BAYESIAN APPROACH TO PAEDIATRIC CLINICAL TRIALS

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It is difficult to conduct clinical trials in children and often the only evidence for treatment efficacy comes from adult trials. Paediatric trials are hampered by a low disease incidence and a low frequency of adverse outcomes that make it impractical to achieve adequate power. Since the paediatrician is willing to utilize efficacy evidence from trials in adults we propose a Bayesian approach that allows a paediatric trial to borrow strength from previous or simultaneous trials in adults. We propose to accomplish this by applying a hierarchical model for which the efficacy parameter from the adult trial and that of the paediatric trail are considered to be draws from a normal distribution with a variance that is elicited from medical experts. This information can be elicited by asking pediatricians for an upper confidence bound on the difference between outcomes in children and adults. We show that with the elicited parameter, one can calculate the sample size required for the pediatric trial and also calculate the posterior distribution of the pediatric efficacy measure. We show that as long as the sample size of the trial is reasonably large, the method presented is relevant to any choice of endpoint and is equivalent to the elicitation of a power prior. This method is applied to a recent trial of Activitated Protein C that was tested in both children and adults. We show that given the positive but not strong results in adults and the negative results in children, the evidence does not strongly support pediatric use unless one believes very strongly in the linkage between pediatric and adult data. We also apply the sample size formula to a proposed study of a medical food in the Management of Acute Lung Injury in both adults and children and show that with a reasonable choice of linkage parameters the pediatric trial is feasible. We feel that the methods we propose have the potential of allowing clinical trials in children that will greatly improve the evidence base of pediatric medicine.