Pelvis RCT: Impact of Surgery on Pain in Lateral Compression Type Pelvic Fractures

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Statistical Analysis

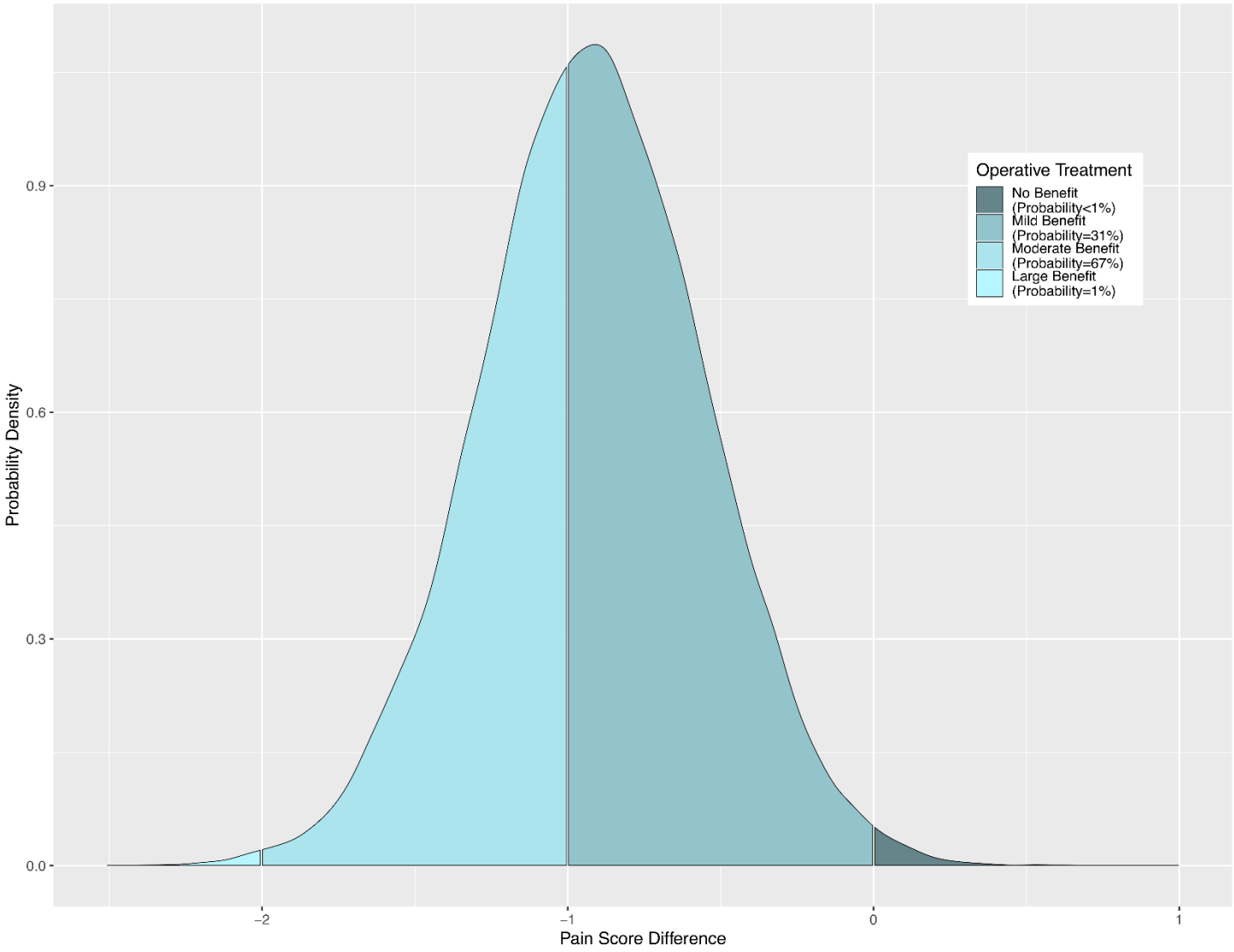
The primary analyses were based on the intent-to-treat principle. The primary analysis for pain and secondary analysis for functional outcome estimated the difference in the average treatment effect based on a longitudinal assessment within the initial 12-weeks after the fracture. This approach uses each patient's multiple outcome assessments to compare the average pain and function experienced over the 12-week period between the treatment groups. For these analyses, we used a Bayesian hierarchical model that applied a prior probability of no treatment difference based on the conflicting evidence in the prior literature [3-6]. This is akin to an initial assumption that there is "no difference" in pain or functional outcome between the treatment groups. In addition to estimating the average treatment effect, we calculated the posterior probability (meaning conditioning the prior distribution on the data at hand) of treatment benefit with operative treatment under various minimally clinical important difference (MCID) thresholds. The models included a dummy variable for each patient as a random intercept, an autoregressive correlation structure, and adjusted for whether the treatment was randomly assigned, the patient's pre-injury narcotic use, and a time-varying covariate that measured narcotic use at each time point. Multivariable linear regression was used to analyze the treatment effect on hospital length of stay and time to mobilization. Outcome data were missing in 16% of the sample at 2-weeks, and 14% of the sample at 6-weeks and 12-weeks, and was therefore imputed using multiple imputation for the final models [16]. To assess possible effect measure modification based on the initial degree of displacement, we stratified the sample to create two subgroups, patients with ≥5mm of displacement and patients with <5mm of displacement. We then calculated the average effect of operative treatment on pain in each of the subgroups. In addition, we compared the average treatment effect of operative fixation on pain with posterior-only fixation compared to operative fixation with anterior and posterior fixation. Additional sensitivity analyses recalculated the pain and function outcomes to separately compare the treatment effects between patients enrolled in the randomized cohort and the observational cohort. The analyses were performed using R Version 3.6.1 (Vienna, Austria) with the packages *lme4, rstan, brms,* and *mice*.

We took two critical steps to understand the potential for biased treatment estimates from pooling the results from the randomized and non-randomized participants. First, we performed sensitivity analyses to separately examine the results for the randomized and non-randomized cohorts. These analyses suggested similar (or even larger) estimated treatment benefits from surgery within the RCT data. Second, we included willingness to be randomized as a potentially confounding variable in our final analysis models, despite there being no evidence that it affected treatment.

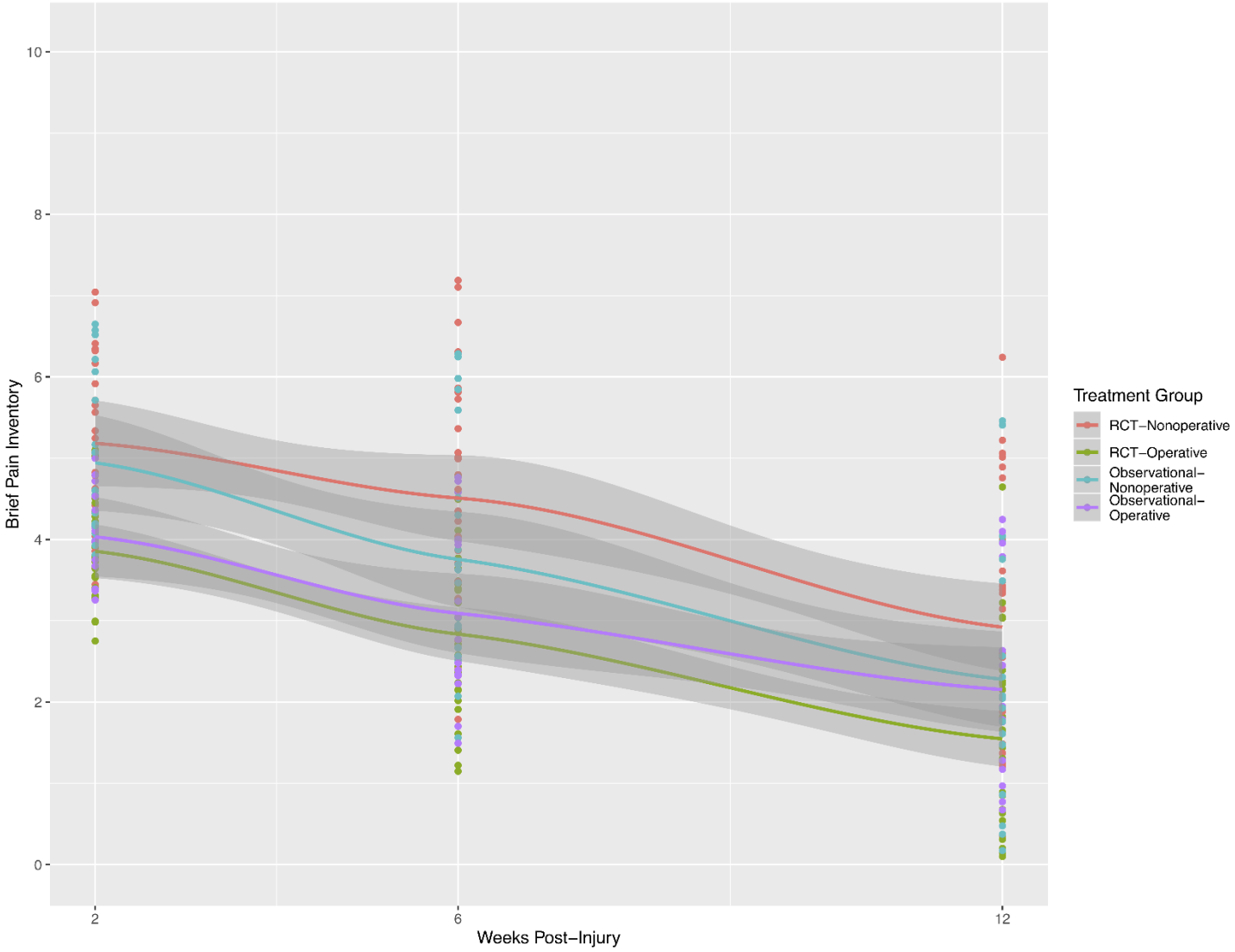
The ability to assess the probability of different magnitudes of treatment benefit is a unique characteristic of Bayesian data analysis, and is not possible with traditional non-Bayesian statistical hypothesis testing. Despite this inherent difference in statistical principles, it should be noted that the average treatment benefits reported from our Bayesian analysis are nearly identical to the results obtained using traditional multilevel linear regression models (results not reported).

Additional results from the described analyses, that were not included in the main article, are provided below.

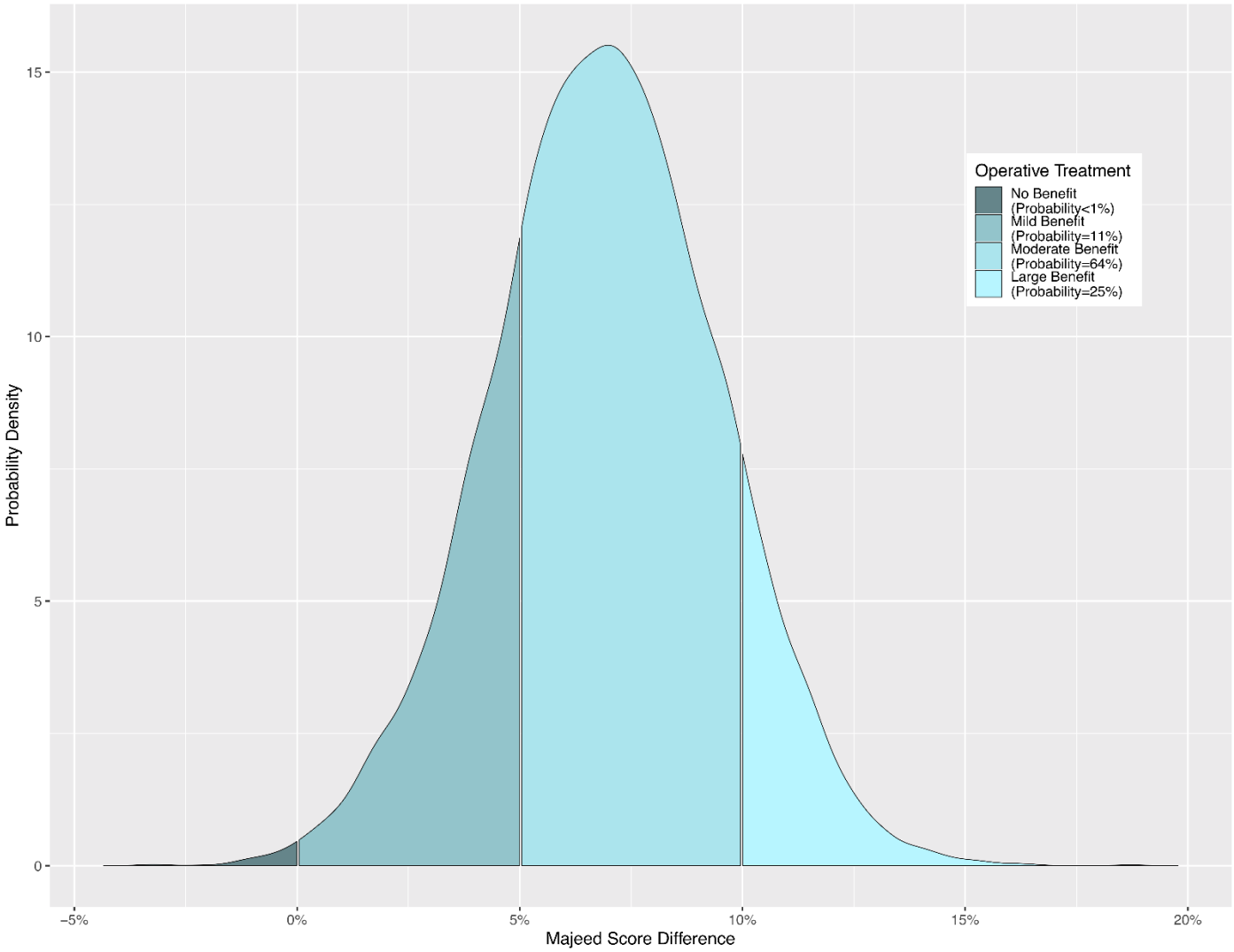
Posterior probability of reduced pain. Posterior probability of reduced pain with operative treatment within 12 weeks of injury.



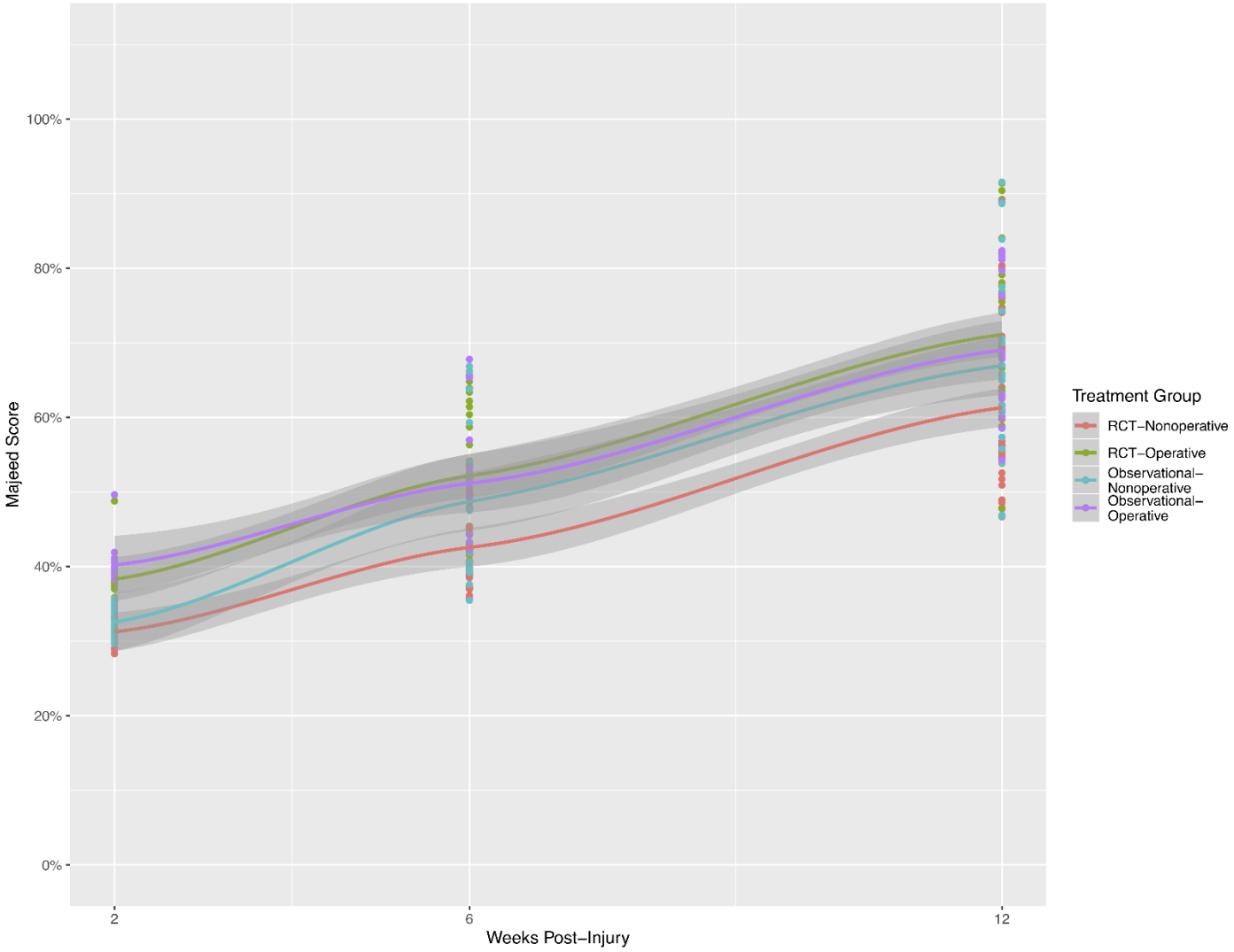
Mean pain stratified between randomized and nonrandomized patients. The mean Brief Pain Inventory scores and 95% credible intervals within the initial 12-weeks of injury for minimally displaced complete lateral compression pelvis fracture patients. The patients are stratified based on their study type (randomized trial versus observation) and treatment type (operative versus nonoperative treatment). The pain scores are adjusted for the study type, prior narcotic use, and narcotic use at each time point.



Posterior probability of improved function. Posterior probability of improved function, measured with the Majeed score, with operative treatment within 12 weeks of injury.



Mean function stratified between randomized and nonrandomized patients. The mean Majeed scores and 95% credible intervals within the initial 12-weeks of injury for minimally displaced complete lateral compression pelvis fracture patients. The patients are stratified based on their study type (randomized trial versus observation) and treatment type (operative versus nonoperative treatment).



Posterior probability of reduced pain, stratified by initial posterior pelvic ring fracture displacement: The posterior probability of surgical fixation achieving a clinically significant reduction in mean BPI pain scores stratified by fracture displacement (<5mm versus ≥5mm). Several possible clinically significant pain reduction thresholds are presented.

	Displacement ≥ 5mm	**Displacement < 5mm**	**Difference in Probability**
Mean Difference in Pain	2.2 (95% CrI: 0.9 - 3.5)	0.9 (95% CrI: 0.1 - 1.8)	
> 0	> 99%	98%	2%
> 0.5	99%	82%	17%
> 1.0	97%	41%	56%
> 1.5	88%	8%	80%
> 2.0	65%	1%	64%