A comparison of migraine prevention therapies in the adult versus pediatric populations using a joint Bayesian network meta-analysis model

Phebe Kemmer1, PhD; Tianle Hu1*, PhD; Fanni Natanegara1, PhD; Zachary Thomas1, PhD; Himanshu Upadhyaya1, MBBS, MS, MBA
1Eli Lilly and Company, Indianapolis, IN, USA

Introduction
- The worldwide prevalence of migraine in children and adolescents is 7.7%. The disorder can cause a significant negative impact on quality of life (e.g., missing school and social activities, etc.).

- Although 8 medications are currently approved for migraine prevention in adult patients, only one (topiramate) has also demonstrated efficacy in the pediatric population, and is FDA-approved for migraine prevention in adolescents.

Objectives
- Synthesize the evidence from adult and pediatric studies of migraine prevention medications, to understand whether we can reasonably extrapolate the treatment effect from adults to pediatric patients.

  1. Perform an extensive literature review, to summarize the effect of treatments studied in adults and pediatric patients.
  2. Use a Bayesian network meta-analysis to assess the similarity between adult vs. pediatric treatment effects.

Literature Review
- We identified results from randomized clinical trials in both adult and pediatric patients in 4 of the medications that are FDA-approved in adults.

- The studies below evaluated efficacy in 8 to 26 weeks of treatment duration, using the outcome of change from baseline in monthly migraine frequency.

- There was generally an improvement in the monthly migraine frequency (negative change from baseline value).

Bayesian network meta-analysis
- To synthesize all the curated summary data above under one framework, a mixture-based meta-analysis was applied to quantify the relationship between the adult and pediatric treatment effects.

- The model assumes the pediatric effects for all 4 drugs above are a mixture of 2 alternative possibilities: one where the adult effects translate to the pediatric effects, and another where the adult effects do not translate to pediatric patients.

- Non-zero prior probability was placed on equivalent treatment effect distributions for adults vs. pediatrics, and remaining probability was allocated to diffuse, independent priors for the adult and pediatric effects separately.

Results
- Evidence for similarity of treatment effects in adult and pediatric patients:
  - There is overlap in adult and pediatric posterior distributions (particularly for propranolol and topiramate)
  - The posterior medians in adult and pediatric patients are below zero for all 4 drugs
  - The posterior probability that the adult and pediatric treatment effects are equal is >0.5

Conclusions
- The literature review and meta-analysis results yield support for the extrapolation of adult effects to the pediatric population.

- The model can be leveraged to yield a posterior predictive distribution of treatment effect in the pediatric population, based on the pivotal studies in the adult population, for future migraine preventive therapies.

Sources:
*Tianle Hu was a full-time employee of Eli Lilly and Company at the time this research was conducted.