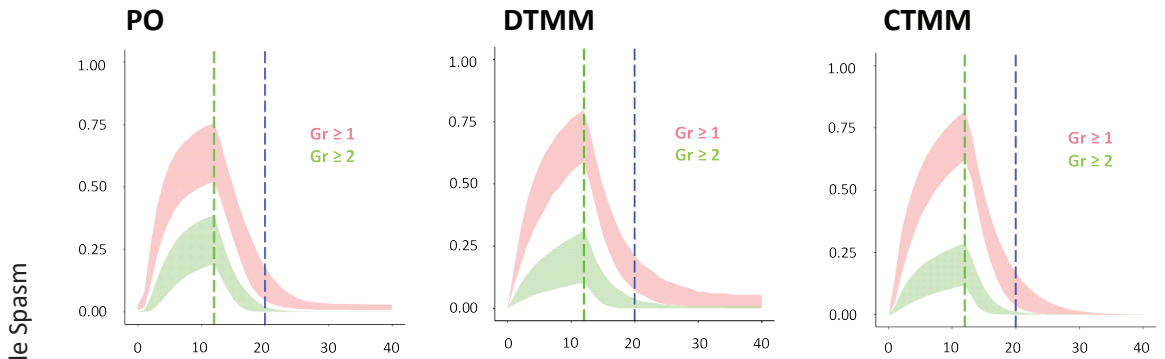


a. Weekly interval:



b. Daily interval:

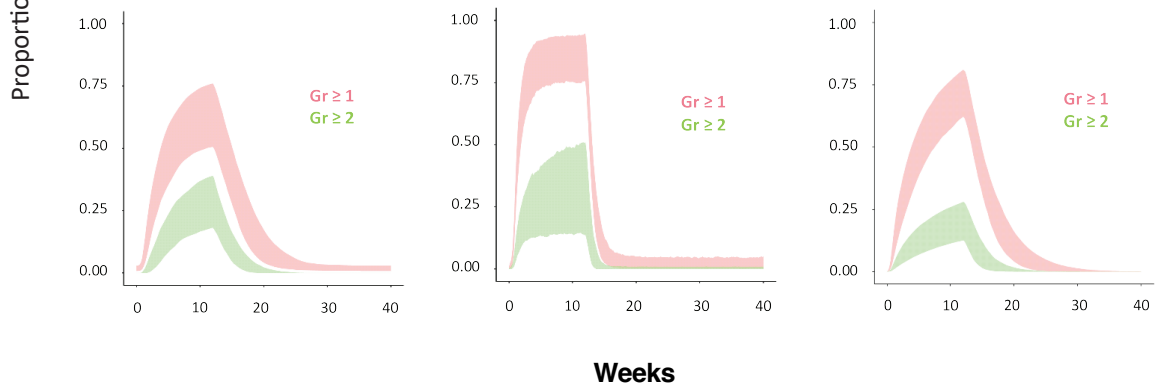


Figure S5: CTS for proportion of muscle spasm after 12-week daily treatment using models developed based on the weekly-spaced dataset.

Simulations included the Inter-individual variability and uncertainty of the parameters from non-parametric bootstrapping; 500 simulations with 200 patients for each simulation. The shaded areas are the 95% prediction intervals. The green and blue dash lines represent week 12 and week 20. The model was simulated for Muscle Spasm observed at frequency of a, weekly interval; b, daily interval. CTS - Clinical trial simulation; PO - Proportional odds model; DTMM - Discrete-time Markov model; CTMM - Continuous-time Markov model.