1. Priors
2. Violin plots
   1. “Show Bayesian monitoring can be done with examples based on violin plot data”
3. Sequential design properties
   1. Fix axis
   2. Make captions match MP
   3. Emphasize sample size reduction and interpretability
4. Further analysis
   1. “Show frequentist properties of a SMBT when enrollment is slow relative to outcome ascertainment”
   2. “Show how the frequentist T1ER inflates as a function of # of times the data are monitored”
5. Priors
   1. Spike & slab
   2. Flat
6. Comparison of spike & slab with flat and regular priors
   1. “Explore alternative distribution for skeptical & enthuastic priors and discuss relationships to OBF and Pocock alpha spending”
      1. More & more spiked 🡪 OBF
      2. Less spiked 🡪 Pocock

Confirm 90% power at 0.35

“Probability of stopping enrollment early NOT probability we conclude treatment works”

Panel graph with speed of enrollment

|  |  |
| --- | --- |
| 4 per month, 4 month lag | 4 per month, 8 month lag |
| 8 per month, 4 month lag | 8 per month, 8 month lag |

Make figures grey scale.

350 dpi

Conclude “regardless of frequency of monitoring good type 1 error rates”

Best case is slow enrollment relative to outcome ascertainment (enrollment is slow but getting good # of outcomes)

\section\*{Meeting Notes 7/19/19}

\begin{itemize}

\item For slides 22/23, it should say nmis not ymis.

\item Violin plots are particular examples.

\item Run replicates of trial to get frequentist properties.

\item Poisson process enrollment, $\lambda$=rate parameter, $1/\lambda$=monthly enrollment. Consider the outcome ascertainment length in months.

\item Interim/final results are consistent if quick/high enrollment relative to outcome ascertainment (think of the extreme example of instant ascertainment). Iterim/final results could be inconsistent if slow/low enrollment relative to outcome ascertainment.

\item The efficacy criteria (proving the null is not true (showing skeptical prior based centered $H\_0$ is now convinced)) is usually not changed in simulations.

\item The futility criteria takes two forms: use futility prior based on intermediate value (between $H\_0$ and $H\_1$) if the intermediate value has clinical significant, otherwise use probability of success (POS). Pick one method to show in the paper, and show the other way is equivalent in the supplement.

\item \textit{Major point: Regardless of the frequency of monitoring there are good type 1 error rates}.

\item Recall the best case for sequential monitoring is slow enrollment relative to outcome ascertainment (outcome ascertainment is quick to provide consistency with interim and final results, enrollment is slow so there is substantial pragmatic benefit to ending trial early if possible).

\item Create panel graph, with Slow, Medium, and High enrollment. Slow=1 subject per month, instantanous outcome ascertainment. Medium=2 subjects per month, 1 month for outcome ascertainment. High=2 subjects per month, 2 months for outcome ascertainment. Show interim and final probability of rejecting $H\_0$. Show how the type 1 error changes in each scenario. There is no gap in Slow case, and gap is highest in High case.

\item Main ideas

\begin{enumerate}

\item Show how the Bayesian monitoring can be done with examples based on violin plot idea. These examples will have variable enrollment rates to show agreement of interim/final.

\item Show frequentist properties of sequential monitoring Bayesian trial when enrollment is slow relative to outcome ascertainment.

\item Show how the frequentist Type 1 error rate inflates as a function of the \# of times the data are monitored.

\item Explore alternative distributions for skeptical and enthuastic priors and discuss relationships to OBF and Pocock $\alpha$-spending. The alternative distributions could be mixtures of Betas.

\end{enumerate}

\end{itemize}