Title: A cost-utility analysis and value of information of biologics for Moderate-to-Severe Crohn's disease: evidence synthesis using Bayesian network meta-analysis

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Authors:
Mark Bounthavong
David L. Veenstra
Emily Beth Devine

Abstract (500 word limit)

Objectives
To evaluate the cost-effectiveness and value of information (VOI) of infliximab, adalimumab, certolizumab pegol, and vedolizumab in Moderate-to-Severe Crohn's disease (CD) from a U.S. payer perspective with evidence synthesis from a Bayesian network meta-analysis (NMA).

Methods
Model and data source
A Markov model was constructed to evaluate the lifetime cost-effectiveness of biologics and active control/placebo in CD. The model used a 3-month cycle with six health states: Moderate-to-Severe, Mild-to-Severe, Remission, Severe/Fulminant, Post-Surgery, and Death. Transition probabilities for the transition from Moderate-to-Severe disease to Remission were estimated using Bayesian NMA. Based on this framework, the comparisons between infliximab, adalimumab, certolizumab pegol, and vedolizumab to active control borrowed strength between each pairwise comparison, and the probabilities for each treatment strategy in the network were estimated. Other transition probabilities and utility values were derived from the literature. Drug costs were based on Medicare Part-B Drug and Biological Average Sales Price Payment files. Costs and quality-adjusted life years (QALYs) were discounted at 3-percent/year. One-way and probabilistic sensitivity analyses (PSA) tested the robustness of the model.

Value of information
Expected value of perfect information (EVPI) was estimated for the affected population; additionally, partial EVPI (EVPPI) was estimated for the transition probability from moderate-to-severe to remission health states and utility values. EVPI was performed using a willingness to pay (WTP) threshold of $150,000/QALY gained. The population EVPI was determined by multiplying the per-patient EVPI by the affected population. EVPI was evaluated for ten years with the rationale that technology will have advanced beyond biologics in CD treatment/management. EVPPI evaluated the transition probabilities for all treatment arms from the Moderate-to-Severe to Remission health states generated from the NMA. Additionally, the uncertainty in utility values for health states was investigated in the EVPPI. The outer loop used the transition probability from one of the treatment strategies while the inner loop continued with the PSA for all the other parameters in the model. A total of 100 outer- and 100 inner-loops were performed to generate the most efficient estimates of EVPPI.

Results
The incremental cost-effectiveness ration (ICER) for infliximab compared to active control was $4,570/QALY. The ICER for adalimumab compared to infliximab was $2.1 million/QALY. Certolizumab pegol and vedolizumab were eliminated by extended dominance. In comparisons between infliximab and active control, the model was robust to all variables in one-way sensitivity analyses. Results comparing adalimumab and infliximab were sensitive to utility values. Reducing the uncertainty would yield a large population EVPI of $459 billion; and the EVPPI identified reducing the uncertainty on the transition probability for infliximab, and the utility values for all the health states, as potential investments in future research.

Conclusions
NMA methods provided the necessary transition probabilities to perform a cost-utility analysis and VOI of biologics for CD. Infliximab was cost-effective relative to active control, unlike adalimumab when compared to infliximab. Future research designed to reduce the uncertainty associated with the transition probability for infliximab and all utility values would yield large benefits to society.