Data Supplement for Simpson et al., Double-Blind Randomized Clinical Trial of Prazosin for Alcohol Use Disorder. Am J Psychiatry (doi: 10.1176/appi.ajp.2018.17080913)

Sensitivity Analyses, Secondary Outcome, and Exploratory Analyses

Sensitivity analyses

1) Using all randomized participants (44 placebo, 48 prazosin) and visit data yielded results similar to the primary analyses for number of drinking days per week and number of heavy drinking days per week, but for number of drinks per week the interaction between condition and week was no longer significant (χ^2=2.54, df=1, p=0.11).

2) Using data for the period after titration was reached and including only subjects who attended at least 70% of visits and for whom the riboflavin trace was present in urine (25 placebo, 20 prazosin) yielded results similar to the primary analyses, except the result for heavy drinking was more pronounced: the odds of heavy drinking for placebo participants were 0.95 (95% CI=0.89, 0.10) times the odds of heavy drinking the previous week, whereas the odds of heavy drinking for prazosin participants were only 0.80 (95% CI=0.73, 0.86) times the odds of heavy drinking the previous week.

3) When we used random-slope models for the 80 participants (40 placebo, 40 prazosin) who completed titration, none of the condition by week interactions was significant (χ^2=0.5; df=1, p=0.81; χ^2=0.73, df =1, p=0.39; χ^2=1.30, df=1, p=0.25; for number of drinks per week, number of drinking days per week, and number of heavy drinking days per week, respectively). Figure

S3 shows individual trajectories and adjusted marginal means by condition and week for each of the primary outcomes, based on the both fixed- and random-slope models.

4) When we used only data from the last week for which interactive voice response system data were reported for the 80 participants (40 placebo, 40 prazosin) who completed titration, the probability of drinking was higher for prazosin participants than placebo participants (0.31, 95% CI=0.24, 0.40 versus 0.24, 95% CI=0.17, 0.32), although this difference was not significant (χ^2=3.49, df=1, p=0.06). The probability of heavy drinking was significantly smaller for prazosin participants than placebo participants (0.07, 95% CI=0.04, 0.12 versus 0.12, 95% CI=0.07, 0.20; test for difference, χ^2=5.98, df=1, p=0.01). There was no difference in the total number of drinks for prazosin versus placebo participants (6.8, 95% CI=3.1, 15.3 versus 6.3, 95% CI=2.8, 14.6).

Secondary outcome

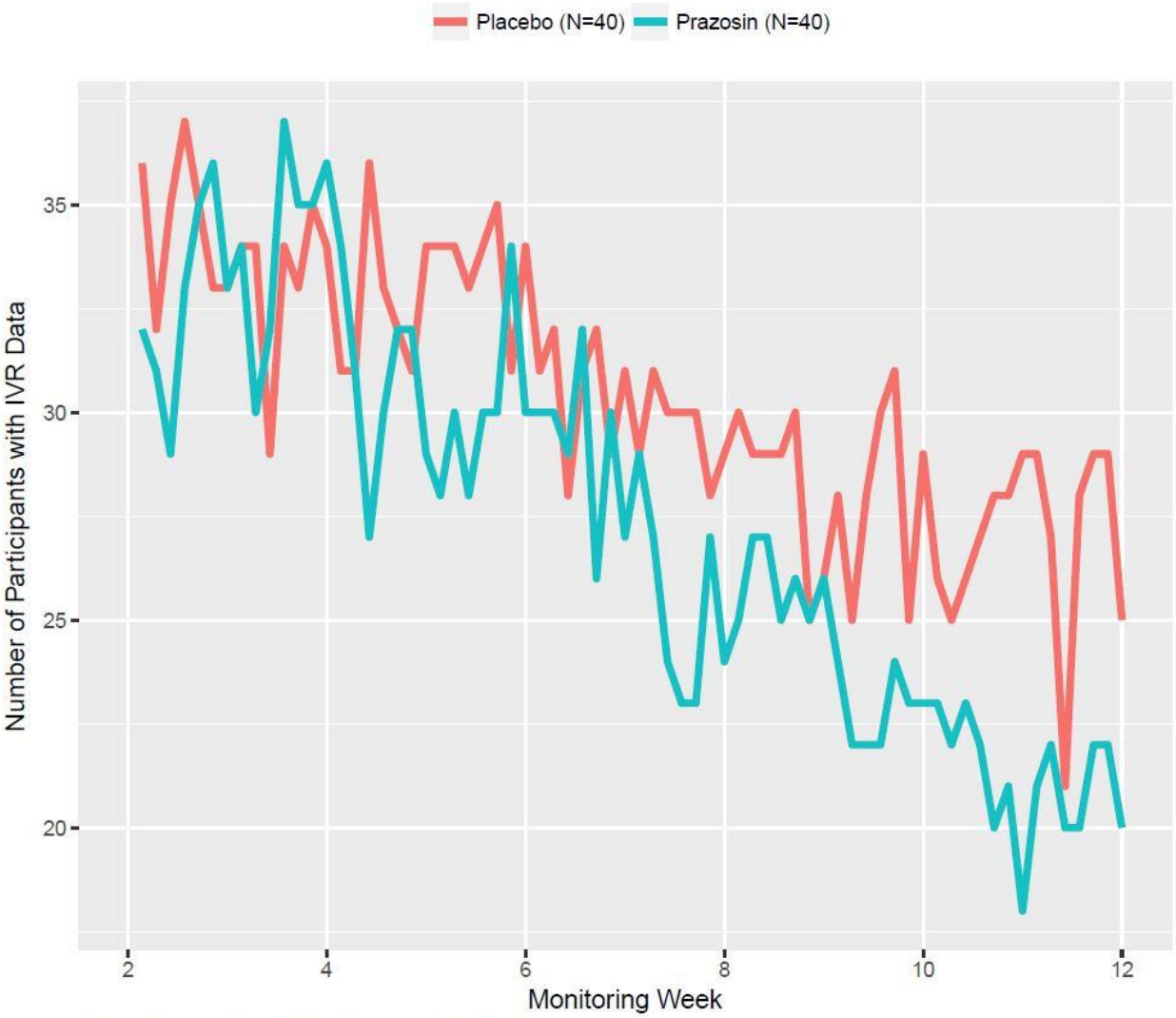
Average craving decreased from week 3 to week 12 for both conditions (fixed-slope model: –0.61, 95% CI=–0.79, –0.44; random-slope model: –0.57, 95% CI=–0.86, –0.28), but there was no difference between conditions in change in craving over time (fixed-slope model: χ^2=0.27, df=1, p=0.60; random-slope model: χ^2=0.21, df=1, p=0.65).

Exploratory analyses

SBP decreased in prazosin participants across the 12-week treatment period by 3.5 mmHg (95% CI=–0.3, 7.4) but increased in placebo participants by 3.1 mmHg (95% CI=–0.5, 6.7) with differences in the 12-week change in SBP by condition of 6.6 mmHg (95% CI=1.4, 11.9, condition-by-week interaction χ^2=6.1, df=1, p=0.01). Similar results were found for the random-

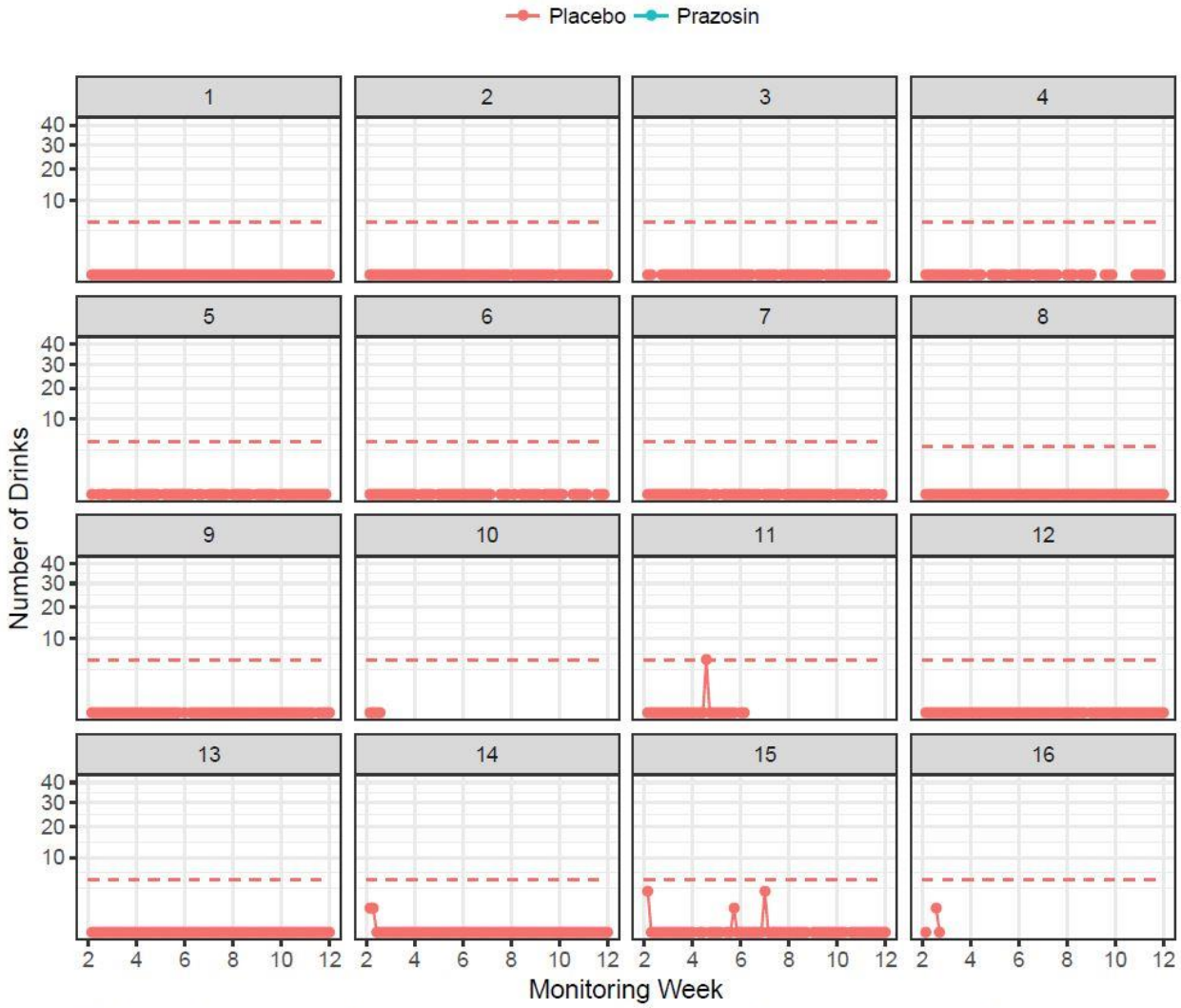
slope models (condition-by-week interaction p=0.04). There was no significant change in DBP for either group (p>0.11) and there was no significant difference in the DBP change by condition for either the fixed- or random-slope models (p>0.26). Neither SBP nor DBP was a significant effect modifier in the difference in improvement in total drinks or heavy drinking days by condition (three-way BP by condition by week interactions p values all >0.26, both fixed- and random-slope models).

Figure S1. Number of Participants with IVR Data by Monitoring Week and Condition, from the End of the Titration Period to the End of the 12−Week Intervention*



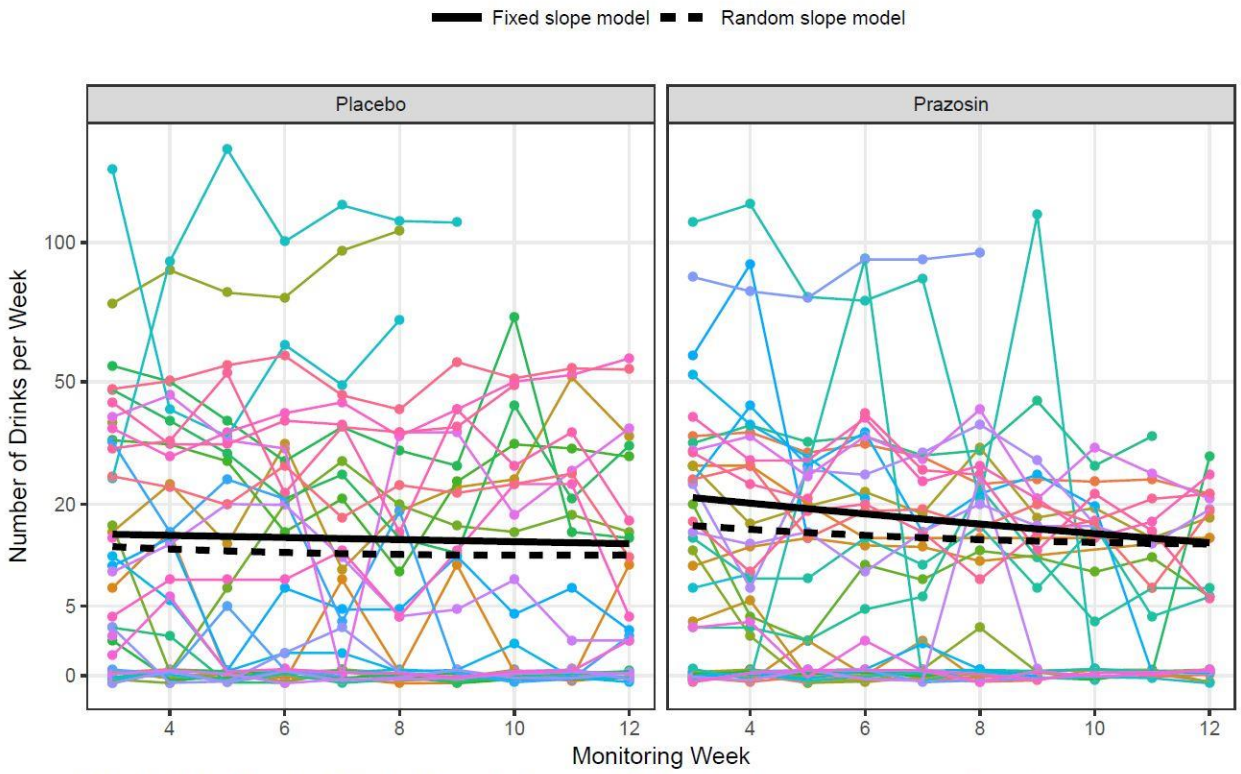
*Based on participants who completed titration.

Figure S2. Total Number of Reported Drinks by Monitoring Week and Participant, from the End of the Titration Period to the End of the 12−Week Intervention*



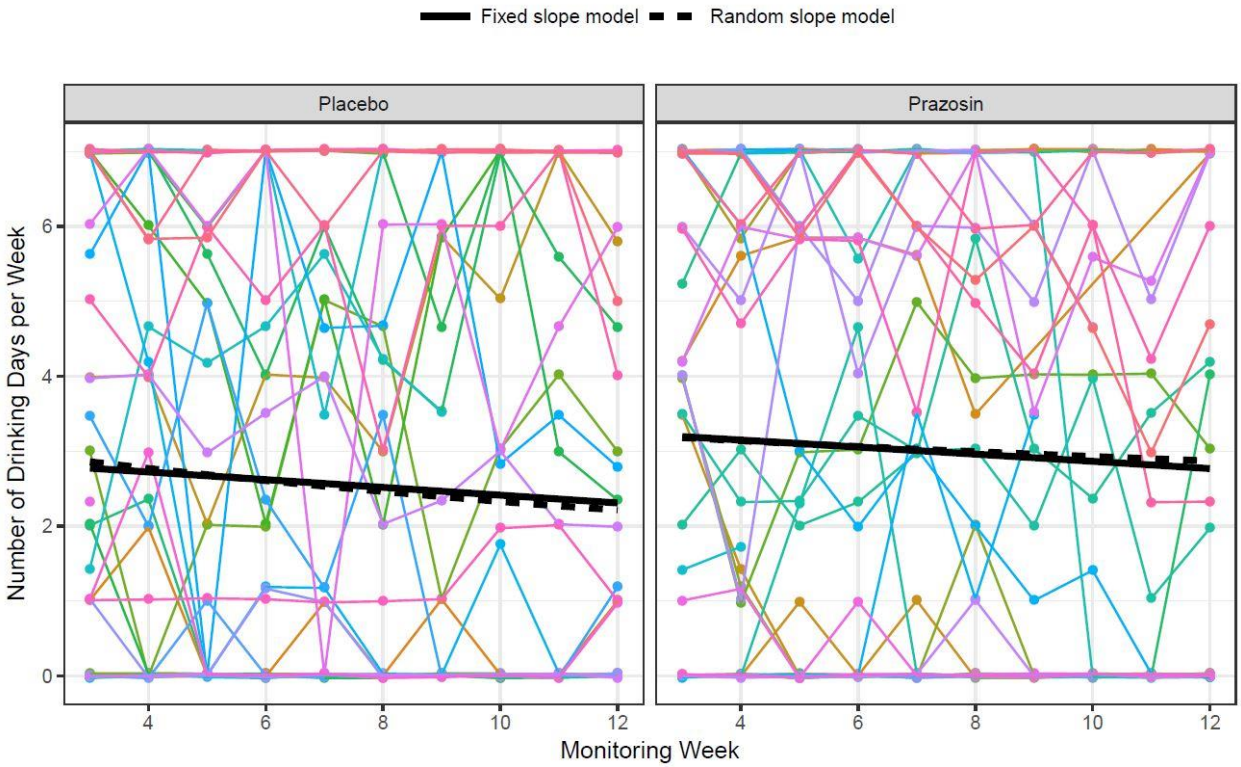
*Plots for the 80 participants (40 Placebo, 40 Prazosin) who completed titration. Plots ordered by condition (Placebo, then Prazosin) and, within condition, by increasing average number of drinks per day in the first 2 weeks after titration. Dashed line denotes cutoff for heavy drinking (4 for women, 5 for men). Y−axis is on square−root scale

Figure S3 A. Individual Participant Trajectories for Number Drinks/Week, and Adjusted Marginal Mean Trajectory From End of Titration Period to End of 12−Week Treatment Period*



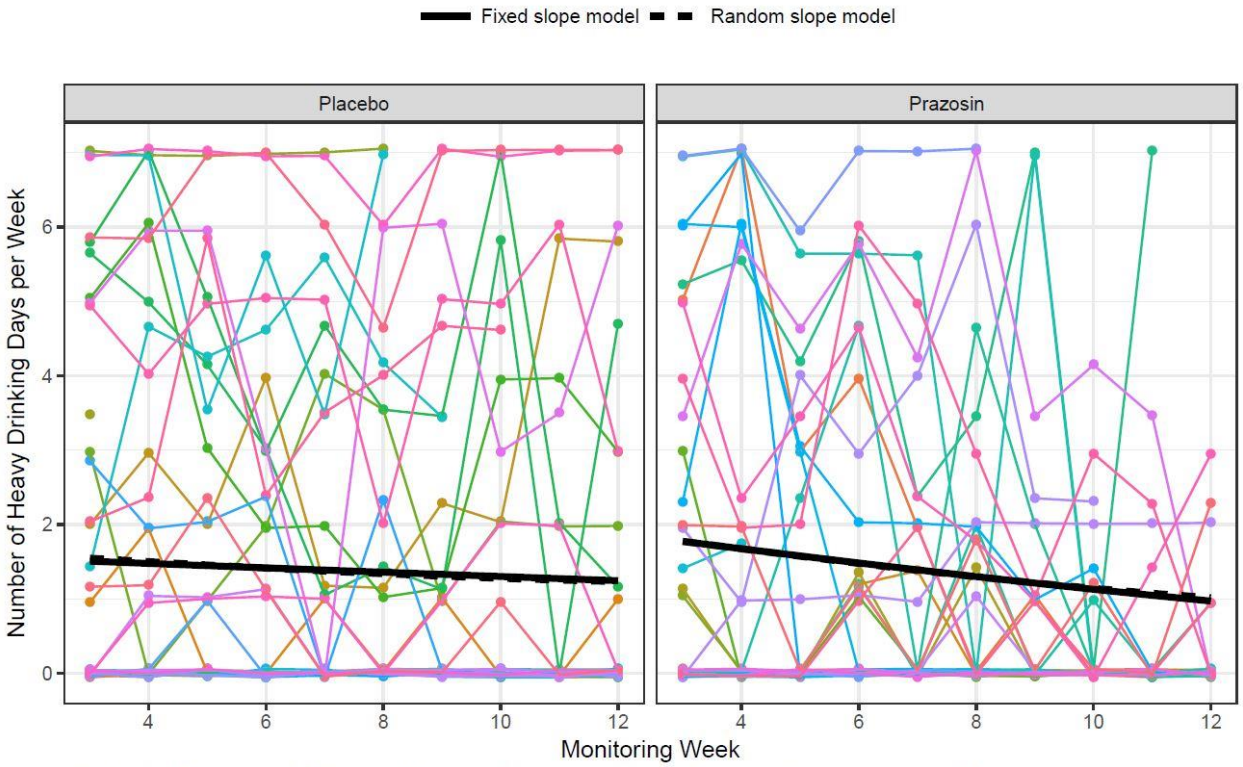
*Plots for the 80 participants (40 Placebo, 40 Prazosin) who completed titration. Y−axis is on square−root scale with trajectories jittered at y=0 to show overlapping lines

Figure S3 B. Individual Participant Trajectories for Number Drinking Days/Week, and Adjusted Marginal Mean Trajectory From End of Titration Period to End of 12−Week Treatment Period*



*Plots for the 80 participants (40 Placebo, 40 Prazosin) who completed titration. Trajectories jittered to show overlapping lines.

Figure S3 C. Individual Participant Trajectories for Number Heavy Drinking Days/Week, and Adjusted Marginal Mean Trajectory From End of Titration Period to End of 12−Week Treatment Period*



*Plots for the 80 participants (40 Placebo, 40 Prazosin) who completed titration. Trajectories jittered to show overlapping lines.