# A Bayesian approach to increase evidence of effectiveness in health economic evaluations of treatments for rare diseases

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**BACKGROUND:** One of the challenges in research for novel technologies for small patient groups arises when establishing clinical effectiveness using conventional statistical analysis. Maximizing power in a trial by increasing the number of subjects not always feasible in rare diseases owing to practical and ethical limitations. Thus, conducting reliable cost-effectiveness analyses is compromised by significant uncertainty related to outcome measures. This challenge is recognised in academia, by public decision-makers and in the pharmaceutical industry. However, not overcoming these challenges can negatively impact access to treatment for patients with rare diseases.

Different initiatives have been made to overcome the problem like innovative reimbursement agreements. However, solving the statistical challenges enables decision-making, which include inputs about cost-effectiveness from health economic evaluations for treatments with small patient groups.

**OBJECTIVE:** This study is a proof of concept (POC) for a method for estimating clinical effects of treatments for which the biochemical mechanisms are well understood using small sample sizes, but without lowering the level of evidence. The method is applied to a study on mannose supplementation for phosphomannomutase 2 deficiency (PMM2 -CDG). PMM2-CDG is a disease for which the metabolic pathways are well understood, but where the rarity of the condition limits the evidence of possible treatments due to lack of power.

**METHODS**: Using Bayesian statistics on clinical trial data, treatment effects can be inferred with reduced standard error by incorporating *in vitro* experiments and knowledge about the physics of the protein catalysts.

**DISCUSSION**: The results of this POC suggest that evidence for clinical treatment effects is attainable for small sample size studies, where lack of power is a major concern. However, researchers should ensure that statistical significance of the *in vitro* treatment effect does not outweigh that of the clinical trial. Thus, new guidelines are warranted and related adjustments in the current framework for economic evaluations is needed.

**CONCLUSION:**

More research is needed to develop a framework, which can enhance evidence in clinical trials with small sample sizes, by using an additional *in virto* estimate. This could potentially overcome the statistical challenges, which are barriers to conduct health economic evaluations

There still seems to be a need for improvement in methodology to make treatment for small sample size studies available to patients

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