Fig. S1

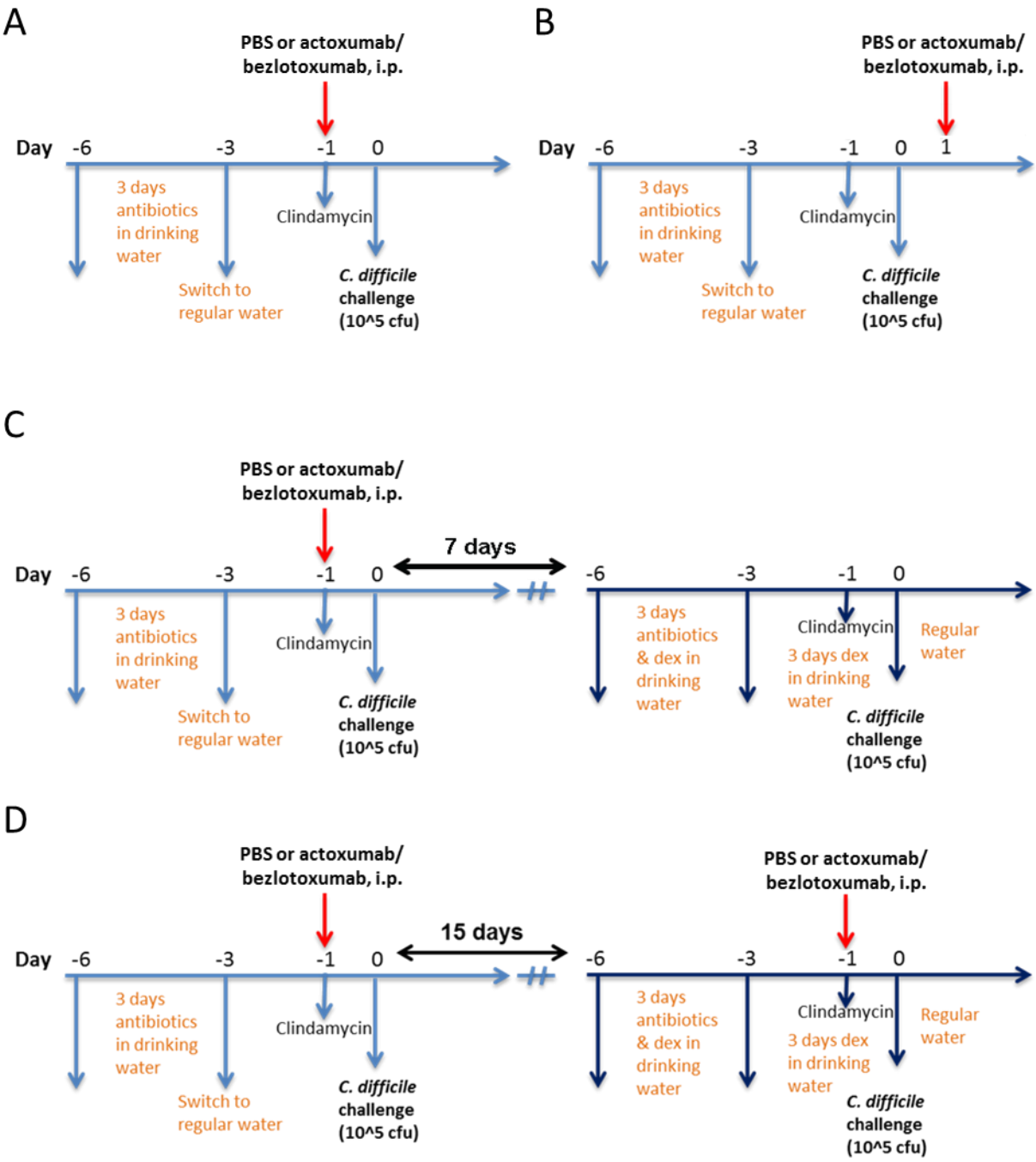

Fig. S1. Schematic representations of timelines for spore challenge models used in this study. A) Prophylactic primary infection. B) Therapeutic primary infection. C) Recurrent infection with single antibody treatment. D) Recurrent infection with two antibody treatments.

Fig. S2

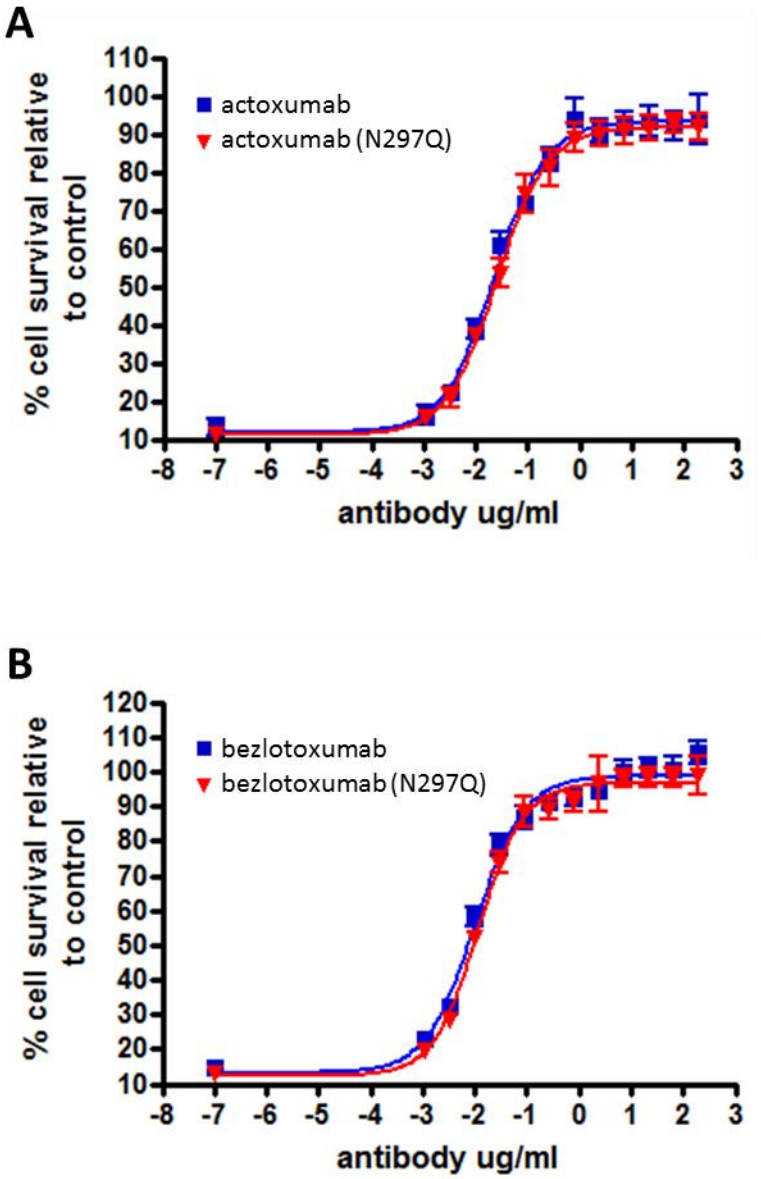

Fig. S2 Neutralization of toxin-induced cell death by wild type and N297Q mutant versions of actoxumab and bezlotoxumab. A) Vero cells were treated with LC_{90} concentrations of TcdA from strain VPI 10463 (ribotype 087) in the presence or absence of increasing concentrations of wild-type or N297Q mutant actoxumab. B) Vero cells were treated with LC_{90} concentrations of TcdB from strain VPI 10463 (ribotype 087) in the presence or absence of increasing concentrations of wild type or N297Q mutant bezlotoxumab. Each point is the mean ± SD of triplicate determinations. Representative experiments are shown.

Fig. S3

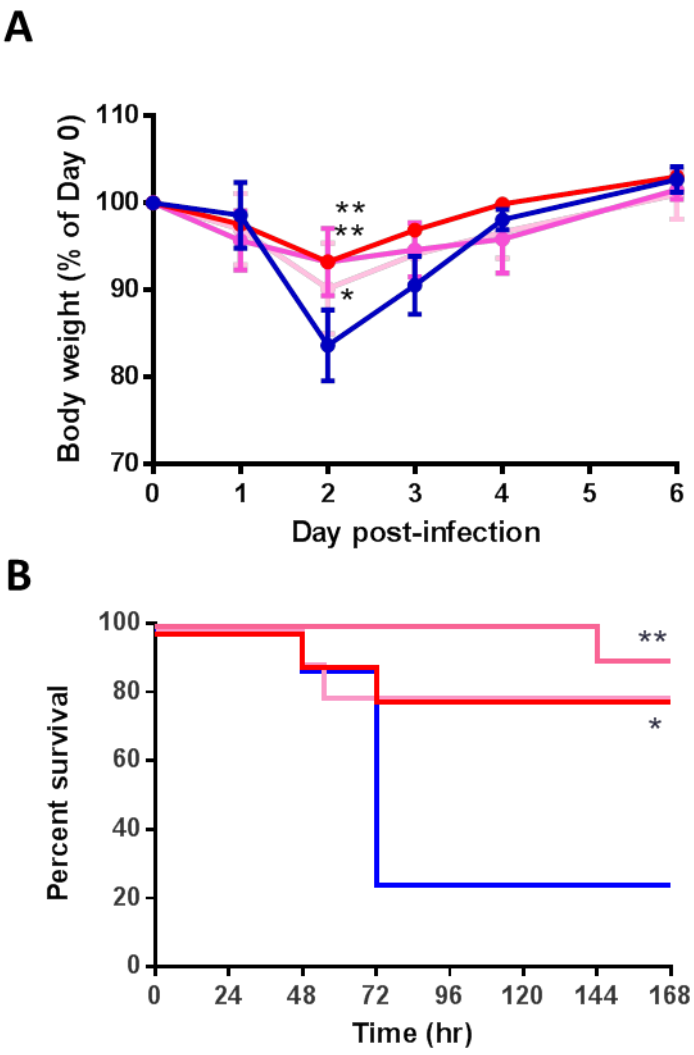

Fig. S3. Actoxumab/bezlotoxumab is protective in both prophylactic and therapeutic paradigms of primary CDI. A) Weights of mice treated with vehicle (blue circles), with 2 mg/kg actoxumab/bezlotoxumab (light pink circles), with 10 mg/kg actoxumab/bezlotoxumab (pink circles), or with 50 mg/kg actoxumab/bezlotoxumab (red circles), 24h prior to challenge with *C. difficile* spores. Each point is the mean ± SEM of 7 to 10 mice, except for vehicle treated mice on days 3-6 when only 2 mice survived. *, $p<0.01$ and **, $p<0.0001$ compared to vehicle-treated mice as assessed by two-way ANOVA with Tukey post-test. B) Survival of mice treated and challenged as described in A) (blue line, vehicle; light pink line, 2 mg/kg actoxumab/bezlotoxumab; pink line, 10 mg/kg actoxumab/bezlotoxumab; red line, 50 mg/kg actoxumab/bezlotoxumab). *, $p<0.05$ and **,$p<0.01$ compared to vehicle-treated mice as determined by Log-rank/Mantel-Cox test.

Fig. S4

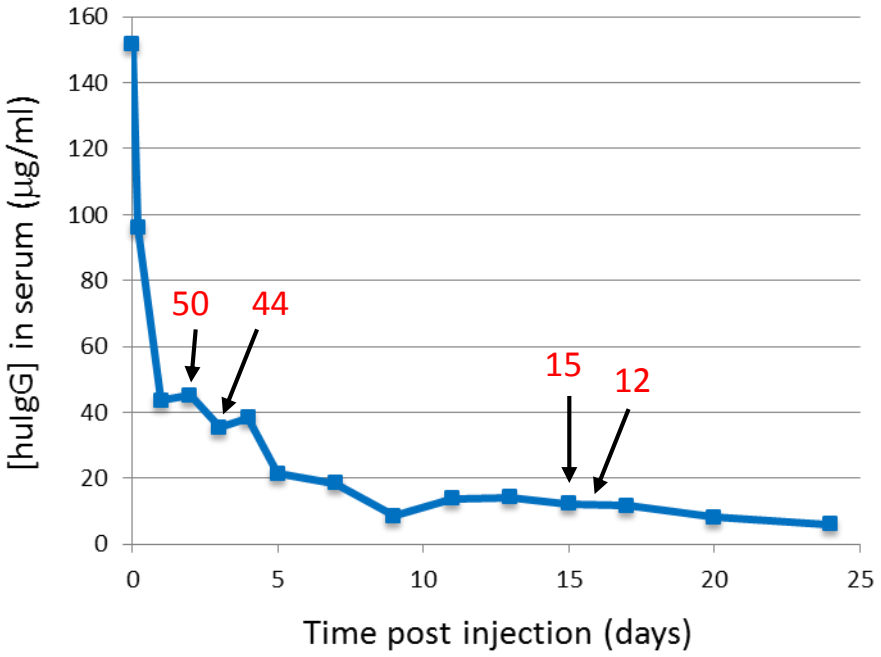

Fig. S4. Pharmacokinetic profile of actoxumab/bezlotoxumab. Three healthy C57BL/6 mice were dosed with 10 mg/kg actoxumab/bezlotoxumab and serum was collected daily for 25 days post dosing. Sera from individual mice on a given day were pooled and human IgG (huIgG) levels were assessed for each pooled sample by ELISA. Values in red indicate serum huIgG concentrations (in µg/ml) in infected mice treated with 10 mg/kg actoxumab/bezlotoxumab, from the experiment shown in Fig. 4A and B at the timepoints indicated by corresponding arrows.