Bayesian Elicitation for rare diseases trials

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Introduction
Small population and rare disease trials often struggle to reach meaningful power levels in their sample size calculations due to limited maximum population size. Statistical methods exist to help overcome this in both Bayesian and frequentist frameworks.
One strong contender is using expert elicited priors in a Bayesian framework.

Methods
A targeted review of small population/rare disease trials since 2009 was carried out, investigating methods used in current research to overcome this problem, looking closely at Bayesian methods. Using learnings from this review, expert prior elicitation was conducted for two trials at ICTU, one for a Bayesian reanalysis and one for the primary trial analysis.

Results
A total of 6,128 articles were screened with 64 eligible trials (4 Bayesian, 60 frequentist). Frequentist trials had planned power ranging from 72-90% (median: 80%) but reported recruiting a mean of 6.6% below the planned sample size (n=38) [median 0%, IQR (-5%, 5%)], most used standard type I error (52 used 5% and 1 used 1%), and the mean standardised effect was high (0.7) with 50% missing their assumed level. Of the 4 Bayesian trials, 3 used informed priors, 2 trials performed sensitivity analysis for the impact on design, 1 performed sensitivity analysis. Historical data, expert consensus or both were used to construct informative priors. Bayesian trials required 30%-2400% fewer participants than using frequentist frameworks. The elicitations were performed remotely during the COVID-19 pandemic but proved fruitful and resulted in sensible priors. Participants and facilitators alike enjoyed and appreciated the process and learnings were carried into following elicitation sessions.

Conclusion
In trials with limited populations, more can be done to overcome this inherent limitation. Bayesian methods, although underutilised, offer promising solutions for such trials. Well performed expert elicitation can contribute to increasing statistical efficiency on Bayesian trials with very small sample sizes.