# How does prevalence affect the size of clinical trials for treatments of rare diseases?*

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## Background

Many rare diseases affect 1 in 100,000 or fewer, thus limiting the potential pool of patients that would be eligible and willing to be recruited to trials. Design and analysis of clinical trials become more challenging.

## Objective

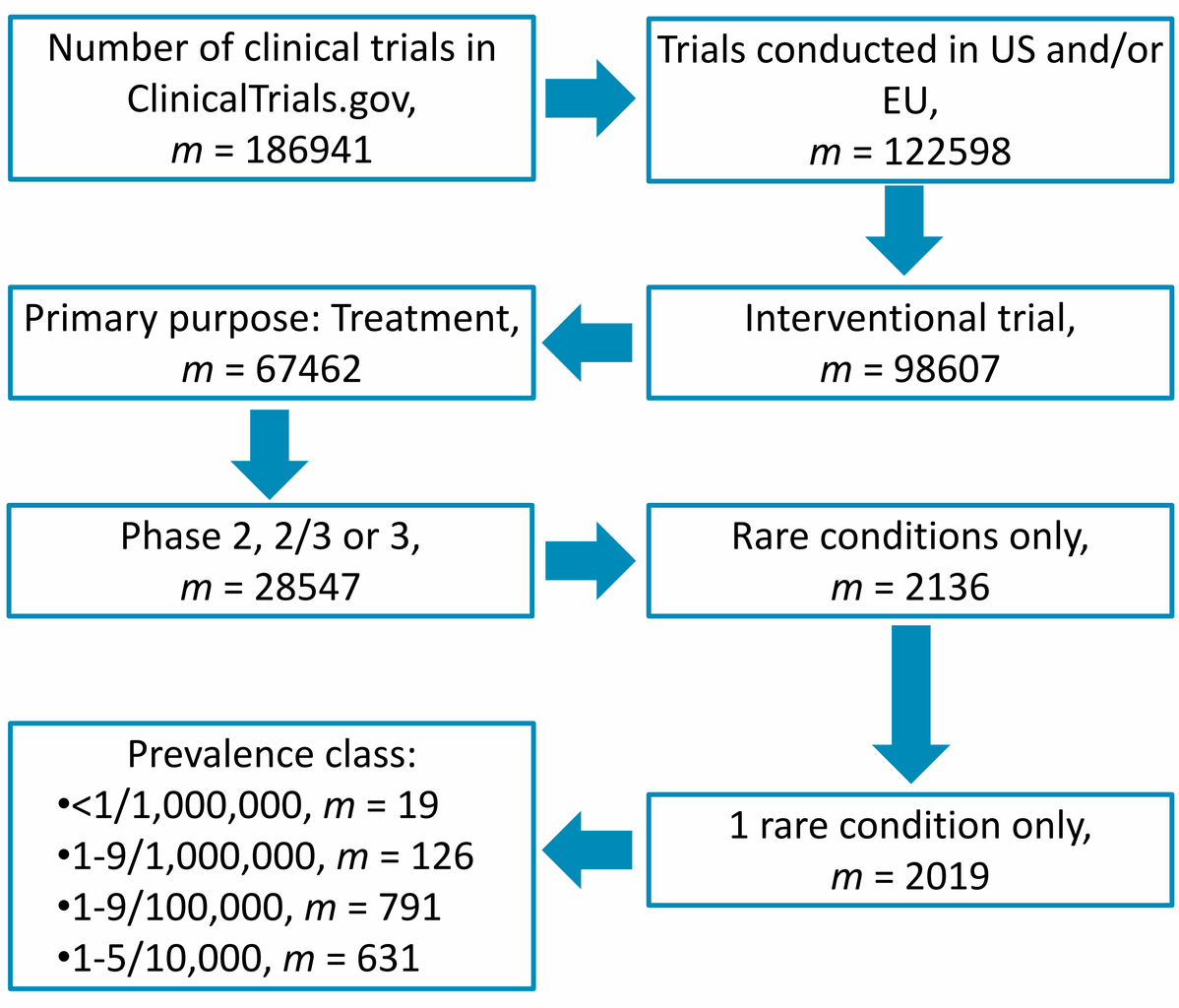
Association between the disease prevalence and sample size for clinical trials in rare diseases allowing for other factors.

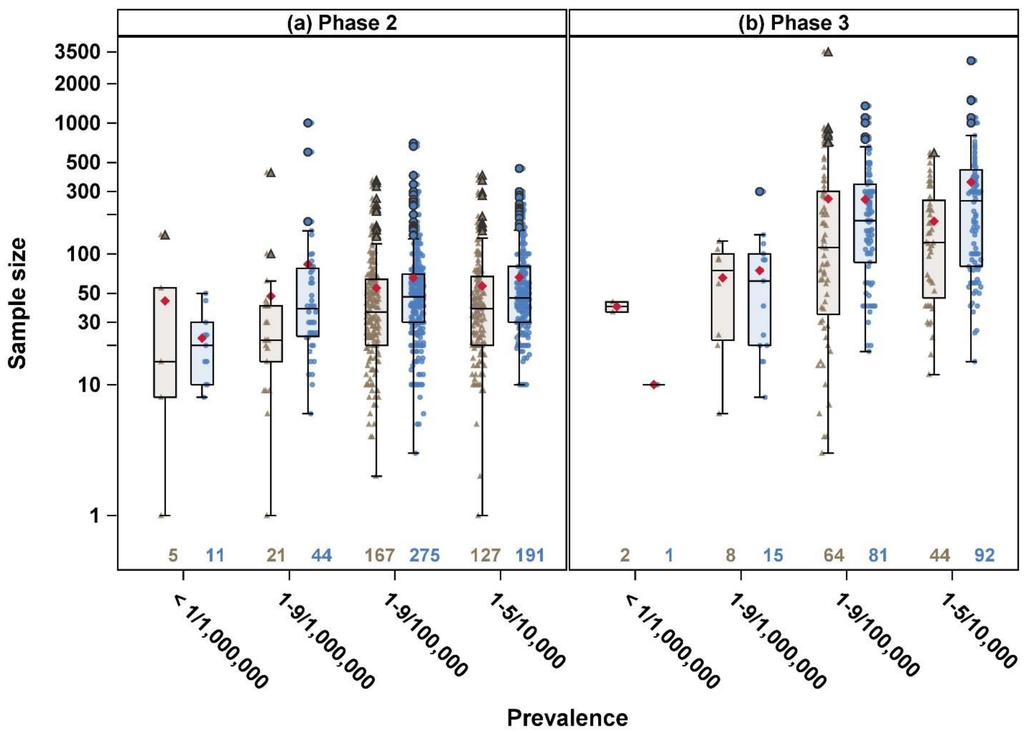
## Methods

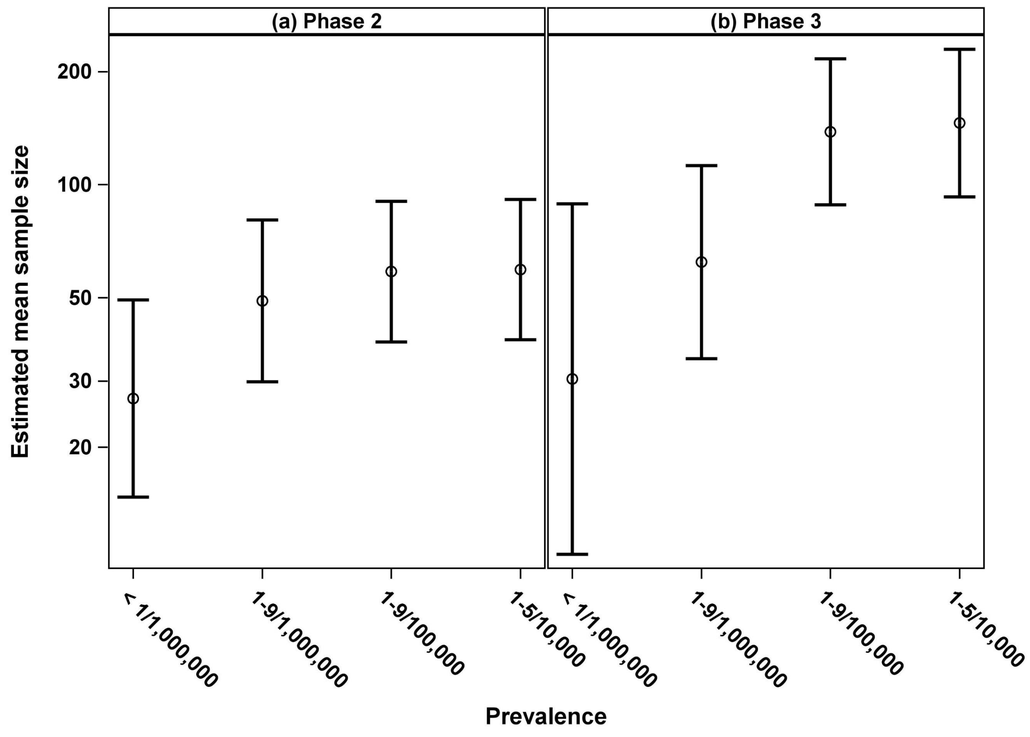
Data from Aggregate Analysis of ClinicalTrials.gov database (AACT)†, a registry of more than 180,000 clinical studies and Orphadata§, a portal for information of rare diseases and their prevalence.

## Statistical analysis

Log of sample size. Analysis of variance and linear regression models. It was expected that prevalence class and phase of study would influence the sample size. Thus, covariates were added in turn to the model that included prevalence, phase and the interaction between prevalence and phase. Significant at $p < 0.05$ level.




## Results

Top Fig: Jittered boxplot with actual (brown triangle) or anticipated (blue dot) sample size by prevalence. More phase 2 than phase 3 trials and the median sample size for phase 3 trials was higher than those in phase 2.

No strong association between prevalence and sample size in phase 2 trials but more indication that the sample size is larger for trials in less rare diseases in phase 3 trials.

Bottom Fig: Fitted mean of sample size and 95% confidence interval back transformed from logarithmic value by prevalence, phase, interaction between prevalence and phase adjusting for gender, age, whether or not there was a DMC, whether or not the intervention was FDA regulated, intervention model, trial regions, number of countries participating in the trial, year that enrolment began and number of treatment arms.

No apparent effect of prevalence in phase 2 but there is in phase 3.

## Conclusion

The fitted mean sample sizes for rare disease trials differ slightly between prevalence classes with slightly larger trials conducted in diseases with higher prevalence.

## References

* Hee *et al*. *Orphanet J Rare Dis*, 2017; 14: 44.
† http://www.ctti-clinicaltrials.org/what-we-do/analysis-dissemination/state-clinical-trials/aact-database
§ http://www.orphadata.org

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Innovative methodology for small populations research

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