

## Title

Interactive simulation-based assessment of “go/no-go” decision making in Duchenne Muscular Dystrophy clinical trials

## Authors

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## Problem Statement

Late stage clinical trials for Duchenne muscular dystrophy (DMD), a rare pediatric disease, have recently failed to demonstrate efficacy through the 6-minute walk test (6MWT) change from baseline (CFB). The 6MWT is a highly variable endpoint in the pediatric DMD population, though currently the primary efficacy endpoint for registration trials. Early assessment of the probability of success and “go/no-go” decisions for new DMD therapeutics is critical, given the limited patient population and multiple competing therapeutics in development.

## Description

Simulations may be useful to explore the probability of making an accurate “go/no-go” decision given clinical trial design and disease progression variables. A disease progression model of DMD was developed for the 6MWT in pediatric boys. An R Shiny app with user-defined inputs simulates clinical trials from the model. The user chooses trial design parameters including sample size, sampling times, drug effect sizes, trial duration, and trial data analysis methods (such as ANOVA, MMRM, or Bayesian). The impact of variable disease progression parameters, including severity of disease progression slope, inter-subject variability, magnitude of drug effect and measurement noise for the 6MWT will also be assessed. The underlying technology supporting these simulations ties together high-performance elastic cloud computing, efficient simulation tools, and a graphical web interface to support interactive decision-making.

## Applications & Learnings

In addition to the specific evaluation of DMD trial performance, this case study will illustrate a general framework for evaluating the operating characteristics of trials in rare pediatric diseases for performance of “go/no-go” decision making using modeling and simulation. The technology used to illustrate this case study is also generalizable to the quantitative support of other pediatric and general drug development decision making scenarios.

## Format

Interactive web app presentation

## Requirements

WI-FI, HD monitor or projector with screen, laptop stand or small table