# MSR179 - Automated Extraction of Cost-Effectiveness Models Data from Health Technology Assessment Submissions Using Large-Language Models (LLMs): Does the Prompting Approach Matter?

**Supplemental Material**

# Methods

## Reviewed Technology Appraisals

The nine technology appraisals (TAs) across three health technology assessment agencies—UK's NICE, Canada's Drug Agency (CDA-AMC), and the US's Institute for Clinical and Economic Review (ICER)—selected for review are summarized in Table 1. TAs were selected to cover a range of diseases.

Table 1.    List of Reviewed TAs

| # | Title | HTA | Indication | Disease area |
|---|-------|-----|-----------|--------------|
| 1 | PC0259. CDA-AMC Reimbursement Review. Nivolumab. Gastric, gastroesophageal junction, or esophageal adenocarcinoma. July 2022 | CDA-AMC | 1L advanced/metastatic GC/GEJC/EAC | Oncology |
| 2 | SR0683. CDA-AMC Reimbursement Review. Somatrogon. Growth hormone deficiency. May 2022 | CDA-AMC | Growth hormone deficiency | Metabolic disorder - pediatric |
| 3 | SR0776. CDA-AMC Reimbursement Review. Elexacaftor-Tezacaftor-Ivacaftor and Ivacaftor. Cystic fibrosis. December 2023 | CDA-AMC | Cystic fibrosis | Respiratory – genetic condition |
| 4 | TA962 (CDF exit). Olaparib for maintenance treatment of BRCA mutation-positive advanced ovarian, fallopian tube or peritoneal cancer after response to first-line platinum-based chemotherapy. Committee Papers | NICE | 1L maintenance ovarian cancer | Oncology |
| 5 | TA823. Atezolizumab for adjuvant treatment of resected non-small-cell lung cancer. Committee Papers | NICE | Adjuvant NSCLC | Oncology |
| 6 | TA853. Avatrombopag for treating primary chronic immune thrombocytopenia. Committee Papers | NICE | Primary chronic immune thrombocytopenia | Hematology |
| 7 | Special Assessment of Outpatient Treatments for COVID-19. Final Evidence Report. Updated June 2023 | ICER | Outpatient treatment for COVID-19 | Infectious disease |
| 8 | Sotatercept for Pulmonary Arterial Hypertension. Final Evidence Report. January 2024 | ICER | Pulmonary arterial hypertension | Cardiovascular |
| 9 | Alzheimer's Disease. An assessment of lecanemab Final Evidence Report. April 2023 | ICER | Early Alzheimer's disease | Neurology |

Abbreviations: 1L = first line; BRCA = breast cancer susceptibility gene; CDA-AMC = Canada's Drug Agency; CDF = Cancer Drugs Fund; EAC = esophageal adenocarcinoma; GC = gastric cancer; GEJC = gastroesophageal junction cancer; HTA = health technology assessment; ICER = Institute for Clinical and Economic Review; NICE = National Institute for Health and Care Excellence; NSCLC = non-small cell lung cancer

## Scoring method

- The LLM extractions were compared against human-validated extractions and scored on a 4-point Likert scale (correct, partially correct, incorrect, and wrongly reporting that information is not available) for simple domains.

- For more advanced domains a 6-point Likert scale was used with the following categories: excellent (the information provided is fully correct and can be used directly), good (the information is correct, but a lot of text is returned, needs rewording before used), fair (unclear whether information is fully correct, needs doublechecks with original text for relevancy), poor (information is not pertinent, confusing, or largely not relevant text is returned), very poor (completely incorrect or not usable at all), and a wrongly reporting that information is not available category.

- To present the results, an automatic extraction for each domain was deemed successful if it achieved one of the first two scores on the Likert scale (correct or partially correct for the simple domains and excellent or good for the advanced domains).

# List of prompts

The list of prompts used for the extraction of each domain is displayed in Table 2.

Table 2.    List of Prompts

| # | Extraction Domain | Prompt 1 | Prompt 1 | Prompt 2 | Prompt 3 | Prompt 1 | Prompt 1 |
|---|---|---|---|---|---|---|---|
| | | **Strategy 1** | **Strategy 2: Chain of Prompt 1 -> Prompt 2-> Prompt 3** | | | **Strategy 3** | **Strategy 4** |
| 1 | **Model Structure** | What model structure was used in the cost-effectiveness model? | What model structure was used in the cost-effectiveness model? | In the document's section discussing the model used for the analysis (often but not always titled "Model Structure"), the authors describe the type of model employed. Common health economic models include decision trees, Markov models, microsimulation models, discrete event simulation models, partitioned-survival models, and compartmental models. Can you identify the type of model used in this analysis? | In the document's section discussing the model used for the analysis (often but not always titled "Model Structure"), the authors describe the type of model employed. Common health economic models include decision trees, Markov models, microsimulation models, discrete event simulation models, partitioned-survival models, and compartmental models. The type of model employed is commonly found at the beginning of the Economic Analysis or Cost-effectiveness Analysis section. Can you identify the type of model used in this analysis? | Same as Prompt 3 but add the following at the end. Use this format: Q: <repeat_question> A: Let's think step by step. <give_reasoning> Therefore, the answer is . | Same as Prompt 3 but add the following at the end. An example of model structure extraction is: "The cost-effectiveness analysis adopted a Markov cohort model" Use this format: Q: <repeat_question> A: Let's think step by step. <give_reasoning> Therefore, the answer is . |
| 2 | **Time horizon** | What time horizon was used in the cost-effectiveness analysis? | What time horizon was used in the cost-effectiveness analysis? | In the cost-effectiveness or economic analysis section of the document, | In the cost-effectiveness or economic analysis section of the document, | Same strategy as above | Same strategy as above An example of time horizon extraction is: |

| # | Extraction Domain | Prompt 1 | Prompt 1 | Prompt 2 | Prompt 3 | Prompt 1 | Prompt 1 |
|---|---|---|---|---|---|---|---|
| | | Keep the extraction focused on the base case analysis | Keep the extraction focused on the base case analysis | where the manufacturer describes the model structure, time horizon is usually specified and it is usually documented in years, such as 10 years, 20 years, 30 years, lifetime. What time horizon was used in developing the cost-effectiveness analysis? Keep the extraction focused on the base case analysis | where the manufacturer describes the model structure, time horizon is usually specified and it is usually documented in years, such as 10 years, 20 years, 30 years, lifetime. This information is usually included as part of the key features of the economic model description. What time horizon was used in developing the cost-effectiveness analysis? Keep the extraction focused on the base case analysis | | "The cost-effectiveness analysis adopted a lifetime horizon (25 years)" Use this format: Q: <repeat_question> A: Let's think step by step. <give_reasoning> Therefore, the answer is . |
| 3 | Cycle length | Which cycle length was used in the cost-effectiveness analysis? Keep the extraction focused on the base case analysis | Which cycle length was used in the cost-effectiveness analysis? Keep the extraction focused on the base case analysis | In the cost-effectiveness analysis section, where the manufacturer describes the model structure, usually also the cycle length is provided. The cycle length is the time duration of one model cycle, and it is usually 1 week, 2 weeks, 3 weeks, one month, 3 months or one year. Which cycle length was used in this assessment? Keep the extraction focused on the base case analysis | In the cost-effectiveness analysis section, where the manufacturer describes the model structure, usually also the cycle length is provided. The cycle length is the time duration of one model cycle, and it is usually 1 week, 2 weeks, 3 weeks, one month, 3 months or one year. You can often find it reported near the time horizon details and the details regarding whether half cycle correction was | Same strategy as above | Same strategy as above An example of cycle length extraction is: "The cost-effectiveness analysis adopted a weekly cycle" Use this format: Q: <repeat_question> A: Let's think step by step. <give_reasoning> Therefore, the answer is . |

| # | Extraction Domain | Prompt 1 | Prompt 1 | Prompt 2 | Prompt 3 | Prompt 1 | Prompt 1 |
|---|---|---|---|---|---|---|---|
| | | | | | implemented or not. Which cycle length was used in this assessment? Keep the extraction focused on the base case analysis | | |
| 4 | List of comparators | What comparators were used in the cost-effectiveness analysis? | What comparators were used in the cost-effectiveness analysis? | In the cost-effectiveness or economic analysis section of the document, the comparators are specified. These comparators are the alternative interventions against which the treatment's cost-effectiveness is evaluated. What comparators were used in the cost-effectiveness analysis? | In the cost-effectiveness or economic analysis section of the document, the comparators are specified. These comparators are the alternative interventions against which the treatment's cost-effectiveness is evaluated. The list of comparators is typically included as a key feature of the economic model development. What comparators were used in the cost-effectiveness analysis? | Same strategy as above | Same strategy as above. An example of list of comparators extraction is: "The cost-effectiveness analysis considered three treatments:<br>• Treatment A<br>• Treatment B<br>• Treatment C"<br>Use this format:<br>Q: \<repeat_question><br>A: Let's think step by step. \<give_reasoning> Therefore, the answer is \. |
| 5 | Health States | What health states were used in the cost-effectiveness analysis? | What health states were used in the cost-effectiveness analysis? | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the model structure, the different health states are usually described. The health states vary based on the disease area, but in general, they represent different levels of well- | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the model structure, the different health states are usually described. The health states vary based on the disease area, but in general, they represent different levels of well- | Same strategy as above | Same strategy as above. An example of health states extraction is: "The cost-effectiveness model included four health states: susceptible, infected, recovered, dead"<br>Use this format:<br>Q: \<repeat_question> |

| # | Extraction Domain | Prompt 1 | Prompt 1 | Prompt 2 | Prompt 3 | Prompt 1 | Prompt 1 |
|---|---|---|---|---|---|---|---|
| | | | | being an individual can experience. What health states were used in the cost-effectiveness analysis? | being an individual can experience. For instance, a cost-effectiveness model used to model a generic disease can have 4 health states: *healthy, sick, recovered, dead*. Economic models use various health states to capture the impact of diseases and interventions on a person's quality of life.<br><br> What health states were used in the cost-effectiveness analysis? | | A: Let's think step by step. <give_reasoning> Therefore, the answer is . |
| 6a | Modeling approach of overall survival – oncology only | What modeling approach was used to extrapolate overall survival outcomes over the model time horizon? Keep the extraction focused on the base case analysis and on the novel treatment assessed | What modeling approach was used to extrapolate overall survival outcomes over the model time horizon? Keep the extraction focused on the base case analysis and on the novel treatment assessed | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the clinical inputs or parameters, survival modeling is usually reported. Common modeling approaches include standard parametric survival models (e.g., Weibull, Gompertz) or more flexible models (e.g. piecewise, splines, K-M combined with standard parametric fits). What modeling approach was used to extrapolate overall | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the clinical inputs or parameters, survival modeling is usually reported. Common modeling approaches include standard parametric survival models (e.g., Weibull, Gompertz) or more flexible models (e.g. piecewise, splines, K-M combined with standard parametric fits). These are usually described as part of the clinical parameters | Same strategy as above | Same strategy as above<br><br>An example of overall survival approach extraction is: "For Treatment A, overall survival was extrapolated using a log-logistic parametric distribution. The log-logistic distribution was selected based on goodness of fit, clinical experts interviews and comparison with available literature"<br>Use this format:<br>Q: <repeat_question><br>A: Let's think step by step. <give_reasoning> |

| # | Extraction Domain | Prompt 1 | Prompt 1 | Prompt 2 | Prompt 3 | Prompt 1 | Prompt 1 |
|---|---|---|---|---|---|---|---|
| | | | | survival outcomes over the model time horizon? Keep the extraction focused on the base case analysis and on the novel treatment assessed | section and some reasoning/justification about the plausibility of the approach is typically reported as well. What modeling approach was used to extrapolate overall survival outcomes over the model time horizon? Keep the extraction focused on the base case analysis. | | Therefore, the answer is . |
| 6b | Modeling approach of XXX outcome* | What modeling approach was used to extrapolate XXX outcome over the model time horizon? Keep the extraction focused on the base case analysis | What modeling approach was used to extrapolate XXX outcome over the model time horizon? Keep the extraction focused on the base case analysis | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the clinical inputs or parameters, XXX outcome modeling is usually reported. Common modeling approaches include parametric models (e.g., Weibull, Gompertz) and semi-parametric models (e.g., proportional hazards). What modeling approach was used to extrapolate XXX outcome over the model time horizon? Keep the extraction focused on the base case analysis | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the clinical inputs or parameters, XXX outcome is usually reported. Common modeling approaches include parametric models (e.g., Weibull, Gompertz) and semi-parametric models (e.g., proportional hazards). These are usually described as part of the clinical parameters section and some reasoning/justification about the suitability of the approach is typically reported as well. What modeling approach was | Same strategy as above | Same strategy as above. An example of XXX outcome extraction is: "For Treatment A, XXX was extrapolated assuming a constant risk of XXX over the time horizon. Alternative assumptions (decrease or increase risk of XXX over the time horizon) were evaluated in scenario analysis" Use this format: Q: <repeat_question> A: Let's think step by step. <give_reasoning> Therefore, the answer is . |

| # | Extraction Domain | Prompt 1 | Prompt 1 | Prompt 2 | Prompt 3 | Prompt 1 | Prompt 1 |
|---|---|---|---|---|---|---|---|
| | | | | | used to extrapolate, XXX outcome over the model time horizon? Keep the extraction focused on the base case analysis | | |
| 7 | Cost categories included in the model | What cost categories were used in the cost-effectiveness analysis? | What cost categories were used in the cost-effectiveness analysis? | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the costs and resource use, the different cost categories are usually reported. For example, cost categories can include drug costs, administration costs, monitoring and disease management costs, terminal care costs, etc. What were the different cost categories considered in the cost-effectiveness analysis? | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the costs and resource use, the different cost categories are usually reported. For example, cost categories can include drug costs, administration costs, monitoring and disease management costs, terminal care costs, etc. These are usually described in the cost and healthcare resource use identification section, which is usually located after the clinical inputs section. What were the different cost categories considered in the cost-effectiveness analysis? | Same strategy as above | Same strategy as above<br><br>An example of cost categories is: "Drug costs, administration costs, monitoring and disease management costs, terminal care costs, adverse events costs"<br>Use this format:<br>Q: <repeat_question><br>A: Let's think step by step. <give_reasoning> Therefore, the answer is . |
| 8 | Approach for utility modeling | What approach was used to model utility as part of the cost-effectiveness analysis? Keep the extraction focused on the base case analysis | What approach was used to model utility as part of the cost-effectiveness analysis? Keep the extraction focused on the base case analysis | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the health-related quality of life measures used, the | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the health-related quality of life measures used, the | Same strategy as above | Same strategy as above<br><br>An example of utility modeling extraction is: "The utility values were assumed independent of treatment but dependent on the CEM |

| # | Extraction Domain | Prompt 1 | Prompt 1 | Prompt 2 | Prompt 3 | Prompt 1 | Prompt 1 |
|---|---|---|---|---|---|---|---|
| | | | | approach for utility modeling is usually described. For example, utilities may be modeled based on time-to-death approach or based on whether patients have progressive disease or not. What approach was used to model utility as part cost-effectiveness model? Keep the extraction focused on the base case analysis | approach for utility modeling is usually described. For example, utilities may be modeled based on time-to-death approach or based on whether patients have progressive disease or not. These details are usually presented after the main treatment effect modeling section, particularly under the health-quality of life section. What approach was used to model utility as part cost-effectiveness model? Keep the extraction focused on the base case analysis | | health states. Adverse event disutilities were also included to capture the impact of adverse events on patients' QoL"<br><br>Use this format:<br><br>Q: \<repeat_question><br><br>A: Let's think step by step. \<give_reasoning> Therefore, the answer is \. |
| 9 | Key critiques from the committee | What were the key critiques made by the health technology agency or the review committee? | What were the key critiques made by the health technology agency or the review committee? | In health technology assessment application document, certain sections are specific to the appraisal made by the health technology agency or an independent review committee. For example, the manufacturer's cost-effectiveness model can be criticized for the model structure employed, the key model health states, the | In health technology assessment application document, certain sections are specific to the appraisal made by the health technology agency or an independent review committee. For example, the manufacturer's cost-effectiveness model can be criticized for the model structure employed, the key model health states, the | Same strategy as above | Same strategy as above<br><br>An example of the key critiques is: "The key critiques included:<br><br>• Critique 1<br>• Critique 2<br>• Critique 3"<br><br>Use this format:<br><br>Q: \<repeat_question><br><br>A: Let's think step by step. \<give_reasoning> Therefore, the answer is \. |

| # | Extraction Domain | Prompt 1 | Prompt 1 | Prompt 2 | Prompt 3 | Prompt 1 | Prompt 1 |
|---|---|---|---|---|---|---|---|
| | | | | clinical and cost inputs as well as the source of data used to inform the model. What were the key critiques made by the health technology agency or the review committee? | clinical and cost inputs as well as the source of data used to inform the model. These are usually described in an independent section of the document, after the manufacturer's submission details. What were the key critiques made by the health technology agency or the review committee? | | |
| 10 | Key modeling assumptions | List the key cost effectiveness modeling assumptions. Keep the extraction focused on the base case analysis | List the key cost effectiveness modeling assumptions. Keep the extraction focused on the base case analysis | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the modeling approach and the model structure, the assumptions made for the analysis are detailed. For example, the manufacturer may specify that a constant risk of mortality was assumed or that adverse events were assumed to happen early near treatment initiation or that the risk of a clinical event was assumed to be independent of patients having already experienced the same event in the past. List the | In the cost-effectiveness or economic analysis section of the document, where the manufacturer describes the modeling approach and the model structure, the assumptions made for the analysis are detailed. For example, the manufacturer may specify that a constant risk of mortality was assumed or that adverse events were assumed to happen early near treatment initiation or that the risk of a clinical event was assumed to be independent of patients having already experienced the same event in the past. These | Same strategy as above | Same strategy as above<br><br>An example of the list of modeling assumptions is provided in the footnotes[+]<br><br>Use this format:<br>Q: <repeat_question><br>A: Let's think step by step. <give_reasoning> Therefore, the answer is . |

| # | Extraction Domain | Prompt 1 | Prompt 1 | Prompt 2 | Prompt 3 | Prompt 1 | Prompt 1 |
|---|---|---|---|---|---|---|---|
| | | | | key cost effectiveness modeling assumptions. Keep the extraction focused on the base case analysis | are usually described after the model structure is presented and after the key modeling inputs are presented. These assumptions can be referred as structural assumptions or modeling assumptions or simplifying assumptions or clinical assumptions or inputs assumptions. List the key cost effectiveness modeling assumptions. Keep the extraction focused on the base case analysis | | |

Abbreviation: CEM = cost-effectiveness model

+ The primary outcome was used in each extraction in place of XXX (e.g., overall survival for cancer indications).

* List of assumptions example for LLM:

- The patient population in the pivotal trial is representative of the disease population under investigation.
- Patients who discontinue treatment will not receive a subsequent treatment but will move to best supportive care.
- A patient can experience any event within a cycle regardless of their previous history.
- A patient can experience only one event within a cycle.
- The probability of experiencing hospitalization increases with age.
- The disutility from clinical events which are not captured as health states is temporary.
- The overall cost of a clinical event is incurred only during the cycle in which the event took place.
- The relative efficacy of treatments is assumed to be maintained while patients are on treatment.