Feasibility and Acceptability of Minimal Modeling Value of Information Analyses for Real-Time Prioritization Decisions Within a Large Cancer Clinical Trials Cooperative Group

Background
Cancer clinical trials groups face excess demand for limited research resources & finite patient populations.

Value of Information (VOI) is a methodology grounded in decision theory that can be used to inform research prioritization decisions.

SWOG is a large cancer research cooperative group that designs and conducts multidisciplinary clinical trials to improve the practice of medicine in preventing, detecting, and treating cancer, and to enhance the quality of life for cancer survivors.

Objectives
Develop efficient process to calculate the value of information (VOI) for SWOG’s trial proposals that is feasible for real-time, prospective evaluations

Provide preliminary assessment of the feasibility, acceptability, strengths, and weaknesses of our modeling approach

Methods
Iterative approach to develop a feasible & efficient process to generate and present VOI information to stakeholders.

Study Sample
• 10 randomized phase II/III trial proposals from the Breast, Gastrointestinal and Genitourinary cancer committees originally reviewed 2008-2013

Value of Information (VOI) Analyses
• Calculated expected value of sample information (EVS) using Bayesian decision theoretic methods
• Prior uncertainty derived from sample size calculation and, prospectively, an expert elicitation exercise of SWOG stakeholders
• Consistent assumptions across trials (e.g. 10 year time horizon for information)
• Final analytical approach developed in collaboration with SWOG stakeholders

SWOG Engagement
• Distributed educational materials & conducted 2 in-person VOI training sessions with SWOG members
• Bi-directional communication between SWOG stakeholders and the research team throughout the modeling development
• Engaged with ~200 SWOG members in total

Results
Began with a traditional VOI Modeling Framework informed by the literature and conceptualization of minimal modeling by Meltzer and colleagues

Customized VOI Modeling Framework to Accommodate Range of SWOG’s Trial Proposals

Many trial proposals used intermediate endpoints (e.g. progression-free survival) and/or events expected over a long time period (>5 years)

Account for age-specific competing causes of death using Markov model framework with up to 3 health states:

Insufficient data from earlier studies to derive an empirical prior distribution of the treatment effect for primary endpoint

Derive prior uncertainty from sample size calculations:
• Created prior distribution of treatment effect such that values under the null and alternative hypotheses align with historical success rates and outcomes of all past cooperative group trials.
• Also use expert elicitation exercise for prospective VOI analyses

Final Customized VOI Modeling Framework

Feasibility
• Focused on primary trial endpoint: appropriate for 8/10 trial proposals (as determined by modeling team, clinical experts, & stakeholders)
• <1 week to construct models and conduct VOI analyses per trial; feasible for use within real-time trial evaluations

Acceptability
• Generally positive feedback from SWOG stakeholders. “What they’re doing is incredibly important… You will see trials with negatives. We need it to make strategic decisions.”
• Many stakeholders felt modeling process particularly expert elicitation, was as useful as VOI results. “We don’t do this often enough. We’re not critical enough to ask directly, what is the likelihood of reaching the trial’s endpoint?”

Incorporated Several Rounds of Stakeholder Feedback:

Strongly divided preferences on incorporating costs in models
• “You can’t say an improvement in survival is a negative because of costs. It’s matter of philosophical differences between clinicians and health economists”

“But what if you were saving costs? Some trials in early stage bladder cancer would do just that... it would reduce downstream medical costs”

Treatment decisions in simulations made to maximize health benefits, reflecting slight majority of stakeholder preferences & treatment adoption decisions in the United States

Concern that population-level VOI would unfairly bias against rare diseases
• “If you compare all the trials in pancreatic cancer versus all the trials in breast cancer, you’ll of course find higher VOI in breast cancer”

Present both the individual-level and population-level VOI results

Conclusions
• We developed an efficient and customized VOI modeling framework that is feasible to use in “real-time” within SWOG’s current trial proposal evaluation process and acceptable to stakeholders
• Prospective use and evaluation of this approach is currently underway within SWOG

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<tr>
<th>Patient level</th>
<th>Population level</th>
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<tr>
<td>Incremental QALYs</td>
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SWOG lacked experience and context for VOI results and expressed need for context to use value of information results to inform prioritization decisions