The value of comparative effectiveness research: projected return on investment of the RxPONDER trial (SWOG S107)

Wong WB, Ramsey SD, Barlow WE, Garrison LP, Veenstra DL

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study examined the value of research from an ongoing clinical trial – the Rx for Positive Node, Endocrine Responsive Breast Cancer (RxPONDER) trial. This assessed the 21-gene assay to predict recurrence and response to chemotherapy for early stage, node-positive breast cancer. This was a good investment for public research funds, especially after stakeholder engagement. The methods used to estimate the expected value of sample information were valid, but the data sources were not described. The conclusions seem robust.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the value of research from an ongoing clinical trial – the Rx for Positive Node, Endocrine Responsive Breast Cancer (RxPONDER) trial. This trial compared the 21-gene profile to predict recurrence and response to chemotherapy versus standard care for early stage, node-positive breast cancer. The expected value of sample information was calculated to assess the value of the clinical trial, given its design and sample size.

Interventions
The two interventions were screening of women using the 21-gene assay, with chemotherapy decisions based on their recurrence score; and usual care, in which all women were recommended adjuvant chemotherapy based on the guidelines of the US National Comprehensive Cancer Network (NCCN).

Location/setting
USA/hospital.

Methods
Analytical approach:
The analysis was based on a mathematical model of the long-term clinical and economic outcomes of using the 21-gene profile to guide chemotherapy decisions, for women with lymph node-positive hormone receptor-positive breast cancer. A lifetime horizon (40 years) was considered. The authors stated that the perspective of the US health care payer was adopted.

Effectiveness data:
The key data for the treatment effect and the patient characteristics were from a subset of participants in a published clinical trial that compared the 21-gene assay with standard care. Other inputs, especially for the long-term analysis, were from other published sources. Some adjustment of the data was required to reflect the population enrolled in the RxPONDER trial, and some assumptions were made. Survival was a key input for the model.

Monetary benefit and utility valuations:
The utility values were from published sources.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure, and they were discounted at an annual rate of 3%. Expected QALYs were converted into monetary values using an incremental net benefit approach.
Cost data:
The analysis included the costs of adjuvant chemotherapy, the 21-gene assay, primary and secondary prophylaxis with granulocyte-colony stimulating factor, and the management of recurrence. The costs of implementing the RxPONDER trial were considered. The cost of adjuvant chemotherapy was from a retrospective claims analysis, and the other costs were from published studies. All costs were in US $ and they were discounted at a yearly rate of 3%. The price year was 2010.

Analysis of uncertainty:
The assessment of the expected value of sample information followed a Bayesian framework that simulated the inputs in the model across their distributions. Different distributions were assigned to groups of inputs. The subsequent value of research was extrapolated to the US population, over a 10-year horizon, using nationwide epidemiological databases. Three willingness-to-pay thresholds were used ($100,000, $150,000, and $200,000 per QALY gained).

Results
Considering the expected costs and QALYs of the two strategies, the expected value of sample information, for an individual patient, was $2,800 at a cost-effectiveness threshold of $100,000 per QALY, $4,700 at a threshold of $150,000 per QALY, or $6,500 at a threshold of $200,000 per QALY.

The cost of the RxPONDER trial was at least $27 million, while its expected value of research ranged from $400 million to $960 million, representing a return of 17 to 39 times the projected cost of the trial.

After consulting stakeholders, information on utilities, costs, and patient preferences was collected as well as survival data, these additional parameters increased the value of the trial by $50 million to $100 million. Among all the outputs, survival had the largest estimated value. Patient preferences added the most to this, on its own.

Authors' conclusions
The authors concluded that the RxPONDER trial was a good investment for public research funds, especially after stakeholder engagement.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the proposed strategy to guide adjuvant chemotherapy was compared with the usual approach recommended by official guidelines.

Effectiveness/benefits:
The clinical data were mainly from a randomised controlled trial that should have had good internal validity. Some assumptions on women’s behaviour and other important inputs, such as long-term survival, were needed. These were tested in the sensitivity analysis, and this was acknowledged as a limitation of the analysis. Data adjustments were made to reflect the population of the RxPONDER trial. QALYs were an appropriate benefit measure, given the impact of breast cancer on patients’ survival and quality of life. No clear information on the derivation of the utility values was given.

Costs:
The cost categories were consistent with the perspective adopted. The costs were presented as category totals and were not broken down to individual items, reducing the transparency of analysis. The unit costs and quantities of resources were not presented separately. No clear description of the data sources was given, but relevant US sources are likely to have been used. The reference year was reported, allowing reflation exercises. Variations in the cost inputs were not considered, but a probabilistic approach was used to assess the uncertainty around the economic inputs.

Analysis and results:
The results were selectively presented as the expected costs and benefits of the two approaches were not reported. Only the incremental net benefit results and the findings of the expected value of sample information analysis were reported. The uncertainty was implicitly addressed, in the probabilistic analyses, within the model framework. The authors acknowledged some limitations to their analysis, mainly due to the lack of good data for some clinical parameters. The model results were specific to the study objective and the US context.
Concluding remarks:
The methods used to estimate the expected value of sample information were valid, but limited information was given on the data sources. The authors’ conclusions appear to be robust.

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