## METHODS

This study was reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards 2022 (checklist found in supplement table 1) [1]. In this study, we developed a probabilistic Markov cohort model to compare the cost-effectiveness of various strategies following anaphylaxis in patients with food allergies. The Markov model is a widely accepted method for modeling the economic outcomes of healthcare decisions. The Markov cohort model is particularly suited to scenarios characterized by recurrent probabilistic risks, such as those associated with food allergies [2], given its ability to model transitions between different health states over a set time horizon.

The target population for this model was Canadian patients with food allergies, aged one year or older. We analyzed the incremental costs and Quality-Adjusted Life Years (QALYs) for two post-anaphylaxis strategies: (1) the routine recommendation for immediate transfer to the emergency department (ED) (‘immediate ED transfer’), and (2) a wait-and-monitor approach at home following the use of an epinephrine auto-injector (‘watchful waiting’). ‘Immediate ED transfer’ is defined as calling for ambulance transport and undergoing an ED evaluation post-anaphylaxis, regardless of epinephrine auto-injector (EAI) use. ‘Watchful waiting’ is defined as patients opting not to transfer to the ED after self-administering an EAI. We evaluated the Incremental Cost-Effectiveness Ratio (ICER) and the incremental net monetary benefit (INMB) using a willingness-to-pay (WTP) threshold of $100,000 per QALY gained—a figure derived from the most recent evidence provided by the Institute for Clinical and Economic Review Value Assessment Framework [3]. This framework upholds $100,000 per QALY as an operational cost-effectiveness threshold, a commonly accepted standard in cost-effectiveness analyses [4]. All costs were reported in 2022 Canadian Dollars (CAD). This study did not include real patients in the analysis and was exempt from institutional review board approval and informed consent requirements. The model was implemented in R version 4.3.1 (R Foundation for Statistical Computing, Vienna, Austria) and is publicly available on the GitHub repository https://github.com/resplab/Allergy\_EAI\_CEA.

### Model Structure

The Markov cohort model we developed included seven health states (Figure 1): (1) No severe allergic reaction; (2) Severe allergic reaction - watchful waiting; (3) Severe allergic reaction - transfer to ED; (4) Severe allergic reaction - hospitalized; (5) Food allergy remission; (6) All-cause mortality; and (7) Food allergy mortality. A severe allergic reaction was defined as an anaphylactic reaction following accidental allergen exposure that required an epinephrine injection. No severe allergic reaction was defined as a patient with a food allergy who did not experienced anaphylaxis.

We designed the base model from a healthcare payer perspective, considering only direct healthcare costs. We incorporated daily cycles into the model to account for the daily risk of allergic reactions and also to incorporate the average duration of hospitalization following severe allergic reactions, as analyzed from the Cross-Canada Anaphylaxis Registry (CCARE) data. In line with the Canadian Agency for Drugs and Technologies in Health (CADTH) guidelines [5], we applied a discount rate of 1.5% per annum to both costs and outcomes.

Patients with a food allergy entered the simulation at one year of age in the ‘no severe allergic reaction’ state. During each cycle of the model, patients either transitioned to a new health state or remained in their current state. Patients with a food allergy would remain in the ‘no severe allergic reaction’ state unless they a) achieved food allergy remission, b) suffered a severe allergic reaction due to accidental exposure, or c) died from causes unrelated to food allergies. When a patient had a severe allergic reaction, they had two options: a) undertake watchful waiting, which assumed immediate resolution of symptoms (within 5-15 minutes) post-EAI administration and without subsequent recurrence, or b) initiate an immediate ED transfer. To enter ‘watchful waiting’ states, patients were required to have access to an EAI in an outpatient setting, while those entered ‘transfer to ED’ state were not required to have an EAI on hand. In the ‘immediate ED transfer’ scenario, all patients with a severe allergic reaction were transferred to the ED regardless of EAI use. In the ‘watchful waiting’ scenario, only patients with an EAI and without a biphasic reaction, defined as the recurrence of symptoms within 72 hours of the initial anaphylactic event, proceeded to watchful waiting, while the rest were transferred to the ED. Mortality could result from two sources: all-cause mortality and food allergy mortality, with all-cause mortality being a risk in any state. Patients who survived a severe allergic reaction would eventually revert to the ‘no severe allergic reaction’ state.

A diagram of allergies

Description automatically generated

#### Figure 1. Model structure

ED: emergency department

### Probability and Events

The parameters used in the model are listed in **Table 1**. The transition probabilities between different states were derived from literature reviews and the analysis of the CCARE data. As our model's age range concluded at 21, when literature provided separate probabilities for patients younger than 18 and those older, we chose the probabilities for the under-18 group to better reflect the majority of our modeled population. We converted all annual probabilities to daily values to align with the model's cycle. The overall probability of experiencing a severe allergic reaction was set based on the CCARE data analysis. In the ‘immediate ED transfer’ scenario, the probability of transferring to the ED equated to the overall probability of experiencing a severe allergic reaction. For the watchful waiting scenario, the probability of entering the ‘watchful waiting’ state was a subset of the overall probability and was calculated based on the likelihood of having access to an EAI and the occurrence of a biphasic reaction. The probability of transferring to the ED was the complement of the probability of entering watchful waiting, derived from the probability of a severe allergic reaction. We assumed hospitalization would only occur in patients transferred to the ED; therefore, the probability of hospitalization was estimated based on the severe allergic fatality from the literature and the overall probability of a severe allergic reaction.

Mortality related to food allergies can occur only in patients who underwent ‘watchful waiting’ state and those transferred to the ED resulting in hospitalization, assuming that patients with more critical symptoms would be hospitalized promptly in the ED. Since the reduction in mortality risk from ‘immediate ED transfer’ compared to ‘watchful waiting’ after in-home EAI use is not clearly studied, we assumed a ten-fold increase in overall food allergy-related fatalities for patients in the ‘watchful waiting’ scenario compared to those in the ‘immediate ED transfer’ scenario. This assumption has been utilized in previous studies[2]. For background mortality, we referred to age-specific, all-cause mortality statistics from the 2022 Canadian life tables[6].

### Resource Use and Costs

In the base case, we considered only the direct medical costs paid by the healthcare payer. All costs were adjusted to daily values within the model to coincide with the model's cycle. The epinephrine cost had two components: the cost for EAI and the epinephrine injection administered in the ED. The price of one EAI, set at $95, was derived from the literature and aligns with costs reported in the British Columbia Pharmacare formulary [7-8]. The cost for epinephrine injection was fixed at $0.8. Dispensing fees and potential market markups were not included in the cost. For patients transferred to the ED in the ‘immediate ED transfer scenario’, the total cost of epinephrine included both the EAI used prior to the ED visit—calculated based on the probability of EAI use (54%) before the ED visit—and the additional epinephrine injection solutions administered in the ED for all patients transferred. In the ‘watchful waiting’ scenario, the cost of epinephrine accounted only for the at-home EAI use for patients transitioning to ‘watchful waiting’ state. For those transferred to the ED because they did not have an EAI at home, the medication cost in the transfer to ED state consisted solely of the epinephrine injection solution.

Regarding medical-related expenses, the ambulance cost was determined based on the fee for uninsured individuals using land ambulance services in British Columbia (BC) [9]. The medical cost of ED visit was derived from the average cost of all-cause ED visits [10]. Similarly, the cost of hospitalization was estimated using the average daily rate for inpatient allergy admissions [7]. The annual background medical costs for patients with allergies were adjusted to remove the average cost of ED visits, calculated at 0.3 days of ED use per year, and were only factored into the state of patients with no severe allergies[7]. Lastly, the background annual medical cost for food allergy remission was estimated by comparing the healthcare expenses of patients with food allergies to those without [11].

### Healthy Utility

For the utility of patients with no severe food allergy (0.92), we utilized the Canadian utility data collected by Dufresne et al. [12], which applied the Short-Form Six-Dimension version 2 (SF-6Dv2) preference value set. The disutility of a severe allergic reaction (-0.09) is derived from a previous study by Carroll et al. in the USA [13]. The utility for food allergy remission was based on the median Health Utilities Index Mark 3 (HUI-3) utility for the Canadian general population of 12–19-year-olds (0.93), as reported in previous literature [14-15].

#### Table 1 Summary of model parameters

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter | Base-case | DSA (lower/upper) | PSA distribution | Source |
| Age at start | 1 year |  |  |  |
| Cycle length | 1 day |  |  |  |
| Discount rate, % per annum | 1.5 |  |  | CADTH [5] |
| Average number of ED visits in patients with food allergy, per year | 0.3 |  | Gamma (α = 0.1111, β = 2.7) | Cardwell et al. (2022) [7] |
| Length of stays after inpatient allergy admission | 1 day |  | Fixed | CCARE registry data |
| Waiting time in ED | 3.6 hours |  | Gamma (α = 0.2749, β = 13.0966). | CIHI [10] |
| Average Length of stay per after inpatient allergy admissiona | 2.1 days |  | Lognormal (0.2541, 0.9878) | Cardwell et al. (2022) [7] |
| Annual probability of Severe allergic reaction following accidental exposure | 0.087 | 0.0696/0.1044 | Beta (α = 66.3345, β = 696.1314) | Analysis of CCARE registry data |
| Probability of patient with known food allergy having an eaib | 0.906 |  | Beta (α = 8.4940, β = 0.8813) | Cardwell et al. (2022) [7] |
| Probability of using an EAI prior to ED visitc | 0.54 |  | Beta (α = 7.6118, β = 6.4841) | Analysis of CCARE registry data |
| Probability of Biphasic reaction dfollowing EAI use | 0.046 |  | Beta (α = 183.5019, β = 3805.6703) | Lee et al. (2015)[16] |
| Probability of ED visit following severe allergic reaction | Watchful waiting scenario: 0.14  Immediate ED transfer scenario: 1 |  | Fixed | Assumption |
| Probability of Hospitalization following ED visit | 0.00168 | 0.01344/0.02016 |  | Assumption |
| Annual probability of Food allergy fatality among patients with food allergy with immediate ED transfer approach | 6.9×10 −7 |  | Beta (α = 99.9999, β = 144927335.2320) | Greenhawt et al. (2023) [17]  Turner et al. (2020) [18] |
| Increased annual fatality in food allergy for patient through watchful waiting strategy | 10 times |  | Fixed | Assumption  Pumphrey and Gowland (2007) [19] |
| Food allergy fatality among hospitalized patients | 0.0045 | 0.0036/0.0054 | Beta (α= 45.8194, β = 10136.2621) | Turner et al. (2020) [18] |
| Annual probability for Food allergy remission | Age 1-6 years: 0.058  Age >6 years: 0 | Age 1-6 years: 0.0464/0.696 | Age 1-6 years: Beta (α= 47.4951, β = 771.3863  )  Age >6 years: fixed | Peters et al. (2022) [20] |
| Cost |  |  |  |  |
| EAI purchase cost, per injector | $95 per injector | $76/$114 | Fixed | BC Pharmacare formulary [8]  Cardwell et al. (2022) [7] |
| Epinephrine solution injection cost in ED | $0.8 | $0.64/$0.96 | Fixed | Assumption |
| Epinephrine cost for patients transfer to EDce | $52.1 | $0.8/$95 | Fixed | Assumption |
| Ambulance cost for ED visit | $848 | $678.4/$1017.6 | Gamma (α = 100, β = 8.48) | BC fee schedule [9] |
| Average hourly wage for all employees in Canada | $31.37 |  | Fixed | Statistics Canada [21] |
| Medical cost for ED visit, per visite | $331($304 adjusted with fixed inflation factor of 1.09) | $264.8/$397.2 | Gamma (α = 100, β = 3.04) | CIHI [10]  Analysis of CCARE registry data |
| Indirect cost for ED visit, per visit | $113 |  | Fixed | CIHI [10]  Statistics Canada [21] |
| Out-of-pocket cost for ED visit, per visitb | $ 95 ($89 adjusted with fixed inflation factor of 1.068) |  | Gamma (α = 100, β = 0.89) | Cardwell et al. (2022) [7] |
| Daily medical cost of hospitalization | $1,866 ($3670 adjusted with fixed inflation factor of 1.068 and average length of stay) | $1492.8/$2339.2 | Gamma (α = 100, β = 36.7) | Cardwell et al. (2022) [7] |
| Indirect cost of hospitalization | $251 |  | Fixed | Analysis of CCARE registry data  Statistics Canada [21] |
| Annual direct medical cost for Canadian with food allergy bg | $1,388($1,393 adjusted with fixed inflation factor 1.068 and ED cost) | $1110.4/$1665.6 | Gamma (α = 100, β = 13.93) | Cardwell et al. (2022) [7] |
| Annual out of pocket costs for Canadian with food allergy bg | $2,577 ($2,440 a with fixed inflation factor 1.068 and ED cost) |  | Gamma (α = 100, β = 24.4) | Cardwell et al. (2022) [7] |
| Annual indirect costs for Canadians with food allergybg | $ 4,421($4,173 with fixed inflation factor 1.068 and ED cost) |  | Gamma (α = 100, β = 41.73) | Cardwell et al. (2022) [7] |
| Annual background medical costs of food allergy remissionb | $569 | $455.2/$682.8 | Fixed | Fox et al. (2009) [11] |
| Utility |  |  |  |  |
| Food allergy | 0.92 | 0.736/1 | Beta (α = 7.0800, β = 0.6157) | Dufresne et al. (2020) [12] |
| Disutility of severe allergic reaction | -0.09 | -0.108/-0.072 | Beta (α = 0.1651, β = 1.6689) | Carroll and Downs (2009) [13] |
| Food allergy remission | 0.93 | 0.744/1 | Beta (α = 8.7708, β = 0.6602) | Guertin et al. (2018) [14]  Mittman et al. (1999) [15] |

Abbreviation: ED, emergency department; BC, British Columbia; CIHI, Canadian Institute for Health Information; CCARE, Cross-Canada Anaphylaxis Registry; CADTH, Canadian Agency for Drugs and Technologies in Health.

a Literature-reported lengths of stay were used in calculating the daily medical costs of hospitalization, according to the literature

b Used the probability reported for <18 years

c Used in ‘immediate ED transfer' scenario

d Biphasic reaction: recurrence of symptoms within 72 hours of initial anaphylactic event

e The cost of epinephrine for patients transferred to the ED was adjusted to include the cost of the EAI for patients who could use it, as well as the cost of the epinephrine solution administered by a provider in the ED.

g Adjusted by deducting related cost in ED

### Analysis

#### Base Case Analysis

The base case analysis was conducted based on the parameters previously described. The main outcomes were the incremental cost and QALYs for ‘immediate ED transfer’ (current practice) compared with ‘watchful waiting’ after receiving an EAI at home. We carried out a cohort analysis with an initial population of 10,000 patients. The incremental cost per QALY was calculated to determine the dominant treatment strategy, with a WTP threshold set at $100,000.

#### Probabilistic Sensitivity Analysis

We conducted a Probabilistic Sensitivity Analysis (PSA) using a Monte Carlo simulation with 1000 iterations to evaluate the uncertainty in our model. The approach to assigning probability distributions for the PSA is outlined in Table 1. In instances where information was insufficient to characterize parameter distributions, we assumed a variance-to-mean ratio of 10%. The results of the PSA are presented in a cost-effectiveness plane and a cost-effectiveness acceptability curve. The cost-effectiveness plane depicts the joint distribution of incremental costs and QALYs, while the cost-effectiveness acceptability curve demonstrates the likelihood that the intervention is cost-effective across a range of WTP thresholds for one QALY.

#### Deterministic Sensitivity Analysis

In our study, a one-way deterministic sensitivity analysis (DSA) was conducted to assess the impact of various parameters on the outcomes of our base-case model. The analysis involved systematic variation of key parameters by 20% above and below their baseline values to determine their impact for majority parameters. These parameters included: utility values, the annual probability of severe allergic reactions and food allergy remission; the probability of hospitalization for patients with severe allergic reactions; the daily fatality rates of hospitalized patients and patients in 'watchful waiting'; the probability of hospitalization; the costs associated with medication in a 'watchful waiting' approach; the annual healthcare costs for patients experiencing non-severe allergic reactions as well as for those in remission; the costs of ambulance services; and the medical costs in the ED and during hospitalization. Additionally, for the variation range of medication costs utilized in the Emergency Department scenario, we used a range from the lowest cost, represented by epinephrine injection solutions, to the highest, represented by EAIs, to adequately reflect the breadth of potential medication costs in the ED setting.

#### Scenario Analysis

We performed a series of scenario analyses to assess the robustness of our results to variation of several parameters at once through 1000 PSA iterations. Scenarios included: (1) 0% discount rate per annum; (2) 3% discount rate per annum; (3) societal perspective; (4) 100-fold increase in overall food allergy-related fatality in watchful waiting scenario; (5) 500-fold increase in overall food allergy-related fatality in watchful waiting scenario; (6) 1000-fold increase in overall food allergy-related fatality in watchful waiting scenario.

## RESULTS

The results from the base-case analysis are presented in Table 2. The discounted total cost for immediate emergency department (ED) transfer over a 20-year horizon was $21,797.71 per patient, compared to $20,640.86 for watchful waiting. The total discounted QALYs were 15.9034 for immediate ED transfer and 15.9026 for watchful waiting. Compared to immediate ED transfer, watchful waiting is less costly with only a minimal reduction in effectiveness. The incremental cost saving was $1,156.85 with a QALY decrease of just 7.276 × 10-4, resulting in an incremental net monetary benefit (INMB) of $1,084.086. Watchful waiting strategy resulted in a slight increase in patient mortality over the model horizon. The per-patient allergy-related fatality associated with the 'watchful waiting' strategy was 1.02 × 10-5, compared to 1.02 × 10-6 for the 'immediate ED transfer' strategy, resulting in a fatality reduction of 9.2 × 10-5 with immediate ED transfer. Consequently, the incremental cost per death prevented with the 'immediate ED transfer' strategy eventually reached $12,586,613.

#### Table 2. Summary of Base-Case Results

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Strategy | Cost ($) | QALYs | Allergic related fatality | Incremental Costs ($) | Incremental QALYs | ICER ($/QALY) | INMB a ($) |
| Watchful and waiting | 20640.8591 | 15.9026 | 1.02 x 10-5 | -1156.8501 | 7.276 X 10-4 | 1,589,854 | 1084.086 |
| Immediate ED transfer | 21797.7092 | 15.9034 | 1.02 x 10-6 | Reference | Reference | Reference | Reference |

Abbreviations: ICER, Incremental Cost-Effectiveness Ratio; INMB, incremental net monetary benefit; QALY, quality-adjusted life-year.

NOTE. Results are presented per-patient over a 20-year horizon

a Incremental net monetary benefit at a willingness-to-pay of $100,000 per QALY gained.

### Deterministic Sensitivity Analyses

The one-way sensitivity analysis revealed the impact of each parameter on ICER when compared to the 'immediate ED transfer' strategy, as shown in Figure 1. Overall, the model was not sensitive to any single parameter. The ‘watchful waiting’ strategy consistently showed a similar, slight reduction in effectiveness and cost when compared to the ‘immediate ED transfer’ strategy across all variations assessed. The value of the 'watchful waiting' strategy was most influenced by the annual probability of a severe reaction, the utility value for non-severe food allergy, and the cost of ambulance services.

A graph with a bar chart

Description automatically generated with medium confidence

**Figure 1. One-Way Sensitivity Analysis of ICER for ‘Watchful Waiting' vs Immediate ED Transfer.** The colored bars indicate the lower (red) and upper (blue) bounds of the parameters in the sensitivity analysis. ED emergency department; QALY, quality-adjusted life-year; ICER, Incremental Cost-Effectiveness Ratio, represents as Incremental Cost per QALY saved.

### Probabilistic Sensitivity Analysis

The results of the PSA are presented in Figure 2. In all PSA iterations, watchful waiting was less costly and offered a minimal reduction in QALYs compared to immediate ED transfer. The probability that the 'watchful waiting' strategy was 100% cost-effective compared to the 'immediate ED transfer' strategy was consistent across all evaluated WTP thresholds (see Figure 3).

A graph showing a number of dots

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**Figure 2. Cost-Effectiveness Plane from Probabilistic Sensitivity Analysis**: Watchful Waiting vs Immediate ED Transfer. Each point represents one iteration from the PSA. Ellipses encompass 95% of iterations; QALY denotes quality-adjusted life-years.

A graph with a line graph

Description automatically generated with medium confidence

Figure 3. Cost-effectiveness Acceptability Curve: Watchful waiting (green line) vs Immediate ED transfer (red line).

### Scenario Analyses

As presented in Table 4, 'watchful waiting' remained the cost-effective strategy across all scenarios, except when the risk of fatality associated with watchful waiting increased to extreme numbers such as 500 and 1,000 times that of fatality in immediate ED transfer. However, when the risk increase was 100 times, 'watchful waiting' strategy still remained cost-effective. Additionally, from the societal perspective, the INMB rose to $1,304, and 'watchful waiting' strategy continued to be cost-effective.

Table 4. Scenario Analyses

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Scenario | Total cost | | Total QALY | | Incremental | | | |
|  | Watchful waiting | Immediate ED transfer | Watchful waiting | Immediate ED transfer | Cost | QALYs | ICER | INMB |
| 100-fold increase in food allergy-related fatality in watchful waiting | 20786.621 | 21949.484 | 15.8915 | 15.8834 | -1162.862 | -0.0080140 | 145103.87 | 361.5097 |
| 500-fold increase in food allergy-related fatality in watchful waiting | 20614.603 | 21833.753 | 15.8920 | 15.8517 | -1219.150 | -0.0403800 | 30191.92 | -2818.5895 |
| 1000-fold increase in food allergy-related fatality in watchful waiting | 20362.792 | 21632.331 | 15.8788 | 15.7981 | -1269.538 | -0.0807000 | 15731.58 | -6800.5102 |
| Societal perspective | 111374.269 | 112751.802 | 15.9052 | 15.9045 | -1377.533 | -0.0007297 | 1887807.32 | 1304.5615 |
| 0% discount rate per annum | 3330.438 | 4654.561 | 18.4476 | 18.4467 | -1324.123 | -0.0008833 | 1499064.19 | 1235.7884 |
| 3% discount rate per annum | 2398.517 | 3411.377 | 13.8083 | 13.8077 | -1012.860 | -0.0006021 | 1682212.76 | 952.6453 |

Abbreviations: ED, Emergency department ICER, Incremental Cost-Effectiveness Ratio; INMB, incremental net monetary benefit; QALY, quality-adjusted life-year

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Supplement

Table 1 Consolidated Health Economic Reporting Standards (CHEERS) Checklist

| **Topic** | **No.** | **Item** | **Location where item is reported** |
| --- | --- | --- | --- |
| **Title** | 1 | Identify the study as an economic evaluation and specify the interventions being compared. |  |
| **Abstract** | 2 | Provide a structured summary that highlights context, key methods, results, and alternative analyses. |  |
| **Introduction** | | | |
| **Background and objectives** | 3 | Give the context for the study, the study question, and its practical relevance for decision-making in policy or practice. |  |
| **Methods** | | | |
| **Health economic analysis plan** | 4 | Indicate whether a health economic analysis plan was developed and where available. | NA |
| **Study population** | 5 | Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics). |  |
| **Setting and location** | 6 | Provide relevant contextual information that may influence findings. |  |
| **Comparators** | 7 | Describe the interventions or strategies being compared and why chosen. |  |
| **Perspective** | 8 | State the perspective(s) adopted by the study and why chosen. |  |
| **Time horizon** | 9 | State the time horizon for the study and why appropriate. |  |
| **Discount rate** | 10 | Report the discount rate(s) and reason chosen. |  |
| **Selection of outcomes** | 11 | Describe what outcomes were used as the measure(s) of benefit(s) and harm(s). |  |
| **Measurement of outcomes** | 12 | Describe how outcomes used to capture benefit(s) and harm(s) were measured. |  |
| **Valuation of outcomes** | 13 | Describe the population and methods used to measure and value outcomes. | NA |
| **Measurement and valuation of resources and costs** | 14 | Describe how costs were valued. |  |
| **Currency, price date, and conversion** | 15 | Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion. |  |
| **Rationale and description of model** | 16 | If modeling is used, describe in detail and why used. Report if the model is publicly available and in which it can be accessed. |  |
| **Analytics and assumptions** | 17 | Describe any methods for analyzing or statistically transforming data, any extrapolation methods, and approaches for validating any model used. |  |
| **Characterizing heterogeneity** | 18 | Describe any methods used for estimating how the results of the study vary for subgroups. | NA |
| **Characterizing distributional effects** | 19 | Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations. | NA |
| **Characterizing uncertainty** | 20 | Describe methods to characterize any sources of uncertainty in the analysis. |  |
| **Approach to engagement with patients and others affected by the study** | 21 | Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study. | NA |
| **Results** | | | |
| **Study parameters** | 22 | Report all analytical inputs (such as values, ranges, references) including uncertainty or distributional assumptions. |  |
| **Summary of main results** | 23 | Report the mean values for the main categories of costs and outcomes of interest and summarize them in the most appropriate overall measure. |  |
| **Effect of uncertainty** | 24 | Describe how uncertainty about analytical judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable. |  |
| **Effect of engagement with patients and others affected by the study** | 25 | Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study. | NA |
| **Discussion** | | | |
| **Study findings, limitations, generalisability, and current knowledge** | 26 | Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice. |  |
| **Other relevant information** | | | |
| **Source of funding** | 27 | Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis. |  |
| **Conflicts of interest** | 28 | Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements. |  |

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