealed significant variation across subjects categorized by carrier-status and treatment arm for response ( $p = 0.04$ ), remission ( $p = 0.0005$ ), and PSS-14 scores ( $p = 0.03$ ).
- Non-carriers receiving celecoxib had the highest rates of response and remission, and the lowest PSS-14 scores.
- Figure 2 shows the week-8 CRP blood levels in all subjects, those receiving celecoxib, and those receiving placebo split by CRP SNP carrier status.
- Figure 3 shows the rates of HAM-D17 response and remission in subjects receiving celecoxib or placebo split by CRP SNP carrier status.



## CONCLUSIONS

- Non-carriers of the CRP SNPs had significantly lower pre-treatment CRP levels, and those receiving celecoxib showed the greatest antidepressant response.
- Carriers did not see significantly improved antidepressant response with celecoxib co-administration, despite reductions in CRP levels, indicating that week-8 CRP levels are not predictive of week-8 antidepressant outcomes.
- Non-carriers of the CRP SNPs may benefit most from celecoxib combination therapy in TRBDD.

**REFERENCES:** 1. Edberg, D. et al., *J Psych Res.* 2018. 102, 1-7    2. Halaris, A. et al., *J Affect Disord.* 2020. 261, 145-152