How Many Sites Should an Orthopaedic Trauma Prospective Multicenter Trial Have? A Marginal Analysis of Completed Trials

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Purpose: Multicenter clinical trials in orthopaedic trauma are crucial to advance the science behind clinical care but are also complex and costly. The orthopaedic trauma research community is called upon to propose gold-standard studies that address the most critical questions while government funding for trials has leveled if not declined. Currently there are no evidence-based approaches for the financial management of multicenter trials in an orthopaedic trauma population. One key cost driver in multicenter trials is the number of participating sites. This project proposes a model for determining the optimal number of sites in a prospective multicenter trial. Our hypothesis is that the optimal number of sites can be determined based on study characteristics, known costs, and predictable site enrollment contributions.

Methods: This study is a retrospective marginal analysis of studies conducted as part of a large orthopaedic research consortium. The analysis utilized the first 12 consortium-sponsored trials that completed enrollment. The studies represented a wide range of consortium research priorities such as infection prevention and reconstructive surgery. The studies varied by injury volume, with the highest enrolling 1054 patients and the lowest enrolling just over 30. The studies also varied by design complexity. The least complex was an observational study with light data collection. The most complex was a placebo-controlled, double-blinded randomized controlled trial. Using enrollment and financial data, the primary analysis was to determine the optimal number of sites for each study by modeling their total cost curves where the curves reflect the marginal cost of each site added to the study. To determine the sensitivity of the model to variation in infrastructure costs, secondary analyses were performed using 2 additional, plausible infrastructure cost models.

Results: For every study, the optimal number of sites was lower than the actual number of sites that participated. Excess sites ranged from 2 to 39 sites. The excess costs associated with these "extra" sites ranged from $17,000 to $330,000 across the 12 studies, with a median excess cost of $96,000. These costs represented, on average, 7% (95% confidence interval: 6%, 9%] of the study budget. The results of the sensitivity analysis demonstrated that as infrastructure costs increase, so does the optimal number of sites as it becomes more advantageous to complete the study as quickly as possible.

Conclusion: Consistent with our hypothesis, we were able to develop a model that determines a clear optimal number of sites based on study characteristics and when costs and site enrollment contributions are predictable. The results indicate that previous trials were not optimized in terms of the number of sites. Hopefully this model can be used by future clinical researchers to answer critical clinical questions in a more cost-effective manner.